CLINICAL PRACTICE

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Screening for *Chlamydia trachomatis* Infections in Women

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This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.*

A 19-year-old woman visits her physician for a preventive health examination. Her medical history is unremarkable. She is sexually active with her boyfriend, and they use condoms inconsistently. She had one prior sexual partner and reports no symptoms of vaginal infections or sexually transmitted diseases. Results from her gynecologic examination are normal. Should this woman be screened for chlamydia, and if so, how?

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THE CLINICAL PROBLEM

EPIDEMIOLOGY

Chlamydia is caused by the gram-negative bacterium *Chlamydia trachomatis* and is the most common infection reported in the United States, with more than 1.5 million cases reported in 2015.[1] The actual number of infections probably exceeds 3 million annually, because most chlamydial infections are asymptomatic and go undetected. Persons between 15 and 24 years of age have the highest reported rates of infection.[2] The rates of chlamydial infection are higher among young women than among men, which reflects screening programs that primarily target women. The prevalence of chlamydial infection varies according to race; according to a U.S. report in 2015, the rate of reported cases among blacks was 5.9 times the rate among whites.[1] The prevalence of chlamydial infection among sexually active non-Hispanic black girls and women 14 to 24 years of age was 13.5%, as compared with 1.8% among non-Hispanic white girls and women.[2] Chlamydial infections are a public health concern in both metropolitan centers and smaller communities.[3]

Sexual risk factors for chlamydial infection (several of which are more common in younger persons) include new sexual partners, more than one (concurrent) sexual partner, a prior case of chlamydial infection or other sexually transmitted disease, and inconsistent condom use.[4] Cervical ectopy, with columnar epithelium extending onto the external surface of the cervix, is common in young women, and this epithelial surface may be friable during intercourse and more susceptible to infection.[5] The rate of transmission of genital *C. trachomatis* infections from men to women and vice versa is approximately 70%, which indicates efficient transmission between sexual partners.[5]

COMPLICATIONS OF CHLAMYDIAL INFECTIONS IN WOMEN

C. trachomatis is an important cause of pelvic inflammatory disease, which results from the ascension of the organism from the cervix to the upper genital tract (uterus

KEY CLINICAL POINTS

SCREENING FOR *CHLAMYDIA TRACHOMATIS* INFECTIONS IN WOMEN

- Chlamydia is the most common infection reported in the United States, with more than 1.5 million reported cases of chlamydial infection in 2015 and many additional unreported cases.
- The highest rates of chlamydial infection are among persons between 15 and 24 years of age.
- Chlamydia is an important cause of pelvic inflammatory disease, infertility, and ectopic pregnancy.
- Data from a randomized, controlled trial and observational data have shown a reduced incidence of pelvic inflammatory disease among young women who undergo screening for chlamydia.
- Modern diagnostic tests are highly sensitive for the detection of chlamydia; testing can be performed on vaginal swabs or urine samples collected by the patient, which eliminates the need for a pelvic examination.
- All sexually active women younger than 25 years of age as well as older women at risk for chlamydia should be offered chlamydia screening annually.

and fallopian tubes) (Fig. 1). Other pelvic inflammatory disease pathogens include *Neisseria gonorrhoeae*, endogenous vaginal bacteria (anaerobes and other microorganisms associated with bacterial vaginosis), and possibly *Mycoplasma genitalium*. In one trial that assessed treatments for pelvic inflammatory disease, *C. trachomatis* was shown to be the most common pathogen (identified in 23% of women).[6]

Quantifying the risk of progression to pelvic inflammatory disease is challenging. In a large community-based study, the 1-year incidence of pelvic inflammatory disease among untreated women with chlamydial infection was approximately 10%.[7] Studies with shorter follow-up suggest that pelvic inflammatory disease develops in 2 to 3% of untreated women within 2 weeks after a positive test for *C. trachomatis*.[8] Acute (symptomatic) pelvic inflammatory disease does not develop in most women with chlamydial infection, either because they receive effective antibiotic treatment or because of spontaneous clearance, which occurs in one in five infected women.[9]

Reproductive sequelae of chlamydial pelvic inflammatory disease include infertility, ectopic pregnancy, and chronic pelvic pain and result from fallopian tube scarring that follows upper genital tract infection — a complex process that involves both tissue injury from acute infection and the host immune response.[10] The reported rate of infertility after one episode of pelvic inflammatory disease was 8%; after a second and third episode, the rate increased to 18% and 38%, respectively.[11] Nearly 10% of first pregnancies after pelvic inflammatory disease are ectopic.[12] Chronic pelvic pain was reported more than 3 times as frequently in women with a history of pelvic inflammatory disease than in those without (18% vs. 5%).[13]

Although most women with tubal factor infertility that is caused by damage to the fallopian tube have no known history of pelvic inflammatory disease, they are more likely to be seropositive for *C. trachomatis* than are fertile women or women with other causes of infertility.[14] Similarly, a history of chlamydia is common in women with ectopic pregnancies.[15] These observations indicate that tubal damage can result from subclinical as well as acute pelvic inflammatory disease through the ascension of chlamydia and other pathogens into the uterus and fallopian tubes, causing inflammation (endometritis in the uterus and salpingitis in the fallopian tubes). One in four women with chlamydial cervicitis has subclinical pelvic inflammatory disease (histologic endometritis in the absence of symptoms of pelvic inflammatory disease), and these women, when followed prospectively, are more likely to have impaired fertility than are women without subclinical pelvic inflammatory disease (Fig. 2).[16,17]

Systematic reviews and meta-analyses have shown that sexually transmitted diseases, including *C. trachomatis*, are associated with increased rates of transmission of and susceptibility to human immunodeficiency virus (HIV) infection.[18,19] In coinfected women, chlamydia increases HIV type 1 shedding in the genital tract, possibly as a result of epithelial friability and recruitment of HIV-infected leukocytes through up-regulation of HIV replication by inflammatory cytokines accompanying sexually transmitted diseases.[18] In a study involving Zairian women, the risk of HIV seroconversion was higher among women with incident chlamydial infection than among wom-

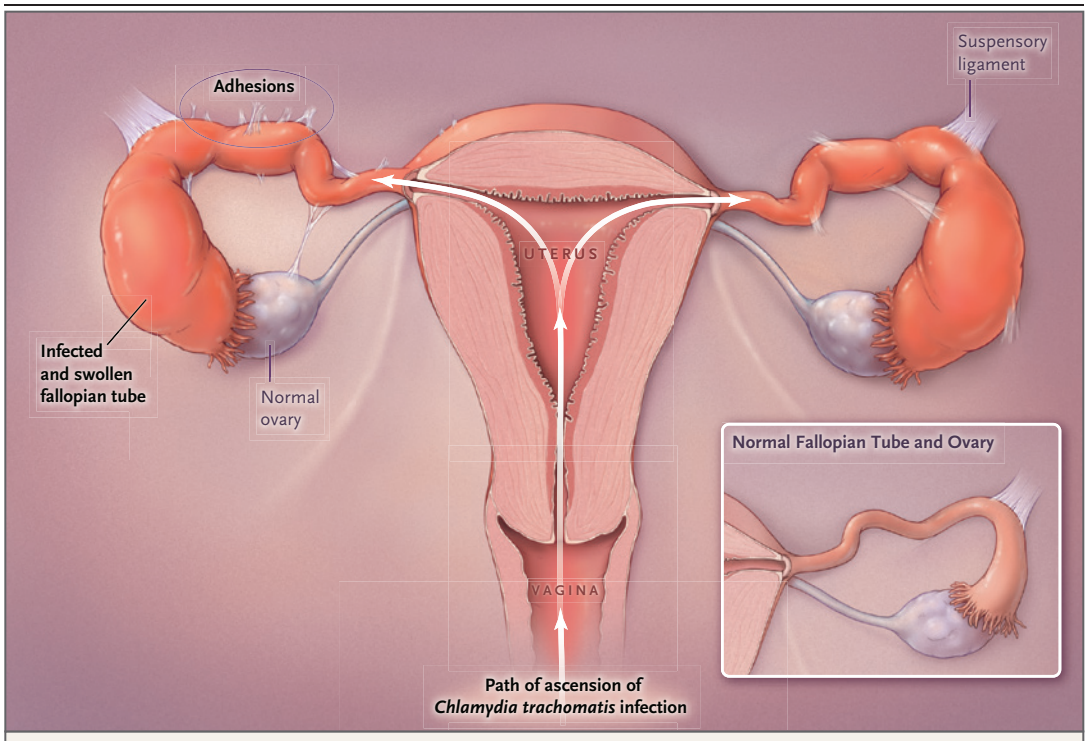

Figure 1. *Chlamydia trachomatis* and Ascension to the Upper Genital Tract in Women.

en without this infection.[20] Mucosal disruption, along with the recruitment of leukocytes in cervicitis, may increase susceptibility to HIV infection. These observations suggest that strategies to reduce chlamydial infections can prevent HIV transmission; however, data showing that population-based efforts to control chlamydia and reduce the spread of HIV are lacking.

STRATEGIES AND EVIDENCE

EVALUATION

In the genital tract, *C. trachomatis* may infect the cervix or urethra, and women may have abnormal vaginal discharge and dysuria. Most urogenital chlamydial infections in women, however, are asymptomatic. Chlamydia can manifest as mucopurulent cervicitis, with a watery or purulent discharge and easily induced bleeding with a swab; more often, physical findings of cervicitis or urethritis are absent, difficult to appreciate, or nonspecific. Chlamydial urethritis is suggested by the combination of dysuria or frequent urination (or both), the presence of leukocytes in urine, and a negative urine culture. Extragenital chlamydial infections may also occur. In one report, rectal infections were identified in 8.6% of women who reported receptive anal intercourse, and pharyngeal infection was identified in 2.6% of women who reported oral sexual contact.[21] Male partners may have symptoms and findings of urethritis (most common), epididymitis, prostatitis, and proctitis, but — as in women — most infections are asymptomatic.

SCREENING TO REDUCE COMPLICATIONS OF CHLAMYDIA

Studies have supported benefits of chlamydia screening to prevent pelvic inflammatory disease. Chlamydia screening in Sweden has coincided with a decreased incidence of acute pelvic inflammatory disease.[22] In one randomized, controlled trial involving 2607 single women in a health maintenance organization who were considered to be at risk for chlamydia (on the basis of risk factors that included young age, race, no pregnancies, douching, and more than one sexual partner in the previous year), the incidence of pelvic inflammatory disease was 56% lower among women who were randomly assigned to a one-time invita-

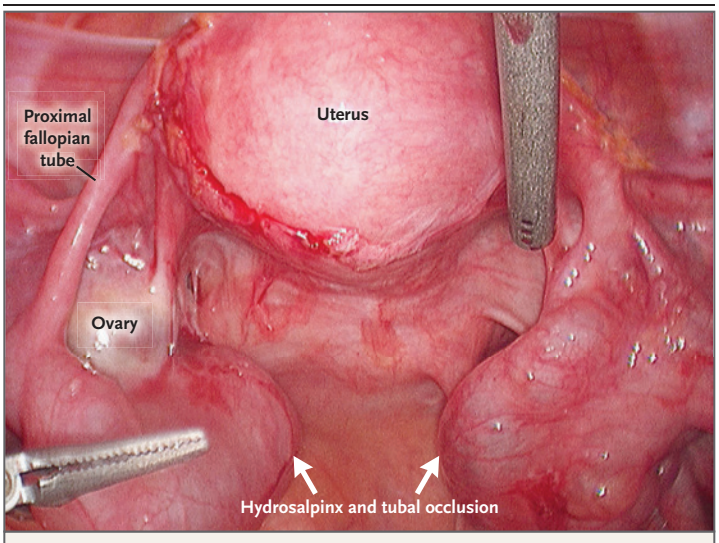

Figure 2. View of the Pelvis in a Woman with Infertility Who Has a History of Chlamydia but No Prior Diagnosis of Acute Pelvic Inflammatory Disease.
Bilateral hydrosalpinx and tubal occlusion can be seen and probably arose subsequent to subclinical pelvic inflammatory disease due to *Chlamydia trachomatis* infection.

tion for chlamydia screening than among women who were assigned to usual care (8 vs. 18 cases per 10,000 woman-months).[23] In another trial involving 2529 sexually active female university students in the United Kingdom who provided vaginal swabs that were randomly assigned to either immediate testing for *C. trachomatis* (intervention group) or testing 1 year later (control group), the rates of incident pelvic inflammatory disease overall were 1.3% and 1.9%, respectively (relative risk, 0.65; 95% confidence interval [CI], 0.34 to 1.22), and among women in whom chlamydia was identified (and treated), the rates of incident pelvic inflammatory disease were 1.6% in the intervention group and 9.5% in the control group (relative risk, 0.17; 95% CI, 0.03 to 1.01).[7] The low number of women who had pelvic inflammatory disease limited the study's power to detect differences between groups. Ecologic studies have shown that chlamydia screening is associated with reductions in the rates of ectopic pregnancies, but these studies cannot determine causality.[24] Data from randomized trials examining the effect of chlamydia screening on ectopic pregnancies, subclinical pelvic inflammatory disease, or infertility are lacking.[25]

SCREENING RECOMMENDATIONS FOR *C. TRACHOMATIS*

Screening Methods

Screening women for chlamydia may be performed with the use of endocervical or vaginal samples or first-catch urine (the initial portion of the urinary stream) specimens. Commercially available nucleic acid amplification tests are very sensitive for the detection of *C. trachomatis* (Table 1) and have replaced less-sensitive methods, both those that use and those that do not use cultures. Despite excellent performance, false positive test results can occur, particularly in populations in which prevalence of *C. trachomatis* infection is low.

Endocervical swabs are collected during a vaginal speculum examination, and the swabs can be analyzed with the use of some liquid-based cervical cytologic testing platforms. Women can undergo screening without a pelvic examination with the use of vaginal swabs or urine samples that they collect themselves. The Centers for Disease Control and Prevention (CDC) considers vaginal swabs to be the preferred specimen type, because nucleic acid amplification tests on vaginal swabs perform as well as those on cervical swabs, and collection of vaginal swabs is easy for most women to perform themselves.[27-29] A first-catch urine specimen is also acceptable but may fail to detect up to 10% of infections.[29] Testing with the use of vaginal swabs or urine samples facilitates screening in venues that are not equipped for a pelvic examination and minimizes discomfort and embarrassment that can deter women from undergoing screening, particularly younger women and women without symptoms who are not as concerned about infection. In two high schools in Pittsburgh, 8% of students who were screened with the use of vaginal swabs received a diagnosis of chlamydial infection; one half of these students had not planned to seek testing.[30]

Home-based screening is also possible and is preferred by some women.[31] A home-based kit is available (www.iwantthekit.org) and, in an early report of its use, detected chlamydia in 10% of women (95% of whom were treated).[32] Home testing may be more cost-effective than screening performed at a clinic.[33] Screening for chlamydia in the rectum and pharynx with the use of laboratory validated assays can be considered in persons who are at risk for infection at those sites.

Table 1. Diagnostic Accuracy of Chlamydia Tests by Specimen Type.*

Specimen Type	Sensitivity	Positive Predictive Value
	percent	
Endocervix		
Transcription-mediated amplification	89.0–97.1	89.4–100
Strand displacement amplification	86.4–96.2	86.9–100
Polymerase chain reaction	86.4–95.8	88.5–100
Vaginal swabs		
Obtained by a clinician		
Transcription-mediated amplification	89.9	92.2
Polymerase chain reaction	93.3	92.1–100
Collected by the patient		
Transcription-mediated amplification	93.3–97.0	94.9–99.4
Strand displacement amplification	96.5	94.8
Polymerase chain reaction	90.7–98.0	87.3–99.4
Urine		
Transcription-mediated amplification	72.0–98.2	92.5–96.5
Strand displacement amplification	93.0–96.2	93.8–94.4
Polymerase chain reaction	84.0–96.1	92.7–99.0

* Specificity and negative predictive values were all 97.5% or greater. All data in the table were adapted from Nelson et al.[26]

Because reinfection is common (occurring in one in five women with chlamydial infection within 1 year after treatment) and is associated with increased risks for ectopic pregnancy and pelvic inflammatory disease, repeat screening 3 months after treatment is recommended to detect new infections.[4,34]

Cost-Effectiveness of Screening

Screening young, sexually active women for chlamydia is generally considered to be cost-effective because it can prevent pelvic inflammatory disease and its sequelae and reduce disease prevalence as a result of earlier detection and treatment.[35] Most analyses have focused on women younger than 25 years of age and screening with the use of cervical samples. Extending the age for screening to 29 years and performing more frequent screening in women with prior infections may also be cost-effective.[35] Collection of vaginal swabs or urine samples by the patient may be more cost-effective than collection by a clinician.[33,36]

Chlamydia Screening in Pregnant Women

Chlamydial infections are linked to preterm birth and low-birth-weight infants, and observational studies have shown lower risks of these complications among treated women than among untreated women.[37,38] Neonatal conjunctivitis may develop in babies born to mothers with untreated chlamydial infections, and chlamydial pneumonitis occurs in up to 30% of babies exposed to chlamydia. All women should undergo screening for *C. trachomatis* in the first trimester of pregnancy, with repeat screening in the third trimester for women at increased risk.[4] Many women undergoing abortion meet the criteria for screening, and therefore the guidelines from the Society of Family Planning propose that screening may be appropriate for at-risk women before surgical or medical abortion.[39]

TREATMENT

Women who test positive for chlamydia should receive either 1 g of azithromycin as a single dose

administered orally or 100 mg of doxycycline administered orally twice daily for 7 days.[4] Cure rates with these two regimens are similar and exceed 95%.[40] In one study comparing azithromycin with doxycycline for the treatment of chlamydia in men and women, in which treatments were observed directly, failures in treatment were rare overall and were seen only with azithromycin.[40] In clinical practice, however, single-dose azithromycin may offer an advantage when adherence to doxycycline is of concern.

Doxycycline is contraindicated in pregnant women. All women who receive treatment for chlamydial infection should return in 3 months for repeat screening, given the high rate of reinfection. A meta-analysis of observational studies showed higher cure rates of rectal chlamydia after doxycycline therapy than after azithromycin therapy.[41]

Women with chlamydial infection should be screened for other sexually transmitted diseases, including gonorrhea, syphilis, and HIV, if they have not been screened previously; hepatitis B vaccination should be considered for unvaccinated women, and human papillomavirus vaccination should be offered to age-appropriate candidates. Counseling on risk reduction should be addressed (recommendations for obtaining a sexual history and prevention counseling are provided elsewhere).[4] Nearly 70% of male partners of women with chlamydial infection are also infected; therefore, sexual partners of persons who received a diagnosis of chlamydial infection should be screened and treated empirically if the sexual contact occurred within 60 days before the diagnosis or development of symptoms.[4] Contraception should be addressed, with a focus on safe sex through condom use and the use of effective contraceptive methods. Among women with known chlamydial cervicitis, insertion of an intrauterine device should be postponed until adequate treatment has been administered.

AREAS OF UNCERTAINTY

For reasons that remain unclear, declines in incidence have not been observed despite chlamydia screening programs.[1,42] This observation is probably explained, at least in part, by better case finding (more screening of persons at high risk and the use of highly sensitive diagnostic tests), but it has also been hypothesized that earlier detection may shorten the natural course of chlamydial infections, impair the protective immune response, and enhance susceptibility to repeat infection.[43] The time between the acquisition of chlamydia and its detection by screening can be lengthy, and the point at which upper genital tract infection occurs during the natural course of infection is unknown; a better understanding of the time frame within which treatment is needed to prevent fallopian tube damage would help guide screening programs. The most effective screening interval for at-risk women is unknown. Conventional standards are lacking to make the diagnosis of various sequelae of chlamydial infections, which complicates the assessment of the effect of screening. Pelvic inflammatory disease is a subjective diagnosis, and tubal factor infertility is also challenging to diagnose and is likely to go unrecognized if women do not pursue infertility evaluations.

Although rates of pelvic inflammatory disease in the United States have declined in association with chlamydia screening, ectopic pregnancy rates have not.[1] It is not known whether screening for *C. trachomatis* reduces the rate of HIV infection. Data are lacking on the benefits of shorter screening intervals and screening women at low risk.

Data from trials evaluating the effect of screening men to reduce the rate of complications in women are also lacking, and routine screening of men is not recommended by the CDC.[4,44] Screening at-risk, sexually active young men (e.g., men attending clinics for sexually transmitted diseases, incarcerated men, and at-risk men who have sex with men) should be considered.

Little is known about the benefit of chlamydia screening in women who have sex with women, who may acquire infection through contact with infected fluid or sharing of sex toys or through sexual contact with a male partner. Among girls and women 15 to 24 years of age who attended

Table 2. Indications for Screening for *Chlamydia trachomatis* in Sexually Active Women.

Young age (<25 yr)
New or multiple sexual partners
Partner with a sexually transmitted disease
Prior sexually transmitted disease (e.g., chlamydia, gonorrhea, syphilis, or trichomoniasis)
Concurrent sexually transmitted disease
Pregnancy
Commercial sex work
Incarceration

Table 3. Chlamydia Screening Recommendations for Sexually Active Nonpregnant and Pregnant Women.*

Organization	Nonpregnant Women		Pregnant Women	
	Age	Screening Interval	Age	Comments
U.S. Preventive Services Task Force[46]	All women ≤24 yr; women >24 yr with risk factors	With new or persistent risk factors	All women ≤24 yr	—
Centers for Disease Control and Prevention[4]	All women ≤24 yr; women >24 yr with risk factors	Annual	All women ≤24 yr; women >24 yr with risk factors	Screen at first prenatal visit; rescreen in third trimester
American College of Obstetricians and Gynecologists[47,48]	All women ≤24 yr; women >24 yr with risk factors	Annual	All	Screen at first prenatal visit (all); rescreen in third trimester all women ≤25 yr of age and women ≥26 yr of age with risk factors
American Academy of Pediatrics[48,49]	All women ≤25 yr	Annual	All	Screen at first prenatal visit (all); rescreen in third trimester all women ≤25 yr of age and women ≥26 yr of age with risk factors
American Academy of Family Physicians[50]	All women ≤24 yr; women >24 yr with risk factors	Not specified	Not specified	—

* Risk factors for chlamydia include new or multiple sexual partners, more than one sexual partner, current sexual partner with a sexually transmitted disease, and sexual partner with other concurrent sexual partners.

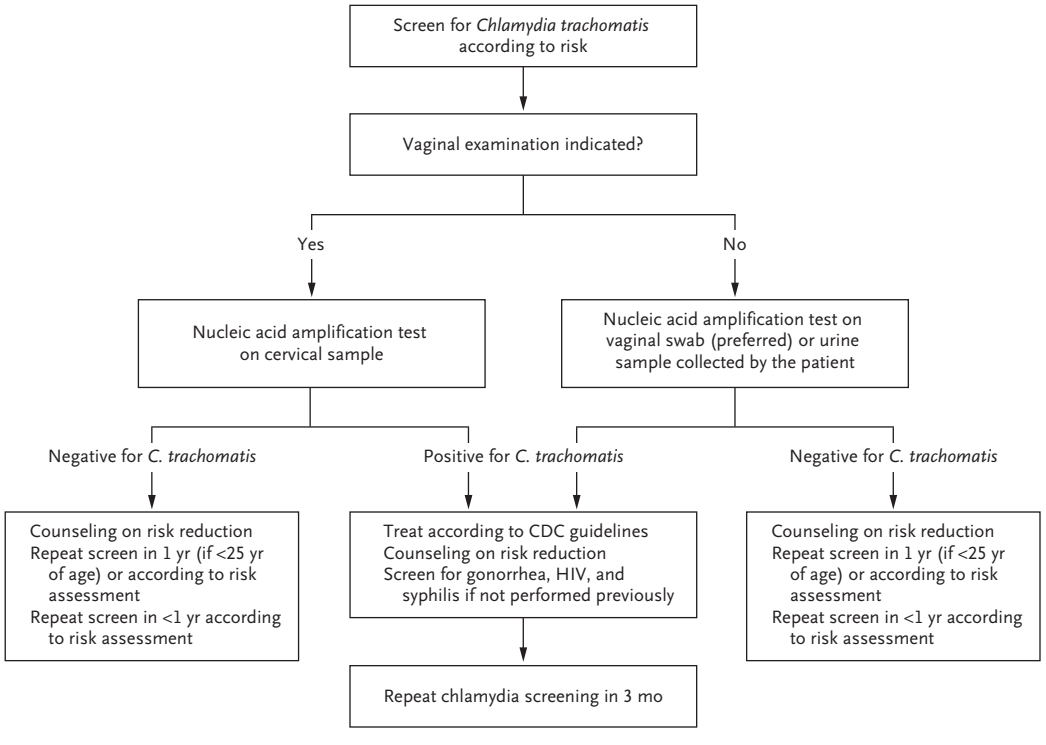

Figure 3. Algorithm for Chlamydia Screening.
CDC denotes Centers for Disease Control and Prevention, and HIV human immunodeficiency virus.

family planning clinics, the rate of chlamydia among women who had sex with women was 7.1%.[45] The recommendations of the CDC for women who have sex with women are the same as those for heterosexual women.[4]

GUIDELINES

The U.S. Preventive Services Task Force endorses chlamydia screening (grade B recommendation [i.e., high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial]) (Table 2).[44] Recommendations from other professional organizations are similar to those from the U.S. Preventive Services Task Force (Table 3). Recommendations in this article are in general accordance with these guidelines (Fig. 3).

SUMMARY AND RECOMMENDATIONS

The woman in our vignette meets criteria for chlamydia screening because she is younger than 25 years of age and sexually active. Assessment of the risks of sexually transmitted diseases and counseling on safer sex, including the use of condoms, are recommended. I would recommend screening with either a vaginal swab (collected by the woman herself or by a clinician) or an endocervical swab obtained by means of pelvic examination, because these specimens have similar sensitivity and specificity for the diagnosis of chlamydial infection when nucleic acid amplification assays are used. Alternatively, testing can be performed by means of a first-catch urine sample, although testing of a urine sample has slightly lower sensitivity than testing of a vaginal or endocervical sample. If the patient tests positive, oral treatment with either 1 g of azithromycin as a single dose or 100 mg of doxycycline twice daily for 7 days is recommended, and a repeat screening test should be performed in 3 months. All sexual partners of this woman should be tested and treated empirically for chlamydia if the sexual contact occurred within 60 days before she received the diagnosis of chlamydial infection or before the symptoms developed.

Dr. Wiesenfeld reports receiving research laboratory supplies from Hologic. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

REFERENCES

1. Sexually transmitted disease surveillance 2015. Atlanta: Department of Health and Human Services, 2016.
2. Torrone E, Papp J, Weinstock H. Prevalence of *Chlamydia trachomatis* genital infection among persons aged 14–39 years — United States, 2007–2012. MMWR Morb Mortal Wkly Rep 2014;63:834-8.
3. Chesson HW, Kent CK, Owusu-Edusei K Jr, Leichliter JS, Aral SO. Disparities in sexually transmitted disease rates across the "eight Americas." Sex Transm Dis 2012;39:458-64.
4. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015; 64(RR-03):1-137.
5. Quinn TC, Gaydos C, Shepherd M, et al. Epidemiologic and microbiologic correlates of *Chlamydia trachomatis* infection in sexual partnerships. JAMA 1996;276: 1737-42.
6. Ness RB, Soper DE, Holley RL, et al. Effectiveness of inpatient and outpatient treatment strategies for women with pelvic inflammatory disease: results from the Pelvic Inflammatory Disease Evaluation and Clinical Health (PEACH) Randomized Trial. Am J Obstet Gynecol 2002; 186:929-37.
7. Oakeshott P, Kerry S, Aghaizu A, et al. Randomised controlled trial of screening for *Chlamydia trachomatis* to prevent pelvic inflammatory disease: the POPI (prevention of pelvic infection) trial. BMJ 2010; 340:c1642.
8. Hook EW III, Spitters C, Reichart CA, Neumann TM, Quinn TC. Use of cell culture and a rapid diagnostic assay for *Chlamydia trachomatis* screening. JAMA 1994; 272:867-70.
9. Geisler WM, Lensing SY, Press CG, Hook EW III. Spontaneous resolution of genital *Chlamydia trachomatis* infection in women and protection from reinfection. J Infect Dis 2013;207:1850-6.
10. Darville T, Hiltke TJ. Pathogenesis of genital tract disease due to *Chlamydia trachomatis*. J Infect Dis 2010;201:Suppl 2: S114-S125.
11. Weström L, Joesoef R, Reynolds G, Hagdu A, Thompson SE. Pelvic inflammatory disease and fertility: a cohort study of 1,844 women with laparoscopically verified disease and 657 control women with normal laparoscopic results. Sex Transm Dis 1992;19:185-92.
12. Buchan H, Vessey M, Goldacre M, Fairweather J. Morbidity following pelvic inflammatory disease. Br J Obstet Gynaecol 1993;100:558-62.
13. Weström L. Effect of acute pelvic inflammatory disease on fertility. Am J Obstet Gynecol 1975;121:707-13.
14. Brunham RC, Maclean IW, Binns B, Peeling RW. *Chlamydia trachomatis*: its role in tubal infertility. J Infect Dis 1985;152: 1275-82.
15. Svensson L, Mårdh PA, Ahlgren M, Nordenskjöld F. Ectopic pregnancy and antibodies to *Chlamydia trachomatis*. Fertil Steril 1985;44:313-7.
16. Wiesenfeld HC, Hillier SL, Krohn MA, et al. Lower genital tract infection and endometritis: insight into subclinical pelvic inflammatory disease. Obstet Gynecol 2002;100:456-63.
17. Wiesenfeld HC, Hillier SL, Meyn LA, Amortegui AJ, Sweet RL. Subclinical pelvic inflammatory disease and infertility. Obstet Gynecol 2012;120:37-43.
18. Johnson LF, Lewis DA. The effect of genital tract infections on HIV-1 shedding in the genital tract: a systematic review and meta-analysis. Sex Transm Dis 2008; 35:946-59.
19. Boily MC, Baggaley RF, Wang L, et al. Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies. Lancet Infect Dis 2009;9:118-29.
20. Laga M, Manoka A, Kivuvu M, et al. Non-ulcerative sexually transmitted dis-

eases as risk factors for HIV-1 transmission in women: results from a cohort study. AIDS 1993;7:95-102.
21. Trebach JD, Chaulk CP, Page KR, Tuddenham S, Ghanem KG. *Neisseria gonorrhoeae* and *Chlamydia trachomatis* among women reporting extragenital exposures. Sex Transm Dis 2015;42:233-9.
22. Kamwendo F, Forslin L, Bodin L, Danielsson D. Decreasing incidences of gonorrhea- and chlamydia-associated acute pelvic inflammatory disease: a 25-year study from an urban area of central Sweden. Sex Transm Dis 1996;23:384-91.
23. Scholes D, Stergachis A, Heidrich FE, Andrilla H, Holmes KK, Stamm WE. Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection. N Engl J Med 1996;334:1362-6.
24. Egger M, Low N, Smith GD, Lindblom B, Herrmann B. Screening for chlamydial infections and the risk of ectopic pregnancy in a county in Sweden: ecological analysis. BMJ 1998;316:1776-80.
25. Gottlieb SL, Berman SM, Low N. Screening and treatment to prevent sequelae in women with *Chlamydia trachomatis* genital infection: how much do we know? J Infect Dis 2010;201:Suppl 2:S156-S167.
26. Nelson HD, Zakher B, Cantor A, Deagas M, Pappas M. Screening for gonorrhea and chlamydia: systematic review to update the U.S. Preventive Services Task Force Recommendations. Evidence Synthesis, No. 115. Rockville, MD: Agency for Healthcare Research and Quality, September 2014.
27. Wiesenfeld HC, Heine RP, Rideout A, Macio I, DiBiasi F, Sweet RL. The vaginal introitus: a novel site for *Chlamydia trachomatis* testing in women. Am J Obstet Gynecol 1996;174:1542-6.
28. Schachter J, McCormack WM, Chernesky MA, et al. Vaginal swabs are appropriate specimens for diagnosis of genital tract infection with *Chlamydia trachomatis*. J Clin Microbiol 2003;41:3784-9.
29. Recommendations for the laboratory-based detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* — 2014. MMWR Recomm Rep 2014;63(RR-02):1-19.
30. Wiesenfeld HC, Lowry DL, Heine RP, et al. Self-collection of vaginal swabs for the detection of chlamydia, gonorrhea, and trichomoniasis: opportunity to encourage sexually transmitted disease testing among adolescents. Sex Transm Dis 2001;28:321-5.
31. Graseck AS, Secura GM, Allsworth JE, Madden T, Peipert JF. Home compared with clinic-based screening for sexually transmitted infections: a randomized controlled trial. Obstet Gynecol 2010;116:1311-8.
32. Gaydos CA, Dwyer K, Barnes M, et al. Internet-based screening for *Chlamydia trachomatis* to reach non-clinic populations with mailed self-administered vaginal swabs. Sex Transm Dis 2006;33:451-7.
33. Huang W, Gaydos CA, Barnes MR, Jett-Goheen M, Blake DR. Cost-effectiveness analysis of *Chlamydia trachomatis* screening via Internet-based self-collected swabs compared with clinic-based sample collection. Sex Transm Dis 2011;38:815-20.
34. Hillis SD, Owens LM, Marchbanks PA, Amsterdam LF, Mac Kenzie WR. Recurrent chlamydial infections increase the risks of hospitalization for ectopic pregnancy and pelvic inflammatory disease. Am J Obstet Gynecol 1997;176:103-7.
35. Hu D, Hook EW III, Goldie SJ. Screening for *Chlamydia trachomatis* in women 15 to 29 years of age: a cost-effectiveness analysis. Ann Intern Med 2004;141:501-13.
36. Andersen B, Gundgaard J, Kretzschmar M, Olsen J, Welte R, Ostergaard L. Prediction of costs, effectiveness, and disease control of a population-based program using home sampling for diagnosis of urogenital *Chlamydia trachomatis* infections. Sex Transm Dis 2006;33:407-15.
37. Martin DH, Koutsky L, Eschenbach DA, et al. Prematurity and perinatal mortality in pregnancies complicated by maternal *Chlamydia trachomatis* infections. JAMA 1982;247:1585-8.
38. Ryan GMJ Jr, Abdella TN, McNeeley SG, Baselski VS, Drummond DE. *Chlamydia trachomatis* infection in pregnancy and effect of treatment on outcome. Am J Obstet Gynecol 1990;162:34-9.
39. Achilles SL, Reeves MF. Prevention of infection after induced abortion: release date October 2010: SFP guideline 20102. Contraception 2011;83:295-309.
40. Geisler WM, Uniyal A, Lee JY, et al. Azithromycin versus doxycycline for urogenital *Chlamydia trachomatis* infection. N Engl J Med 2015;373:2512-21.
41. Kong FYS, Tabrizi SN, Fairley CK, et al. The efficacy of azithromycin and doxycycline for the treatment of rectal chlamydia infection: a systematic review and meta-analysis. J Antimicrob Chemother 2015;70:1290-7.
42. Rekart ML, Gilbert M, Meza R, et al. Chlamydia public health programs and the epidemiology of pelvic inflammatory disease and ectopic pregnancy. J Infect Dis 2013;207:30-8.
43. Brunham RC, Pourbohloul B, Mak S, White R, Rekart ML. The unexpected impact of a *Chlamydia trachomatis* infection control program on susceptibility to reinfection. J Infect Dis 2005;192:1836-44.
44. LeFevre ML. Screening for chlamydia and gonorrhea: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2014;161:902-10.
45. Singh D, Fine DN, Marrazzo JM. *Chlamydia trachomatis* infection among women reporting sexual activity with women screened in family planning clinics in the Pacific Northwest, 1997 to 2005. Am J Public Health 2011;101:1284-90.
46. Final recommendation statement — chlamydia and gonorrhea: screening. Rockville, MD: U.S. Preventive Services Task Force, September 2014 (https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/chlamydia-and-gonorrhea-screening).
47. Guidelines for women's health care: a resource manual. 4th ed. Washington, DC: American College of Obstetricians and Gynecologists, 2014.
48. Guidelines for perinatal care. 7th ed. Washington, DC: American Academy of Pediatrics and the American College of Obstetricians and Gynecologists, 2012.
49. Committee on Adolescence, Society for Adolescent Health and Medicine. Screening for nonviral sexually transmitted infections in adolescents and young adults. Pediatrics 2014;134(1):e302-e311.
50. Summary of recommendations for clinical preventive services. Leawood, KS: American Academy of Family Physicians, January 2017 (http://www.aafp.org/dam/AAFP/documents/patient_care/clinical_recommendations/cps-recommendations.pdf).