Chlamydia control: components of an effective control strategy to reduce the incidence of chlamydia trachomatis

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ABSTRACT (ABSTRACT)

Abstract: Genital chlamydia infection is the most frequently reported communicable disease in North America. Ten to forty percent of infected women will develop pelvic inflammatory disease. The resulting human and fiscal tragedy is preventable. This paper gives a practical and conceptual overview of options in chlamydia control. While promotion of behavioural change remains crucial, several other public health strategies show remarkable promise in reducing the burden of this infection. These include focused screening of high risk groups, employment of amplified DNA technology for screening, introduction of single dose treatment, and partner notification provided by health care workers. The technology and resources to apply these approaches are within our reach. If we can mobilize them, we can render chlamydia infections a rarity. Key words: Chlamydia, STD control, Partner notification, Screening, Azithromycin ACKNOWLEDGEMENTS: The author wishes to acknowledge Ms. Dorothy Rachar and Ms. April Accola for assistance in manuscript preparation, and the staff of the Division of STD Prevention and Control, Laboratory Centre for Disease Control, Bureau of HIV/AIDS and STD, for provision of data and organizing the meeting on national goals for STD, Health Canada. INTRODUCTION Few consider the problem of genital infection with Chlamydia trachomatis on the same scale as those of other preventable diseases such as mumps, polio and measles. Perhaps the fact that genital chlamydia infection is the most frequently reported communicable disease in North America indicates that we should (CDC, 1996; CDC, 1993; Gully &Rwetsiba, 1992). Between 10-40% of chlamydia infected women will suffer from pelvic inflammatory disease (PID), a condition affecting one million women annually in the United States alone (CDC, 1991). American costs associated with chlamydia and its complications were estimated at $2 billion US for 1994 (Institute of Medicine, 1996). This human and fiscal tragedy is preventable because cost-effective means to dramatically reduce the burden of morbidity are at hand in almost all developed nations. All that is required is the will to deploy them. In the United States in 1995, the CDC received nearly half a million reports of chlamydia infection for a rate of 182 per 100,000 population (CDC, 1997). Reports of infection underestimate true incidence because many people remain undiagnosed. In Canada, the chlamydia rate has fallen from 162 to 123 per 100,000 of the population between 1992 and 1995 (Personal communication, J. Doherty, Bureau of STD and AIDS, Laboratory Centre for Disease Control, Health Canada, 1997). Indeed, incidence may be slowly declining in a number of countries, although this is usually in settings where control efforts are clearly in place (Crowley, Homer &Nelki, 1994; Hillis et al., 1994; Garland, Gertig, &McInnes, 1993; Patrick &Bowie, 1994). Enthusiasm about general population trends must be tempered by continued high rates of infection occurring among females less than 25 years of age. For example, in 1995, Canadian women aged 15-19 years had a chlamydia infection rate of 1080 per 100,000; the rate for 20-24 year old women was 1009 per 100,000 (see Table 1). However, many chlamydia infections go undetected and untreated. Sexually active females in this age group carry prevalence rates as high as 5-10% (CDC, 1993, Garland et al., 1993). Control efforts for these young women are hampered by underdiagnosis and undertreatment of their male partners (Garland et al., 1993; Patrick &Bowie, 1994). Among especially vulnerable populations such as male and female street youth, cumulative incidence as measured by serological survey is as high as 22% (Ram et al., 1996). Chlamydia rates also vary among the provinces and territories (see Table 2). CONCEPTUALIZING CHLAMYDIA CONTROL A useful conceptual tool in fine tuning public health efforts at sexually transmitted disease (STD) control is the reproductive rate of an STD. The reproductive number or reproductive rate (text not transcribed) represents the mean number of people secondarily infected from an individual carrying a given STD. If text not transcribed is less than one, prevalence of infection

declines over time; greater than one, prevalence increases. Although a formula describing its determinants is mathematically simplistic, it remains conceptually useful: R"Symbol not transcribed" = betacD The reproductive number or reproductive rate (hereafter referred to as R) is the mean number of new infections generated by infected persons over the lifetime of their infection (in a fully susceptible population).

FULL TEXT

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persons over the lifetime of their infection (in a fully susceptible population). The phrase in brackets means that the infected person is encountering new uninfected partners who would not have been exposed except through him/her. (beta) is the probability of transmission from an infected to an uninfected person, (c) is the contact rate between infected and susceptible individuals, and (D) is the average duration of infectivity of infected individuals. Programs that promote sexual and reproductive health focus primarily on reduction of (beta) and (c) in the above equation. For example, the probability of transmission from an infected person (beta) is often addressed through promotion of condom use or suggestion of lower risk (non-insertive) sexual practices; reducing the contact rate between infected an uninfected individuals (c) might involve efforts to reduce number of sexual partners, to maintain "monogamous" relationships or, among the young, to encourage postponement of sexual involvement or abstention from high risk sexual activity. These and other behavioural interventions are common elements in attempts to control bacterial and viral STDs and unwanted pregnancy (see Maticka-Tyndale, 1997). In practice, these behaviours are sometimes difficult to influence although there has been some notable success in increasing condom use in particular populations (Maticka-Tyndale, 1997). When an STD is curable (e.g., chlamydia), it is also possible to reduce text not transcribed by shortening the duration of infectivity (D). This is achieved through screening, diagnosis and cure of patients and their partners. Indeed, this sometimes maligned approach to STD control carries considerable evidence of efficacy and most probably explains declines in the incidence of syphilis and gonorrhea over the last decade. Happily, this proven approach is also ideally suited to controlling chlamydia and highlights the treatment-related declines in bacterial STDs in contrast to the static or modest changes in viral STDs such as human papillomavirus (HPV) and herpes simplex virus (HSV). In determining how to best influence the duration of infectivity (D) for chlamydia, it is instructive to make comparisons with another readily diagnosed and curable bacterial STD. The rate of reporting of gonorrhea declined tenfold in Canada between 1981 and 1994 (Division of STD Prevention and Control, Bureau of STD and AIDS, Laboratory Centre for Disease Control, Health Canada, October, 1996). Why have declines in chlamydia infections been less impressive? To begin with, there is evidence that chlamydia has been more widespread in the population and less concentrated in subgroups that have been motivated to change their sexual behaviour in response to the AIDS pandemic. A number of factors may also have conspired to make the duration of infectivity for gonorrhea shorter than that for chlamydia. Patients with gonorrhea are more frequently symptomatic than those with chlamydia, thus leading to a greater likelihood of their seeking care. Accurate diagnostics for gonorrhea have been widely available for decades; whereas, those for chlamydia only became available in the 1980s. Single dose therapy with high efficacy virtually assured that people who were treated for gonorrhea would be cured. Until recently, treatment of chlamydia has required compliance with a week of oral medication. Finally, public health services in many jurisdictions have been more dedicated to providing partner notification for gonorrhea than for chlamydia. Below, I discuss how correction of these discrepancies can lead to improved chlamydia control. Evidence of the efficacy of such modified strategies continues to mount. SCREENING PRACTICES A majority of women and many men infected with chlamydia will have mild or no symptoms (CDC, 1993). Indeed, 50% of women with infertility associated with tubal scarring give no history compatible with PID resulting from chlamydia infection (Sellors, Mahoney, Chernesky, &Rath, 1988). Because of the frequently subtle presentation, screening recommendations focus on identifying asymptomatic people at risk. The 1993 CDC guidelines suggest annual screening of all sexually active females under 20 years of age and screening of those 20 or over if additional risk factors are identified (e.g., no barrier contraception, new partners in last 3 months) (CDC, 1993). Recently, it has been reported that age-based criteria may prevent a similar volume of PID at a slightly reduced cost (Howell, Quinn, Brathwaite, &Gaydos, 1996). But does screening have a clear positive impact on patients and populations? A randomized trial of chlamydia screening among patients of an HMO indicated that asymptomatic women screened and treated for Chlamydia trachomatis had a rate of subsequent PID 50% lower than women who were not screened (Scholes et al., 1996). There is also good ecological evidence of success on a population scale. Routine screening was introduced in Region X family planning clinics in the USA and was followed by a decline in prevalence among those screened from 9.3% in 1988 to 3.3% in 1994 (CDC, 1997). The importance of resulting reductions in chlamydia incidence to morbidity from PID is underscored when one notes that dramatic reductions in the incidence of gonorrhea and chlamydia infections have correlated with impressive declines in PID

morbidity and costs in Sweden (Westrom, 1988; Kamwendo, Forslin, Bodin, &Danielsson, 1996). It is also important to look at scenarios where testing is unnecessary. Testing to determine that treatment has effected a cure is not a cost effective strategy when currently recommended chlamydia therapy is employed (Schiotz &Csango, 1992). Given a much lower rate of new sexual partners after the age of 30, screening should be more selective after that age in order to conserve laboratory resources for a younger population at higher risk. TESTING TECHNOLOGY The efficiency of screening practices is highly dependent on the accuracy of the diagnostic tests employed. While widespread use of confirmatory technologies has ensured a low false positive rate in most screening systems, systems depending on enzyme immunoassay (EIA), direct fluorescent antibody and chlamydia cell culture are missing one out of every three to five infections among people screened (Black, 1997). In contrast, tests based on amplified nucleic acid technology have a sensitivity of up to 95% (Quinn et al., 1996), and use of this technology in practice greatly enhances diagnosis. This technology has the added advantage of excellent performance on urine specimens, thus opening the door to wider screening of young adult males who have been deterred from testing by the requirement for a urethral swab. Cost-benefit analyses suggest that under most circumstances, screening using DNA amplification yields an advantage in terms of outcome and net cost over other methods (Genc &Mardh, 1996). Preliminary use of a dynamic model of transmission, prevalence and associated costs indicates that improved sensitivity of the test and improved compliance with screening from young males would be expected to reduce prevalence, morbidity and net costs associated with chlamydia infections over a broad range of assumptions (Personal communication, N. Meagher and R. Hanvelt, Department of Health Care and Epidemiology, University of British Columbia, 1997). It has been suggested that since EIA technology detects infections with higher chlamydia burden, it may remain relevant to public health screening where the goal is to reduce transmission. EIA positive patients may or may not be more infectious than those positive only by amplified nucleic acid test. However, one can offer no measure of reassurance to an EIA negative woman that her "low-burden" infection poses no threat to fertility. SINGLE DOSE THERAPY In treating symptomatic and asymptomatic people, the medication should be carefully chosen. While doxycycline regimens have proven high efficacy, a number of studies indicate poor compliance in STD treatment populations and associated treatment failure (Katz, Caine, &Jones, 1992; Augenbraun, Wallace, Bubauchet, &McCormack, 1996; Bachman, Stephens, Richey, &Hook, 1996). A one gram single dose of azithromycin has been shown to have equivalent efficacy with doxycycline for proven chlamydia infections and for STD syndromes where chlamydia is a commonly implicated cause (Martin et al., 1992; Stamm et al., 1995; Ossewaarde et al., 1992). Despite its higher cost, a number of studies document that improved compliance rates with single dose therapy will prove cost-effective in the treatment of chlamydia infections by reducing health care costs from complications (F. Marra, Marra, &Patrick, 1997; Haddix, Hillis, &Kassler, 1995). PARTNER NOTIFICATION It seems remarkable that some jurisdictions will strongly recommend screening an asymptomatic population before partner notification strategies are in place. Over 50% of male and female partners of people infected with chlamydia are themselves infected (Viscidi et al., 1993). Notification and treatment of partners is an extremely efficient means of chlamydia control. With an 82% success rate, notification by health care workers (provider referral) has proven more effective in assuring notification and treatment of contacts to bacterial sexually transmitted diseases than notification by patients (Katz et al., 1992). Partner notification also has direct benefits to the index client. The rate of re-infection of index patients is six times lower when provider referral is used to verify contact treatment than when referral is left up to the client (Ramstedt, Forssman, &Johannisson, 1991). Mathematical modelling of the Swedish success in reducing PID morbidity strongly suggests that a comprehensive partner notification scheme was a key component of the campaign (Ripa &Bauman, 1995). PHYSICIAN EDUCATION The development of screening and treatment guidelines may not be enough to ensure adequate practice at the primary care level. Surveys of physicians have found that while most are up-to-date in employing recommended therapy, many have not adapted their practices to fully comply with screening guidelines (e.g., McDougall, Mathias, O'Connor, &Bowie, 1992). It is important to complement screening and treatment guidelines with adequate continuing medical education programming and evaluation. CONCLUSIONS AND RECOMMENDED GOALS Independent evidence exists to suggest that each of the measures discussed in this paper can contribute to reducing the prevalence and burden of chlamydia. These include focused screening of high risk groups, employment of

amplified DNA technology for screening, introduction of single dose treatment and partner notification provided by health care workers. There remain questions about how these strategies best work in combination, and which are the most crucial to population disease control. However, the most successful STD control models do employ a combination of strategies (e.g., Ripa &Bauman, 1995). Goals for the control of genital chlamydia infection in Canada should take into account epidemiological targets, proven means by which they may be achieved, and surveillance requirements to assure a reasonable level of evaluation (see Table 3). Success over time can be monitored by consistent surveillance with an awareness of potential confounding factors. It has been suggested that since the objective of most chlamydia control measures is to reduce the duration of infectivity (D), programs should monitor that parameter as an indicator of success. In most cases, however, such an effort would not be practical, as the duration of infection will very rarely be known or easily ascertained. Tracking laboratory reports of positive chlamydia tests is simpler and of clear value, as long as its interpretation takes into account the number of tests performed in different settings and the performance characteristics of the technology employed. Cross-sectional prevalence studies conducted at intervals are of value in determining the impact on clientele at family practice and sexually transmitted disease clinics, and in supporting data from more passive surveillance. It is also important to monitor the burden of complications. Indeed, influencing these is the true raison d'etre of control efforts. PID can be monitored by tracking ICD-9 coded diagnoses at such locations as hospitals and surgical day care centres. Such tracking is limited because most PID is managed outside of hospitals, and economic pressures may reduce the likelihood of hospitalization over time. Finally, PID is a syndrome frequently caused by organisms other than Chlamydia trachomatis. Nevertheless, tracking PID diagnoses over time in large populations is of some value in determining whether control programs are working. Ectopic pregnancy, due to its acuity and requirement for urgent management, will perhaps more consistently meet with a registered diagnosis. Its surveillance is therefore less likely to be confounded than that of PID, but would prove only a late indicator of the success or failure of a given program. STD control stands at the threshold of its greatest opportunity in 15 years. We have at our disposal all the necessary diagnostic, public health and therapeutic tools to engineer a dramatic decline in the prevalence and morbidity associated with the continent's most frequently reported communicable disease. If we can muster enough enthusiasm to mobilize these resources, we can render chlamydia infections a rarity. Such an accomplishment would match our greatest achievements in vaccine preventable disease. Our patients, our health care budgets and our economies will reap the dividend. Table 1 Reported cases and rates(f.*) of genital chlamydia in Canada by province/territory and sex, 1995 Male Female Total(f.1) Province/Territory Cases Rates Cases Rates Cases Rates Newfoundland 45 15.6 229 79.8 274 47.6 Prince Edward Island 27 40.2 85 123.4 112 82.3 Nova Scotia 282 61.0 906 190.7 1189 126.8 New Brunswick 150 39.8 539 140.6 689 90.7 Quebec 1759 48.7 5278 141.9 7048 96.1 Ontario 2762 50.4 8794 156.5 11556 104.1 Manitoba 754 133.7 2148 374.6 2902 255.1 Saskatchewan 514 101.8 1456 285.0 1970 194.0 Alberta 1158 83.7 3830 280.9 4988 181.6 British Columbia 1057 56.5 3602 190.2 4660 123.7 Yukon 34 222.6 122 821.8 156 518.0 Northwest Territories 197 577.7 633 1996.0 831 1262.4 Canada 8739 59.6 27622 184.9 36376 122.9 f.* Per 100,000 f.1 Totals include cases not specified for sex. Source: Division of STD Prevention and Control, Laboratory Centre for Disease Control, Bureau of HIV/AIDS and STD, Health Canada, 1996. Table 2 Reported cases and rates(f.*) of genital chlamydia in Canada by age category and sex, 1995 Male Female Total(f.1) Province/Territory Cases Rates Cases Rates Cases Rates Less than 1 18 9.2 30 16.2 49 12.8 1-4 4 0.5 4 0.5 8 0.5 5-9 1 0.1 10 1.0 11 0.6 10-14 23 2.3 482 49.2 504 25.2 15-19 1662 163.8 10427 1080.4 12091 610.7 20-24 3356 323.8 10166 1008.9 13523 661.6 25-29 1757 155.1 3603 324.0 5361 238.8 30-39 1429 53.6 2239 85.7 3668 69.5 40-59 384 10.5 441 12.1 826 11.3 60+ 32 1.5 30 1.1 62 1.3 Age Not Specified 73 -- 190 -- -- 271 Total 8739 59.6 27622 184.9 36376 122.9 f.* Per 100,000 f.1 Totals include cases not specified for sex. Source: Division of STD Prevention and Control, Laboratory Centre for Disease Control, Bureau of HIV/AIDS and STD, Health Canada, 1996. Table 3 Goals for Chlamydia Control in Canada By the year 2000 The national rate of reporting of genital chlamydia infection should be less than 80 per 100,000 (Each jurisdiction should strive for a 1/3 reduction from 1995 rates) The rate in women aged 15-24 should be less than 500 per 100,000 (Each jurisdiction should st rive for a 50% reduction from 1995 rates) Rates of PID hospitalization for females aged 15-44 should be less than 120 per 100,000 By the year 2010 The national rate of reporting of genital chlamydia infection should be less than

50 per 100,000 (Each jurisdiction should strive for a 2/3 reduction from 1995 rates). The rate in women aged 15-24 should be less than 200 per 100,000 (Each jurisdiction should strive for an 80% reduction from 1995 rates) Rates of PID hospitalization for females aged 15-44 should be less than 80 per 100,000 Ectopic pregnancy rate should decline by 30% compared to 1996 to less than 14 per 1,000 pregnancies Surveillance Needs All provinces and territories should continue surveillance based on positive laboratory tests for chlamydia; this should be interpreted in the context of the volume of testing conducted and changes in technology employed LCDC should standardize its definitions for PID and ectopic pregnancy and track these conditions from national databases Surveys of screening seeking behaviour in 15-24 year old Canadians and evaluations of primary care practice in this regard should be conducted periodically Control Strategies Screening should be offered to all sexually active women and men between the ages of 15-24 Amplified DNA technology should be available to the majority of primary care physicians Single dose therapy should be introduced in each province or territory as soon as possible All health jurisdictions should perform partner notification, screening and treatment for contacts to proven genital chlamydia infection as a top priority program Behavioural Targets Reduce the number of sexual partners Delay the onset of sexual activity Increase condom use Increase other safer sex practices References Augenbraun, M., Wallace, T., Bubauchet, L., &McCormack, W. 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DETAILS

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