

Risk factors for genital chlamydial infection

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OBJECTIVE: To discuss the occurrence of genital chlamydia in developed countries and review the literature assessing the potential risk factors for this sexually transmitted disease.

DATA SOURCES: A MEDLINE search was performed for all English citations from 1985 to 2000 that contain the keywords "Chlamydia trachomatis", "chlamydial infections", "risk factors" and "sex behaviour". All relevant references cited in articles that were obtained from the search were also included.

DATA EXTRACTION: All articles obtained from the above sources were examined, and were included in the review if they met the following criteria: primary study examining sociodemographic or behavioural risk factors associated with genital chlamydial infection using multivariate analysis; study subjects 12 years of age and older; and study setting in a developed country.

DATA SYNTHESIS AND CONCLUSIONS: Genital chlamydial infection has become the most commonly reported bacterial infection in North America over the past decade. Thirty-eight cross-sectional studies and six cohort studies were included in the present review. Most studies demonstrated that young men and women are at higher risk of being infected with chlamydia than older subjects. Chlamydia seems to be found in a diverse group of people, and unlike gonorrhoea, is not concentrated in low income, minority core groups with high rates of partner change. However, a number of studies have shown that communities with well-established control programs are beginning to demonstrate this pattern. There is no clear evidence that chlamydia is associated with type of partners, contraceptive use, or age at first intercourse. Future research should follow this sexually transmitted disease as it evolves through the epidemiological stages to ensure that preventive and treatment services are reaching those people who are most likely to be infected.

Key Words: *Epidemiology; Genital chlamydia; Risk factors; Sexually transmitted diseases*

Genital chlamydial infection is a sexually transmitted disease (STD) of public health importance. Infection with the intracellular bacterium *Chlamydia trachomatis* can cause urethritis, cervicitis, pharyngitis, proctitis or epididymitis, although asymptomatic infections are quite common, occurring in up to 70% of infected women and 50% of infected men (1,2). Untreated chlamydial infection can lead to pelvic inflammatory disease (PID) in 10% to 40% of affected women, which can result in infertility, ectopic pregnancy and chronic

Les facteurs de risque de chlamidiose génitale

OBJECTIF : Discuter de l'occurrence de chlamidiose génitale dans les pays industrialisés et examiner la documentation scientifique évaluant les facteurs de risque potentiels de cette maladie transmise sexuellement.

SOURCES DE DONNÉES : Une recherche sur toutes les citations des mots clés « Chlamydia trachomatis », « chlamidiose », « facteurs de risque » et « comportement sexuel » entre 1985 et 2000 a été exécutée dans MEDLINE. Toutes les références pertinentes citées dans les articles obtenus grâce à cette recherche ont également été incluses.

EXTRACTION DES DONNÉES : Tous les articles obtenus dans les sources précédentes ont été examinés et inclus dans l'analyse s'ils respectaient les critères suivants : étude primaire portant sur les facteurs de risque sociodémographiques ou comportementaux associés avec une chlamidiose génitale au moyen d'une analyse multivariée, étude de sujets de 12 ans et plus et étude menée dans un pays industrialisé.

SYNTHÈSE DES DONNÉES ET CONCLUSION : Depuis dix ans, la chlamidiose génitale est devenue l'infection bactérienne la plus déclarée en Amérique du Nord. Trente-huit études transversales et six études de cohortes ont été incluses dans la présente analyse. La plupart des études ont démontré que les jeunes hommes et femmes courent un risque plus élevés d'être infectés par la chlamydia que les personnes plus âgées. La chlamydia semble s'observer dans un groupe varié de la population et, contrairement à la gonorrhée, elle n'est pas concentrée dans des noyaux minoritaires à faible revenu présentant un roulement élevé de partenaires. Cependant, plusieurs études ont démontré que les collectivités disposant de programmes de contrôle bien établis commencent à afficher ce schéma. Il n'existe pas de preuve manifeste selon laquelle la chlamydia est reliée au type de partenaires, à l'usage de contraceptifs ou à l'âge de la première relation sexuelle. Les prochaines recherches devraient porter sur les phases épidémiologiques de cette maladie transmise sexuellement, pour garantir que les services préventifs et de traitements atteignent les personnes les plus susceptibles d'être infectées.

pelvic pain (3,4). As well, chlamydial infection during pregnancy may cause complications such as spontaneous abortion, premature rupture of fetal membranes, premature delivery, low birth weight and neonatal infections including conjunctivitis and pneumonia (4-6). The economic burden of this disease is also great. The 1990 baseline burden of illness estimate for *C trachomatis* in Canada, which includes the costs of diagnostic and screening tests, and treatment of uncomplicated genital chlamydia and cases of PID, female infertility and ectopic preg-

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nancy attributable to this infection, was \$89 million for men and women combined (7). In comparison, the direct and indirect costs of treating genital chlamydia and its complications in the United States was estimated to be approximately US\$2 billion in 1994 (3).

The present paper provides an overview of the occurrence of genital chlamydia in developed countries and summarizes the potential risk factors associated with the disease. These risk factors may be either causally related to disease outcome (such as number of partners or use of barrier contraceptives), a marker or indicator of certain sexual or health care behaviours that directly affect a person's risk of infection (including socioeconomic status or race) or both (such as age). The ability to identify populations at increased risk is important for targeting screening and prevention programs.

DATA AND METHODS

To find epidemiological studies that examined the risk factors related to genital chlamydial infection, a MEDLINE search was performed for all English citations from 1985 to 2000 that contain the keywords "*Chlamydia trachomatis*", "chlamydial infections", "risk factors" and "sex behaviour". The reference lists from retrieved articles were searched manually to find further relevant studies. Studies were included in the present review if they met the following criteria: the study was published in 1985 or later; the study was a primary study examining sociodemographic and behavioural risk factors associated with chlamydial infection using multivariate analysis; and study subjects were 12 years of age and older. As well, the study had to be located in Canada, the United States, Australia, New Zealand or Europe, because the epidemiology of genital chlamydia in developing countries is very distinct from that of developed countries, due to differences in health care accessibility, public sector resources, health care-seeking behaviours and gender inequalities (8). Three articles that exclusively compared repeat cases to initial cases of genital chlamydia were excluded (9-11) from this review to make comparisons among studies more meaningful, because all other studies compared infected individuals to individuals who were not infected. In addition, three articles were eliminated because the method of detection for chlamydial infection was not given (12), had low specificity (microimmunofluorescence) (13), or was based solely on self-reported disease status (14). Overall, 44 studies examining risk factors for genital chlamydial infection were included in the review, including 38 cross-sectional studies in which disease and exposure status were assessed at a single time for each study subject, and six prospective cohort studies that examined the predictors of incident infections in susceptible study subjects over a period of time. Only eight of these studies looked at risk factors for chlamydia in males. The studies are described in Tables 1 and 2.

OCCURRENCE OF GENITAL CHLAMYDIA

Genital chlamydia has become the most commonly reported bacterial STD in North America and Europe (15). However, accurate time trends in the incidence of chlamydia are difficult to define because of changes in reporting, increased detection due to improved laboratory tests and increasing laboratory surveillance (16). Gerbase et al (17) estimated that the average annual incidence rates for people aged 15 to 49 years were similar in North America, western Europe and Australasia at 2146/100,000 for males and 3073/100,000 for females in 1995.

This translates into 1.64 million new cases in males and 2.34 million new cases in females in North America, compared with 2.30 million males and 3.20 million females in western Europe, and 120,000 males and 170,000 females in Australasia.

In Canada, reported genital chlamydial infections decreased steadily between 1991 and 1997, from an annual national reported incidence of 171.7/100,000 persons to 112.7/100,000 persons (18). However, increases in genital chlamydia incidence have been reported by some provinces since 1998, due in part to the introduction of nucleic acid amplification tests that have a substantially higher sensitivity than previous tests (19). In 2000, the annual national reported incidence was 151.1/100,000 persons. Annual reported incidence rates are consistently higher among females than among males. In 2000, the reported incidence rates were highest at 1236.1/100,000 among women aged 15 to 19 years and 1179.4/100,000 among women aged 20 to 24 years. In contrast, the reported incidence of genital chlamydia peaked at 472.8/100,000 among men aged 20 to 24 years in 2000 (18). This sex differential reflects the combination of screening of asymptomatic females during routine pelvic examinations and low rates of testing in men (18).

In the United States, reported incidence rates of genital chlamydia increased from 50.8 cases/100,000 persons in 1987 to 236.6/100,000 in 1998. In addition to increased screening, especially for asymptomatic women, this trend is also due to improved reporting and an increase in the number of states requiring reporting. As with people in Canada, the incidence was highest in females aged 15 to 19 years, at 2359.4/100,000 cases, and in 20- to 24-year old women, at 1952.7/100,000 in 1998 (20). The 1992 National Health and Social Life Survey found that 3.2% of 3159 American men and women between the ages of 18 and 59 years reported having had chlamydia in their lifetime, and the annual incidence of chlamydia was estimated to be 500/100,000 population (21). According to the 1988 National Survey of Family Growth (NSFG), 1.7% (95% CI 1.4 to 2.0) of 8450 women aged 15 to 44 years reported ever having had chlamydia. However, these self-reported rates are likely to be underestimates because chlamydia is a less well-known STD; for example, only 36.6% of the NSFG sample had ever heard of chlamydia (14).

In England and Wales, surveillance reports were based on returns from genitourinary medicine (GUM) clinics and microbiological laboratories. In 1996, 29,656 new cases were reported from laboratories and 31,857 new cases were reported from 213 GUM clinics (22). Annual incidence rates for males seen at GUM clinics remained relatively stable – under 100/100,000 males between 1988 and 1996, with highest incidence rates among males aged 20 to 24 years in 1996. For females, the annual incidence increased from 95 cases/100,000 females in 1993 and 125 cases/100,000 females in 1996, with the highest incidence for females aged 16 to 19 years in 1996 (23). However, only about 10% of *C trachomatis* infections are identified in GUM clinics, and reporting from laboratories is neither mandatory nor complete (22,24). Studies and surveillance estimates based on data from STD and GUM clinics also may not provide accurate estimates for the disease frequency among the general population because their clientele are not necessarily representative of the sexually active population that is at risk for STDs (25).

Genital chlamydial infections have been reportable in Swedish laboratories since 1982 and became nationally notifi-

TABLE 1
Description of cross-sectional studies of chlamydia

Year*	Location	Author (reference)	Study site	Study subjects	Eligibility criteria	Primary method of detection
1985	United States	Harrison et al (32)	University clinic	162 females	Consecutive nonpregnant patients	Culture
	United States	McCormack et al (33)	University clinic	431 females	Consecutive patients	Culture
1986	United States	Handsfield et al (70)	Two family planning clinics	1059 females	Consecutive patients who have had intercourse, ≥ 14 years	Culture
	United States	Karam et al (74)	Hospital emergency room	85 males	Asymptomatic, heterosexual, sexually active in past three months, ≥ 18 years	Culture
1987	United States	Addiss et al (71)	Four family planning clinics	335 females	Patients having a pelvic exam	DFA
1989	United States	Oh et al (101)	One teen family planning clinic	376 females	Consecutive patients, 12 to 18 years	Culture
	United States	Phillips et al (37)	Four private practices, one hospital-based OB/GYN practice	1141 females	Consecutive nonpregnant patients having a routine pelvic examination, 18 to 50 years	Culture
1990	United States	Addiss et al (87)	Two family planning clinics, one community health centre	849 females	Patients having a pelvic examination	Culture
	Denmark	Bro and Juul (91)	29 general practices	577 females	Nonpregnant women complaining of discharge or having a pelvic examination	Culture
	United States	Johnson et al (94)	University clinic	2271 females	Patients having a pelvic examination	Culture
	United States	Malotte et al (95)	University clinic	1320 females	Patients having a pelvic examination	EIA
	Canada	Pereira et al (79)	STD clinic	247 females	Consecutive patients	Culture
	The Netherlands	Thewessen et al (96)	STD and abortion clinics	1052 females	Consecutive patients	Culture
	United States	Winter et al (72)	Four family planning clinics	889 females	Consecutive patients attending for physical examination or contraceptive counselling	EIA
1991	Canada	Masse et al (103)	One primary health clinic	717 females	Patients having a pelvic examination excluding those presenting specifically for an STD or who have taken antibiotics in past six weeks	Culture
	Canada	Vincelette et al (111)	23 provider sites [†]	2018 females 838 males	Symptomatic or history of contact with known or suspected partner or history of multiple partnerships or presenting for an abortion	EIA
1992	Australia	Hart (51)	STD clinic	3533 females	Consecutive sexually active patients	EIA
	United States	Hook et al (78)	STD clinic	400 females 400 males	Consecutive patients	Culture

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TABLE 1 (CONTINUED)
Description of cross-sectional studies of chlamydia

Year*	Location	Author (reference)	Study site	Study subjects	Eligibility criteria	Primary method of detection
	United States	Humphreys et al (88)	22 family planning clinics	11,793 females	Consecutive patients	EIA
	Sweden	Ramstedt et al (54)	Family planning clinics	5785 females	Consecutive patients, ≤ 25 years	Culture
	Canada	Sellers et al (56)	Two family planning clinics	1002 females	Patients having a pelvic examination, ≥ 16 years	Culture or EIA
	United States	Weinstock et al (90)	Four family planning clinics	1348 females	Consecutive patients attending for physical examination or contraceptive counselling who were not screened in the past year, 13 to 50 years	DFA
1993	United States	Addiss et al (81)	Five family planning clinics	1757 females	All patients having a pelvic examination	DFA (nonurban) EIA (urban)
	United Kingdom	Evans et al (92)	Genitourinary medicine clinic	1025 females	Consecutive, new attenders	Culture
	United States	Han et al (73)	10 provider sites [†]	1531 females	Different criteria at sites	Culture
	Australia	Hart (50)	STD clinic	6125 females 12,170 males	Consecutive patients	EIA
	Australia	Hart (52)	STD clinic	7992 males	Consecutive patients	EIA
	United States	Stergachis et al (55)	Two primary care clinics	1804 females	Symptomatic or having a pelvic examination in clinic A or randomly chosen at clinic B, 15 to 34 years	Culture
1995	Canada	Jolly et al (53)	Public health laboratory reports	400 females	Random sample of those tested at public health laboratory	EIA
1996	United States	Finelli et al (93)	Five STD, five family planning and five college health clinics	5128 females	Patients presenting for a pelvic examination or symptoms, 12 to 29 years	EIA
	United States	Gershman et al (68)	52 family planning clinics	12,926 females	Patients having a pelvic examination, presenting for symptoms, a history of risk or a recent contact with a partner with STD	NAH
1997	United States	Han et al (24)	Four family planning clinics	8920 females	Patients having a pelvic exam or presenting symptoms	EIA
	United States	Marrazzo et al (36)	12 provider sites [†]	4968 females 5150 males	Consecutive patients, ≥ 12 years	LCR
	United States	Mosure et al (89)	160 family planning clinics	148,650 females	Sexually active patients having a pelvic examination, 15 to 19 years	DFA
	The Netherlands	Van Duynhoven et al (25)	STD clinic	1288 females 1696 males	Consecutive patients	Culture and NAH

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TABLE 1 (CONTINUED)
Description of cross-sectional studies of chlamydia

Year*	Location	Author (reference)	Study site	Study subjects	Eligibility criteria	Primary method of detection
1998	United Kingdom	Oakeshott et al (97)	30 general practices	1049 females	Consecutive patients attending for a cervical smear test, < 35 years	EIA
1999	Denmark	Munk et al (77)	Population-based survey	522 females	Randomly selected from a population-based cohort, 20 to 29 years	PCR
	Belgium	Vuylsteke et al (35)	17 school medical centres	1433 females	Students due for medical check-up, ever had intercourse, 16 to 18 years	LCR

*Year of publication; †A combination of provider sites may include any of the following: family planning clinics, private physician offices, obstetrics/gynecology clinics, emergency rooms, hospital outpatient clinics, correctional centres, student health centres, adolescent clinics, abortion clinics or STD clinics; DFA Direct fluorescent antibody; EIA Enzyme immunoassay; LCR Ligase chain reaction; NAH Nucleic acid hybridization; OB/GYN Obstetrics/Gynecology; PCR Polymerase chain reaction; STD Sexually transmitted disease

TABLE 2
Description of prospective cohort studies of chlamydia

Year*	Location	Author (reference)	Study site	Study subjects	Eligibility criteria	Primary method of detection
1991	Sweden	Rahm et al (104)	One adolescent clinic	301 females	Sexually active adolescent attenders	Culture
1994	Netherlands	Prins et al (98)	STD clinic	234 females 155 males	Consecutive patients, heterosexual, reported ≥ 5 partners in the past six months, ≥ 18 years	Culture
1996	United States	Mosure et al (69)	160 family planning clinics	26,921 females	Sexually active patients having a pelvic examination who were tested for chlamydia on two or more occasions between 1988 and 1992, 15 to 19 years	DFA
	United States	Oh et al (99)	Adolescent clinics	216 females	Sexually active patients having pelvic examinations who had at least two visits with indications for repeat screening during the study period	Culture
1998	United States	Burstein (34)	Three middle school clinics	188 females	Consecutive patients	LCR
	United States	Burstein et al (82)	Family planning, STD and school-based clinics	3202 females	Consecutive patients, 12 to 19 years	PCR

*Year of publication. DFA Direct fluorescent antibody; LCR Ligase chain reaction; PCR Polymerase chain reaction; STD Sexually transmitted disease

able in 1988 (26). The incidence of genital chlamydia began to decrease during the late 1980s, in association with the implementation of routine screening of women, increased screening among men, contact tracing and the establishment of youth clinics (16,26-29). The number of reported cases dropped from approximately 40,000 cases in 1987 to 14,000 cases in 1996, which has been accompanied by a corresponding reduction in the number of cases of PID and ectopic pregnancy (29-31).

RISK FACTORS FOR GENITAL CHLAMYDIA

A summary of the relationships between genital chlamydia and the various risk factors observed in the studies reviewed is shown in Tables 3 and 4.

Age

Younger age is shown consistently to be associated with increased risk of chlamydial infection among the sexually active population. Highest incidence rates of infection are reported consistently in adolescents and young adults in Canada and the United States (18,20). Twenty-nine of 34 studies of females and five of seven studies of males have shown a significant relationship between age and chlamydial infection in multivariate analysis. In the majority of studies that did not demonstrate an association between age and chlamydial infection, study populations were restricted to adolescents and young adults, such as at university health services or school-based clinics, where the risk of being infected was

more likely to be uniform across the subpopulation (32-36). Phillips et al (37) set the cut-off age at 30 years, which may have been too high to detect an age differential; in fact, they did find that women aged 24 years and younger had the highest prevalence of chlamydia.

There are a number of reasons why adolescents are at greater risk for genital chlamydial infection than older people. A higher risk in adolescent females may be associated with certain aspects of physical development that make this group more vulnerable to sexually transmitted infections, including the persistence of columnar epithelium on the cervix, which supports the growth of *C trachomatis*, and changes in vaginal flora and mucus production (38,39). As well, older women may have acquired partial immunity after initial or serial infections in the past (6). Differences in the prevalence of infection between adolescents and adults are also often attributed to differences in sexual behaviours. In the United States, the proportion of adolescent women who reported having had premarital intercourse increased from 28.6% in 1970 to 51.5% in 1988 (40), and sexual debut during early adolescence is often associated with greater numbers of sex partners (40-44). The difference in number of sexual partners according to age may also largely be a function of marital status (41). Finally, adolescents may be less able to implement the complex act of correct condom use (39) or to communicate effectively about sexuality (45), and may be less likely to acknowledge the risks associated with their sexual behaviour (46). Therefore, in addition to universal screening for adolescents and young adults, as is generally recommended (47,48), these results also highlight the need for more proactive sexual health education strategies for adolescents and young adults for the primary prevention of chlamydia and other STDs.

Race and/or ethnicity and socioeconomic status

The relationships among race, socioeconomic status (SES) and genital chlamydial infection are not clear. Race/ethnicity and socioeconomic status are often considered together because they are strongly interrelated (49). Only 10 of 23 studies in females and one of four studies in males indicated a higher risk of chlamydial infection in nonwhite people compared with white people in multivariate analysis. SES was not associated with chlamydia in multivariate analysis using any measure for males and females, including employment status (50-52), income (53-55), level of parents' education (33), use of Medicaid (37) or occupation (56).

Although gonorrhoea is often shown to be concentrated in low income, minority communities (57-59), genital chlamydial infection does not seem to demonstrate this pattern (9,60,61). One potential reason why such a clearly delineated high-risk or 'core' group was not identified for chlamydia in these studies is that these two STDs are likely to be at different epidemiological stages. In other words, while genital chlamydial infection is still widely prevalent throughout the sexually active population, gonorrhoea has become concentrated in those segments of the population that have low or no access to well-established prevention and treatment programs for gonorrhoea (62). The distribution of an STD in a population is also influenced by the various combinations of sexual, health care and provider behaviours (51). For example, gonorrhoea is often more prevalent in low-income, minority communities than higher-income, white communities (63,64). Because it is generally recommended that people with gonorrhoea and their partners also be treated for chlamydia (47,65), the rate of

chlamydial infection in some low-SES minority communities may be lower than expected because of frequent exposure to dual antibiotic treatment (60). Race and SES may also be markers for health care seeking behaviours. Poor, uninsured, minority patients may be less likely to seek medical care or to seek care later than their more affluent, insured, nonminority counterparts (66). For instance, women of higher SES may be more likely to have routine examinations, and thus, the detection of asymptomatic cases in this group may bias reporting of chlamydia upward. Nevertheless, after the establishment of coordinated screening, surveillance and health education for chlamydia, this STD, in time, may become more concentrated within core groups where access to STD services is limited. This pattern has already been observed in areas where chlamydia control programs have been introduced (61,67). In fact, race is shown to be an important risk factor in most studies published after 1994, including three studies in which a chlamydia control program was well-established (24,68,69). Further evidence of the potential for such core groups is given in three studies that demonstrated that nonwhite men and women were significantly more likely to have recurrent chlamydial infections than white study subjects (9-11).

Three methodological issues should be mentioned. First, a number of studies that did not demonstrate a significant relationship between racial group and chlamydia had samples that were either predominantly white or predominantly black (32,50,70-74), and a small proportion of subjects with the exposure of interest make it difficult to detect differences among groups. Second, some studies may be affected by a diagnostic bias. For example, if providers are more likely to screen for and report cases of chlamydia in nonwhites, these cases may be systematically over-represented in the study (12). Third, definitions of race may not be clear, especially for those individuals of mixed parentage, which may result in misreporting of this potential risk factor or inconsistencies between studies (75).

In general, although SES does not seem to be a salient risk factor for chlamydia at this point in time, a person's racial or ethnic group has become a more important risk factor in the past few years. Although race should not necessarily be used as a screening criterion, it may be a marker for other underlying problems, including sexual and health care seeking behaviours or SES (75,76). A deeper understanding of the relationship between SES and race and/or ethnicity is required. Race is a characteristic that is not modifiable, but it does present an opportunity for improving primary prevention in communities where this is an important factor, such as through culturally sensitive education programs.

Number and type of partners

Multiple partnerships may increase the likelihood of encountering a sexually transmitted pathogen through the increased probability of choosing a partner with infection, while having new or casual sexual contacts may be related to increased risk because of a reduced familiarity between partners (21).

Munk et al (77) used polymerase chain reaction to detect *C trachomatis* in 525 women who were randomly selected from a population-based cohort. Women who reported having five to nine partners in their lifetime were almost five times more likely to have genital chlamydia than women who reported four or fewer lifetime sexual partners (OR 4.8, 95% CI 1.8 to 12.7). However, women who reported 10 or more lifetime sex-

TABLE 3
Risk factors for chlamydia in females

Year*	Author (reference)	Age	Race	Socio-economic status	Number of partners			Type of partners			Barrier contraceptive use	Oral contraceptive use	Age at first intercourse
					Lifetime	Past Year	Recent	New	Casual	Regular			
1985	Harrison et al (32)	†	-		-							+	
	McCormack et al (33)	-	+	-	+	-					-	-	
1986	Handsfield et al (70)	+	-			†	†	+			+		-
1987	Addiss et al (71)	+	-					†					-
1989	Oh et al (101)											+	
	Phillips et al (37)	†	+	-			-				†		†
1990	Addiss et al (87)	+	†			+	†	†			†	†	†
	Bro and Juul (91)	+									†	†	
	Johnson et al (94)		-				+	+			-	-	
	Malotte et al (95)	+					†	+			-	†	
	Pereira et al (79)	+			-		-				-	+	-
	Thewessen et al (96)	+					+				-	†	
	Winter et al (72)	+	-				-				†	†	
1991	Masse et al (103)	+				-		-					-
	Rahm et al (104)					†							-
	Vincelette et al (110)	+				+							
1992	Hart (51)	+	+	-			-			+		+	
	Hook et al (78)	+			-	-	-	-	-	-			-
	Humphreys et al (88)	+				+		+			+	-	
	Ramstedt et al (54)	+		†							+		
	Sellors et al (56)	†		†				+					
	Weinstock et al (90)	+	†					+			+	-	
1993	Addiss et al (81)	+				+	†	†			+	-	
	Evans et al (92)	+	†		-	+					-	†	†
	Han et al (73)	+	-				+					+	
	Hart (50)	+	-				-			+		+	
	Stergachis et al (55)	+	+	†		+		-			-	-	
	Prins et al (98)	+						-					
1995	Jolly et al (53)	+	+	-									
1996	Finelli et al (93)	+	†								-		
	Gershman et al (68)	+	+				+	†					
	Mosure et al (69)		+				+	+			+	+	
1997	Han et al (24)	+	+				+						-
	Marrazzo et al (36)	+	-				+				-		
	Mosure et al (89)		+				+	+			+	+	
	Oh et al (99)		-		-		-				-		
	Van Duynhoven et al (25)	+			+						+	+	
1998	Burstein et al (34)						-	-			-		
	Burstein et al (82)						+	†			+		
	Oakeshott et al (97)	+	+			+					-		
1999	Munk et al (77)	+			+						-		
	Vuylisteke et al (35)	†			+	†					†		†

*Year of publication; †Positive correlation, statistically significant in single factor analysis only; +Positive correlation, statistically significant in multivariate analysis; -No correlation; Blank space Not determined

TABLE 4
Risk factors for chlamydia in males

Year*	Author (reference)	Age	Race	Socio-economic status	Number of partners			Type of partners			Barrier contraceptive use	Age at first intercourse
					Lifetime	Past Year	Recent	New	Casual	Regular		
1986	Karam et al (74)	+	-		†	+	-					-
1991	Vincelette et al (111)	+				-						
1992	Hook et al (78)	-					-	+	+	-		
1993	Hart (50)	+	-	-			+			-		
	Hart (52)	+	-	-			+			†		
1994	Prins et al (98)						-					
1997	Van Duynhoven et al (25)	+					+		†		+	
	Marrazzo et al (36)	†	+				+				+	

*Year of publication; †Positive correlation, statistically significant in single factor analysis only; +Positive correlation, statistically significant in multivariate analysis; -No correlation; Blank space Not determined

ual partners had a reduced risk of having chlamydia (OR 2.8, 95% CI 0.9 to 8.8). The authors suggested that women with multiple sex partners acquire immunity against chlamydial infection from repeated exposure, although this immunity may be strain-specific or short-lived. Van Duynhoven et al (25) documented a similar pattern for women at an STD clinic in the Netherlands, while McCormack et al (33) found that the risk of being seropositive for *C trachomatis* antibodies increases with greater numbers of lifetime sex partners for women. Hook et al (78) also found that, for both men and women, those reporting the highest number of lifetime partners (30 or more) had a lower proportion of chlamydia diagnoses than those reporting fewer partners. This trend was not documented in several other studies because the number of lifetime partners was measured as a dichotomous variable (32,35,74,79). The number of partners in the past year may also be an important risk factor for infection in women, because 10 of 14 studies found a positive correlation between multiple partners and infection in either single factor or multivariate analysis.

However, the relationship between the number of recent partners (in the past one, two, three or six months), type of sex partners (new, casual or regular) and genital chlamydia is not consistent across the studies for males or females. This may be partly explained by using the classic model for the transmission of STDs, which defines the reproductive rate (R_0), or the mean number of new infections generated by an infected person over the lifetime of his or her infection, as a product of the probability of transmission from an infected to uninfected person (β), the rate of sex partner change (c), and the average duration of infectivity (D) (3,62,80).

$$R_0 = \beta c D$$

Because chlamydia is frequently asymptomatic or only mildly symptomatic, it often goes untreated. The duration of infectivity is therefore often long, and the rate of partner change can remain low for the disease to be sustained in a given population (80). With the implementation of control programs, more asymptomatic cases are treated, causing the duration of infectivity to decrease, and therefore, the rate of

partner change must increase correspondingly to maintain the STD in the population (62). As a result, the STD becomes concentrated in the small proportion of the population that is characterized by high rates of new partner acquisition or the 'core' group (61,80). As with race and SES, as chlamydia control programs become more widely established, there will likely be an increase in the importance of the number and type of partners in determining risk of genital chlamydial infection. This pattern has been demonstrated in areas where chlamydia control programs have been in place for a year or more. In all five studies set in populations with well-established screening programs, reporting recent multiple partnerships was significantly associated with a 1.2 to 2.2-fold increase in risk in multivariate analysis (24,68,69,81,82). In three of those studies, reporting having a new partner was significant before adjusting for other variables (68,81,82), and in Mosure et al's (69) study, published in 1996, this variable was significant in multivariate analysis (OR 1.7, 95% CI 1.5 to 1.9).

Another possible explanation for those inconsistencies may be that the relationship between the number and type of partners and chlamydial infection may be offset by other behaviours. For instance, in the 1991 United States National Survey of Men, men who reported having multiple partners and one-night stands were significantly more likely to report using condoms than men who did not report these behaviours (41,83). There are also methodological reasons for the inconsistency between reported number and type of partners, and chlamydial infection. First, the time frame of the question may bias the observed relationships. Because of the high proportion of asymptomatic cases and the relatively long incubation period for symptomatic cases (seven to 21 days) (84,85), cases that are detected are less likely to be newly acquired (25,55,61,78). Therefore, reporting new or casual partners in the past one to three months may be a less relevant risk behaviour because the most recent partner(s) may not be the source of the infection. Second, the results may be biased because these behaviours are self-reported. It is possible that men over-report the number of sexual partners while women under-report in effort to provide more socially desirable responses (86). As well, the classifica-

tion of a sexual relationship by its partners may be discordant (78). Differential misclassification may over- or underestimate the association between the exposure and outcome. Third, information on the number and type of partners does not tell whether partners are concurrent or sequential, or commercial or private, the frequency of sex, the sexual practices that are engaged in, or the type of contraceptive that is employed, all of which are factors that can influence a person's risk of infection (21).

Contraceptive use

The relationship between the use of condoms and other barrier contraceptives (diaphragm or cervical cap), and genital chlamydial infection is inconsistent across the studies. Use of a barrier method was shown to be associated with reduced risk of infection compared with the use of other methods of contraception in two of five studies in females (33,54,70,71,87). Compared with no contraceptives, use of a barrier method was protective against chlamydia for females in three of five studies (32,69,81,88,89). Only one of 10 studies found female barrier users to be significantly less likely to be infected than female nonusers (37,55,79,90-96). Although these studies did not consider consistency of use, when this factor is accounted for, the results are similar. Consistent users of barrier contraceptives were not shown to have a significantly reduced risk of infection compared with inconsistent users in multivariate analysis in six studies in women and one study in men (25,34,35,72,82,97). Han et al (24) found that unprotected sex in the past three months was associated with almost twice the risk of having chlamydia compared with not having unprotected sex for two of four samples from New York family planning clinics. Prins et al (98) did not find a significant relationship between chlamydial infection and the estimated number of unprotected sexual encounters with commercial or private partners for men or women. Using a condom at the last sexual encounter was not significantly associated with decreased risk of infection for female adolescents in Oh et al's study (99), but it was protective for adolescent males in the study by Marrazzo et al (36).

There are three possible reasons for these inconsistencies. First, individuals may have become infected before barrier use and started to use barriers after their symptoms appeared. Second, individuals may over-report barrier contraceptive use. Third, it is unclear how best to measure consistent and correct barrier use (100). Some studies established a time frame for use (eg, past three months, last sexual encounter), while others measured 'current' use of barriers. However, despite these weak results, this risk factor is modifiable, and consistent use of barrier contraceptives, especially condoms, should be encouraged.

Use of oral contraceptive pills (OCP) is thought to increase the risk of chlamydial infection by inducing ectopy, making more cervical epithelial cells susceptible to infection. Alternatively, ectopy induced by OCP may make sampling more efficient and thus improve detection of *C trachomatis* by culture (77,101,102). Users of OCP may also be less likely to use barrier contraceptives. OCP users tend to have higher prevalences of infection compared with nonusers, but this association is not significant after adjusting for other variables in the majority of studies reviewed (24,32,33,51,55,56,72,81,87,90-92,94,95,103,104). Only two studies found that oral contraceptive users were significantly more

likely to have chlamydia than nonusers after controlling for other risk factors (69,79), while Mosure et al (89) found that OCP users had a 20% decreased risk of being infected with chlamydia compared with females who did not use any method of contraception. Therefore, the relationship between OCP use and chlamydial infection is not clear. Harrison et al (32) suggested that cervical ectopy is a better predictor of infection. In their study, cervical ectopy was correlated significantly with use of OCP, while chlamydial infection was related strongly to ectopy, regardless of contraceptive practice. However, while eight of 10 studies examining this risk factor found that women with cervical ectopy were more likely to be infected with *C trachomatis* (32,55,70,72,81,94,96,103), only two of those studies showed this relationship to be significant after adjusting for other variables (55,94).

Evans et al (92) found that the use of an intrauterine device (IUD) was protective compared with nonuse (relative risk 0.4, 95% CI 0.2 to 0.9). The authors hypothesized that the IUD may enhance local immune function or may accelerate the development of squamous cells in the cervical epithelium, which discourages infection by *C trachomatis*. However, no significant difference was found for IUD use compared with the use of other methods in two studies (33,79) or for IUD use compared with nonuse in three studies (50,91,96).

Age at first intercourse

Age at first intercourse may be causally related to sexually transmitted infections through the biological mechanisms affecting adolescents that were discussed earlier (16). It may also be an indicator of other aspects of sexual activity that will directly increase risk, including multiple partnerships and recruitment of nonregular partners (44,105,106). Four of seven studies that looked at this risk factor found a higher risk of infection in women who had early age of sexual debut in single factor analysis, but none of these studies demonstrated a significant relationship in multivariate analysis. Karam et al (74) found no relationship between age at first intercourse and chlamydial infection in men; however, the sample size of 85 males may have been too small to detect statistically significant differences between groups. There is some evidence that age at sexual debut may be modifiable (107), but it may be equally important to examine the causes of early age at sexual debut and its determinants, such as sexual abuse, to establish the best point of intervention.

Other risk factors

A number of other risk factors have been identified (through multivariate analysis) to be associated with genital chlamydial infection. Chlamydia rates tend to be highest in men and women who are single, although only three studies identified marital status as a significant risk factor in multivariate analysis (52,55,90). The effect of marital status is mediated largely through its impact on number of partners (105,108,109). Current pregnancy was associated with a 1.4- to 1.8-fold risk of being infected in three studies (50,88,89); not only does it indicate inconsistent or nonuse of contraceptives, this relationship has also been attributed to increased hormonal levels and lower immunity during pregnancy (77). However, the results for a history of pregnancy were mixed – two studies found that nulliparity was protective against infection (35,51), and two found it to be associated with an increased risk of the infection (55,77), while Addiss et al (87) found that women

with one child or no children were at five times greater risk for chlamydia than women with two or more children. This may be due to involuntary infertility following 'silent' chlamydial PID. Suspected exposure to chlamydia (24,51,52,91,110) or having a symptomatic partner (32,35,71) is associated with an increase in risk of the infection in a number of studies, which highlights that, as chlamydia becomes more concentrated in core groups, contact tracing will become an increasingly important control strategy.

IMPLICATIONS FOR FUTURE STUDIES

There are several methodological issues that should be considered when designing further studies. First, the majority of studies were cross-sectional in design, and are therefore unable to demonstrate temporality between cause and effect. Disease and exposure status are assessed at the same time in cross-sectional studies, whereas in cohort studies, it is possible to observe whether the risk behaviour of interest preceded the infection. It should be noted, however, that the results found in the prospective cohort studies were similar to those observed in the cross-sectional studies. Second, sexual behaviours were self-reported in all studies, and therefore, may be affected by recall bias and/or a social desirability bias, which is a common issue in STD research (111). Third, the sources of study subjects differed for these studies. While most studies were based in family planning clinics, many of the studies reviewed were conducted in STD clinics. STD clinic populations are fairly homogeneous, often reporting higher numbers of partners and lower SES than the general population (112,113). Therefore, these populations may not be representative of the general population. However, there were no distinguishable differences in the results from STD clinics compared with the various study settings. Fourth, several different diagnostic tests of variable sensitivities and specificities (85) were used to detect *C trachomatis* in these studies. However, Gershman and Barrow (68) suggested that, although tests with lower sensitivities than the gold standard of

cell culture plus a nucleic acid amplification assay may underestimate the prevalence of chlamydia in a sample, the risk factor relationships should not be substantially affected unless the tests were differentially sensitive according to exposure status. Fifth, we need to establish uniform methods of measuring these risk factors. Lastly, further studies should examine the risk factors for chlamydial infection among males. The high level of asymptomaticity and the low levels of testing among males make them an important reservoir for chlamydial infection.

CONCLUSION

The most useful demographic or behavioural risk factor for genital chlamydia is age. Adolescents, and young men and women are consistently at higher risk of being infected with chlamydia than older subjects. Chlamydia seems to be found in a diverse group of people, and does not necessarily discriminate according to racial or ethnic groups, or SES. Number of partners in the past year has been found to be positively correlated with chlamydial infection in women in several studies, although there has been no clear evidence that chlamydial infection is associated with recent number of partners, type of partners, contraceptive use or age at first intercourse.

Chlamydia is in a relatively early epidemiological stage. Like gonorrhoea, as more control programs are implemented, people with limited access to preventive and treatment programs will become more dominant in the epidemic, and chlamydia may become concentrated in lower-income minority groups with high rates of partner change. A number of studies reviewed in the present article have shown that communities with well-established control programs are already demonstrating this pattern. More studies need to be conducted as this STD evolves through the epidemiological stages, both before and after the implementation of such programs, to ensure that preventive and treatment services are reaching those people who are most likely to be infected.

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