

## ORIGINAL ARTICLE

## Pharyngeal Chlamydia trachomatis is not uncommon any more

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**Background.** The significance of Chlamydia trachomatis (Ct) infection in the pharynx, and possible symptoms, are under discussion. Most studies have involved only homo/bisexual men. We report findings of pharyngeal Ct (PhCt) infections in patients with long-lasting throat discomfort and the prevalence of PhCt in genitally Ct-infected young people in a Swedish primary care setting. **Method.** Sub-study 1 (SS1) included 48 persons aged 15–35 y, with pharyngeal discomfort for more than 14 days. Sub-study 2 (SS2) included 150 persons, aged 15–35 y, with genital Ct. Questionnaires concerning symptoms, sexual behaviour and sexual identity were completed for both groups. Samples for Ct testing were taken from the pharynx, and in SS1, samples were also collected to ascertain genital Ct. **Results.** In SS1, 2 of 48 persons (4%) with pharyngeal discomfort had PhCt. In all, 35 of the 48 persons (73%) included in SS1 reported unprotected oral sex during the previous year. In SS2, 11 of 92 women (12%) and 4 of 58 men (7%) tested positive for PhCt. More women (94%) than men (83%) had given unprotected oral sex. Persons with PhCt had more symptoms from the upper respiratory tract ( $p = 0.04$ ). **Conclusions.** Some primary care patients with long-lasting throat discomfort have a PhCt infection. PhCt infection is not uncommon in genitally infected sexually active people. More heterosexual women than heterosexual men had given unprotected oral sex and were infected by Ct in the pharynx. Thus, research on PhCt should not focus on homo/bisexual men only. Information about Ct should include the risk of contracting a PhCt infection as well as a gender perspective.

**Keywords:** Chlamydia, pharyngitis, oral sex, gender**Introduction**

Chlamydia trachomatis (Ct) is the most common sexually transmitted infection (STI) in the USA and Europe, including Sweden [1–3]. In Sweden, 37,780 cases were reported in 2009, constituting a 96% increase in 10 y [3]. The increase was greatest in the age group 15–19 y.

There may be few or no symptoms of a genital Ct infection [4]. Untreated, Ct may cause an uncomplicated infection in the lower genitals, but it may also ascend, causing infection in the uterus, fallopian tubes and testicles. Of women with a Ct infection, 2–10% are affected by salpingitis [5], and Ct is the most common reason for epididymitis in young men [6]. Infertility and ectopic pregnancy in women [7] are well-known consequences.

Changes in sexual behaviour and attitudes explain, at least in part, the increasing numbers of Ct-infected young persons [8–10]. The age of sexual debut has

lowered internationally, young persons have more sexual partners than just a decade ago, while having sex the first night of an encounter has become increasingly common [11,12,13]. Furthermore, the attitude to temporary sexual contacts has become more positive [9,14]. Condom use has remained relatively low, and first-date intercourse without a condom has increased [11,12].

As part of the changing sexual behaviour, oral-genital contact has become more common among young persons [8,9]. Oral sex is usually carried out without barrier protection [13–15]. It is well-known that syphilis, herpes simplex virus, human papillomavirus and Neisseria gonorrhoeae can infect the pharynx, which is considered to be of epidemiological importance as a transmission route [16]. Oral-genital transmission is also established regarding Ct [8]. Such transmission and the prevalence of pharyngeal Ct (PhCt) has mainly been investigated among homosexual men (MSM) [17,18]. In a large study involving

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MSM from San Francisco, USA conducted in 2003, 6.6% of those with a Ct infection were only infected in the throat. One of 10 infected had local pharyngeal symptoms [19]. In a recent Swedish study of 234 homosexual men, 13% of those tested for PhCt (85% of all) were infected; 9% of those with urethral Ct had only practised oral sex [18].

There are few studies concerning the prevalence of PhCt among heterosexuals, and we have found none regarding lesbian women. In a Japanese study involving Ct-positive women with symptomatic cervicitis, a high prevalence of PhCt was detected: in 75.0% of prostitutes and 21.9% among other women [20]. In a study of women and men attending an outpatient clinic for STIs in Sweden, 7% of the women and 2.7% of the men with genital Ct infections tested positive in the pharyngeal samples [21]. In another Swedish study, 2.3% of patients attending a venereological clinic, and confirming engagement in unprotected oral sex within the last 6 months, were Ct-positive in the pharynx; 12.9% were positive genitally [13].

To sum up, there is limited knowledge regarding the prevalence of PhCt infection in young women and men, together with the importance of oral sex as a possible route of transmission of Ct, and symptoms connected to PhCt. According to the Swedish Communicable Disease Act [22], a person infected with Ct is obliged to participate in partner notification. Persons identified in this way are equally obliged to attend a clinic for Ct testing. In the County of Norrbotten, in the north of Sweden, where the present study was performed, there were approximately 900 persons with genital Ct infections in a population of 250,000 inhabitants in 2007 (information from the Department of Communicable Disease Prevention and Control in Norrbotten County). Most of those tested had attended Primary Health Care Centres for examination and treatment. Due to the suspicion of/concern for an STI, urine samples, and in women also cervical samples, were collected for Ct tests. In these situations, the attendees occasionally asked if Ct might infect the throat as well. The question was raised due to throat discomfort and/or having had oral sex with a genitally infected person. Furthermore, during the last years quite a few young patients attending Porsö Primary Health Care Centre, where 2 of us (AK, AF) work as general practitioners, have reported long-lasting throat discomfort, without any specific cause being identified. Some of these patients recovered when treated with doxycycline. When some of these persons were tested in a non-systematic manner, 1 of them turned out to be PhCt-positive. This was the starting point for the investigation presented herein. Our hypothesis was that more heterosexual women than men would be PhCt carriers due to anatomical differences, and

because we assumed that more women than men give oral sex.

The aim of the study was to answer the following questions: (1) Does Ct infection constitute a differential diagnosis in young persons with prolonged throat discomfort? What are the symptoms, if any? and (2) How common is PhCt infection in young persons with genital Ct, and does the prevalence differ between women and men?

## Materials and methods

### *Study populations and study design*

This was a descriptive study, divided into 2 sub-studies: (1) sub-study 1 (SS1) included 48 persons, 15–35 y of age, attending Porsö Health Care Centre between March 2007 and May 2009, due to throat symptoms lasting more than 14 days; (2) sub-study 2 (SS2) included 150 persons, 15–35 y old, with a verified genital Ct infection, who attended Porsö Health Care Centre and Gällivare Centre for Young Persons during the period March 2007 to May 2009, or Luleå and Piteå centres for young persons during the period May 2008 to May 2009.

Two questionnaires were completed for both groups, one concerning throat symptoms (continuous pain, recurrent pain, discomfort, swollen lymph nodes) and the other concerning sexual behaviour (unprotected oral sex within the last year, and if they considered themselves to be hetero-, bi- or homosexuals). Samples for Ct were taken from the pharynx, and in SS1, samples were also collected to ascertain genital Ct. At the time the study was planned, the standard method for PhCt testing employed pharyngeal swabs. Ct only grows in the respiratory epithelium of the pharynx, not in the epithelial cells in the tonsils. Thus, all samples were taken by swab (thorough scraping) from the posterior pharyngeal wall. Standard cultures for the detection of beta-haemolytic streptococci in pharyngeal swabs, and beta-haemolytic streptococci, pneumococci, Haemophilus influenzae, and Moraxella catarrhalis in nasopharyngeal swabs were also conducted. The participants received detailed information about the study, both in writing and verbally, during the visit. Two weeks after treatment, the attending doctor or midwife contacted the participants over the phone, filling in a short form concerning recovery and experiences from participating in the study.

The studies were carried out in parallel to ordinary work. Hence, no or few participants were included when there were intermittent staff shortages. Approximately one third of all people attending our centres, positive for genital Ct, were included in SS2. There was no systematic exclusion of patients from the study due to staff shortages. Eleven persons declined

to participate in SS2. In SS1, 8 cases were excluded due to a lack of data. In SS2, 10 cases were excluded for the same reason.

### *Chlamydia trachomatis* analysis

The analysis of Ct was done by multiplex strand displacement amplification (SDA; a DNA amplification) using BD-ProbeTec reagents (Becton Dickinson). The method is well studied and has a high sensitivity [23]; although not certified for PhCt, it is well proven [24].

### Statistical analysis

The analyses were carried out using Excel and SPSS v. 15.0 (SPSS Inc., Chicago, IL, USA). Results are given as frequencies, but for some populations and proportions we also carried out hypothesis testing. Confidence intervals (95% CI) and a version of the standard method for comparing 2 proportions were used. This 'plus 4 estimate' method has been shown to have superior performance to other methods in several respects, particularly coverage probability and small sample characteristics [25].

### Ethical approval

Ethical approval was received from the Regional Research Ethics Committee. Written consent was obtained from each participant. Ordinary examinations and treatments were carried out as usual. Records were kept according to standard procedures. Partner notifications and treatments were performed irrespective of whether the patient participated in the study or not.

## Results

In SS1, 2 of the 48 included persons (4%) tested positive for PhCt: 1 woman and 1 man (Table I). Both were also found to have genital Ct infections, and neither of them had positive pharyngeal or nasopharyngeal cultures for other common respiratory tract pathogenic bacteria. One of these patients recovered

Table I. Sub-study 1, showing the number of participants, median age, sex, and proportion positive for pharyngeal *Chlamydia trachomatis*.

	Women	Men	Total
Number of participants	21	27	48
Median age, y	23	22	23
Positive PhCt (proportion)	1 (5%)	1 (4%)	2 (4%)

PhCt, pharyngeal *Chlamydia trachomatis*.

fully with doxycycline treatment, while symptoms were ameliorated in the other, without a full recovery. He was, however, negative when re-tested for PhCt. Of the participants in SS1, 35 of the 48 (43%) had engaged in unprotected oral sex during the past year. A majority, 45 of 48 (94%), identified themselves as heterosexuals, and 1 as bisexual. Two left the question unanswered.

In SS2, 15 of the 150 included persons tested positive for PhCt: 11 women and 4 men (Table II). A majority, 142 of the 150 persons (95%) included in this study, identified themselves as heterosexuals, 7 as bisexual, and 1 person left the question unanswered. Of the 150 persons, 141 had engaged in unprotected oral sex during the past year. Of those with confirmed PhCt, all 15 had received and 14 had given unprotected oral sex. One female participant with PhCt denied having given oral sex during the year before testing. However, she had received oral sex and engaged in deep kisses. At follow-up, she was asked more detailed questions about oral sex, but maintained her story and was very credible. Of the 15 participants with PhCt and symptoms from the upper respiratory tract (URT) in SS2, all had recovered at the follow-up a fortnight later.

We found that a higher proportion of the women (12%) compared to the men (7%) had PhCt. However, this difference was not statistically significant ( $p = 0.44$ ; Table II). Similarly, we found that women had given unprotected oral sex to a higher degree than men, 92% vs 83% ( $p = 0.07$ ), and that men had received unprotected oral sex to a greater extent than women, 91% vs 85% ( $p = 0.33$ ).

We also investigated whether the participants in SS2 had experienced URT symptoms. There was a statistically significant difference, with a higher frequency

Table II. Sub-study 2, showing the number of participants, sex, median age, pharyngeal *Chlamydia trachomatis* findings, presence of symptoms in the upper respiratory tract, and answers regarding having given or received oral sex.

	Women	Men	Total
Number of participants	92	58	150
Median age, y	20	22	21
Participants with PhCt	11 (12%)	4 (7%)	15 (10%)
Upper respiratory tract symptoms in persons with PhCt	6 (55%)	4 (100%)	10 (67%)
Upper respiratory tract symptoms in persons without PhCt	31 (39%)	16 (30%)	47 (35%)
Participants who had given oral sex	85 (92%)	48 (83%)	133 (89%)
Participants who had received oral sex	78 (85%)	53 (91%)	131 (87%)

PhCt, pharyngeal *Chlamydia trachomatis*.

of URT symptoms in the group with PhCt ( $p = 0.04$ ). These symptoms could, however, not be specified.

## Discussion

The question constituting the basis for SS1 was whether PhCt should be considered as a differential diagnosis in young persons with prolonged throat discomfort. This study showed that PhCt should be considered in these patients. We found that both patients exhibiting PhCt also had a genital Ct infection. In clinical practice, a way of investigating the possible differential diagnosis of PhCt in patients with long-standing pharyngeal discomfort could be to exclude Ct by a urine sample. Such a procedure might make it easier for the clinician to raise the question about PhCt, and avoid the difficulties inherent in sampling from the pharynx. However, this procedure also implies that PhCt will run undiscovered in a few cases. A study of MSM has shown that pharyngeal infection alone is more common than a combination of pharyngeal and genital infection [20]. In addition, oral sex is common among young people, often practised instead of vaginal intercourse, and often considered as 'safe sex' [13,15,26,27].

In SS2, symptoms linked to PhCt infections could not be specified. However, symptoms from the upper respiratory tract were significantly more common in patients with PhCt than in those without ( $p = 0.04$ ). This finding is in contrast to those of previous studies, showing that symptoms are rare in persons with PhCt [13,28].

We found a higher prevalence of PhCt in persons with genital Ct than reported in previous similar studies [13,21]. PhCt was more common in women than in men, reaching prevalences in women equal to those earlier found in MSM [26]. It has been suggested that PhCt might be of significance in the transmission of Ct in MSM, and pharyngeal testing is often recommended in MSM [1]. This is in contrast to the recommendations regarding heterosexuals [1]. All persons with PhCt in the present study had engaged in oral sex. Sexually active young persons increasingly engage in oral sex, and 1 study even reported oral sex to be more common than vaginal sex [11,27]. Our figures concerning frequencies of unprotected oral sex were equal to, or exceeded, those found earlier, and reached the ranges previously described in studies of MSM [9,18,19,26]. This implies that research concerning pharyngeal transmission of Ct and other STIs should involve both women and men, regardless of their sexual identity. Furthermore, public information on STIs should highlight the risk of contracting Ct infections by practising oral sex. In our study, it was more common for women than men to give unprotected oral sex. Likewise it was more common

for men to receive unprotected oral sex (Table II). Together, these findings highlight the exposed position of heterosexual women with regard to PhCt infection.

We had expected higher numbers of participants in both studies. Furthermore, we expected to finish the studies in a shorter time period. However, both participating centres suffered long periods of heavy ordinary workload and organizational changes, causing discontinuities in the study. However, we do not believe that these setbacks affected the results in any substantial way.

Although we did our utmost to prevent any kind of bias in the patients selected for the studies, the physicians involved in SS1 reported more uneasiness in inviting women than men. This might explain why more men than women were included in SS1, despite our assumption that women run a higher risk of contracting PhCt. This might also have lowered the number of PhCt carriers in SS1. These feelings of uneasiness might indicate a general emotional obstacle towards involving heterosexuals, perhaps both in research and in practise, regarding orally transmitted STIs. In addition, our illogical discouragement of heterosexual women carries a gender bias, as well as the risk of missed diagnosis.

One possible source of error in the present study is the way in which sampling for PhCt was carried out. An oral wash might have revealed more PhCt cases [8].

The finding of a woman who had contracted PhCt although she had not been giving oral sex during the last year, illustrates the limited knowledge of carriage and transmission of Ct infections that we have today. The theoretical route of transmission in her case could have been ophtho-pharyngeal (secretions from the eyes were not analyzed), hand-pharyngeal or pharyngeal-pharyngeal. Alternatively, this person might have carried Ct in her pharynx for more than a year [29]. This study highlights the need for larger studies to address the question of the role of PhCt in the transmission of Ct.

Without being a common cause, PhCt should be considered in the differential diagnosis of sexually active persons attending medical care for long-lasting throat discomfort. A significant level of pharyngeal symptoms found through detailed questions about symptoms in a questionnaire, supports a linkage between PhCt infection and non-specific pharyngeal symptoms.

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