Chlamydial cervicitis: a research study from general practice

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SUMMARY. *Chlamydia trachomatis* was isolated from the cervix in five out of 294 women at routine cervical cytology screening. Significant sera antibody titres were obtained from six out of 115 isolate-negative women similarly screened. The antibody response increased in proportion to the past frequency and severity of cervical pathology and sexually transmitted disease.

It is suggested that the true incidence of chlamydial genital infection in general practice will be five times as high as the current cervical isolation rate.

Introduction

CHLAMYDIA TRACHOMATIS is an intracellular parasite which is particularly dangerous in the female genital tract. It is a small, Gram-negative bacterium with a complex life cycle, infection being by elementary bodies which form intracytoplasmic inclusions in affected cells.

Early work having produced evidence of an association between chlamydial genital infection and chlamydial ocular infection,[1] many of the clinics dealing with sexually transmitted disease (STD) now test both partners for *C. trachomatis*. This is because approximately 50 per cent of males and 30 per cent of their female partners, routinely diagnosed as having non-specific genital infection, are in fact infected with this organism[2]—in the urethra in the male and in the cervix in the female.

Chlamydial cervicitis is frequently associated with hypertrophic cervical erosion and mucopurulent cervicitis,[2] and these macroscopically discernible features have been reported as showing significant correlation with non-specific inflammation noted in cervical cytology examinations.[3] Oriel and co-workers[4] reported similar findings—cervical ectopy with purulent exudate together with inflammatory changes in cervical cytology—but did not consider these signs to be pathognomonic because they were also seen in some women infected with other microbes.

The micro-immunofluorescent test has facilitated serotyping from ocular, genital and rectal infections, and the measurement of type-specific antibody in the sera of patients gives a sensitive indication of chlamydial infection.[5]

In order to assess the current and possible past practice rates for chlamydial genital infection in women, a combination of cervical isolation and serological tests for *C. trachomatis* was undertaken.

Method

Isolation study

The isolations for *Chlamydia trachomatis* were done on consecutive patients during routine cervical cytology screening in two stages: in 1973–75, 255 women were tested; in 1979, 102 women were tested. Twenty-three women were common to both stages and therefore the total number of different women involved was 334 (Figure 1).

After first wiping the cervix free from discharge, an adequate endomucosal scrape was taken on a swab. The transport and isolation techniques are detailed elsewhere.[6]

Serological study

This study was also done in two stages but on smaller numbers of women for laboratory reasons: in 1975, the last 31 women from the stage 1 isolation study were tested; in 1979, the first 92 women from the stage 2 isolation study were tested. Four women (not any of the 23 women common to both stages of the isolation study) were common to both stages of the

Figure 1. *Numbers of patients from each year group taking part in the isolation and serological studies. (Total number of women screened = 334)*

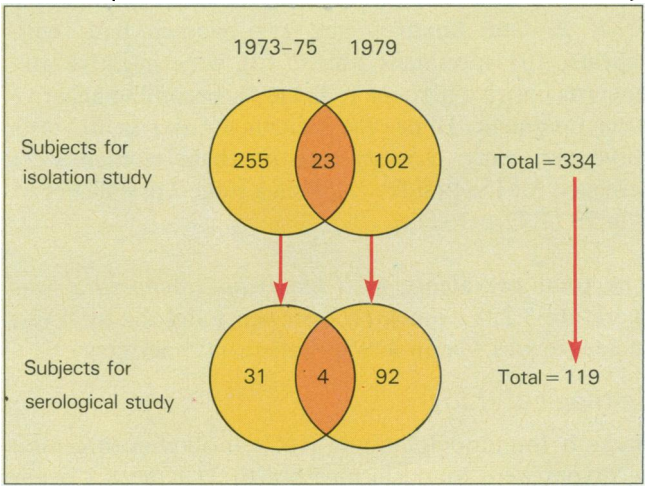

Table 1. Some features of the five women who were isolate positive.

	Past history			Details at time of diagnosis							Follow up		
Patient code	Cytological inflammation	Neoplasia	STD	Age (years)	Symptoms	Risk	Contraception	Recent chemotherapy	Cervix macro-/microscopic	Titres[1] and serotypes	Time lapse (years)	Risk	Macro-/microscopic
1	−	+	+	21	Discharge	Single permissive	Pill	Nil	e/neo	2 rising to 64 in a week. BDE	1	ISQ	n/inflammation
2	+	−	+	22	Intermenstrual bleeding	Husband's infidelity	Nil	Oxytetracycline	e/*Trichomonas vaginalis*	Not done	4	Nil, divorced and remarried	n/n
3	+	+	+	29	Discharge	Separated, permissive	IUCD	Nil	e/neo	8 CED SA2 L11L 111G1	5	ISQ	n/inflammation
4	−	−	−	36	Postcoital bleeding	Separated, permissive	Nil	Nil	e/n	8 ESA2G I L11	2	Nil, regular cohabitant	n/n
5	+	−	−	36	Nil	Husband's infidelity	IUCD	Nil	e/neo	8 8 32 32 32 32. C A B E D I1. 64 4 4 8 16 16. SA2 L111FG 1 L11	3	Divorced, occasionally permissive	e/inflammation

Abbreviations: STD, sexually transmitted disease; e, ectopy (erosion); neo, neoplasia; ISQ, as before; n, normal; IUCD, intrauterine contraceptive device.

serological study and therefore the total number of different women involved was 119 (Figure 1).

Five millilitres of venous blood was withdrawn and centrifuged at the surgery. Stage 1 sera were sent to a laboratory in the United States, while stage 2 sera was assayed in London at the Clinical Research Centre by a comparable method (see Discussion).

Results

Isolation study

Stage 1. Two hundred and fifty-five women had, with repeats, 289 specimens tested for chlamydial isolation; 58 specimens from 40 of the women had to be discounted because 39 specimens were contaminated and 19 were lost. Of the remaining 231 specimens from 215 women, 223 were negative and four were positive, becoming negative after treatment—a prevalence of four in 227 (1.76 per cent). The four isolations were from the initial screening of the 215 women, giving a prevalence of 1.86 per cent.

Stage 2. One hundred and two women had, with repeats, 103 specimens tested; 101 were negative and one was positive (patient 1, Table 1), becoming negative after treatment. Hence the incidence was 1 in 102 tests (0.98 per cent). Seventy-nine of these women were screened for the first time, giving a stage 2 prevalence of 1 in 79 (1.27 per cent).

The total prevalence of *Chlamydia trachomatis* was therefore 5:294 women (1.7 per cent) and the total test incidence was five in 329 specimens (1.5 per cent).

Serological study

Stage 1. Immunoglobulin G (IgG) antibodies to genital serotypes were found in nine out of 31 women (29 per cent), their serum titre^{-1} levels ranging from 2 to 64. Three of the women were isolate-positive, with serum titre^{-1} levels of 8, 8, and 64, respectively.

Table 2. 1975 and 1979 titre^{-1} antibody levels in the four women common to stages 1 and 2.

	1975	1979
Patient 1	0	0
Patient 2	2	2
Patient 3	0	4
Patient 4	0	8

Stage 2. IgI antibodies to genital serotypes were found in 50 out of 92 women (54 per cent), their serum titre^{-1} levels ranging from 2 to 64. There was a positive isolation from one of these women. Before treatment, her serum titre^{-1} levels rose from 2 to 64 in one week. Six other women had significant serum titre^{-1} levels: 1 out of 16 in three women, 1 out of 32 in two and 1 out of 64 in the sixth patient; all were isolate-negative.

Stages 1 and 2. The 1975 and 1979 titre^{-1} antibody levels in each of the four women common to both stages is shown in Table 2. As none of these women had a positive isolate, this serology suggests that patients 3 and 4 were exposed to chlamydial infection in the interim.

Table 1 includes the titre levels of four of the five women who were isolate-positive. The other women did not undergo chlamydial serology.

Comparison with cytology results. The titre levels of the 115 isolate-negative women were compared relative to their current and previous cytology results.

Sixty women (52 per cent) had serum titre^{-1} levels of zero, but for two no adequate previous records were available. For 29 of the remaining 58 women there was a previous history of cervical inflammation, neoplasia or STD, or a combination of these conditions. Therefore in 50 per cent of these women there was no evidence of previous chlamydial genital infection.

Thirty-three women (29 per cent) had serum titre^{-1} levels of 2 or 4, but for eight women no adequate previous records were available. For 20 of the remaining 25 women there was a previous history of cervical pathology or STD, or both. Therefore in 20 per cent of these women there was no evidence of previous chlamydial genital infection.

Twenty-two women (19 per cent) had serum titre^{-1} levels of more than 8, but for six women no adequate previous records were available. In all the remaining 16 women there was a previous history of cervical pathology or STD or both.

Discussion

This has been the largest isolation study of the few undertaken in general practice and the only one to indicate the rates for chlamydial genital infection in women. Copeman and Treharne had no positive cervical cultures in 200 women,[7] and the results of a two-year prospective study are awaited with interest.[8]

Chlamydial cervicitis, being a sexually transmitted disease is more frequent in 'high risk' groups of women,[6,9] and it has been shown that high inclusion counts in infected women are obtained significantly more often from women with cervical ectopy.[10] Table 1 illustrates both these facts. Furthermore, for the serum antibody level to be relatively increased in the presence of genital pathology is perhaps an indication of past chlamydial genital infection. In both stages of the present study the micro-immunofluorescent method of Wang[11,12] was used to assay IgG antibodies to the genital strains of the chlamydial serotypes. Matching the isolate and serology results reveals the inconsistency of single testing for chlamydial cervicitis, especially in general practice, where isolate positivity is likely to be low compared with STD clinics.

Two of the four isolate-positive women who had genital serotypes had a titre^{-1} of 8, which is not acceptable as positive on a single test, and one of the other two women (patient 1, Table 1) would have been recorded with a titre^{-1} level of only 2 had she not been retested after a week. By contrast, six women who were isolate-negative had titre^{-1} levels $\geq$ 16, which were regarded as indicative of a past infection (B. Thomas, pers. communication).

Of the 119 women concurrently tested for isolates and antibodies, four were isolate-positive and six others were seropositive. Overall the serology study suggests an exposure to infection of almost three times that obtained by single culture testing.

Present isolation rates are 40 per cent from STD clinics, and 1–2 per cent from family planning clinics.[13] If allowance is made for wastage of *in vitro* specimens, the total practice prevalence could be in the order of 8.5 per cent and not 6.9 per cent as suggested by this study.

Options for identifying chlamydial cervicitis

Cervical culture is necessary for a precise diagnosis but, for most general practitioners, obtaining satisfactory facilities for this difficult procedure is unrealistic. What remains therefore is to maintain a high index of suspicion in women at risk, including contacts of asymptomatic men with non-gonococcal urethritis (NGU),[14] and also to be constantly on guard for its complications.

Like idiopathic infection, *Chlamydia* (with secondary organisms) can cause acute salpingitis leading to ectopic gestation and infertility[15] and also acute pelvic inflammatory disease.[16] Such infections can also produce a persistent reservoir of cervicitis with danger from latency[17] and pelvic infection with only ephemeral symptoms.[6] Cervicitis is reported via cervical cytology as severe non-specific inflammation (NSI). When a women has this, she should be treated empirically. During pregnancy, the infection can lead to prematurity, stillbirth, neonatal death and postpartum pelvic inflammation.[18] *Chlamydia trachomatis* can be isolated from the endocervix in 15 per cent of mothers whose babies have proven chlamydial conjunctivitis, a trachoma-like 'inclusion blenorrhoea',[16] and it is the primary invader in 30–50 per cent of infants with sticky eyes.[13] Often with such an antecedent history, a pertussoid, eosinophilic, neonatal pneumonia from *C. trachomatis* has been documented, and neonatal upper respiratory tract infection.[2] In infancy, otitis[2,19] and vaginitis[19] have also been postulated.

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This report is largely contained in an MD thesis.[6]

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International migration

In 1982 the numbers of both immigrants and emigrants increased and reached the highest level for some years, with immigrants increasing more than emigrants. The number of immigrants rose sharply from 153,000 in 1981 to 225,000 in 1982, an increase of 47 per cent and the highest annual total since 1970. The number of emigrants rose by 11 per cent from 1981, to reach 259,000, the highest total since 1974. As a consequence, the net outflow fell from 79,000 to 34,000 in 1982. Changes in these flows related mainly to UK citizens, rather than Commonwealth citizens or aliens.

Source: Office of Population Censuses & Surveys. *OPCS Monitor* 1983; MN 83/3: 1.