Oral contraceptive use and prevalence of infection with Chlamydia trachomatis in women

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SUMMARY One thousand and eighty non-pregnant women aged 16-34 years, presenting for the first time at a clinic for sexually transmitted diseases (STD), were examined and screened for infection with Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis, and Candida species. The respective prevalence rates were 21·1%, 20·7%, 13·4%, and 27·8%. Isolation rates for C trachomatis, either occurring alone or in association with other genital infections, were significantly greater in women using oral contraceptive agents. This was not because oral contraceptive users were more promiscuous.

The findings strengthen the case for providing a routine chlamydial culture service for women attending STD clinics. They also indicate that the likelihood of chlamydial infection in women taking oral contraceptives is increased.

Introduction

Infection with Chlamydia trachomatis is now recognised as a major cause of genital tract infection. In contrast to infections in men, who usually present with nongonococcal urethritis, those in women often have no specific symptoms or signs. Unless routine cultures for this organism are undertaken, such infection is easily overlooked. Several recent studies have suggested that chlamydial infection is promoted by the use of oral contraceptive agents,2-4 although this is disputed by others.5-9 If such an effect does exist, it is not clear whether this is secondary to differences in the sexual behaviour of oral contraceptive users and non-users leading to increased exposure to C trachomatis or due to a specific hormonal effect causing increased susceptibility to the organism.

Since 1975 women with new complaints attending the department of genitourinary medicine at Leeds General Infirmary have had specimens taken routinely for the culture of C trachomatis at their first attendance. The aims of the present study were: (1) to compare the isolation rate for C trachomatis with that for other major genital pathogens and to compare the rate in 1979 with that found in a previous study10; and (2) to examine more closely the possible association between chlamydial infection and the use of oral contraceptive agents.

Patients and methods

The study population consisted of 1080 consecutive non-pregnant women aged between 16 and 34 years presenting for the first time to the department of genitourinary medicine, Leeds General Infirmary, Leeds, between 1 January and 30 September 1979.

SPECIMEN COLLECTION

After a full history had been taken, patients were examined in the lithotomy position. Specimens for immediate microscopy and the appropriate culture were taken from the urethra and cervix for the identification of N gonorrhoeae and from the posterior fornical pool for T vaginalis and Candida species. The methods of specimen collection, cultural techniques, and diagnostic criteria have been described.11

Specimens for culture for C trachomatis were collected by rotating a cottonwool swab in the cervical canal and on any exposed ectopic columnar epithelium. The swabs were then placed in transport medium (McCoy cell growth medium with 0·5% glucose and 10% sorbitol) and stored at 4°C before being transferred to the virology laboratory. The method used for isolating C trachomatis in untreated McCoy cells has been described.12

DATA ANALYSIS

For analysis of the results patients were divided into two groups, those who used oral contraceptives and those who used other methods or no contraception at all. Demographic and clinical data on the two groups

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Accepted for publication 17 November 1980
infected with *C trachomatis* were compared. In this study the presence of cervicitis was defined as the presence of mucopurulent or purulent cervical secretion showing >5 white cells per high-power field (× 100 magnification) associated with one or more of the following: hyperaemia of the ectocervix, hypertrophic ectopy of the columnar epithelium, and contact bleeding from the endocervical canal. Statistical analysis was made by the $\chi^2$ test with Yates's correction.

**Results**

**Isolation Rates**
The isolation rates for *C trachomatis, N gonorrhoeae, T vaginalis,* and *Candida* species in the 1080 women studied are given in table I. *C trachomatis* was found in 160 (26·6%) of all 601 oral contraceptive users compared with only 72 (15%) of all 479 non-users ($P<0.001$). *T vaginalis* was found significantly less frequently in oral contraceptive users (11%) than in non-users (16·5%) ($P<0.02$). There were no significant differences between oral contraceptive users and non-users in the incidences of *N gonorrhoeae, Candida* species, or of women uninfected with any of these four pathogens.

**Table I** Isolation rates in relation to use of oral contraceptives

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>All women</th>
<th>Users</th>
<th>Non-users</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
</tr>
<tr>
<td><em>Chlamydia trachomatis</em></td>
<td>223</td>
<td>21·5</td>
<td>160</td>
</tr>
<tr>
<td><em>Neisseria gonorrhoeae</em></td>
<td>224</td>
<td>20·7</td>
<td>125</td>
</tr>
<tr>
<td><em>Trichomonas vaginalis</em></td>
<td>145</td>
<td>13·4</td>
<td>66</td>
</tr>
<tr>
<td><em>Candida</em> species</td>
<td>300</td>
<td>27·8</td>
<td>180</td>
</tr>
<tr>
<td>No pathogen isolated</td>
<td>360</td>
<td>33·3</td>
<td>187</td>
</tr>
<tr>
<td>Total No of patients</td>
<td>1080</td>
<td></td>
<td>601</td>
</tr>
</tbody>
</table>

* $\chi^2 = 20·6; P<0.001$

† $\chi^2 = 6·5; P<0.02$

**Single Infections**
Use of oral contraceptives in women with single infections is shown in table II. The number of oral contraceptive users in men infected with *C trachomatis* alone was significantly increased compared with those infected with each of the other three pathogens alone and with those uninfected with any of these organisms ($P<0·002$). The incidence of infection with *C trachomatis* alone was 10·8% of all oral contraceptive users in the study population compared with 5·2% of all non-users ($\chi^2 = 10·2; P<0·002$).

**Table II** Use of oral contraceptive agents in women with single infections

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Total No of women</th>
<th>Users</th>
<th>Statistical difference†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
</tr>
<tr>
<td><em>C trachomatis</em> alone</td>
<td>90</td>
<td>65</td>
<td>72·2</td>
</tr>
<tr>
<td><em>T vaginalis</em> alone</td>
<td>43</td>
<td>16</td>
<td>37·2</td>
</tr>
<tr>
<td><em>N gonorrhoeae</em> alone</td>
<td>68</td>
<td>36</td>
<td>52·9</td>
</tr>
<tr>
<td><em>Candida</em> species alone</td>
<td>113</td>
<td>64</td>
<td>56·6</td>
</tr>
<tr>
<td>No pathogen isolated</td>
<td>360</td>
<td>187</td>
<td>51·9</td>
</tr>
</tbody>
</table>

*Of oral contraceptive agents
†In use of oral contraceptives compared with isolation of *C trachomatis* alone

**Concomitant Infections**
The incidences of concomitant infection with *C trachomatis* in all women infected with *N gonorrhoeae, T vaginalis,* and *Candida* species were 37·5%, 29·0%, and 16·0% respectively (table III). In each of these groups, the incidence of concomitant infection with *C trachomatis* was significantly increased in oral contraceptive users compared with non-users.

Thus, whether occurring as the sole pathogen or in association with another genital pathogen, infection with *C trachomatis* was significantly more common in oral contraceptive users than in non-users.

**Table III** Isolation rates of *Chlamydia trachomatis* in women with mixed infections

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Total No of women</th>
<th>Users</th>
<th>Non-users</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
</tr>
<tr>
<td><em>N gonorrhoeae</em></td>
<td>224</td>
<td>84</td>
<td>37·5</td>
</tr>
<tr>
<td><em>T vaginalis</em></td>
<td>145</td>
<td>42</td>
<td>29·0</td>
</tr>
<tr>
<td><em>Candida</em> species</td>
<td>300</td>
<td>48</td>
<td>16·0</td>
</tr>
</tbody>
</table>

*Of oral contraceptive agent
†Based on numbers of users and non-users of oral contraceptives with each condition given in table I
Oral contraceptive use and prevalence of infection with Chlamydia trachomatis in women

TABLE IV Demographic data on women with chlamydial infection

<table>
<thead>
<tr>
<th>Data</th>
<th>All</th>
<th>Users*</th>
<th>Non-users*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients</td>
<td>232</td>
<td>160</td>
<td>72</td>
</tr>
<tr>
<td>Age less than 25 years</td>
<td>72-8</td>
<td>74-4</td>
<td>69-9</td>
</tr>
<tr>
<td>Marital state</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Single</td>
<td>69-4</td>
<td>71-9</td>
<td>63-9</td>
</tr>
<tr>
<td>% Married</td>
<td>10-8</td>
<td>7-5†</td>
<td>18-1</td>
</tr>
<tr>
<td>% Divorced/separated</td>
<td>19-8</td>
<td>20-6</td>
<td>18-1</td>
</tr>
<tr>
<td>Ethnic group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Caucasian</td>
<td>90-5</td>
<td>91-3</td>
<td>88-9</td>
</tr>
<tr>
<td>Job status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Employed</td>
<td>54-3</td>
<td>60-6%</td>
<td>40-3</td>
</tr>
<tr>
<td>% Student</td>
<td>15-1</td>
<td>16-3</td>
<td>12-5</td>
</tr>
<tr>
<td>Reason for attendance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Known contacts of NSU</td>
<td>36-6</td>
<td>36-3</td>
<td>37-5</td>
</tr>
<tr>
<td>% Known contacts of gonorrhoea</td>
<td>34-5</td>
<td>34-3</td>
<td>34-7</td>
</tr>
<tr>
<td>% Other</td>
<td>28-9</td>
<td>29-3</td>
<td>27-8</td>
</tr>
<tr>
<td>No of sexual partners in previous 3 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% 0</td>
<td>0-4</td>
<td>1-4</td>
<td></td>
</tr>
<tr>
<td>% 1</td>
<td>68-5</td>
<td>70-0</td>
<td>65-3</td>
</tr>
<tr>
<td>% 2</td>
<td>23-3</td>
<td>25-0</td>
<td>19-4</td>
</tr>
<tr>
<td>% 3 or more</td>
<td>7-8</td>
<td>5-0‡</td>
<td>13-9</td>
</tr>
<tr>
<td>No of pregnancies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% 0</td>
<td>59-8</td>
<td>66-3</td>
<td>45-8</td>
</tr>
<tr>
<td>% 1</td>
<td>20-7</td>
<td>20-0</td>
<td>22-2</td>
</tr>
<tr>
<td>% 2 or more</td>
<td>19-4</td>
<td>13-8†</td>
<td>31-9</td>
</tr>
</tbody>
</table>

*Of oral contraceptive agents

age, ethnic group, or reason for attendance. Non-users infected with C trachomatis differed from their counterparts using oral contraceptives; more were likely to be married (p<0-05), to be unemployed (p<0-01), to admit to three or more sexual partners in the preceding three months (p<0-05), and to have had multiple pregnancies (p<0-01). No significant differences were shown in the proportions in each group admitting to multiple sexual partners in the three months before attendance at the clinic between oral contraceptive users and non-users in the groups of women with gonorrhoea alone, trichomoniasis alone, candidosis alone, or with no infection.

Concomitant infections
In women with chlamydial and concomitant infections there were no significant differences between oral contraceptive users and non-users in the incidence of gonorrhoea, trichomoniasis, candidosis, or infection with other STDs (table V).

Clinical features
The clinical details of women infected with C trachomatis alone are shown in table VI. Of the 90 women 60 (66·7%) were asymptomatic; there were no differences in the presence and type of symptoms between oral contraceptive users and non-users. However, oral contraceptive users infected with C trachomatis alone had cervicitis significantly more often than non-users (p<0-01).

Table V Concomitant infections in women infected with C trachomatis

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>All</th>
<th>Users*</th>
<th>Non-users*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients</td>
<td>232</td>
<td>160</td>
<td>72</td>
</tr>
<tr>
<td>% With no other infection</td>
<td>38-8</td>
<td>40-6</td>
<td>34-7</td>
</tr>
<tr>
<td>% With N gonorrhoeae</td>
<td>36-2</td>
<td>36-9</td>
<td>34-7</td>
</tr>
<tr>
<td>% With T vaginalis</td>
<td>18-1</td>
<td>17-5</td>
<td>19-4</td>
</tr>
<tr>
<td>% With Candida species</td>
<td>20-7</td>
<td>23-8</td>
<td>13-9</td>
</tr>
<tr>
<td>% With other STD</td>
<td>10-3</td>
<td>9-4</td>
<td>12-5</td>
</tr>
</tbody>
</table>

*Of oral contraceptive agents

Table VI Clinical features in women infected with C trachomatis alone

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Total No</th>
<th>Users*</th>
<th>Non-users*</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>60</td>
<td>67-6</td>
<td>64-0</td>
</tr>
<tr>
<td>Excessive vaginal discharge</td>
<td>27</td>
<td>20-2</td>
<td>32-0</td>
</tr>
<tr>
<td>Frequency/dysuria</td>
<td>5</td>
<td>6-2</td>
<td>4-0</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>4</td>
<td>4-6</td>
<td>4-0</td>
</tr>
</tbody>
</table>

*Of oral contraceptive agents

Discussion
The isolation of C trachomatis from 21% of women aged between 16 and 34 years attending the Leeds clinic is comparable with the isolation rates found in a smaller previous study in the same department and in recent studies elsewhere in England. It is noteworthy that only 75 (37%) of all 232 infections with C trachomatis occurred in women who were known contacts of men with nongonococcal urethritis and who would therefore routinely have received antichlamydial therapy. This finding supports the view of those who consider that a service for culture of C trachomatis is essential and as important as that for culture of N gonorrhoeae in women attending STD clinics. We have found that infected women are usually asymptomatic and that there are no reliable clinical indicators of infection. Seventy-three per cent of women infected with C trachomatis alone had some degree of cervicitis,
although this was usually minor. The most frequent
clinical abnormality was cervical mucopus associated
with contact bleeding from the endocervical canal.
We also noted that a small percentage of women in
whom no pathogen other than C trachomatis could
be isolated also had a vulvovaginitis with a frothy
mucopurulent vaginal discharge with or without
cervical abnormalities.

The finding of a reduced incidence of tricho-
omoniasis in oral contraceptive users in this study, in
which the diagnosis was made by both microscopy
and culture, confirms an earlier report, in which the
diagnosis was made by microscopy alone. The
present study suggests a clear association between C
trachomatis infection, whether occurring alone or
with concomitant gonorrhoea, trichomoniasis, or
candidosis, and the use of oral contraceptive agents.
It confirmns previous studies of both selected and
non-selected groups of women attending STD clinics
and a gynaecological clinic, which showed a similar
increased incidence of chlamydial infection in oral
contraceptive users. We found no evidence that this
effect was related to increased promiscuity in such
women. Indeed non-users of oral contraceptives with
chlamydial infection had multiple sexual partners
significantly more often. It is still not clear, however,
whether the increased isolation rate is due to a greater
infectivity in oral contraceptive users—perhaps
because of increased exposed susceptible columnar
epithelium—or to easier detection of C trachomatis
by present cultural methods, possibly as a result of a
stimulative effect of steroids on the growth of C
trachomatis within the cervical epithelium.

This study clearly emphasises the importance of
a routine chlamydial culture service in women
attending STD clinics, particularly as the number of
young women using oral contraceptive agents is
increasing and may well serve to increase the
potential reservoir for chlamydial infection within
the community.

We are grateful for the technical help and expertise
of Dr M F Hambling and Mr J J O'Neill in the iso-
alation of C trachomatis and to Mrs C Treweek and Mrs
E Welch for secretarial assistance.

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Oral contraceptive use and prevalence of infection with Chlamydia trachomatis in women.
G R Kinghorn and M A Waugh

Br J Vener Dis 1981 57: 187-190
doi: 10.1136/sti.57.3.187

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