

General practice update: chlamydia infection in women

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SUMMARY. *The prevalence of cervical Chlamydia trachomatis infection in general practice populations ranges between 2% and 12%. Untreated infection can cause pelvic inflammatory disease, tubal infertility and ectopic pregnancy. These risks are increased by cervical invasive procedures, especially termination of pregnancy. However, most women with chlamydia infection have no symptoms. General practitioners and practice nurses carrying out pelvic examinations should have facilities for taking endocervical specimens for chlamydia. Routine chlamydia screening, should be considered if the local prevalence of infection is over 6%. Otherwise chlamydia testing should be offered to women requesting termination of pregnancy and to those who have risk factors: aged less than 25 years, absence of barrier contraception, recent change of sexual partner, vaginal discharge, friable cervix or sterile pyuria. Women found to have chlamydia infection need appropriate antibiotics, advice about contact tracing and referral to a genitourinary medicine clinic. Good communication between general practitioners and genitourinary physicians is essential. Both general practitioners and practice nurses have an important role to play in reducing the prevalence of cervical chlamydia infection and its potentially devastating consequences.*

Keywords: *chlamydia infections; women's health; morbidity; screening; diagnosis.*

Introduction

CERVICAL *Chlamydia trachomatis* infection in women is common,¹ often asymptomatic² and may have serious consequences.³ In 1994 the Communicable Disease Surveillance Centre received 13 787 laboratory reports of genital chlamydia infection in women,⁴ making it the most prevalent sexually transmitted bacterial infection in England and Wales.

In men *C trachomatis* causes urethritis and epididymitis, and in the newborn it causes conjunctivitis and pneumonitis.⁵ However, the most serious consequences occur in women in whom it may result in pelvic inflammatory disease, tubal infertility, ectopic pregnancy and chronic pelvic pain.⁶ It has been estimated that in the United Kingdom the cost of treating genital chlamydia infections and their sequelae is at least £50 million per year.⁵

The aim of this paper is to review published research on chlamydia infection in women and to make practical recommendations for its diagnosis, management and prevention in contemporary general practice.

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© British Journal of General Practice, 1995, 45, 615-620.

Natural history of chlamydia infection in women

It is generally accepted that cervical chlamydia infection can cause pelvic inflammatory disease, tubal infertility and ectopic pregnancy. However, the natural history of the disease is still uncertain,⁷ mainly because as many as 70% of women with chlamydia infection have no symptoms.³ The remainder may have mild symptoms of vaginal discharge, intermenstrual bleeding, lower abdominal pain or dysuria.^{7,8} Untreated, chlamydia may persist at the cervix for many months⁹ or years or may disappear spontaneously. However, failure to detect chlamydia in cervical swabs does not exclude tubal chlamydia disease.³

Chlamydia can be detected in samples from the fallopian tubes of up to half of the women with pelvic inflammatory disease in developed countries.¹⁰ More than 10% of women who have one episode of pelvic inflammatory disease, and over 50% of those who have three episodes, develop tubal infertility.^{11,12} The risk of ectopic pregnancy is increased 10-fold after an episode of pelvic inflammatory disease.¹¹

However, much pelvic inflammatory disease due to chlamydia infection is 'silent' or subclinical.¹³ Plasma cell endometritis has been found in 40% of women thought to have uncomplicated chlamydial cervicitis.¹⁴ Laparoscopy is usually regarded as the best method of assessing tubal infection, but the serosa can appear normal in women with smouldering chlamydial tubal disease.¹⁵ Indeed, the first sign that a woman has had previous chlamydia infection may be when she presents with infertility.³

Serological and animal studies provide further evidence that chlamydia can cause infertility and ectopic pregnancy. Three out of four women with tubal infertility or ectopic pregnancy have serum antibodies to chlamydia compared with one out of four fertile women.^{16,17} In monkeys serial inoculation of chlamydia into the ovarian tubes causes distal tubal obstruction.¹⁸ The risk of untreated cervical chlamydia causing infertility is estimated to be between 2% and 4%,^{19,20} although the exact risk is unknown. More than half of infertile women with an identifiable aetiology have tubal damage; the majority of these have evidence of chlamydia infection.¹⁷

In clinical studies, treatment produces microbiological cure, but it is unclear whether this prevents morbidity.²¹ In one small

KEY POINTS

- General practices should stock chlamydia swabs and appropriate slides or transport medium
- Chlamydia specimens should contain endocervical cells, not cervical discharge
- Screening should be undertaken:
 - Routinely if prevalence over 6%
 - Of at-risk groups: aged under 25 years, recent change of sexual partner, absence of barrier contraception, mucopurulent vaginal discharge, friable cervix, sterile pyuria
 - Before cervical invasive procedures, especially termination of pregnancy
- Management
 - Appropriate antibiotics
 - Treatment of sexual partners
 - Follow up by genitourinary clinic
- Prevention
 - When appropriate offer advice on safer sex

general practice study of women treated for chlamydia infection, 19% presented with pelvic inflammatory disease, infertility or ectopic pregnancy during 22 months' follow up.²²

In summary, chlamydia infection in women causes few symptoms but may have serious consequences. Before recommendations about screening can be made it is essential to define the prevalence of cervical chlamydia infection in different populations.⁵

Prevalence of cervical chlamydia infection in general practice

A systematic review of the literature was conducted to determine the prevalence of cervical chlamydia infection in general practice populations. MedLine was searched using the following terms: chlamydia infections, cervicitis, prevalence, screening and family practice. Citations in articles were reviewed and references provided by colleagues were examined. Authors were written to where there were missing data²³ or unusual results.²⁴ To ensure that the review contained clinically significant studies applicable to primary care in the UK, only reports from UK general practice in which over 100 women were screened were included.

Two studies using culture were not included because the prevalence of chlamydia infection was unexpectedly low.^{24,25} In one,²⁴ a study from the same practice two years later found a much greater prevalence of infection using a direct fluorescent antibody test.²⁶ In the other,²⁵ serological results from the same patients indicated a higher prevalence of infection, as did a contemporary study in the same city.¹ Authors of both studies attributed the low detection rate to the problems of using culture in general practice.^{24,25}

The prevalence of cervical chlamydia infection varies between 2% and 12% in UK general practices and is higher in inner city populations (Table 1). Studies in primary care from Belgium,³³ Denmark,³⁴ Norway,^{19,35} Sweden³⁶ and the United States of America³⁷⁻⁴⁰ show similar prevalences. The prevalence of chlamydia infection varies between different populations, particularly with respect to age and socioeconomic group. It is usually higher in women with symptoms such as vaginal discharge^{1,23,28} or in those requesting termination of pregnancy²⁷ than in asymptomatic women attending for cervical smears.^{31,32}

Selective versus routine screening

General practitioners need to have estimates of the prevalence of cervical chlamydia infection in their own local population in order to decide whether selective or routine screening is appropriate.^{29,41} This could be done by using 'spotter practices'. However, this will only give the prevalence of infection in women who have pelvic examinations in general practice and will not be truly representative of the population. If the prevalence is at least 6%⁴² or 7%,⁴³ as in some inner city practices,^{1,29,30} it may be cost effective to screen all sexually active young women who attend for a speculum examination, but at least two years should elapse between repeated tests.¹⁹ It has been suggested that even at a prevalence of 2% it may still be cost effective to screen routinely.⁴⁴ However, such calculations are controversial as they depend on many factors including the specificity and sensitivity of the test used and estimates of the risk of untreated chlamydia causing complications, as well as the costs of treatment at every stage. The potential costs of untreated chlamydia infection which may be considered in cost-benefit calculations are shown in Figure 1.

The prevalence of cervical chlamydia infection in some primary care populations may be low.^{31,39,40} Many studies have attempted to define groups of women at higher risk in whom screening is more cost effective. Generally, infection is more common in younger women (those aged less than 25 years), women with a recent change of sexual partner, women who do not use barrier contraceptive methods, and women with mucopurulent vaginal or cervical discharge, a friable cervix which bleeds on contact or sterile pyuria.^{1,8,29,34,39-41,45-47} Selective screening

Potential costs of untreated chlamydia

- Pelvic inflammatory disease
- Ectopic pregnancy
- Tubal infertility
- Chronic pelvic pain
- Complications in sexual partners
- Transmission to neonates

Figure 1. Potential costs of untreated cervical chlamydia infection.

Table 1. Prevalence of cervical chlamydia infection in UK general practices.

First author, year of publication	Location	No. of practices	Study populations	Age range (years)	Test used	No. infected/ no. studied	Prevalence (%)
Southgate, 1983 ¹	East London	3	Women having speculum examination	15-45	Culture	19/248	8
Longhurst, 1987 ²³	Central London	1	Women having speculum examination	Pre-menopausal	DFA	18/169	11
Southgate, 1989 ²⁷	East London	4	Women requesting termination of pregnancy	16-44	DFA	12/103	12
Owen, 1991 ²⁸	Cardiff	1	Women with lower genital tract symptoms. Mainly social classes 3 and 4	15-65	DFA	25/386	6
Smith, 1991 ²⁹	Glasgow	1	Women attending for cervical smear. Mainly social class 3	19-58	Culture	24/197	12
Oakeshott, 1992 ³⁰	Southeast London	2	Women having speculum examination. Mainly social classes 4 and 5	17-45	DFA	36/409	9
Thomson, 1994 ³¹	Fife	10	Women attending for cervical smear	15-40	DFA	5/287	2
Oakeshott, 1995 ³²	South London	28	Women attending for cervical smear	17-35	EIA	39/1255	3

DFA = direct fluorescent antibody test. EIA = enzyme immunoassay.

based on such predictors may be an effective and efficient strategy in low prevalence settings.⁴⁶ However, other workers point out that as many as 30% of women with infection may be missed.⁴⁷ History and examination are unreliable in identifying women at risk.^{27,42,48} In one study general practitioners failed to predict the presence of chlamydia in 72% of infected women, despite taking a full history and performing a pelvic examination.³⁹

Cervical swabs for chlamydia should always be included in the investigation of vaginal discharge or pelvic inflammatory disease.^{1,10} Screening should also be offered to women undergoing cervical invasive procedures since they are at increased risk of developing upper genital tract infection.⁴⁹ Women undergoing termination of pregnancy have a high prevalence of chlamydia infection^{27,50} and a high risk of developing postoperative pelvic inflammatory disease. In one study 60% of women with untreated cervical chlamydia infection developed symptoms of pelvic inflammatory disease following a termination of pregnancy.⁵¹ For the few who develop tubal infertility this may be their only pregnancy. Chlamydia screening is also recommended before insertion of an intrauterine device³³ or dilatation and curettage.²⁹

The effectiveness of routine chlamydia testing has been well demonstrated in Halmsted, Sweden.⁵² A programme of widespread screening and assiduous contact tracing and treatment reduced the prevalence of chlamydia infection in women aged 20–24 years from 90 per 1000 women tested in 1984 to 47 per 1000 in 1988. During these five years a similar 40%–50% fall in prevalence was shown in all age groups. Comparable results have been obtained in the USA.⁴⁷ Although attitudes to sexual health, particularly in Sweden, may have made the problem easier to deal with,⁵ general practitioners in the UK have much to learn from their example.

Chlamydia tests in general practice

Since chlamydia can only be diagnosed by microbiological tests, all general practitioners and practice nurses performing pelvic examinations should have equipment to take specimens for chlamydia.¹ However, it is likely that at present many practices do not have the appropriate swabs or slides.⁴⁹ For women undergoing a speculum examination, taking an endocervical specimen for chlamydia is almost as simple and quick as taking a high vaginal swab (though a different transport medium or special slides are required). The cost is similar to that of a high vaginal swab: between £5 and £10 for the kit and laboratory costs.^{30,42} The clinical benefits may be much greater. General practitioners should liaise with their local laboratories to ensure they are offered an efficient service for the detection of chlamydia infection.

Taking specimens

Chlamydia are small bacteria that need to be inside cells to multiply,⁵ preferring the columnar epithelium of the cervix. It is essential, therefore to sample columnar cells from the endocervix and an ectropion if present. Pus and cervical discharge should be removed before sampling. Specimens for chlamydia should therefore be taken at the end of a pelvic examination after cleaning the cervix (in practice if a cervical smear or other swabs have been taken first, cleaning may not be necessary). A cotton tipped swab should be rotated gently in the endocervix for at least 10 seconds to obtain as much material as possible. It is essential to obtain a good quality specimen in order to minimize false negative results.⁴⁸ Cervical swabs give the greatest diagnostic yield, although in a few cases chlamydia may only be detected in urethral or urine samples. In general, fewer organisms are present in urethral or urine samples and cervical swabs are preferable.⁵³

Tests used

Culture. Culture is regarded as the gold standard. *Chlamydia trachomatis* is an intracellular bacterium and is isolated from cell culture. However, this test is difficult to organize in general practice as it involves storing specimens in a liquid nitrogen container at -180°C .¹ Great care is required to ensure viability of organisms in transit. It has been used successfully in some research studies in general practice,^{1,29} but less so in others.^{24,25,54} Currently most chlamydia tests in general practice use antigen detection tests (direct fluorescent antibody tests and enzyme immunoassay) rather than culture, as storage and transport of specimens is less complicated.

Direct fluorescent antibody test. This test has been used successfully in many studies in UK general practice.^{23,27,30} The swab is smeared onto two wells on a teflon-coated slide, air dried, fixed with acetone or methanol and put into a slide box. It can then be stored at 4°C for up to seven days if necessary²³ before being transported to a hospital laboratory. At the laboratory the fixed material is stained with a fluorescein-labelled monoclonal antibody and examined by fluorescent microscopy. An advantage of this method is that it allows some evaluation of the quality of the specimen.³⁰ Compared with culture, the specificity of the direct fluorescent antibody test is greater than 98% and its sensitivity is greater than 90%.²

Enzyme immunoassay. Cotton-tipped swabs are placed in transport medium and should be sent to the laboratory within two days. This test measures antigen-antibody reactions through an enzyme-linked immunoabsorbent assay and requires a spectrophotometer. As this test has a specificity of only between 92% and 97%,² a positive result is usually confirmed using the direct fluorescent antibody test.⁵⁵ This may increase the specificity to 100%.⁵⁶ Sensitivity (between 67% and 91%^{2,56}) may be lower than using the direct fluorescent antibody test, but some laboratories prefer it as it is less labour intensive.

Near patient tests. Rapid enzyme immunoassay tests, also known as sideroom or desktop tests, are being promoted in general practice. They take less than 30 minutes and can be done in the surgery. Unfortunately, their use is limited by their low sensitivity,^{57,58} time consuming nature and difficulties with quality control. In a recent study of near patient testing in 12 UK practices⁵⁹ the chlamydia desktop assay was one of the three tests least used, and no practice wished to retain the kits when they were offered free at the end of the study.

DNA detection tests. DNA testing of endocervical samples or first-void urine samples using polymerase or ligase chain reaction to enhance sensitivity can be very reliable.⁵⁷ However, these tests require special laboratory facilities, are more expensive than other tests and are not yet suitable for routine use.¹² The possibility of screening a first-void urine sample for chlamydia by a sensitive, non-invasive test is appealing, but further research is required to confirm a report of successful screening of urine specimens with the ligase chain reaction.⁶⁰

At present the direct fluorescent antibody test and the enzyme immunoassay are probably the most suitable tests for general practice. However, no test is completely reliable, and the possibility of a false negative or false positive result should always be borne in mind.⁶¹ Whenever there is doubt about the result the patient should be referred to the local genitourinary clinic where she can be counselled and retested using a sensitive method.⁶¹

Management of women with cervical chlamydia infection

It is generally recommended that women diagnosed with cervical chlamydia infection in general practice be treated and referred to a genitourinary medicine clinic for follow up.^{62,63} This is because these clinics offer counselling and contact tracing with the assistance of health advisers. In addition they can review compliance with treatment, perform a test of cure if required, and screen for other sexually transmitted infections.

The management of women with chlamydia infection in a general practice that had a specific research interest in chlamydia was comparable with management in genitourinary clinics.²⁸ However, it is likely that management would be less complete elsewhere. One survey of general practitioners whose patients had chlamydia detected in urine samples found that 59% of patients were referred to genitourinary clinics for treatment and contact tracing.⁸ An earlier study found that only 25% of general practitioners would prescribe antibiotic therapy effective against chlamydia for a woman with suspected pelvic inflammatory disease; only 39% considered referring the woman's male partner for clinical investigation.⁶⁴ Some women with cervical chlamydia infection may initially be reluctant to attend a genitourinary clinic. However, if the implications of the diagnosis are explained, and if there is good communication between general practitioners and local genitourinary physicians,³¹ many women can be persuaded to attend.

Draft recommendations for the management of women diagnosed as having cervical chlamydia infection in general practice, drawn up in consultation with general practitioners and genitourinary medicine physicians, are shown in Figure 2. The antibiotic treatment accords with Centers for Disease Control guidelines.⁶⁵ Doxycycline is more effective than erythromycin, treatment failure 3% and 37%, respectively.⁶⁶ A single dose of azithromycin 1 g is also effective for uncomplicated cervical chlamydia infection and ensures compliance, but is expensive.¹² If pelvic inflammatory disease is suspected a minimum of two weeks' antichlamydial treatment should be included in the antibiotic regimen. The patient should be advised not to have sex with her partner until they have both completed their courses of treatment.

A test of cure is not routinely recommended^{12,65} but may be done if there is a risk that the patient or her partner has not complied with treatment, reinfection might have occurred, or a less effective antibiotic was used. It should be done between two and four weeks after completion of treatment.¹² It also provides an opportunity for further patient education.

Prevention

Strategies to reduce the prevalence of cervical chlamydia infection in general practice populations include encouraging safer sex, increasing screening and improving treatment and contact

tracing among women found to be infected. Increasing rates of condom use in women who are not in long-term relationships is a more effective approach than attempting to limit the number of sexual partners.^{67,68} However, since barrier methods are unreliable in preventing pregnancy, it is essential that effective contraception such as the oral contraceptive pill should also be advocated — the 'double dutch' method.⁶⁹ One USA study found that following an education programme the proportion of women who reported using condoms in the previous month had increased from 16% to 31% over five years.⁴⁷ However, the authors estimated that this accounted for only a small proportion of the concurrent reduction in the prevalence of chlamydia infection which was mainly a result of improved screening and management.⁴⁷

Unfortunately, UK general practitioners are unable to prescribe condoms.⁷⁰ A study from Newcastle found that few general practitioners gave opportunistic sexual health education to women attending for cervical smears.⁷¹ In some areas family health services authorities provide free condoms to practices with an interest in sexual health and to those running clinics for teenagers.⁷² Although these have mostly been well received by both general practitioners and patients, it is not clear whether such strategies actually increase condom use in patients most at risk. It seems sensible to consider offering advice about how to avoid sexually transmitted infections (backed up by leaflets and condoms if possible) to all sexually active young women, especially when they attend for pelvic examinations.

Conclusion

One aim of the UK government white paper, *The health of the nation*, is to reduce the incidence of sexually transmitted diseases and their consequences.^{73,74} Strategies to control cervical chlamydia infection have so far been hampered by the lack of symptoms, haphazard screening programmes, insensitive tests and inadequate contact tracing.^{5,7} However, a programme of widespread screening and effective treatment and contact tracing in Sweden has been shown to halve the prevalence of cervical chlamydia infection in all age groups.⁵² Since many pelvic examinations for cervical smears and family planning take place in general practice surgeries, general practitioners and practice nurses have a vital role to play in order to achieve similar successes in the UK.

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Action points in case of positive chlamydia test result

- Recall and counsel patient
- Treat with doxycycline 100 mg twice daily for seven days; if patient pregnant or lactating, treat with erythromycin 500 mg four times a day for seven days or 250 mg four times a day for 14 days
- Emphasize that patient's sexual partner must be treated
- Refer to genitourinary clinic for follow up and contact tracing, and give patient a clinic leaflet

Figure 2. Suggested management of women diagnosed as having cervical chlamydia infection in general practice.

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Acknowledgements

We thank Professor Sean Hilton and Dr David Carrington for advice, and the 'south Thames research and development project grant scheme' for funding.

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Colorectal cancer

COLORECTAL carcinoma is one of the three most common carcinomas in the United Kingdom (excluding skin cancer) and results in 16 000 deaths each year. Of the 24 000 new cases of colorectal carcinoma that present each year, 23% are rectal, 24% sigmoid and 22% occur in the right colon. Each year 6000 colorectal carcinomas are successfully resected.

Secondary prevention by faecal occult blood screening has attracted much attention but there has always been interest in primary prevention of this condition. Dietary advice was promoted when an association was shown between colorectal carcinoma and the high fat diet of people in western countries. This paper from the United States of America investigates the possible protective effect of exercise which has been highlighted by other researchers.

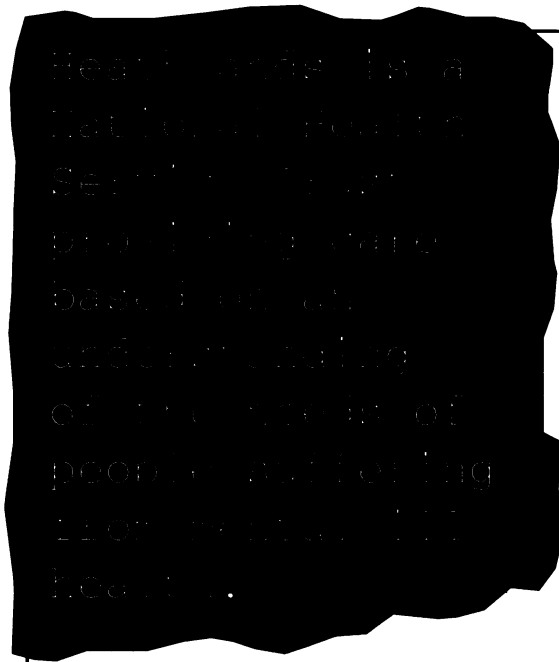
This is a retrospective descriptive study, using community controls, of men with adenocarcinoma of the right colon and rectum. Physical activity, both occupational and leisure, and diet were evaluated by validated questionnaires. Men who exercised for leisure vigorously for two hours or more each week had a decreased risk of cancer of the right colon. Occupational exercise did not protect against colorectal carcinoma. Adjustment for diet was not thought to affect the associations. There was no association between physical activity and rectal carcinoma.

It must be noted, however, that a greater proportion of cases with carcinoma of the right colon had a history of smoking and annual incomes of less than \$20 000 compared with controls; this may have affected the results. To prove a causal association between physical activity and reduced risk of colorectal carcinoma would require a prospective study and greater control for socioeconomic factors. General practice in the United Kingdom would provide an ideal environment for such a study.

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Source: Longnecker MP, Gerhardtsson de Verdier M, Frumkin H, Carpenter C. A case-control study of physical activity in relation to risk of cancer of the right colon and rectum in men. *Int J Epidemiol* 1995; **24**: 42-50.

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A wide range of services are provided at a number of facilities throughout western Surrey and north east Hampshire. Many of these activities are provided in a traditional manner in hospitals in Frimley, Knaphill near Woking, and Guildford. However, Heathlands Mental Health NHS Trust is improving the way that mental health care is provided to local people. Community based services are bringing easier access, better individual care and an end to reliance on institutions.

Our new services include:

- * Local Community Mental Health Care Centres where teams of nurses, psychologists, occupational therapists, social workers will be based with psychiatrists providing some out-patient clinics.
- * Support in the home to people living in the community and those moving from the long-stay institutions.
- * A rehabilitation unit to help people to re-adjust to life back home following illness.
- * Care homes for older people who need 24-hour nursing support.
- * An acute in-patient service for the people who need urgent nursing care.
- * Help with getting back to work following an illness.
- * Help with transportation to and from our services.

A range of specialist services including psychiatric care and follow up for mentally disordered offenders; support for families; help with welfare rights; and treatment for people with substance misuse problems, such as drugs or alcohol.

Plans for these services and developments are progressing and if you would like any further information then please contact our Information Section at: Heathlands House, The Ridgewood Centre, Old Bisley Road, Frimley, Camberley, Surrey, GU16 5QE, phone 01276 692919 fax 01276 678174.

Heathlands
Mental Health NHS Trust