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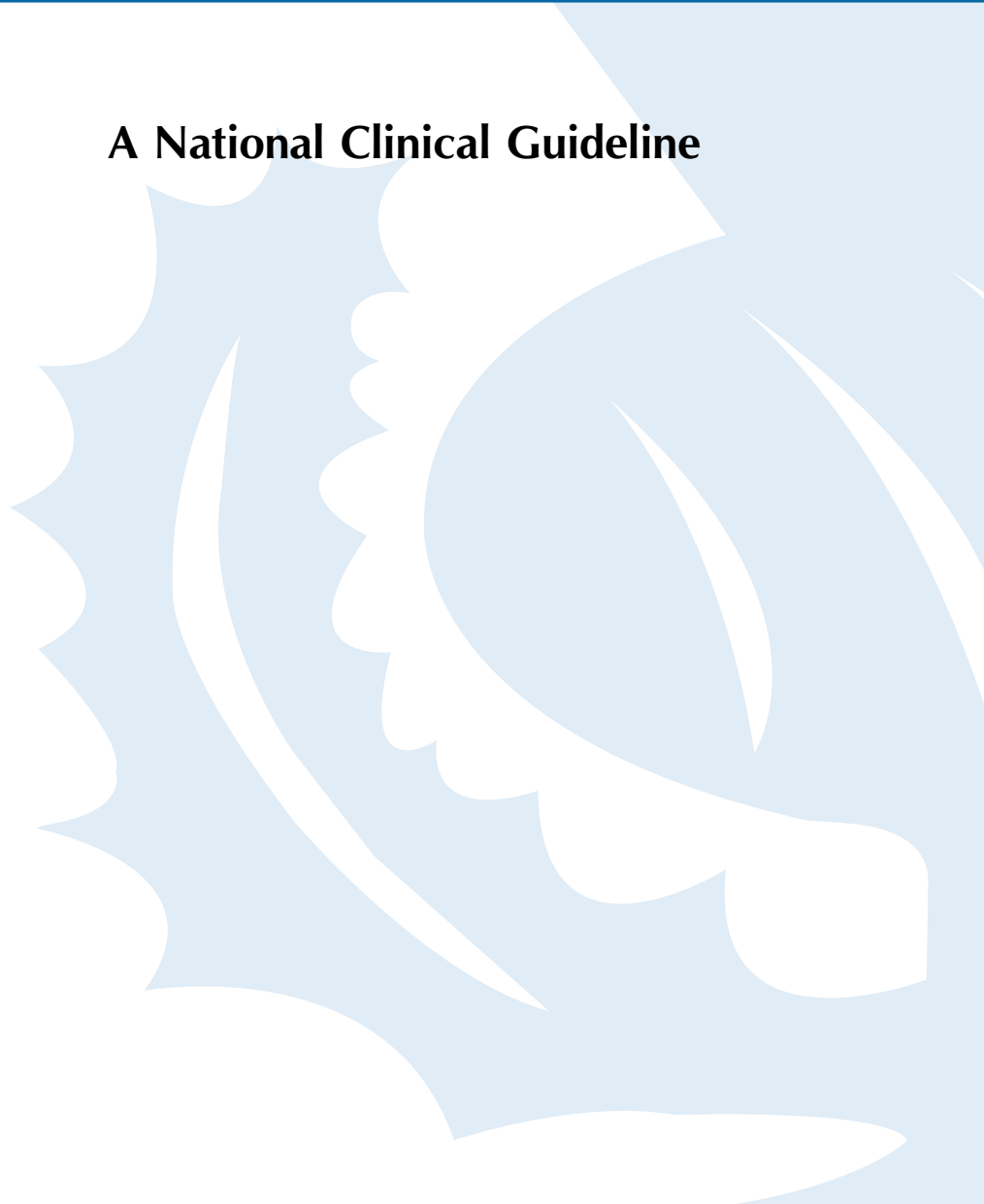
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Scottish
Intercollegiate
Guidelines
Network

Management of Genital *Chlamydia trachomatis* Infection

A National Clinical Guideline

March 2000



KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

The definitions of the types of evidence and the grading of recommendations used in this guideline originate from the US Agency for Health Care Policy and Research¹ and are set out in the following tables.

STATEMENTS OF EVIDENCE

<i>Ia</i>	Evidence obtained from meta-analysis of randomised controlled trials.
<i>Ib</i>	Evidence obtained from at least one randomised controlled trial.
<i>IIa</i>	Evidence obtained from at least one well-designed controlled study without randomisation.
<i>IIb</i>	Evidence obtained from at least one other type of well-designed quasi-experimental study.
<i>III</i>	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.
<i>IV</i>	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

GRADES OF RECOMMENDATIONS

A	Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. <i>(Evidence levels Ia, Ib)</i>
B	Requires the availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation. <i>(Evidence levels IIa, IIb, III)</i>
C	Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. <i>(Evidence level IV)</i>

GOOD PRACTICE POINTS

<input checked="" type="checkbox"/>	Recommended best practice based on the clinical experience of the guideline development group.
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Notes for users of the guideline

DEVELOPMENT OF LOCAL GUIDELINES

It is intended that this guideline will be adopted after local discussion involving clinical staff and management. The Area Clinical Effectiveness Committee should be fully involved. Local arrangements may then be made for the derivation of specific local guidelines to implement the national guideline in individual hospitals, units and practices and for securing compliance with them. This may be done by a variety of means including patient-specific reminders, continuing education and training, and clinical audit.

SIGN consents to the copying of this guideline for the purpose of producing local guidelines for use in Scotland. For details of how to order additional copies of this or other SIGN publications, see inside back cover.

STATEMENT OF INTENT

This report is not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve.

These parameters of practice should be considered guidelines only. Adherence to them will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the doctor in light of the clinical data presented by the patient and the diagnostic and treatment options available.

Significant departures from the national guideline as expressed in the local guideline should be fully documented and the reasons for the differences explained. Significant departures from the local guideline should be fully documented in the patient's case notes at the time the relevant decision is taken.

A background paper on the legal implications of guidelines is available from the SIGN Secretariat.

REVIEW OF THE GUIDELINE

This guideline was issued in March 2000 and will be reviewed in 2002 or sooner if new evidence becomes available. Any amendments in the interim period will be noted on the SIGN website. Comments are invited to assist the review process. All correspondence and requests for further information regarding the guideline should be addressed to:

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Abbreviations

AIDS	Acquired immune deficiency syndrome
DNA	Deoxyribonucleic acid
GUM	Genito-urinary medicine
HIV	Human immune deficiency virus
IUD	Intrauterine device
LCR	Ligase chain reaction
NGU	Non-gonococcal urethritis
NSU	Non-specific urethritis
PCR	Polymerase chain reaction
PID	Pelvic inflammatory disease
RCT	Randomised controlled trial
SDA	Strand-displacement amplification
SIGN	Scottish Intercollegiate Guidelines Network
SNAP	Scottish Needs Assessment Programme
STI	Sexually transmitted infection
TMA	Transcription-mediated amplification
TOP	Termination of pregnancy

Summary of recommendations

TESTING FOR GENITAL *CHLAMYDIA TRACHOMATIS* INFECTION

It is important that the reason for, implications of, and results of any test carried out are explained to the individual being tested.

B The recommended laboratory test is a nucleic acid amplification test (e.g. LCR or PCR).

PATIENTS WITH SYMPTOMS/SIGNS OF CHLAMYDIAL INFECTION

B Testing for *Chlamydia trachomatis* infection should be performed in women and men with symptoms and signs which may be attributable to chlamydial infection:

- **Women**
 - vaginal discharge
 - post coital/intermenstrual/breakthrough bleeding
 - inflamed/friable cervix (which may bleed on contact)
 - urethritis
 - pelvic inflammatory disease
 - lower abdominal pain in the sexually active
 - reactive arthritis in the sexually active.
- **Men**
 - urethral discharge
 - dysuria
 - urethritis
 - epididymo-orchitis in the sexually active
 - reactive arthritis in the sexually active.

ASYMPTOMATIC PATIENTS

Testing for genital *Chlamydia trachomatis* infection should be performed in the following **specific circumstances**:

- A**
 - all women undergoing termination of pregnancy
- B**
 - all patients attending genitourinary medicine clinics
 - all patients with another sexually transmitted infection, including genital warts
 - sexual partners of those with chlamydial infection
 - mothers of infants with chlamydial conjunctivitis or pneumonitis
 - all women undergoing uterine instrumentation, including IUD insertion, who have risk factors for chlamydial infection
 - semen and egg donors
- C**
 - sexual partners of those with suspected chlamydial infection.
- B** **Opportunistic testing** could be considered in the following groups of women:
 - women younger than 25 years and sexually active
 - women aged 25 years or older with two or more partners in the last year or a change of sexual partner in the last year.

ANTIMICROBIAL TREATMENT FOR GENITAL CHLAMYDIAL INFECTION

- B** Initiate treatment without waiting for laboratory confirmation of infection in patients with symptoms and signs attributable to chlamydial infection and their sexual partners.

UNCOMPLICATED INFECTION

- A** Uncomplicated genital *Chlamydia trachomatis* infection may be treated with any one of the following (*listed alphabetically*):

- azithromycin 1g stat
- doxycycline 100mg twice daily for 7 days
- lymecycline 300mg once a day for 10 days
- minocycline 100mg once a day for 9 days
- ofloxacin 200mg twice daily for 7 days.

- B** Taking into account the issue of compliance with therapy, it is recommended that uncomplicated genital *Chlamydia trachomatis* infection is treated with azithromycin 1g stat.

UNCOMPLICATED INFECTION IN PREGNANCY

- A** In pregnancy, uncomplicated genital chlamydial infection should be treated with:

- erythromycin 500mg four times a day for 7 days
- or*
- amoxicillin 500mg three times a day for 7 days.

- A** All women undergoing termination of pregnancy should receive antimicrobial therapy effective against chlamydial infection at the time of the procedure.

UPPER GENITAL TRACT INFECTION IN WOMEN (CHLAMYDIAL SALPINGITIS / PID)

- C** The recommended treatment for upper genital tract infection in women is:

- doxycycline 100mg twice daily for a minimum of 10 days plus metronidazole 200mg three times a day or 400mg twice daily for the first 7 days
- ofloxacin 400mg twice daily may be used as an alternative to doxycycline
- clindamycin 450mg four times a day may be used as an alternative to metronidazole.

UPPER GENITAL TRACT INFECTION IN MEN (CHLAMYDIAL EPIDIDYMO-ORCHITIS)

- C** The recommended treatment for upper genital tract chlamydial infection in men is:

- doxycycline 100mg twice daily for 7 to 14 days
- or*
- oxytetracycline 250mg four times a day for 7 to 14 days.

FOLLOW UP AND TEST OF CURE

- Follow up should be offered approximately two to three weeks after initiating therapy.
- B** Patients should be interviewed at follow up with regard to compliance with therapy and risk of re-infection.
- B** In those patients who have been compliant with therapy and in whom there is no risk of reinfection, a test of cure need not be performed.
- Some patients, especially those who had asymptomatic chlamydial infection, may prefer the reassurance of test of cure.
- B** Test of cure/re-infection established by molecular amplification assay should be performed a minimum of three weeks after the initiation of therapy, to avoid false positive results.
- When women have been treated with amoxicillin in pregnancy, practitioners should maintain a high index of suspicion should symptoms suggestive of chlamydial infection develop in the infant.

PARTNER NOTIFICATION

- B** Patients should be referred to trained health advisers for support with partner notification.
- B** Patients should be offered the choice of patient, provider, or conditional referral for partner notification:
 - *Patient referral*: index patients themselves inform their sexual contacts to seek treatment.
 - *Provider referral*: the health care provider informs a patient's contacts anonymously that they should seek treatment.
 - *Conditional referral*: the health care provider notifies contacts if the patient has not done so after a given number of days.
- C** In men with symptomatic chlamydial infection, contact all partners over the four weeks prior to onset of symptoms.
- C** In women and asymptomatic men, contact all partners over the last six months or the most recent sexual partner (if outwith that time period).

HEALTH EDUCATION

- C** Sexual health promotion should be an integral part of contraception provision wherever this is offered.
- B** All patients with chlamydial infection should receive appropriate health education, including relevant reading materials.
- B** Opportunities should be taken to deliver education in a wide variety of non-health care settings. Education about chlamydial infection should be integrated with other sexual health education and condom promotion initiatives.

1 Introduction

1.1 BACKGROUND

Sexually active individuals are at risk of a range of sexually transmitted infections (STIs), of which *Chlamydia trachomatis* is the most prevalent bacterial infection. Genital chlamydial infection can cause considerable short and long term morbidity with accompanying costs to the individual and the health service.² The sequelae of chlamydial infection include pelvic inflammatory disease (PID), ectopic pregnancy and tubal infertility in women, epididymo-orchitis in men, and reactive arthritis.^{3,4}

1.2 THE NEED FOR A GUIDELINE

Genital *Chlamydia trachomatis* infection is asymptomatic in up to 70% of women and at least 50% of men.³⁻⁵ As a result, there may be limited testing of those with chlamydial infection. This will lead to few cases being identified, and a perception that there is no significant problem.

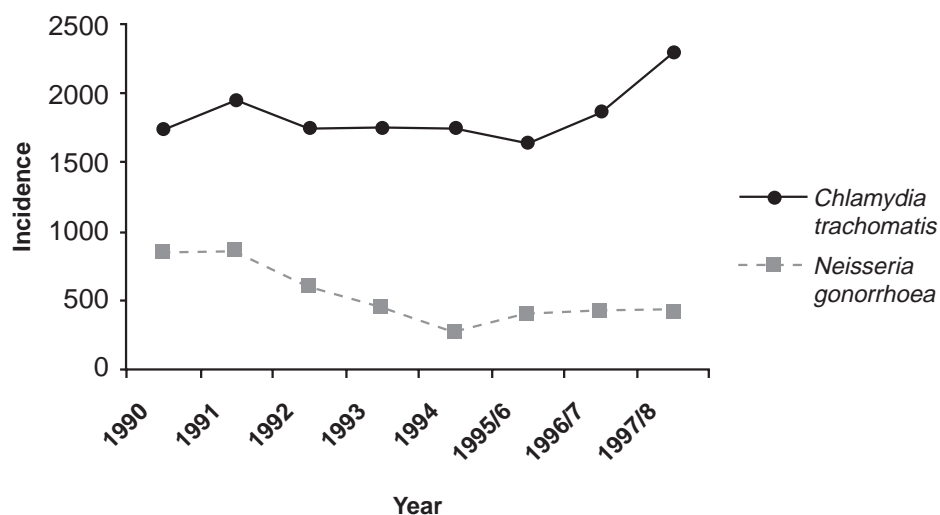
Patients who may have chlamydial infection (either with or without symptoms) present in many different medical settings. In addition to genito-urinary medicine (GUM) departments, patients may be seen in general practice, family planning and Brook Advisory Clinics, obstetrics & gynaecology and other hospital departments. A group set up under the auspices of the Scottish Needs Assessment Programme (SNAP) reviewed sexually transmitted disease services in Scotland and uncovered clear evidence of variation in practice in the management of *Chlamydia trachomatis* infection in these settings.⁶ For example:

- Only 30 of 63 gynaecology units undertook screening for chlamydial infection prior to termination of pregnancy (TOP), although it is known that 6-10% of women undergoing TOP will be positive for chlamydial infection. Of these, 25% are likely to develop postoperative salpingitis if the chlamydial infection remains untreated.⁷⁻⁹
- In family planning clinics, only eight of 13 clinics surveyed screened for chlamydial infection prior to insertion of an intrauterine device (IUD), despite the risk of ascending infection at the time of insertion.^{10,11}
- General practitioners in Scotland send approximately 22,000 tests for chlamydial infection per annum, compared with 60,000 tests for the diagnosis of gonococcal infection. This is completely at variance with the respective prevalence of the two conditions. For example, in the year ending March 1998, there were 396 reported cases of gonococcal infection compared with 2,277 cases of chlamydial infection (see *Figure 1*).¹²
- No facilities for routine contact tracing of chlamydial infection exist outwith GUM departments.

Advances in understanding the natural history of the infection and of diagnostic methods have resulted in a wealth of research, mainly in the United States and Scandinavia, on the effectiveness of early diagnosis in reducing the impact of the disease.¹³⁻²⁰

Figure 1

DIAGNOSES OF *CHLAMYDIA TRACHOMATIS* AND *NEISSERIA GONORRHOEA* AT SCOTTISH GUM CLINICS, 1990-1997/8



A guideline for the management of genital *Chlamydia trachomatis* infection has the potential to encourage the uptake of effective practice in the identification and treatment of chlamydial infection. Appropriate testing for chlamydial infection in defined clinical settings should lead to lower complication rates for individuals and, in tandem with wider access to contact tracing, should lead to significant falls in re-infection rates and a reduced pool of infection within the community.

1.3 REMIT OF THE GUIDELINE

This SIGN guideline was developed by a multidisciplinary guideline development group. The remit of the guideline is encompassed by two key questions:

- In which circumstances should potential chlamydial infection be sought routinely in adults?
- What is the optimum management of patients identified as *Chlamydia trachomatis* positive?

The guideline is based on a systematic review of the evidence base (see Annex 1 for further details). Consideration was also taken of the recommendations in the reviews carried out by the Centers for Disease Control,³ the Canadian Task Force on Periodic Health Examination,⁴ the Central Audit Group in Genitourinary Medicine,²¹ the Royal College of Obstetricians and Gynaecologists Study Group on the Prevention of Pelvic Infection,²² Leicestershire Genital Chlamydia Guidelines,²³ and the CMO's Expert Advisory Group on *Chlamydia trachomatis*.² The Canadian review and the Leicestershire guidelines were based on critical appraisal of published literature. In the remaining reviews, in depth considerations of the literature were undertaken by national experts.

1.4 LIMITATIONS OF THE GUIDELINE

Assessment of the cost-effectiveness of testing and treating the general and at risk population for *Chlamydia trachomatis* is hampered by the fact that much of the epidemiological research on chlamydial infection was carried out using older methods of detection with reduced sensitivity. This led to an underestimate of the prevalence of chlamydial infection in both symptomless patients and in those with possible complications such as PID. In addition, the guideline group identified several areas where there is little or no published evidence (see *recommendations for research, section 7.2*).

A detailed analysis of cost-effectiveness was beyond the remit of this guideline, which is concerned primarily with clinical effectiveness. However, the guideline has clear resource implications in terms of the cost of testing – especially in low-prevalence populations – and the cost of antimicrobial therapy. These might be offset by both the rationalisation of gonococcal testing, in keeping with the current epidemiology, and by the reduction in inpatient stays and outpatient visits resulting from the complications of chlamydial infection such as PID, ectopic pregnancy, infertility, and neonatal pneumonitis and conjunctivitis.

2 Laboratory tests

2.1 LABORATORY TESTS FOR *CHLAMYDIA TRACHOMATIS*

The diagnostic tests that are currently available include cell culture, antigen detection and DNA amplification tests.²⁴⁻²⁶

There is clear evidence that a modern molecular approach to amplifying deoxyribonucleic acid (DNA), such as ligase chain reaction (LCR) or polymerase chain reaction (PCR), provides a sensitivity approaching 100% and that this is superior to the 60-80% achievable by either cell culture or antigen detection.²⁴⁻³²

Evidence level IIa

In addition, LCR and PCR can be performed on urine samples, eliminating the need for invasive sampling and simplifying the procedures for obtaining samples.³¹

The role of newer tests such as transcription-mediated amplification (TMA) and strand-displacement amplification (SDA) needs to be clarified.³³⁻³⁵

Given the exquisite sensitivity of molecular methods, independent confirmation of positive results by another method is difficult. Medico-legal cases should continue to be investigated by cell culture, as this remains the only test validated in a court of law.³

B The recommended laboratory test for *Chlamydia trachomatis* is a nucleic acid amplification test (e.g. LCR or PCR).

2.2 OBTAINING SPECIMENS

Specimens from a variety of sites are suitable for testing. In women a cervical swab, first void urine (i.e. the first part of the stream) and vaginal swab are equally sensitive, although each may miss a small number of positives. Self-taken vaginal swabs are also acceptable specimens for diagnostic purposes.^{24, 36, 37}

Evidence level IIb

The test chosen will depend on the clinical situation. For example, if a vaginal examination is being carried out it is likely that a cervical swab will be submitted. If no examination is planned, then a specimen of urine may be preferred.^{31, 38}

- In women who are undergoing a vaginal examination, the specimen should be an endocervical swab.
- In women not undergoing a vaginal examination, a first void urine (i.e. the first part of the stream) should be obtained.
- A self-taken vaginal swab is an alternative specimen for women who cannot void urine at the time of the visit.

In men, urethral swabs and first void urine have equal sensitivity, but urethral sampling causes discomfort.^{31,38}

Evidence level IIa

B In men, a first void urine is the sample of choice.

3 Testing for genital chlamydial infection

This section addresses testing in:

- individual patients with symptoms and/or signs suggestive of genital chlamydial infection
- groups in the population who do not have symptoms of genital chlamydial infection but may have asymptomatic disease.

- ☑ It is important that the reason for, implications of, and results of any test carried out are explained to the individual being tested.

3.1 TESTING PATIENTS WITH SYMPTOMS/SIGNS OF CHLAMYDIAL INFECTION

Failure to diagnose or delay in the diagnosis of chlamydial infection is potentially harmful. Lower genital tract infection may spread to cause PID or epididymitis. Delay in treating PID increases the subsequent risk of infertility.³⁹ Failure to diagnose chlamydial infection as the cause of PID reduces the likelihood of contact tracing being carried out. This carries a risk of re-infection for the index case⁴⁰ along with a risk of morbidity for untreated sexual partners (see section 3.2).

In women, symptoms of chlamydial infection include increased vaginal discharge, post coital and/or intermenstrual bleeding, lower abdominal pain and dysuria. Signs include a mucopurulent cervical discharge, cervical friability and adnexal tenderness on vaginal examination.^{13,15,39,41-55}

Evidence level IIa

In men, symptoms include urethral discharge and/or dysuria. Signs include a mucoid or mucopurulent urethral discharge, microscopy of which reveals numerous pus cells.⁵⁶⁻⁵⁹ Epididymo-orchitis causes scrotal pain and swelling, with tender swelling of the epididymis on examination.⁶⁰⁻⁶²

Reactive arthritis occurs in about 1% of men following chlamydial infection of the urethra^{63,64} but occurs more rarely following chlamydial infection in women.⁶⁵ Rectal infection in either men or women rarely causes signs or symptoms.⁶⁶ Chlamydial infection may present with right hypochondrial pain due to perihepatitis.⁶⁷

Evidence level IIb

B Testing for *Chlamydia trachomatis* should be performed in women and men with symptoms and signs which may be attributable to chlamydial infection:

- **Women**
 - vaginal discharge
 - post coital/intermenstrual/breakthrough bleeding
 - inflamed/friable cervix (which may bleed on contact)
 - urethritis
 - pelvic inflammatory disease
 - lower abdominal pain in the sexually active
 - reactive arthritis in the sexually active.
- **Men**
 - urethral discharge
 - dysuria
 - urethritis
 - epididymo-orchitis in the sexually active
 - reactive arthritis in the sexually active.

3.2 TESTING ASYMPTOMATIC GROUPS FOR CHLAMYDIAL INFECTION

3.2.1 SPECIFIC CIRCUMSTANCES FOR TESTING

The risk of morbidity from the spread of chlamydial infection is immediate in:

- **Termination of pregnancy**
 Failure to treat chlamydial infection carries approximately a 25% risk of post-abortal salpingitis.^{7-9, 68-74} | Evidence level Ib

Women undergoing TOP are at increased risk of chlamydial infection.^{69, 74-80} | Evidence level IIa
- **IUD insertion**
 No studies have specifically demonstrated the benefit of testing prior to IUD insertion (with a view to preventing ascending infection), but there have been two studies that showed that giving an antimicrobial agent effective against chlamydial infection at the time of IUD insertion reduced the rate of salpingitis.^{10, 11} | Evidence level III
- **Semen and egg donation**
 Semen and egg donors should be tested for chlamydial infection to reduce the risk of transmission of infection to the recipient.⁸¹

In most circumstances the goal is to reduce the long term morbidity for individuals, their sexual partners and the wider community. There is good evidence that specific groups of patients have an increased likelihood of being infected with *Chlamydia trachomatis*:

- **Attendees at GUM clinics**^{2, 12, 82-84} and persons with STIs presenting in other clinics.^{2, 85-87} | Evidence level IIb
- **Sexual partners of chlamydia-positive individuals** are clearly at risk of infection and therefore of morbidity.⁸⁸⁻⁹² Treating them will also reduce the risk of re-infection of the index case. | Evidence level IV
- **Sexual partners of those with conditions for which *Chlamydia trachomatis* is a frequent (but undiagnosed) cause**, such as PID⁹³ or epididymo-orchitis.⁹⁴ | Evidence level IIb
- **Mothers of infants with chlamydial conjunctivitis or pneumonitis** are likely to have genital chlamydial infection.⁹⁵⁻⁹⁷

Testing for genital *Chlamydia trachomatis* infection should be performed in the specific circumstances of:

- A**
 - all women undergoing termination of pregnancy
- B**
 - all patients attending genitourinary medicine clinics
 - all patients with another STI, including genital warts
 - sexual partners of those with chlamydial infection
 - mothers of infants with chlamydial conjunctivitis or pneumonitis
 - all women undergoing uterine instrumentation, including IUD insertion, who have risk factors for chlamydial infection (see section 3.2.2)
 - semen and egg donors
- C**
 - sexual partners of those with suspected chlamydial infection.

- ☑ In patients with another STI the test should be offered by the doctor providing initial care.
- ☑ In women undergoing TOP, the ultimate responsibility for ensuring testing lies with the gynaecologist undertaking the procedure. However, local arrangements may favour the test being carried out by the referring doctor (see section 4.3).

3.2.2 OPPORTUNISTIC TESTING

Prevalence and risk factors for chlamydial infection have been identified from studies set in UK general practice^{28, 42, 98, 99-104} and family planning clinics.¹⁰⁵⁻¹¹⁰ These studies have limitations in terms of representativeness, sample size, types of analyses conducted and testing strategies,¹¹¹ but the risk factors described in UK populations are similar to those reported from the United States.^{13, 45, 112-116} Risk factors consistently identified for chlamydial infection in women in these and other studies include age <25 years, two or more sexual partners within the last year and/or a recent partner change.^{15, 46, 84, 115, 117, 118}

Evidence level IIa

One London study found that a selective screening strategy based on age <25 and two or more partners in the past year detected 87% of infections while testing only 49% of the study population.²⁸

A randomised controlled trial of population based screening using criteria such as these has demonstrated reduced PID morbidity over one year.⁴¹

Evidence level Ib

B Opportunistic testing could be considered in the following groups of women:

- women younger than 25 years and sexually active
- women aged 25 years or older with two more partners in the last year or a change of sexual partner in the last year.

There are little data on men outwith GUM clinics. It is therefore not possible to make a recommendation on opportunistic screening in men.

There is increasing support for opportunistic screening in sexually active women attending general practice. However, questions remain about interval of screening, funding, training and organisational aspects.

- ☑ All clinicians treating sexually active women should maintain a high level of awareness of the need to offer a screening test for genital *Chlamydia trachomatis* infection to women who have an increased risk of infection.
- ☑ Testing should be carried out wherever the patient is seen, i.e. in general practice, antenatal clinics, family planning clinics or gynaecology departments. It is appreciated that opportunistic testing in general practice will most likely be offered during consultations relating to sexual health, e.g. contraception, cervical smears, pregnancy.

The guideline development group recognises the resource implications associated with these recommendations (see section 1.4).

4 Antimicrobial treatment for genital chlamydial infection

The management of confirmed *Chlamydia trachomatis* infection incorporates appropriate antimicrobial therapy, partner notification (see section 5), advice to abstain from sex until both the index case and current partner(s) have been treated, and relevant health education (see section 6).

4.1 CHOICE OF ANTIMICROBIAL AGENT

The choice of antimicrobial agent is governed by efficacy, incidence of side effects, cost, and compliance.

There are no randomised controlled trials (RCTs) of the treatment of genital chlamydial infection with any agents compared to placebo, as the original trials of antimicrobial agents for the treatment of non-gonococcal urethritis (NGU) established the efficacy of tetracyclines and erythromycin long before *Chlamydia trachomatis* was identified.¹¹⁹⁻¹²¹ Once it became clear that *Chlamydia trachomatis* was the aetiological agent in 50% of cases of NGU, it was ethically unjustifiable to carry out placebo-controlled trials of antichlamydial agents. Rather, newer agents have been compared with older drugs such as tetracyclines or erythromycin.^{119, 122-126}

Evidence level IIIb

The newer tetracyclines, minocycline and doxycycline are as effective as older tetracyclines and erythromycin, as is ofloxacin. Ciprofloxacin and norfloxacin have been shown to be ineffective.¹²⁷ Doxycycline is generally better tolerated than minocycline¹⁰ and as a result has tended to be used as the control against which other drugs are compared. As erythromycin has rarely been used in RCTs, the group could find insufficient evidence to support its use, except in the treatment of uncomplicated infection in pregnancy. Although equally effective, the four times a day regimen of older treatments meant that doxycycline was more often used as a comparator in studies.

Evidence level IIIa

Given the high cure rate (>90%) with all the agents used, equivalence of effectiveness of therapy, rather than improved effectiveness, was sought. All treatment regimens reviewed are oral, for outpatient use.

It has been shown that compliance with oral therapy for STIs over several days is sub-optimal, and gets worse the more frequent the daily dosage. Compliance may be poor for many reasons, ranging from patients being asymptomatic, the symptoms of infection clearing quickly, or the presence of side effects, through to the chaotic lifestyle of some patients.¹²⁹⁻¹³²

Evidence level IIIa

4.2 UNCOMPLICATED INFECTION

Azithromycin 1g stat, ofloxacin 200 or 300mg twice daily for seven days, minocycline 100mg for nine days and lymecycline 300mg for 10 days are all as effective as doxycycline 100mg twice daily for seven days.^{127,133-144}

Evidence level Ib

A Uncomplicated genital *Chlamydia trachomatis* infection may be treated with any one of the following (listed alphabetically):

- azithromycin 1g stat
- doxycycline 100mg twice daily for 7 days
- lymecycline 300mg once a day for 10 days
- minocycline 100mg once a day for 9 days
- ofloxacin 200mg twice daily for 7 days.

B Taking into account the issue of compliance with therapy, it is recommended that uncomplicated genital *Chlamydia trachomatis* infection is treated with azithromycin 1g stat.

4.3 UNCOMPLICATED INFECTION IN PREGNANCY

In women with ongoing pregnancy, erythromycin may not be well tolerated and there is evidence that amoxicillin 500mg three times a day for seven days is equivalent to erythromycin 500mg four times a day for seven days in the treatment of uncomplicated genital chlamydial infection.^{145, 146} In vitro studies suggest that amoxicillin may not always eradicate chlamydial infection but may render the infection latent.¹⁴⁷ A small study has shown that some infants develop chlamydial infection despite apparently successful treatment of the mother.¹⁴⁸ Therefore a negative test of cure does not necessarily equate with absence of transmission during delivery.^{145,146}

Evidence level Ia

A Uncomplicated genital chlamydial infection in pregnancy should be treated with:

- erythromycin 500mg four times a day for 7 days
or
- amoxicillin 500mg three times a day for 7 days.

When women have been treated with amoxicillin in pregnancy, practitioners should maintain a high index of suspicion should symptoms suggestive of chlamydial infection develop in the infant.

Women undergoing TOP should routinely be tested for chlamydial infection (see section 3.2) There is evidence that giving antichlamydial therapy at the time of the procedure reduces the risk of PID regardless of the result of the test,⁷⁴ but the test should still be performed to allow partner notification to prevent reinfection.

Evidence level Ib

A All women undergoing TOP should receive antimicrobial therapy effective against chlamydial infection at the time of the procedure.

4.4 UPPER GENITAL TRACT INFECTION IN WOMEN

(CHLAMYDIAL SALPINGITIS / PID)

All studies on the treatment of pelvic inflammatory disease use clinical end-points as their primary assessment of efficacy. There are no satisfactory studies where microbial test of cure for chlamydial infection is the primary end-point.

The current Centers for Disease Control (CDC) treatment guidelines³ for PID incorporate anti-gonococcal therapy. Their recommendations are based on the high prevalence of gonorrhoea in the USA and are not directly applicable to Scotland, where the incidence is lower. Adapting the guidelines for the UK, where there is presently a low prevalence of gonorrhoea, the following are recommended as treatment for chlamydial salpingitis.

Evidence level IV

- C** The recommended treatment for upper genital tract infection in women is doxycycline 100mg twice daily for a minimum of 10 days plus metronidazole 200mg three times a day or 400g twice daily for the first 7 days.
- C** Ofloxacin 400mg twice daily may be used as an alternative to doxycycline.
- C** Clindamycin 450mg four times a day may be used as an alternative to metronidazole.

4.5 UPPER GENITAL TRACT INFECTION IN MEN

(CHLAMYDIAL EPIDIDYMO-ORCHITIS)

The literature search undertaken for this guideline did not identify any reliable evidence on the treatment of upper genital tract infection in men. Historically, tetracyclines have been used successfully, with current practice favouring doxycycline and oxytetracycline.¹⁴⁹

Evidence level IV

- C** The recommended treatment for upper genital tract chlamydial infection in men is:
 - doxycycline 100mg twice daily for 7-14 days
 - or
 - oxytetracycline 250mg four times a day for 7-14 days.

4.6 INITIATION OF TREATMENT

In symptomatic patients treatment should be initiated at the first consultation rather than awaiting laboratory confirmation of infection. There is evidence in PID that delay in starting treatment increases the risk of impaired fertility.³⁹ Partners should be treated without waiting for laboratory confirmation.¹⁵⁰

Evidence level IIIb

- B** Initiate treatment without waiting for laboratory confirmation of infection in patients with symptoms and signs attributable to chlamydial infection and their sexual partners.

4.7 FOLLOW UP AND TEST OF CURE

The quality of evidence available to determine the role of test of cure is inevitably poor. Many patients fail to return and thus cannot be included in studies. However, conclusions can still be drawn regarding the management of the self-selecting group of patients who return for follow-up.¹⁵¹⁻¹⁵⁶ These studies provided no conclusive evidence as to the optimal timing of follow-up. However, prolonged delay on follow-up increases the risk of re-infection from untreated partners.

Evidence level III

Follow up should be offered approximately 2-3 weeks after initiating therapy.

B Patients should be interviewed at follow-up with regard to compliance with therapy and risk of re-infection.

B In those patients who have been compliant with therapy and in whom there is no risk of reinfection, a test of cure need not be performed.

Some patients, especially those who had asymptomatic chlamydial infection, may prefer the reassurance of test of cure.

Health professionals should be aware that if a test of cure is to be done using a molecular amplification assay, it should not be done within three weeks to avoid false positive results due to persistence of non-viable organisms.¹⁵⁷

Evidence level IIIb

B Test of cure/re-infection established by molecular amplification assay should be performed a minimum of three weeks after the initiation of therapy, to avoid false positive results.

5 Partner notification

The treatment of sexual contacts prior to resumption of sexual intercourse is the strongest predictor for preventing re-infection.⁴⁰ This may be particularly important in salpingitis, as there is evidence that repeated infections increase the risk of tubal infertility.¹⁵⁸ Therefore, effective partner notification (also referred to as contact tracing) forms an essential component of management of chlamydial infection.¹⁵⁹

Evidence level IIb

Trained interviewers have been shown to identify more partners than routine health care providers for patients with gonorrhoea or *Chlamydia trachomatis*.¹⁶⁰

B Patients should be referred to trained health advisers for support with partner notification.

At present the only NHS staff trained to carry out partner notification are health advisers in GUM departments.

Choice of method of partner notification is based on resource availability as well as patient/partner acceptability.¹⁶¹ It is the role of the health adviser to advise individual patients on the best approach in their circumstances. The options are:

- **Patient referral** (or self-referral), when index patients themselves inform their sexual contacts to seek treatment.
- **Provider referral**, when the health care provider informs a patient's contacts anonymously that they should seek treatment. This is obviously more time consuming for the health care provider.
- **Conditional referral**, where the health care provider notifies contacts if the patient has not done so after a given number of days.

There is no evidence that any one of the traditional methods of patient, provider or conditional referral is superior to the others.¹⁶⁰

Evidence level IIb

B Patients should be offered the choice of patient, provider or conditional referral for partner notification.

Where a patient requests assistance, health care providers should be available to notify partners.¹⁶¹ Where this is not possible then the health care provider should inform the patient that they should advise all recent sexual partners to seek treatment. There is evidence that simple forms of patient assistance directed at improving patient referral, such as a telephone call, can be effective.¹⁶⁰

Evidence level IIb

One study from Denmark has demonstrated superior partner testing rates where male partners were asked to mail a sample of urine from home, rather than attend a clinic.¹⁶² The acceptability of this approach has not been tested in the UK.

Evidence level IIa

There is no clear evidence regarding the length of time over which previous sexual partners should be sought. The guideline development group endorses the recommendations of the Central Audit Group in Genitourinary Medicine:¹⁶³

Evidence level IV

- C** In men with symptomatic chlamydial infection, contact all partners over the four weeks prior to onset of symptoms.
- C** In women and asymptomatic men, contact all partners over the last six months or the most recent sexual partner (if outwith that time period).

6 Health education in primary prevention and prevention of reinfection

There are relatively few studies available on the effectiveness of sexual health promotion in the context of STIs other than HIV/AIDS. While such studies may be relevant, it cannot be assumed that sexual health promotion effective in the context of a predominantly fatal virus can be automatically transferred to a treatable bacterial infection such as chlamydial infection.

Studies have been undertaken to evaluate the effectiveness of a range of intervention programmes, for example to promote condom use.¹⁶⁴⁻¹⁶⁷ Community interventions to increase awareness of chlamydial infection and other STIs, promote prompt treatment seeking, and reduce high-risk sexual behaviours have also been reported.^{5,6} However, few of the studies reviewed meet the required methodological standards, and the effects of the interventions on subsequent behaviour are inconclusive. It is therefore not possible to recommend any particular intervention.

One of the most important components of any educational effort will be the reduction of stigma associated with chlamydial infection, STIs in general, and GUM services.¹⁷⁰

While there is a lack of evidence about educational interventions that will alter behaviour, some general points can be ascertained from the social science literature. There are three distinct groups to which education should be targeted: patients, the general public, and health professionals.

6.1 PATIENTS

6.1.1 PRIMARY PREVENTION

Sexual health promotion should be an integral part of contraception provision. Risk of STIs should be discussed where non-barrier contraception is being offered as well as possible condom use in addition to other contraceptive methods.¹⁷¹ It is important that sexual health education in primary care is also targeted at men, for example, when attending for new patient checks or for travel advice.¹⁶⁹

Evidence level IV

C Sexual health promotion should be an integral part of contraception provision wherever this is offered.

6.1.2 PREVENTION OF REINFECTION

Successful treatment and control of STI involves a complex set of behaviours: prompt seeking of health care, compliance with therapy, referral of sexual partners, return for follow up and prevention of re-exposure.¹⁵⁹ The educational needs of patients are likely to vary according to age, gender, social class, social vulnerability, sexual orientation and ethnicity.¹⁷²

Evidence level III

B All patients with chlamydial infection should receive appropriate health education, including relevant reading materials.

Valuable information for patients is contained in the leaflets “*What is chlamydia?*”, produced by the Family Planning Association and “*What do you know about Chlamydia and NSU?*” produced by the Health Education Board for Scotland (see Annex 2).

6.2 GENERAL PUBLIC

An essential precondition for any screening strategy would be education of the general public, to increase awareness of chlamydial infection and reduce stigma.

Knowledge of chlamydial infection among the general population and among GUM clinic attenders has been found to be low.¹⁷³ Education campaigns that have used multimedia advertising to increase awareness about other sensitive issues (e.g. HIV/AIDS, or the Zero Tolerance of Violence Against Women campaign) have proved successful.^{174, 175} It is the translation of increased awareness into behaviour change that is problematic.

Evidence level III

B Opportunities should be taken to deliver education in a wide variety of non-health care settings e.g. youth clubs, community centres, schools. Education about chlamydial infection should be integrated with other sexual health education and condom promotion initiatives.

6.3 HEALTH PROFESSIONALS

The communication skills needed to discuss sexual health and to elicit a sexual history have traditionally been awarded relatively little attention in undergraduate curricula.¹⁷¹ The educational needs of staff providing care outwith specialised sexual health centres therefore requires attention.¹⁷⁶ Specific issues to be addressed include strategies to initiate and discuss sexual health issues within a consultation, especially when the consultation is unrelated to sexual health.¹⁷¹

Medical educators should include sexual history skills as an essential part of undergraduate education. The skills required for sexual history taking should also form part of postgraduate medical training, as well as training for practice nurses and health advisers.

7 Recommendations for audit and research

7.1 KEY POINTS FOR AUDIT

7.1.1 NATIONAL TARGETS

- number of laboratories using molecular amplification methods to diagnose chlamydial infection
- proportion of cases of diagnosed chlamydial infection that are asymptomatic
- the ratio of testing for gonococcal and chlamydial infection compared with their current epidemiology
- numbers of patients attending GUM health advisers, having been referred by their GP.

7.1.2 REGIONAL TARGETS

- number of tests per head of population
- number of tests carried out in men
- development and dissemination of educational materials to health professionals and the general public.

7.1.3 TARGETS WITHIN DEPARTMENTS, CLINICS, HEALTH CENTRES ETC.

General

- % of patients with chlamydial infection who receive treatment within four weeks
- rates of referral to GUM health advisers from other settings.

Diagnostic testing

- % of women with suspected PID tested for chlamydial infection
- % of men with epididymitis tested for chlamydial infection.

Testing specific asymptomatic groups

- % of women tested before TOP
- % of women tested prior to IUD insertion.

Follow up rate

- partner notification success rates.

7.2 RECOMMENDATIONS FOR RESEARCH

The CMO's Expert Advisory Group on *Chlamydia trachomatis*² recommended that research should be undertaken to collect evidence on the effectiveness of strategies for prevention in the United Kingdom. The Department of Health has provided funding to conduct these more rigorous studies.

During the development of this guideline, the group identified the following areas where specific evidence is lacking:

Testing

- is full STI testing essential in people identified with chlamydial infection in the community?
- what are the incidence and re-infection rates? This might generate some guidance as to how often repeat testing should be undertaken.

Patients and partners

- the effectiveness of methods of partner notification and follow up
- should partners be tested first or just treated? What further opportunities for partner notification would be lost by not testing partners prior to treatment?
- patients' needs and views, particularly information and support needs for partner notification
- what evidence is there that asking and recording information about sexual history, number of partners, etc is acceptable to patients?
- the social, cultural and psychological factors that are implicated in sexual behaviour and, more specifically, in health and sick role behaviours of patients with chlamydial infection and other STIs. On the basis of this applied research, health promotion interventions can be designed and evaluated.

Cost issues

- the cost-effectiveness of single dose azithromycin therapy in the UK.

Efficacy

- the efficacy of azithromycin in the treatment of PID and epididymo-orchitis.

Annex 1

DETAILS OF SYSTEMATIC REVIEW UNDERTAKEN FOR THE GUIDELINE

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by the SIGN Information Officer in collaboration with members of the guideline development group. Searches were carried out on Medline, Embase, Social citation index, Cinahl and the Cochrane Library.

Articles relating to *Chlamydia pneumoniae* were excluded. All articles that were not related to the treatment of genital *Chlamydia trachomatis* infection were excluded. Where sufficient evidence was felt to be available in the English literature, the non-English literature was not reviewed. Studies involving drugs that are not available in the UK, studies from developing countries and those focusing specifically on HIV/AIDS were also excluded.

Papers were only included if they adhered to recognisable methodological principles, including adequate sample size, a clearly identified hypothesis and measure of outcome, and accurate reporting of results. Whenever possible randomised trials have been discussed, but due to the paucity of sound randomised controlled trials in some of the areas covered by the remit of this guideline, a number of clinical studies have also been included.

In relation to the antimicrobial treatment of *Chlamydia trachomatis*, studies reporting small numbers (<50 cases), and those not specifically relating to chlamydial infection were excluded.

Annex 2

KEY MESSAGES FOR PATIENTS

These notes are provided for possible use by clinicians in discussing investigations and treatment options with patients who may have chlamydial infection. They are not intended for direct distribution to patients, but might be incorporated into locally-developed patient information materials.

Chlamydial infection:

- is the commonest bacterial STI in Scotland
- is curable
- is asymptomatic in the majority of patients and thus may remain undiagnosed for long periods of time
- may be diagnosed within a stable relationship
- can result in serious morbidity if not treated, for example PID, tubal infertility and ectopic pregnancy
- is sexually transmitted, so attempts should be made to notify partners, avoiding sex until they have been treated
- using condoms helps protect against all STIs

Valuable information for patients is contained in the leaflets *“What is chlamydia?”*, produced by the Family Planning Association, FPA Scotland, Unit 10 Firhill Business Centre, 76 Firhill Road, Glasgow G20 7BA, and *“What do you know about Chlamydia and NSU?”* produced by the Health Education Board for Scotland, Woodburn House, Canaan Lane, Edinburgh EH10 4SG.

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Quick Reference Guide



SIGN

Management of Genital *Chlamydia trachomatis* Infection

SIGN Publication
Number

42

TESTING FOR *CHLAMYDIA TRACHOMATIS* (Ct) SHOULD BE PERFORMED:

In women with symptoms and signs which may be attributable to Ct:

- B** – vaginal discharge
- postcoital/intermenstrual/breakthrough bleeding
- inflamed/friable cervix (which may bleed on contact)
- urethritis
- pelvic inflammatory disease (PID)
- lower abdominal pain in the sexually active
- reactive arthritis in the sexually active.

Opportunistically:

- B** – in women younger than 25 years and sexually active
- in women aged 25 years or older with two or more partners in the last year or a change of sexual partner in the last year.

- All clinicians treating sexually active women should maintain a high level of awareness of the need to offer a screening test for genital *Chlamydia trachomatis* infection to women who have an increased risk of infection.

- It is important that the reason for, implications of, and results of any test carried out are explained to the individual being tested.

In men with symptoms and signs which may be attributable to Ct:

- B** – urethral discharge
- dysuria
- urethritis
- epididymo-orchitis in the sexually active
- reactive arthritis in the sexually active.

In other specific circumstances:

- A** – all women undergoing termination of pregnancy
- B** – all patients attending genitourinary medicine clinics
- B** – all patients with another sexually transmitted infection (STI), including genital warts
- B** – sexual partners of those with Ct
- B** – mothers of infants with chlamydial conjunctivitis or pneumonitis
- B** – all women undergoing uterine instrumentation who have risk factors for Ct
- B** – semen and egg donors
- C** – sexual partners of those with suspected Ct (e.g. PID, epididymo-orchitis).

LABORATORY TEST

- B** The recommended laboratory test is a nucleic acid amplification test (LCR or PCR).

SAMPLING

- In women who are undergoing a vaginal examination, the specimen should be an endocervical swab.
- In women not undergoing a vaginal examination, a first void urine (i.e. the first part of the stream) should be obtained.
- A self-taken vaginal swab is an alternative specimen for women who cannot void urine at the time of the visit.

- B** In men a first void urine is the sample of choice.

KEY

A

B

C

indicates grade of recommendation



good practice point

TREATMENT

Uncomplicated infection in women and men:

- A – azithromycin 1g stat *or*
- doxycycline 100mg twice daily for 7 days *or*
- ofloxacin 200mg twice daily for 7 days *or*
- minocycline 100mg once a day for 9 days *or*
- lymecycline 300mg once a day for 10 days.

B Taking into account the issue of compliance with therapy, it is recommended that uncomplicated genital Ct infection is treated with azithromycin 1g stat.

Upper genital tract infection in men:

- C – doxycycline 100mg twice daily for 7 to 14 days *or*
- oxytetracycline 250mg four times a day for 7 to 14 days.

Uncomplicated Ct infection in pregnancy:

- A – erythromycin 500mg four times a day for 7 days *or*
- amoxicillin 500mg three times a day for 7 days
- A All women undergoing termination of pregnancy should receive antimicrobial therapy effective against Ct at the time of the procedure.

Upper genital tract infection in women:

- C – doxycycline 100mg twice daily for a minimum of 10 days plus metronidazole 200mg three times a day or 400 mg twice daily for the first 7 days
- ofloxacin 400mg twice daily may be used as an alternative to doxycycline
- clindamycin 450mg four times a day may be used as an alternative to metronidazole.

INITIATION OF TREATMENT

B Initiate treatment without waiting for laboratory confirmation of infection in patients with symptoms and signs attributable to chlamydial infection and their sexual partners.

PARTNER NOTIFICATION

B Patients should be referred to trained health advisers for support with partner notification.

B Patients should be offered the choice of patient, provider or conditional referral.

C In men with symptomatic Ct infection, contact all partners over the four weeks prior to onset of symptoms.

C In women and asymptomatic men, contact all partners over the last six months or the most recent sexual partner (if outwith that time period).

Patient referral: index patients themselves inform their sexual contacts to seek treatment.

Provider referral: the health care provider informs a patient's contacts anonymously that they should seek treatment.

Conditional referral: the health care provider notifies contacts if the patient has not done so after a given number of days.

FOLLOW-UP

B Patients should be interviewed at follow-up with regard to compliance with therapy and risk of re-infection.

B In those patients who have been compliant with therapy and in whom there is no risk of re-infection, a test of cure need not be performed.

B Test of cure/re-infection established by molecular amplification assay should be performed a minimum of three weeks after the initiation of therapy, to avoid false positive results.

HEALTH EDUCATION

B All patients with Ct infection should receive appropriate health education, including relevant reading materials.

B Opportunities should be taken to deliver education in a wide variety of non-health care settings (e.g. youth clubs, community centres, schools). Education about chlamydial infection should be integrated with other sexual health education and condom promotion initiatives.

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Derived from the national clinical guideline recommended for use in Scotland by the Scottish Intercollegiate Guidelines Network (SIGN)

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Available on the SIGN website: www.sign.ac.uk

This guideline was issued in March 2000 and will be reviewed in 2002