Complete Summary

GUIDELINE TITLE

Chlamydia trachomatis. In: Sexually transmitted infections: UK national screening and testing guidelines.

BIBLIOGRAPHIC SOURCE(S)

Carder C, Mercey D, Benn P. Chlamydia trachomatis. In: Ross J, Ison C, Carder C, Lewis D, Mercey D, Young H. Sexually transmitted infections: UK national screening and testing guidelines. London (UK): British Association for Sexual Health and HIV (BASHH); 2006 Aug. p. 26-32. [9 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Chlamydia trachomatis infection

GUIDELINE CATEGORY

Diagnosis
Evaluation
Screening

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Urology

INTENDED USERS

Advanced Practice Nurses
Clinical Laboratory Personnel
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

- To provide advice on what tests for *Chlamydia trachomatis* are most appropriate in a United Kingdom genitourinary (GU) clinic setting (excluding human immunodeficiency virus [HIV]-infected patients)
- To provide a basis for audit
- To support clinics when bidding for additional resources to meet national standards

TARGET POPULATION

Individuals in the United Kingdom with or at risk for *Chlamydia trachomatis* infection

INTERVENTIONS AND PRACTICES CONSIDERED

1. Nucleic acid amplifications tests (NAATs) (first choice test for urethral, cervical, and first catch urine specimens)
2. Tissue culture (TC)
3. Direct fluorescent antibody (DFA)
4. Enzyme immune assay (EIA)
5. "Point of care"/serological tests/leukocyte esterase tests (considered but not recommended)
6. Sampling according to pack inserts from manufacturer's kits from the following sites as appropriate: cervix, urethra, pharynx, rectum, and vulva/vagina
7. Special considerations for screening of heterosexual women, heterosexual men, homosexual men, young women, young men, pregnant women, sexual contacts, sex workers, and victims of sexual assault
8. Test of cure when appropriate

MAJOR OUTCOMES CONSIDERED

Test sensitivity and specificity

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A Medline search using the terms *Chlamydia trachomatis*, *diagnosis*, and *genital* from 1996 to Jan 2004 was conducted, and the most relevant references are included.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Ia: Evidence obtained from meta-analysis of randomised controlled trials

Ib: Evidence obtained from at least one randomised controlled trial

IIa: Evidence obtained from at least one well designed controlled study without randomisation

IIb: Evidence obtained from at least one other type of well designed quasi-experimental study

III: Evidence obtained from well designed non-experimental descriptive studies

IV: Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The guidelines have been developed following the methodological framework of the Appraisal of Guidelines Research and Evaluation instrument (AGREE - adapted as described in *Int J STD and AIDS* 2004 15:297-305).

The extent to which the guideline represents the views of intended users has been addressed primarily by the authorship coming from the multidisciplinary membership of the Bacterial Special Interest Group (BSIG). As practising clinicians the authors were able to draw on their experience of applying the tests to symptomatic and asymptomatic patients, but it was not feasible to obtain formal input from representative patients.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grading of Recommendations

A. Evidence at level Ia or Ib
B. Evidence at level IIa, IIb, or III
C. Evidence at level IV

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

After drafting, other health care professionals and professional bodies in genitourinary (GU) medicine were asked to comment, the draft guidelines posted on the British Association for Sexual Health and HIV (BASHH) website for 3 months, and all comments reviewed before final publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the level of evidence (**I-IV**) and grade of recommendation (**A-C**) are provided at the end of the "Major Recommendations" field.

Available Tests

Nucleic Acid Amplification Tests (NAATs)

The role of the nucleic acid amplification technology in the routine diagnosis of *Chlamydia Trachomatis (C. trachomatis)* infections is evolving rapidly. Three commercial assays are now available for routine use:

- Polymerase chain reaction (PCR; Roche Diagnostics)
- Strand displacement amplification (SDA; Becton Dickinson)
- Transcription mediated amplification (TMA; GenProbe)

Although these commercial assays differ in their target sequence and their method of amplification, it is their ability to produce a positive signal from theoretically a single copy of the target DNA or RNA (see pack inserts from the kit manufacturers) that has lead to the reported increased sensitivity of NAATs. Similar to other nonculture tests, NAATs do not require viable organisms.

With the advent of molecular diagnostic technology, it is now appreciated that no single test provides 100% sensitivity and specificity. Currently, NAATs are proving to be the best tests on the market. There is no room for complacency, however, as further work is required to eliminate test problems, such as inhibitors, contamination, reproducibility, and hormonal factors, that have played a part in lowering sensitivity.

Confirming Positive NAATs by Another Technique

Only another NAAT is sensitive enough to confirm a positive result. This approach needs further evaluation, as it is rare that individual laboratories will be able to offer more than one NAAT platform.

Equivocal Results

Re-test the original sample (according to manufacturer's instructions).

Inhibition

Inhibitors can be identified from all sites, in particular first-void urine. An internal amplification control to identify inhibition should be used and is available using some of the commercial kits. The Gen-Probe TMA test has a stage in the extraction process which the manufacturer claims removes the majority of inhibitors and therefore no inhibitory control is needed (see individual manufacturer's instructions).

Pooling Samples

This is possible and improves cost efficiency but is not licensed. Optimal pool sizes will vary according to the prevalence in the population being tested.

Tissue Culture (TC)

The traditional method of diagnosing *C. trachomatis* was by cell culture. However, few laboratories in the United Kingdom (UK) still offer this service. Cell culture procedures are expensive, labour intensive and time consuming.

Although chlamydiae are bacteria, they cannot be cultivated in non-living or cell free media. Tissue culture techniques vary among laboratories. With no standardised protocol it is difficult to compare interlaboratory performance. Cell culture detects only viable organisms, and hence, as with any other bacterial investigation the specimen collection and transport to the laboratory has to be optimal, irrespective of which laboratory method is to be used. Even under ideal conditions the sensitivity is probably no more than 75%, although specificity should be 100% if a *C. trachomatis*- major outer membrane protein (MOMP)-specific stain is used.

Direct Fluorescent Antibody (DFA)

Specimen material is obtained with a swab or brush, which is then rolled over the specimen well of a slide. Once air dried and fixed the specimen can be stained using either a MOMP or lipopolysaccharide (LPS) fluorescein-labelled monoclonal antibody that binds to *C. trachomatis* elementary bodies. Stained elementary bodies can then be identified using a fluorescence microscope. This technique is ideally suited for small numbers. It can give a quick turnaround time, but its sensitivity and specificity are dependent on the expertise of the laboratory. DFA detects both viable and non-viable organisms.

This is the only test allowing simultaneous assessment of specimen adequacy.

Enzyme Immuno Assay (EIA)

There are many commercially available EIA tests on the market for detecting *C. trachomatis* infection. They detect chlamydial LPS with a monoclonal or polyclonal antibody that has been labelled with an enzyme. The enzyme converts a colourless substrate into a coloured product, which is detected by a spectrophotometer.

As the EIA detects LPS, there is a potential that cross reaction occurs with other microorganisms causing a false positive reaction, hence it is vital that confirmation either by DFA or blocking antibody test is performed.

Sensitivity has been shown to be lower than for NAATs.

"Point of Care"/Serological Tests/Leukocyte Esterase Tests

As they stand at present, these tests are not advised for diagnosis of genital *C. trachomatis* in the genitourinary medicine (GUM) setting (**Grade of Recommendation C**).

Recommendations

Because of the superior sensitivity and good specificity of NAATS these are the tests of choice for urethral, cervical and first catch urine specimens (**Grade of Recommendation A**).

Sites for Testing

Guidance on how to take samples can be made by following the pack inserts from the different manufacturer's kits.

First Catch Urine (FCU) — Grade of Recommendation C

- First 15 to 50 mls of urine passed anytime of the day. Patient must not have urinated for at least one hour (maybe 2 hours for some kits). Follow manufacturer's instructions.
- First catch urine (FCU) is both male and female licensed for most NAATs, although less sensitive than from urethral or endocervical specimens.
- Male urine is licensed for some EIAs, shown to be sensitive with symptomatic, relatively insensitive for asymptomatic males.
- Female urine is unsuitable for EIAs.
- Urine is suitable but not ideal for DFA, needs expertise.
- Urine is unsuitable for tissue culture techniques.

Cervical, (Cx)

Cervical samples are suitable for all tests. Taken under speculum examination, the swab inserted into the os using the manufacturer's swab collection packs and rotated two or more times for 15 to 30 seconds (**Grade of Recommendation C**).

Urethral, (Ur)

- Both male and female urethral samples are suitable for all tests.
- For men the swab is inserted into the urethra 2 to 4 cm and rotated one or more times (**Grade of Recommendation C**).

Pharynx, (Ph)

- Pharyngeal samples licensed for tissue culture technique (**Grade of Recommendation A**).
- DFA is licensed for pharyngeal swab specimens but not suitable for large throughput use (**Grade of Recommendation C**).
- Not licensed for most EIAs.
- NAAT not licensed but increasing work on validation means that for any centre without access to culture this is the test of choice (**Grade of Recommendation C**).

Rectal, (Re) (obtained via proctoscopy)

- Rectal samples validated for tissue culture technique (**Grade of Recommendation A**).
- DFA is licensed for rectal swab specimens but not suitable for large throughput use (**Grade of Recommendation C**).

- Not licensed for EIA testing owing to the cross reaction with other organisms leading to false positive EIA results.
- Routinely available NAATs for *C. trachomatis* will detect all serovars including lymphogranuloma venereum (LGV) serovars and are licensed for genital specimens. There are no licensed NAATs for the detection of *C. trachomatis* in rectal specimens but data is available supporting the validity of these tests for use with rectal specimens and therefore for centres without access to culture this is the test of choice (**Level of Evidence III, Grade of recommendation B**).

Vulval-Vaginal, (VV)

Not licensed for use with NAATs, but demonstrated by a number of workers to produce equivalent sensitivity to cervical testing.

Table 1: Summary of Recommended Tests for Use with Different Sites of Samples

	Sites					
Test	**FCU**	**Cx**	**Ur**	**Ph**	**Re**	**VV**
NAAT	1	1	1	3	3	3
ELISA	4	2	2	5	5	5
DFA	2	2	2	2	2	5
TC	5	2	2	1	1	5

FCU, first catch urine; Cx, cervix; Ur, urine; Ph, pharynx; Re, rectal; VV, vulval/vaginal; NAAT, Nucleic Acid Amplification Tests; ELISA, enzyme-linked immunosorbant assay; DFA, direct fluorescent antibody; TC, tissue culture

Key

1. Test of choice
2. Acceptable, but not first choice
3. Not licensed, although encouraging work being performed
4. Only for use in asymptomatic males
5. Not recommended

All recommendations are at level B unless stated otherwise.

Screening in the Following Patient Groups

Owing to the frequently asymptomatic nature of genital *C. trachomatis* there is no difference in the screening guidelines for those showing symptoms to those who do not.

Frequency of Repeat Testing in an Asymptomatic Patient

This is in part being addressed by the Department of Health (DoH) Chlamydia Screening Programme. Re-exposure to a possible source of chlamydia should lead to re-screening if the patient re-presents.

Heterosexual Women

Cervical or vulval-vaginal (clinician or self taken) or first catch urine (**Grade of Recommendation A**)

Heterosexual Men

Urethral or first catch urine (**Grade of Recommendation A**)

Homosexual Men

Urethral or first catch urine (**Grade of Recommendation A**)

Young Women

- Offer non-invasive tests if speculum examination is declined
- Vulval-vaginal (clinician or self-taken) or first catch urine (**Grade of Recommendation A**)

Young Men

- Offer non-invasive testing if urethral specimen is declined
- First catch urine (**Grade of Recommendation A**)

Pregnant Women

As for heterosexual women. See notes below on test of cure (TOC).

Contacts

No different advice

Sex Workers

No different advice

Sexual Assault Victims

Culture was the recommended method for detecting *C. trachomatis* at all exposed sites following sexual assault in adults because of 100% specificity (**Grade of Recommendation C**). This guideline recommends that a NAAT be taken from all exposed sites in addition to a chlamydial culture (if culture is available) owing to the low sensitivity of culture and lack of availability.

Test of Cure (TOC)

Test of cure is not routinely recommended if standard treatment has been given, there is confirmation that the patient has adhered to therapy and there is no risk of re-infection. However, if these criteria cannot be met or if the patient is pregnant a TOC is advised. This should be taken using the same technique as used for the initial testing. Ideally, a minimum of 3 to 5 weeks post treatment is required as NAATs will demonstrate residual DNA/RNA even after successful treatment of the organism (**Grade of Recommendation A**).

Definitions:

Levels of Evidence

Ia: Evidence obtained from meta-analysis of randomised controlled trials

Ib: Evidence obtained from at least one randomised controlled trial

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IIb: Evidence obtained from at least one other type of well designed quasi-experimental study

III: Evidence obtained from well designed non-experimental descriptive studies

IV: Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

Grading of Recommendations

A. Evidence at level Ia or Ib
B. Evidence at level IIa, IIb, or III
C. Evidence at level IV

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Accurate diagnosis of *Chlamydia trachomatis* infection

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The availability of different microbiology tests may vary and use of optimal tests as outlined in this guideline may have resource implications.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Carder C, Mercey D, Benn P. Chlamydia trachomatis. In: Ross J, Ison C, Carder C, Lewis D, Mercey D, Young H. Sexually transmitted infections: UK national screening and testing guidelines. London (UK): British Association for Sexual Health and HIV (BASHH); 2006 Aug. p. 26-32. [9 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Aug

GUIDELINE DEVELOPER(S)

British Association for Sexual Health and HIV - Medical Specialty Society

SOURCE(S) OF FUNDING

No specific or external funding was sought or provided in the development of this guideline.

GUIDELINE COMMITTEE

Screening Guidelines Steering Committee
Clinical Effectiveness Group (CEG)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: Caroline Carder, University College, London Hospitals Trust; Danielle Mercey, UCL; Paul Benn, Camden, PCT

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Caroline Carder has been funded to attend conferences by various diagnostic companies.

Danielle Mercey: None declared

Paul Benn: None declared

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from British Association for Sexual Health and HIV Web Site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Specifications for the development of UK guidelines on the management of sexually transmitted infections (STIs) and closely related conditions 2005. London (UK): British Association of Sexual Health and HIV (BASHH); 2005. 14

p. Electronic copies: Available in Portable Document Format (PDF) from the British Association for Sexual Health and HIV Web site.

Additionally, auditable outcome measures can be found in the original guideline document.

PATIENT RESOURCES

None available

NGC STATUS

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