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# Diagnosis of *Chlamydia trachomatis* Infection

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## 1. Introduction

With the use of molecular medicine as part of routine laboratory evaluation of patients, the diagnosis of infection with has undergone a metamorphosis in the last 30 years. However, it remains a debated process as molecular testing is to date not accepted as definitive in most clinical settings, and more historic testing methods like cell culture, has not been completely rendered redundant[1]. Infection with *Chlamydia trachomatis* is therefore a complex condition to diagnose, and requires a clear understanding of testing methods and the inherent advantages and disadvantages to each. The modern approach to the diagnosis of *Chlamydia trachomatis* typically involves a combination of assays as part of screening and confirmation[2].

Patients very often manifest very few clinical symptoms and rarely seek medical assistance. For this reason, continued transmission occurs to sexual partners[3] causing *Chlamydia trachomatis* to be the most common sexually transmitted bacterial infection worldwide[3, 4]. Due to these disease and pathogen characteristics, prevalence of this pathogen seems to be increasing in both developing and developed countries[5-8]. Correct diagnosis of infection with *Chlamydia trachomatis* is essential as false negative results may have significant impact on societal health[9]. Chlamydial infections has been associated with a higher risk of acquiring HIV-1 infection[4, 10] as well as cervical cancer[11] and adverse outcomes with pregnancy[12, 13]. For these reasons, early correct diagnosis of infection with Chlamydia trachomatis is essential to prevent long-term sequelae associated with prolonged infection.

## 2. Specimens, collection and transport

### 2.1 Clinical specimens

*Chlamydia trachomatis* is very often asymptomatic in female patients, but may present with cervicitis, endometritis, pelvic inflammatory disease or Bartholin abscesses[14, 15]. Urethritis and proctitis is often a secondary manifestation, found in conjunction with other sites of infection[16]. In heterosexual men, urethral infection accounts for most symptomatic cases[17, 18], with ascending infection causing epididymitis[19]. Among homo- and bisexual men, sites of infection are also predominantly the urethra[20], but further includes the

rectum[21]. Infection in infants may cause conjunctivitis as well as pneumonia, particularly in early infancy [22, 23]. Serovars L1-3 is associated with lymphogranulomavenereum (LGV), and is particularly prevalent in areas of Africa, Asia and South America[24]. Clinically, these patients present with a painless genital ulcer, which later progress to lymphadenopathy[24]. They occasionally develop systemic symptoms[25].

### 2.2 Specimen collection

Chlamydiae are intracellular organisms, and it is therefore essential to obtain host cells with the clinical sample to so ensure yield of organisms[2]. The sensitivity and specificity of any test for *Chlamydia trachomatis*, is highly dependent on sampling and adequacy of the sample obtained[26-28]. This holds true irrespective of testing type, whether it be culture, where viable organisms need to be obtained, or nucleic acid based testing, where non-viable genetic material can be obtained[29]. Although relatively standardized methods for sampling is advocated for direct testing, certain commercially available tests have unique sampling requirements, stipulated in the package insert[2].

In women, the endocervix is most commonly targeted for obtaining samples for culture, by utilizing either a swab or a cytologic brush. In the case of swabs, careful consideration should be taken as certain types of swabs may actually inhibit growth by being directly toxic to either the organisms or the cell culture[30]. Similarly, wooden-shafted swabs also inhibit growth. Optimal sample can be obtained using Dacron, cotton, rayon or calcium alginate-tipped swabs with plastic shafts[31]. Prior to obtaining the sample, the cervical os should be cleared of secretions and discharges, to so reduce bacterial contamination and possible toxicity. This also improves the quality and ease of interpretation of direct fluorescent antibody stains[32, 33]. Sampling should be performed by inserting the swab approximately 1-2 cm into the cervical os, rotating it, and keeping it in situ for 15 to 30 seconds. Using swabs are less likely to induce bleeding[34], which in itself may also inhibit culture, but typically has a lower cell yield than cytological brushes[28]. For this reason, some authors have advocated against the use of a cytological brush, provided sampling with a swab is performed adequately[35]. Furthermore, culture yields have been improved by combining endocervical with urethral sampling[36]. Sampling is similar to male urethral sampling, however, the swab is inserted only 1cm past the urethral opening[2].

In male patients, the anterior urethra is the site of choice for optimal sampling, especially for culture purposes. A dry swab is inserted 3 to 4 cm past the meatal opening of the urethra, rotated and removed. It is important to note that urination should best be avoided for at least 1 hour prior to sampling, as this significantly reduces the yield of cells obtained during sampling[2].

Cases of conjunctivitis should be investigated by first removing the gross purulent discharge. Thereafter, the eye should be swabbed on the palpebral conjunctival surface, to so obtains some epithelial cells[2].

In cases of LGV, sampling can be in the form of swabs from ulcers, saline aspirates from the bubo or biopsies. To ensure adequacy of deep-seated ulcers, these biopsies may be best performed under direct vision through proctoscopy[37].

### 2.3 Specimen transport

Culture yield is significantly improved if samples are transported to the laboratory for processing within 48 hours, and kept at 2 to 8°C during this time. The practice of freezing samples should be restricted to settings where significant delay is expected, as freezing at -70°C is associated with up to 20% loss in viability, and freezing at -20°C even higher losses[30, 38].

Various formulations of transport media have been used[39-41] as it may improve yield. This is because it typically contains fetal bovine serum to improve viability as well as antimicrobials, to suppress growth by other organisms. The formulation used is similar to transport media used for rickettsiae, but not viral transport media, as this typically contains penicillin[39, 40, 42].

### 2.4 Sampling for non-culture-based testing

Although typically very similar to culture based testing, non-culture based testing requires sampling and transport as specified by the manufacturers for the particular assay[43, 44]. Urine-based testing has also been advocated for molecular testing. This has the added advantage that simultaneous testing can be performed for other pathogens like *Neisseria gonorrhea* as well as being non-invasive. However, the yield on urine samples are greater if it is a first-catch sample obtained 1 to 2 hours after prior urination, to so increase the amount of columner epithelial cells[45, 46]. If sampling is performed in excess of 3 hours after last void, specificity and sensitivity is reduced in females, but in male patients, controversy still exists[47, 48]. Some authors have reported that preceding cleaning performed in culture samples for females, should not be performed in this setting to so improve yield[46]. Novel testing methods now include sampling the vaginal introitus or vulva with promising results. The major advantage to this is that patients can self-sample[49].

## 3. Laboratory methods

### 3.1 Direct detection

#### 3.1.1 Culture-based testing

Historically, culture-based testing was considered the gold standard for diagnosis of *Chlamydia trachomatis*, and specificity was considered to approach 100%[50-52]. This high specificity is at the cost of sensitivity, which in a best-case scenario is estimated at 70 to 85%[52]. Appropriate sampling and transport is absolutely essential to ensure organism viability.

Culture is performed using cell monolayers in dram or shell vials. Cell types permissive to infection include McCoy cells[53-55], HeLa229 cells[56, 57] and BGMK cells[58, 59]. Certain pretreatment steps have been advocated to improve culture yield. These include administration of DEAE-dextran[56, 60], sonication[61] and centrifugation[60]. These cell cultures are maintained using Eagle's minimal essential medium (EMEM) with additional amino acids, vitamins, glucose, foetal calf serum and L-glutamine[2]. Although blind passaging has been shown to improve recovery by 3 to 10%[62], it leads to a significantly delay in obtaining results.

Following culture, the presence of *Chlamydia trachomatis* needs to be confirmed. Firstly, various stains have been used including various Romanovsky stains and iodine staining. These

methods lack sensitivity and specificity and require an experienced microscopist[54, 63, 64]. The iodine stain is based on the premise of glycogen binding. However, normal cervical cells also contain glycogen, and therefore may impact on specificity[2]. Fluorescent dye based confirmation shows improved sensitivity and specificity, as it utilizes fluorescently labeled antibodies targeting either the major outer membrane protein (MOMP) or the chlamydial lipopolysaccharide (LPS) following approximately 48 to 72 hours of incubation. Sensitivity seems to be higher with MOMP based assays, as these are more widely distributed on the cells within culture[1]. Alternatively, these methods can also be applied to shell vial based cultures, to so improve turn-around times of results and sensitivity[54, 55].

### 3.1.2 Antigen detection methods

Wide arrays of validated immunoassays are currently available[65-77]. Direct fluorescent antibody (DFA) testing can be utilized directly on clinical samples. As for culture-based confirmation, two antigenic sites can be utilized as targets, namely the MOMP and LPS. Assays targeting the LPS are specific to Chlamydia spp and are not considered specific to *Chlamydia trachomatis*. These antigens are not as widely distributed as MOMP, and sensitivity of these assays are therefore inferior to those targeting MOMP[2]. The MOMP based assays show specificity for *Chlamydia trachomatis*. These assays are validated for use on endocervical smears and male urethral swabs[78-80] but can be applied to urethral samples[78, 81], conjunctival swabs[82, 83], rectal smears[84] and respiratory samples from infants[85, 86]. DFA testing is a rapid method, with the added advantage providing simultaneous information on the quality of the sample, by way of visualizing presence of columner epithelium in adequate samples. However, the process is laborious and requires an experienced microscopist[2]. Evaluation of DFA methods with external quality programs by the College of American Pathologist (ACP) showed significant variability in results depending on the experience level of the laboratory[80]. It has been clearly established that in the absence of a quality assurance program, more than 10% of samples will be of inadequate quality for processing[27, 35]. For this reason, specimen adequacy can be evaluated by direct examination of the sample – an advantage that only the DFA assays hold.

Immunochemical detection (EIA) can be performed either directly, targeting LPS or indirectly, by detecting anti-Chlamydial antibodies (discussed later). The LPS antigen is more abundant albeit irregularly distributed as compared to MOMP antigen. Prior to performing the EIA assays, samples are lysed, releasing large amounts of LPS thereby improving sensitivity. However, cross-reaction may occur with gram negative organisms to the detriment of specificity[62, 87-89]. To alleviate this issue, some manufacturers produce blocking assays to verify all positive results[90]. With these assays, positive tests are repeated following a pretreatment step where Chlamydial-specific monoclonal antibodies are added to the sample. True positive results will test negative on blocking assays, where false positive results will remain positive[91].

Point-of-Care testing assays are also available. These assays utilize EIA technology targeting LPS, with similar diagnostic problems with poor specificity as with laboratory based testing[65, 92, 93].

Molecular detection of nucleic acids are becoming more common, utilizing various molecular technologies. These can either utilize biological amplification (detection of ribosomal RNA) or laboratory based amplification technology like polymerase chain reaction (PCR)[94]. DNA

probes have been designed in commercially available assays targeting the 16S rRNA[95, 96]. These assays are estimated to be 1 log more sensitive as compared to EIA based assays. Specificity is reduced if samples are blood stained, as this may cause autofluorescence[2]. Some manufacturers also produce a confirmatory competitive assay, similar to those described for EIA[44, 97] to improve specificity. Furthermore, certain manufacturers offer combined assays testing for both *Chlamydia trachomatis* and *Neisseria gonorrhea*[98]. Nucleic acid amplification techniques offers the advantage of being highly sensitive and providing a platform for less invasive sampling[52]. Sensitivity may in fact be a diagnostic problem, as DNA amplification techniques have obtained positive results from environmental samples obtained from health care settings[2]. However, provided that sampling is performed with the same care as for culture, this should only be a theoretical diagnostic issue. Commercially available techniques utilized have largely focused on PCR[94, 99, 100], ligase chain reaction[101, 102] and strand displacement assays (SDA)[103], amongst others[104, 105]. Further development into real-time[106, 107] and multiplexed based platforms[108], as well as nesting steps[109] has also improved diagnostic utility.

Inherent to the nature of nucleic acid detection methods, genetic variation may lead to a reduction in sensitivity of assays. A genetic variant was described in Sweden in 2007, which contained a 377bp deletion in the cryptic plasmid[9]. This resulted in false negative results by both the Roche COBAS AMPLICOR and Abbott LCx C trachomatis assays[110, 111], and on a community level, to unrestricted spread to these stains[110, 111]. For this reason, some authorities have called for all diagnostic assays to target at least two genetic sites within the pathogen[112].

### 3.2 Indirect detection

Historically, serological testing has been used in investigation of women with pelvic inflammatory disease[113], ectopic pregnancies[114], recurrent miscarriages[12] and tubal infertility[115]. Despite this, serological testing to identify Chlamydia specific antibodies is not considered to be useful in the diagnosis of genital tract infection, for a number of reasons. Firstly, these antibodies are long-lived and do not distinguish between previous and current infection. Comparing antibody titers from acute and convalescent sera typically makes this distinction. This sampling window may be required to be as long as 1 month, and this type of diagnostic delay is not acceptable in modern laboratory medicine. Secondly, positivity is not specific for *Chlamydia trachomatis*, but rather Chlamydia spp., rendering interpretation of positive serology even more problematic[2]. Serological testing is considered appropriate in only two clinical settings. Firstly, use of Chlamydia specific IgM in the diagnosis of pneumonitis in infants, and secondly, significant rise in Chlamydial titers (≥32) in the diagnosis of LGV[24]. The practical application of this test is more difficult as the initial ulcers are typically painless and patients often do not present at health care facilities in the acute phase[2].

Various testing procedures have been employed in detecting Chlamydial antibodies. Historically, complement fixation (CF) was utilized in many diagnostic laboratories. For this method, a single titer of ≥256 is strongly predictive of LGV versus a titer lower than 32 showing good performance as a rule out test[116]. A further consideration with this assay is the requirement of biosafety level (BSL) 3 conditions[117]. Additionally, high quality antigen is not always available as these reagents are usually prepared from guinea pigs, which can be co-infected with *Chlamydia psittaci* [118].

Microscopic immunofluorescence testing (MIF) was long considered the test of choice for the diagnosis of chlamydial pneumonitis in infants, as this was utilized to identify IgM specifically[119, 120]. Historically, it was used in the description of the original 15 serovars described for *Chlamydia trachomatis* [121, 122]. This assay however is laborious and time-consuming and is therefore usually not employed as a routine diagnostic test[2] as this antigen is produced from infected egg yolk in the form of elementary bodies[2].

Enzyme immunoassay methods (EIA) are commercially available, typically targeting the LPS. A positive result in isolation does not distinguish between active or previous infection and may also be due to cross-reaction with antibodies for *Chlamydia pneumonia* or *psittaci*[123, 124]. Generally, EIA based testing is considered to be less sensitive compared to immunofluorescent-based testing[125], however, recently developed assays seem to show adequate sensitivity and specificity for use in a high throughput setting[126]. In a recent study by Baud et al, various serological platforms were evaluated. The CT-IgG-pELISA by Medac (Wedel, Germany) and automated epifluoroscence immunoassay by InoDiag (Signes, France) performed adequately, but still inferior to conventional immunofluorescence assays. The CT pELISA by R-Biopharm (Darmstadt, Germany) had sensitivities and specificities comparable to gold standard assays. These authors therefore considered this assay as an alternative option in a high throughput setting[126].

## 4. Defining the new "Gold Standard" assay

The FDA expanded its definition of a true positive result in 1992 to include a combination of culture and non-culture based testing[127]. The Centers for Disease Control and Prevention (CDC) classifies diagnosis as definitive, presumptive and suggestive (Table 1)[87].

| | |
|---|---|
| Definitive<br>Requires either of criteria | 1. Culture isolation with confirmation<br>2. Any two of the following<br>- DFA of exudate<br>- EIA of exudate<br>- NAT testing |
| Presumptive<br>Requires both criteria | • Presence of clinical symptoms<br>• Detection by non-culture based test |
| Suggestive<br>Requires 1st criterion with either 2nd or 3rd | • Clinical symptoms<br>• Exclusion of other causes of discharge or exudate<br>• Sexual exposure to person with *C trachomatis* or nongonococcal urethritis, mucopurulent cervicitis or PID |

Table 1. Diagnostic criteria for *Chlamydia trachomatis* published by the CDC[87]

The definition of the so-called "Gold Standard" testing assay is important for two reasons. Firstly, all commercially available tests will be measured against this standard to define performance characteristics. In the past, performance was gauged simply on culture results, leading to overestimation of sensitivity[2]. And secondly, this will impact on testing algorithms depending on local epidemiology and prevalence[128]. The issue of prevalence is particularly complex in the case of Chlamydial infection as this not impacts on test

performance, but it has also been shown that females in low prevalence settings (defined as ≤5%) seem to have a lower chlamydial load, further reducing testing sensitivity[129-131]. In its most extreme form, asymptomatic patients seem to have the worst sensitivity in testing[132]. Therefore, in these settings, the CDC advocates highly sensitive testing with confirmation of all positive samples[15].

Recently, some authors have not only advocated use of NAT testing as the only gold standard[133], but rather specific assays like the BD ProbeTec ET (Becton Dickinson Diagnostic Systems, Maryland, USA), the COBAS TaqMan ST test v2.0 (Roche Diagnostics, New Jersey, USA) and the Aptima Combo 2 (Gen-Probe, San Diego, USA)[134]. Not only are these assays highly sensitive and specific, these can be easily implemented in a high throughput laboratory[133, 135-138].

## 5. Comparison of methods

Currently, three molecular assays dominate molecular diagnostics of *Chlamydia trachomatis*. The Gen-Probe Aptima Combo 2 (AC2) targets the 23S rRNA molecule, whereas the Roche Cobas TaqMan CT assay targets both the cryptic plasmid and the *omp*1 gene. The Abbot RealTime CT m2000 PCR targets two parts of the cryptic plasmid[139]. All of these assays can successfully detect the new variant strain, first described in Sweden[140]. Despite very good performance by all these assays, the Gen-Probe assay seems to have superior sensitivity (99.3%) and equally good specificity (99.9%) as the Abbott m2000 assay. The Roche TaqMan assay shows superior specificity (100%), but with sensitivity estimated at 82.4%[139]. These platforms have differing performance characteristics and use different pre-amplification processing steps. Since the quality of results is comparable, the true choice of assay lies by en large in the platform and pre-processing preferences.

## 6. References

[1] CDC: Sexually transmitted diseases clinical practice guidelines. In. Edited by Prevention CfDCa; 1991.

[2] Black C: Current methods of Laboratory Diagnosis of *Chlamydia trachomatis* Infections. *Clin Microbiol Rev* 1997, 10(1):160-184.

[3] Peipert J: Clinical practice. Genital chlamydial infections. *N Engl J Med* 2003, 349:2424-2430.

[4] Manavi K: A review on infection with *Chlamydia trachomatis*. *Best Pract Res Clin Obstet Gynaecol* 2006, 20:941-951.

[5] Baud D, Jaton K, Bertelli C, Kulling J, Greub G: Low prevalence of *Chlamydia trachomatis* infection in asymptomatic young Swiss men. *BMC Infect Dis* 2008, 8:45.

[6] Fine D, Dicker L, Mosure D, Berman S: Increasing chlamydia positivity in women screened in family planning clinics: do we know why? *Sex Transm Dis* 2008, 35:47-52.

[7] Lind I, Bollerup A, Farhot S, Hoffman S: Laboratory surveillance of urogenital *Chlamydia trachomatis* infections in Denmark 1988-2007. *Scand J Infect Dis* 2009, 41:334-340.

[8] Spiliopoulou A, Lakiotis V, Vittoraki A, Zavou D, Mauri D: *Chlamydia trachomatis*: time for screening? *Clin Microbiol Infect* 2005, 11:687-689.

[9] Rockett R, Goire N, limnios A, Turra M, Higgens G, Lambert S, Bletchly C, Nissen M, Sloots T, Whiley D: Evaluation of the cobas 4800 CT/NG test for detecting *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. *Sex Transm Infect* 2010, 86:470-473.

[10] Sangani P, Rutherford G, Wilkinson D: Population-based interventions for reducing sexually transmitted infections, including HIV infection. *Cochrane Database Syst Rev* 2004, 2:CD001220.

[11] Simonetti A, Melo J, Souza Pd, Bruneska D, Filho JdL: Immunological's host profile for HPV and *Chlamydia trachomatis*, a cervical cancer cofactor. *Microbes Infect* 2009, 11:435-442.

[12] Baud D, Regan L, Greub G: Emerging role of Chlamydia and Chlamydia-like organisms in adverse pregnancy outcomes. *Curr Opin Infect Dis* 2008, 21:70-76.

[13] Mardh P: Influence of infection with *Chlamydia trachomatis* on pregnancy outcome, infant helath and life-long sequelae in infected offspring. *Best Pract Res Clin Obstet Gynaecol* 2002, 16:847-864.

[14] Bleker O, Smalbraak D, Shutte M: Bartholin's abscess: the role of *Chlamydia trachomatis*. *Genitourin Med* 1990, 66:24-25.

[15] CDC: Recommendations for the prevention and management of *Chlamydia trachomatis* infection. *Morbid Mortal Weekly Rep* 1993, 42(RR-12):1-39.

[16] Dunlop E, Goh B, Darougar S, Woodland R: Triple culture tests for the diangosis of Chlamydial infection of the female genital tract. *Sex Transm Dis* 1985, 12:68-71.

[17] Stamm W, Cole B: Asymptomatic *Chalmydia trachomatis* urethritis in men. *Sex Transm Dis* 1986, 13:163-165.

[18] Zelin J, Robinson A, Ridgway G, Allason-Jones E, Williamson P: Chlamydial urethritis in heterosexual men attending a genitourinary medicine clinic: prevalence, symptoms, condom usage and partner change. *Int J STD AIDS* 1995, 6:27-30.

[19] Berger R, Alexander E, Harnish J, Paulsen C, Monda G, Ansell J, Homes K: Etiology and therapy of acute epididymitis: prospective study of 50 cases. *J Urol* 1979, 121:750-754.

[20] Stamm W, Koutsky L, Benedetti J, Jourden J, Brunham R, Holmes K: *Chlamydia trachomatis* urethral infections in men. Prevalence, risk factors, and clinical manifestations. *Ann Intern Med* 1984, 100:47-51.

[21] Rompalo A, Roberts P, Johnson K: Empirical therapy for the management of acute proctitis in homosexual men. *JAMA* 1988, 260:348-353.

[22] Claesson B, Trollfors B, Brolin I, Granstrom M, Henrichsen J, Jodal U, Juto P, Kallings I, Kanclerski K, Lagergard T: Etiology of community-acuired pneumonia in children based on antibody response to bacterial and viral antigens. *Pediatr Infect Dis* 1989, 8:856-862.

[23] Hammerschlag M, Cummings C, Roblin P, Williams T, Delke I: Efficacy of neonatal ocular prophylaxis for the prevention of chlamydial and gonococcal conjunctivitis. *N Engl J Med* 1989, 320(769-772).

[24] Perine P, Osoba A: Lymphogranuloma venereum. In: *Sexually transmitted diseases.* Edited by Holmes K, Mardh P, Sparling P, Wiesner P. New York: McGraw Hill Book Co; 1990: 195-204.

[25] Pearlman M, McNeely S: A review of the microbiology, immunology, and clinical implications of *Chlamydia trachomatis* infections. *Obstet Gynaecol* 1992, 47:448-461.

[26] Howard C, Friedman D, Leete J, Christensen M: Correlation of the precert of positive *Chlamydia trachomatis* direct fluorescent antibody detection tests with the adeuacy of specimen collection. *Diagn Microbiol Infect Dis* 1991, 14:233-237.

[27] Kellogg J, Seiple J, Klinedinst J, Levisky J: Impact of endocervical specimen uality of apparent prevalence of *Chlamydia trachomatis* infections diagnosed using an enzyme-linked immunosorbent assay method. *Arch Pathol Lab Med* 1991, 115:1223-1227.

[28] Moncada J, Schachter J, Shipp M, Bolan G, Wilber J: Cytobrush in collection of cervical specimens for detection of *Chlamydia trachomatis*. *J Clin Microbiol* 1989, 27:1863-1866.

[29] Kellogg J, Seiple J, Klinedinst J, Stroll E: Impact of endocervical specimen quality on apparent prevalance of *Chlamydia trachomatis* infections diagnosed using polymerase chain reaction, abstr. In: *Abstracts of the 95th General Meeting of the American Society for Microbiology 1995 American Society for Microbiology: 1995; Washington DC*. 86.

[30] Mahony J, Chernesky M: Effect of swab type and storage temperature on the isolation of *Chlamydia trachomatis* from clinical specimens. *J Clin Microbiol* 1985, 22(865-867).

[31] Mardh P, Zeeberg B: Toxic effect of sampling swabs and transportation test tubes on the formation of intracytopasmic inclusions of *Chlamydia trachomatis* in McCoy cell cultures. *Br J Vener Dis* 1981, 57:268-272.

[32] Embil J, Thiebaux H, MAnuel F, Pereira L, MacDonald S: Sequencial cervical specimens and the isolation of *Chlamydia trachomatis*: factors affecting detection. *Sex Transm Dis* 1983, 10:62-66.

[33] Hobson D, Karayiannis P, Byng R, Rees E, Tait I, Davies J: Quantitative aspects of chlamydial infection of the cervix. *Br J Vener Dis* 1980, 56:156-162.

[34] Akane A, Matsubara K, Nakumura H, Takahashi S, Kimura K: Identification of the heme compound copurified with deoxyribonucleic acid (DNA) from bloodstains, a major inhibitor of polymerase chain reaction amplication. *J Forensic Sci* 1994, 39:362-372.

[35] Kellogg J, Siple J, Klinedinst J, Levinsky J: Comparison of cytobrushes with swabs for recovery of endocervical cells and for Chlamydiazyme detection of *Chlamydia trachomatis*. *J Clin Microbiol* 1992, 30:2988-2990.

[36] Jones R, Katz B, Vanderpohl B, Caine V, Batteiger B, Newhall W: Effects of blind passage and multiple sampling on recovery of *Chlamydia trachomatis* from urogenital specimens. *J Clin Microbiol* 1986, 24:1029-1033.

[37] Fedorko D, Smith T: Chlamydial infections. In: *Laboratory methods for the diagnosis of sexually transmitted diseases.* Edited by Wentworth B, Judson F, Gilchrist M, 2nd edn. Washington DC: American Public Health Association; 1991: 95-125.

[38] Reeve P, Owen J, Oriel J: Laboratory procedures for the isolation of *Chlamydia trachomatis* from the human genital tract. *J Clin Pathol* 1975, 28:910-914.

[39] Gordon F, Harper I, Quan A, Treharne J, Dwyer R, Garland J: Detection of Chlamydia (Bedsonia) in certain infections of man. 1. Laboratory procedures: comparison of yolk sac and cell culture for detection and isolation. *J Infect Dis* 1969, 120:451-462.

[40] Nash P, Krenz M: Culture media. In: *Manual of clinical microbiology.* Edited by Balows A, Hausler W, Herrmann K, Isenberg H, Shadomy H, 5th edn. Washington DC: American Society for Microbiology; 1991: 1226-1288.

[41] Bovarnick M, Miller J, Snyder J: The influence of certain salts, amino acids, sugars and proteins on the stability of rickettsiae. *J Bacteriol* 1950, 59:509-522.

[42] Salmon V, Kenyon B, OVerall J, Anderson R: USe of a universal transport media in a commercial polymerase chain reaction assay for *Chlamydia trachomatis*, abstr. In: *Abstracts 6f the 10th Annual Clearwater Virology Symposium 1994: 1994*. 33.

[43] Hosein I, Kaunitz A, Craft S: Detection of cervical *Chlamydia trachomatis* and *Neisseria gonorrhoeae* with deoxyribonucleic acid probe assays in obstetric patients. *Am J Obstet Gynecol* 1992, 167:588-591.

[44] Limberger J, Biega R, Evancoe A, McCarthy L, Slivienski L, Kirkwood M: Evaluation of culture and the Gen-Probe PACE 2 assay for detection of *Neisseria gonorrhoea* and *Chlamydia trachomatis* in endocervical specimens transported to a state health laboratory. *J Clin Microbiol* 1992, 30:1162-1166.

[45] Chernesky M, Castriano S, Sellors J, Stewart I, Cunningham I, Landis S: Detection of *Chlamydia trachomatis* antigens in urine as an alternative to swabs and cultures. *J Infect Dis* 1990, 161(124-126).

[46] Chernesky M, Jang D, Chong S, Lee H, Sellors S, Mahony J: Order of urine collection affects the diagnosis of *Chlamydia trachomatis* infection in men by ligase chain reaction, GenProbe Pace II, Chlamydiazyme, and leukocyte esterase testing. In: *Abracts of the 11th Meeting of the International Society for STD Research 1995: 1995*. 180.

[47] Sellors J, Chernesky M, Pickard L, Jang D, Walter S, Krepel J, Mahony J: Effect of time elapsed since previous voiding on the detection of *Chlamydia trachomatis* antigens in urine. *Eur J Clin Microbiol Infect Dis* 1993, 12:285-289.

[48] Sugunendran H, Birley H, Mallinson H, Abbott M, Tong C: Comparison of urine, first and second endourethral swab for PCR based detection of genital *Chlamydia trachomatis* infection in male patients. *Sex Transm Dis* 2001, 77(6):423-426.

[49] Wiesenfeld H, Heine R, DiBiasi F, Repp C, Rideout A, Macio I, Sweet R: Self collection of vaginal introitus specimens: a novel approach to *Chlamydia trachomatis* testing in women, abstr 040. In: *Abstracts of the 11th Meeting of the International Society for STD Research 1995: 1995*. 42.

[50] Chernesky M, Jang D, Lee H, BUrczak J, Hu H, Sellors J, Tomazic-Allen S, Mahony J: Diagnosis of *Chlamydia trachomatis* infections in men and women by testing first-void urine by ligase chain reaction. *J Clin Microbiol* 1994, 32:2682-2685.

[51] Chernesky M, Jang D, Luinstra K, Chong S, Pickard L, Sellors J, Mahony J: Ability of ligase chain reaction and polymerase chain reaction to diagnose female lower genitourinary *Chlamydia trachomatis* infection by testing cervical swabs and first void urine. In: *Chlamydial infections Proceedings of the Eighth International Symposium on Human Chlamydial Infections: 1994; Bologna, Italy*. 326-329.

[52] Lee H, CHernesky M, Schachter J, Burczak J, Andrews W, Muldoon S, Leckie G, Stamm W: Diagnosis of *Chlamydia trachomatis* genitourinary infection in women by ligase chain reaction assay of urine. *Lancet* 1995, 345:213-216.

[53] Smith T, Brown S, Weed L: Diagnosis of *Chlamydia trachomatis* infections by cell cultures and serology. *Lab Med* 1982, 13:92-100.

[54] Stamm W, Tam M, Koester M, Cles L: Detection of *Chlamydia trachomatis* inclusions in McCoy cell cultures with fluorescein-conjugated monoclonal antibodies. *J Clin Microbiol* 1983, 17:666-668.

[55] Yoder B, Stamm W, Doester C, Alexander E: Microtest procedure for isolation of *Chlamydia trachomatis*. *J Clin Microbiol* 1981, 13:1036-1039.
[56] Kuo C, Wang S, Wentworth B, Grayston J: Primary isolation of TRIC organisms in HeLa 229 cells treated with DEAE-dextran. *J Infect Dis* 1972, 125:665-668.
[57] Rota T, Nichols L: Infection of cell culture by trachoma agent. Enhancement by DEAE-dextran. *J Infect Dis* 1971, 124:419-421.
[58] Johnston S, Siegel C: Comparison of Buffalo Green Monkey Kidney cells and McCoy cells for the isolation of *Chlamydia trachomatis* in shell vial centrifugation culture. *Diagn Microbiol Infect Dis* 1992, 15:355-357.
[59] Krech T, Bleckmann M, Paatz R: Comparison of Buffalo Green Monkey cells and McCoy cells for isolation of *Chlamydia trachomatis* in a microtitre system. *J Clin Microbiol* 1989, 27:2364-2365.
[60] Rota T, Nichols R: *Chlamydia trachomatis* in cell culture. 1. Comparison of efficiencies of infection in several chemically defined media, at various pH and temperature values, and after exposure to diethylaminoethyl-dextran. *Appl Microbiol* 1973, 26:560-565.
[61] Warford A, Carter T, Levy R, Rekrut K: Comparison of sonicated and nonsonicated specimens for the isolation of *Chlamydia trachomatis*. *Am J Clin Pathol* 1985, 83:625-629.
[62] Barnes R: Laboratory diagnosis of human chlamydial infections. *Clin Microbiol Rev* 1989, 2:119-136.
[63] Schoenwald E, Schmidt B, Steinmetz G, Hosmann J, Pohla-Gubo G, Luger A, Gasser G: Diagnosis of *Chlamydia trachomatis* infection - culture versus serology. *Eur J Epidemiol* 1988, 4:75-82.
[64] Stephens R, Kuo C, Tam M: Sensitivity of immunofluorescence with monoclonal antigodies for detection of *Chlamydia trachomatis* inclusions in cell culture. *J Clin Microbiol* 1982, 16:4-7.
[65] Skulnick M, Chua R, Simor A, Low D, Khosid H, Fraser S, Lyons E, Legere E, Kitching D: Use of the polymerase chain reaction for the detection of *Chlamydia trachomatis* from endocervical and urine specimens in an asymptomatic low-prevalence population of women. *Diagn Microbiol Infect Dis* 1994, 20:195-201.
[66] Basarab A, Browning D, Lanham S, O'Connell S: Pilot study to assess the presence of *Chlamydia trachomatis* in urine from 18-30-year-old males using EIA/IF and PCR. *Fam Plann Reprod Health Care* 2002, 28(1):36-37.
[67] Altaie S, Meier F, Centor R, Wakabongo M, Toksoz D, Harvey D, Basinger E, Johnson B, Brookman R, Dalton H: Evaluation of two ELISA's for detecting *Chlamydia trachomatis* from endocervical swabs. *Diagn Microbiol Infect Dis* 1992, 15:579-586.
[68] Biro F, Reising S, Doughman J, Kollar L, Rosenthal S: A comparison of diagnostic methods in adolescent girls with and without symptoms of Chlamydia urogenital infection. *Pediatrics* 1994, 93:476-480.
[69] Chan E, Brandt K, Horsman G: A 1-year evaluation of Syva Microtrak Chlamydia enzyme immunoassay with selective confirmation by direct immunofluorescent-antibody assay in a high-volume laboratory. *J Clin Microbiol* 1994, 32:2208-2211.
[70] Clark L, Sierra M, Daidone B, Lopez N, Covino J, McCormack W: Comparison of the Syva Microtrak enzyme immunoassay and Gen-Probe PACE 2 with cell culture for

diagnosis of cervical *Chlamydia trachomatis* infection in a high-prevalence female population. *J Clin Microbiol* 1993, 31:968-971.

[71] Domeika M, Bassiri M, Mardh P: Diagnosis of genital *Chlamydia trachomatis* infection in asymptomatic males by testing urine by PCR. *J Clin Microbiol* 1994, 32:2350-2352.

[72] Gaydos C, Reichart C, Long J, Welsh L, Neumann T, Hook E, Quinn T: Evaluation of Syva enzyme immunoassay for detection of *Chlamydia trachomatis* in genital specimens. *J Clin Microbiol* 1990, 28:1541-1544.

[73] Matthews R, Pandit P, Bonigal S, Wise R, Radcliffe K: Evaluation of an enzyme-linked immunoassay and confirmatory test for the detection of *Chlamydia trachomatis* in male urine samples. *Genitourin Med* 1993, 69:47-50.

[74] Moncada J, Schachter J, Bolan G, Nathan J, Shafer M, Clark A, Schwebke J, Stamm W, Mroczkowski T, Martin D: Evaluation of Syva's enzyme immunoassay for the detection of *Chlamydia trachomatis* in urogenital specimens. *Diagn Microbiol Infect Dis* 1992, 15:663-668.

[75] Moncada J, Schachter J, Shafer M, Williams E, Gouriay L, Lavin B, Bolan G: Detection of *Chlamydia trachomatis* in first catch urine samples from symptomatic and asymptomatic males. *Sex Transm Dis* 1994, 21:8-12.

[76] Talbot H, Romanowski B: Factors affecting urine EIA sensitivity in the detection of *Chlamydia trachomatis* in men. *Genitourin Med* 1994, 70:101-104.

[77] Thomas B, MacLeod E, Hay P, Horner P, Taylor-Robinson D: Limited value of two widely used enzyme immunoassays for detection of *Chlamydia trachomatis* in women. *J Clin Pathol* 1994, 13:651-655.

[78] Tam M, STamm W, Handsfield H, Stephens R, Kuo C, Holmes K, Ditzenberger K, Kreiger M, Nowinski R: Culture-independent diagnosis of *Chlamydia trachomatis* using monoclonal antibodies. *N Engl J Med* 1984, 310:1146-1150.

[79] Thomas B, Gilchrist C, Taylor-Robinson D: Detection of *Chlamydia trachomatis* by direct immunofluorescence improved by centrifugation of specimens. *Eur J Clin Microbiol Infect Dis* 1991, 10:659-662.

[80] Woods G, Bryan J: Detection of *Chlamydia trachomatis* by direct fluorescent antibody staining, Results of the College of American Pathologists proficiency testing program, 1986-1992. *Arch Pathol Lab Med* 1994, 118:483-488.

[81] Stamm W, HAriison H, ALexander E, Cles L, Spence M, Quinn T: Diagnosis of *Chlamydia trachomatis* infection by direct immunofluorescence staining of genital secretions- multicenter trial. *Ann Intern Med* 1984, 101:638-641.

[82] Bell T, Kuo C, Stamm W, Ram M, Stephens R, Holmes K, Grayston J: Direct fluorescent monoclonal antibody stains for rapid detection of infant *Chlamydia trachomatis* infections. *Pediatrics* 1984, 74:224-228.

[83] Rapoza P, Quinn T, Kiessling L, Green W, Taylor H: Assessment of neonatal conjunctivitis witha direct fluorescent monoclonal antibody stain for Chlamydia. *JAMA* 1986, 255:3369-3373.

[84] Rompalo A, Suchland R, Rice C, Stamm W: Rapid diagnosis of *Chlamydia trachomatis* rectal infection by direct fluorescence staining. *J Infect Dis* 1987, 155:1075-1076.

[85] Friis B, Kuo C, Wang S, Mordhorst C, Grayston J: Rapid diagnosis of *Chlamydia trachomatis* pneumonia in infants. *Acta Pathol Microbiol Immunol Scand Sect* 1984, 92:139-143.

[86] Paisley J, Lauer B, Melinkovich P, Bitterman B, Feiten D, Berman S: Rapid diagnosis of *Chlamydia trachomatis* pneumonia in infants by direct immunofluorescence microscopy of nasopharyngeal secretions. *J Pediatr* 1986, 109:653-655.

[87] CDC: False-positive results with the use of chlamydial tests in the evaluation of suspected sexual abuse. *Morbid Mortal Weekly Rep* 1991, 39:932-935.

[88] Kellogg J, Seiple J, Hick M: Cross-reaction of clinial isolates of bacteria and yeasts with the chlamydiazyme test for chlamydial antigen, before and after use of a blocking agent. *Am J Clin Pathol* 1992, 97:309-312.

[89] Stamm W: Diagnosis of *Chlamydia trachomatis* genitourinary infections. *Ann Intern Med* 1988, 108:710-717.

[90] Malenie R, Joshi P, Mathur M: *Chlamydia trachomatis* antigen detection in pregnancy and its verification by antibody blocking assay. *Indian J Med Microbiol* 2006, 24(2):97-100.

[91] Newhall W, DeLisle S, Fine D, Johnson R, Hadgu A, Matsuda B, Osmond D, Campbell J, Stamm W: Head-to-head evaluation of five different nonculture chlamydia tests relative to a quality assured culture standard. *Sex Transm Dis* 1994, 21:S165-166.

[92] Blanding J, Hirsch L, Stranton N, Wright T, Aarnaes S, Maza Ldl, Peterson E: Comparison of the Clearview Chlamydia, the PACE 2 assay, and culture for detection of *Chlamydia trachomatis* from cervical specimens in a low-prevalence population. *J Clin Microbiol* 1993, 31:1622-1625.

[93] Kluytmans J, Goessens W, Mouton J, Rijsoort-Vos Jv, Niesters H, Quint W, Habbema L, Wagenvoort J: Evaluation of Clearview and Magic Lite test, polymerase chain reaction, and cell culture for the detection of *Chlamydia trachomatis* in urethral specimens from males. *J Clin Microbiol* 1993, 32:568-570.

[94] Khan E, Hossain M, Paul S, Mahmud M, Rahman M, Alam M, Hasan M, Mahmud N, Nahar K: Molecular diagnosis of genital *Chlamydia trachomatis* infection by polymerase chain reaction. *Mymensingh Med J* 2011, 20(3):362-365.

[95] Altwegg M, Burger D, Lauper U, Schar G: Comparison of Gen-Probe PACE 2, Amplicor Roche, and a conventional PCR for the detection of *Chlamydia trachomatis* in genital specimens. *Med Microbiol Lett* 1994, 3:181-187.

[96] Kluytmans J, Niesters H, Mouton J, Quint W, Ijpelaar J, Rijsoort Jv, Habbema L, Stoltz E, Michel M, Wagenvoort J: Performance of a nonisotopic DNA probe for detection of *Chlamydia trachomatis* in urogenital specimens. *J Clin Microbiol* 1991, 29:2685-2689.

[97] Stary A, Teodorowicz L, Horting-Muller I, Nerad S, Storch M: Evaluation of the Gen-Prove PACE2 and the Microtrak enzyme immunoassay for diagnosis of *Chlamydia trachomatis* in urogenital samples. *Sex Transm Dis* 1994, 21:26-30.

[98] Melton M, Hale Y, Pawlowicz M, Halstead D, Wright S: Evaluation of the Gen-Probe PACE 2C system for *Chlamydia trachomatis* and *Neisseria gonorrhoea* in a high prevalence population, abstr. In: *Abtracts of the 95th General Meeting of the American Society for Microbiology 1995: 1995; Washington DC*. 138.

[99] Mullis K, Faloona F: Specific synthesis of DNA in votro via a polymerase-catalyzed chain reaction. *Methods Enzymol* 1987, 55:335-350.

[100] Saiki R, Scharf S, Faloona F, Mullis K, Horn G, Erlich H: Enymatic amplification of B-globin genomic sequences and restriction site analysis for diagnosis of sickle cell anaemia. *Science* 1985, 230:1350-1354.

[101] Dille J, Butzen C, Birkenmeyer L: Amplification of *Chlamydia trachomatis* DNA by ligase chain reaction. *J Clin Microbiol* 1993, 31:729-731.

[102] Harinda V, Underhill G, Tobin J: Screening for genital chlamydia infection: DNA amplification techniques should be the test of choice. *Int J STD AIDS* 2003, 14(11):723-726.

[103] Haugland S, Thune T, Fosse B, Wentzel-Larsen T, Hjelmevoll S, Myrmel H: Comparing urine samples and cervical swabs for Chlamydia testing in a female population by means of Strand Displacement Assay (SDA). *BMC Womens Health* 2010, 25(10):9.

[104] Masek B, Arora N, Quinn N, Aumakhan B, Holden J, Hardick A, Agreda P, Barnes M, Gaydos C: Performance of three nucleic acid amplification tests for detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* by use of self-collected vaginal swabs obtained via an Internet-based screening program. *J Clin Microbiol* 2009, 47(6):1663-1667.

[105] Matthews-Greer J, McRae K, LaHaye E, Jamison R: Validation of the Roche COBAS Amplicor system for *Chlamydia trachomatis*. *Clin Lab Sci* 2001, 14(2):82-84.

[106] Sevestre H, Mention J, Lefebvre J, Eb F, Hamdad F: Assessment of *Chlamydia trachomatis* infection by Cobas Amplicor PCR and in-house LightCycler assays using PreservCyt and 2-SP media in voluntary legal abortions. *J Med Microbiol* 2009, 58(Pt 1):59-64.

[107] Jaton K, Bille J, Greub G: A novel real-time PCR to detect *Chlamydia trachomatis* in first-void urine or genital swabs. *J Med Microbiol* 2006, 55:1667-1674.

[108] Bhalla P, Baveja U, Chawla R, Saini S, Khaki P, Bhalla K, Mahajan S, Reddy B: Simultaneous detection of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* by PCR in genitourinary specimens from men and women attending an STD clinic. *J Commun Dis* 2007, 39(1):1-6.

[109] Jalal H, Stephen H, Al-Suwaine A, Connex C, Carne C: The superiority of polymerase chain reaction over an amplified enzyme immunoassay for the detection of genital chlamydial infections. *Sex Transm Dis* 2006, 82(1):37-40.

[110] Herrmann B: A new genetic variant of *Chlamydia trachomatis*. *Sex Transm Infect* 2007, 83:253-254.

[111] Unemo M, Olcen P, Agne-Stadling I: Experiences with the new genetic variant of *Chlamydia trachomatis* in Orebra county, Sweden - proportion, characteristics and effective diagnostic solution in an emergent situation. *Euro Surveill* 2007, 12:E5-6.

[112] Whiley D: False-negative results in nucleic acid amplification tests-do we need to routinely use two genetic targets in all assays to overcome problems caused by sequence variation? *Crit Rev Microbiol* 2008, 34:71-76.

[113] Ness R, Soper D, Richter H, Randall H, Peipert J, Nelson D, Schubeck D, McNeley S, Trout W, Bass D *et al*: Chlamydia antibodies, chlamydia heat shock protein, and adverse sequelae after pelvic inflammatory disease: the PID Evaluation and Clinical Health (PEACH) Study. *Sex Transm Dis* 2008, 35:129-135.

[114] Machado A, Guimaraes E, Sakurai E, Fioravante F, Amaral W, Alves M: High titers of *Chlamydia trachomatis* antibodies in Brazilian women with tubal occlusion or previous ectopic pregnancy. *Infect Dis Obstet Gynecol* 2007, 24816.

[115] Arya R, Mannion P, Woodcock K, Haddad N: Incidence of genital *Chlamydia trachomatis* infection in the male partners attending an infertility clinic. *J Obstet Gynaecol* 2005, 25:364-367.

[116] Meyer K, Eddie B: The influence of tetracycline compounds on the development of antibodies in psittacosis. *Am Rev Tuberc* 1956, 74:566-571.

[117] Biosafety in microbiological and biomedical laboratories. In. Edited by Services UDoHaH. Washington DC: US Government Printing Offices; 1988: 88-8395.
[118] Schachter J: Manual of clinical microbiology, 2nd edition edn. Washington DC: American Society for Microbiology; 1980.
[119] Wang S, Grayston J: Immunologic relationship between genital TRIC, lymphogranuloma venereum, and related organisms in a new microtiter indirect immunofluorescence test. *Am J Ophthalmol* 1970, 70:367-374.
[120] Wang S, rayston J, Alexander E, Holmes K: Simplified immunofluorescence test with trachoma-lymphogranuloma venereum (*Chlamydia trachomatis*) antigens for use as a screening test for antibody. *J Clin Microbiol* 1975, 1:250-255.
[121] Lampe M, Suchland R, Stamm W: Nucleotide sequence of the variable domains within the major outer membrane protein gene from serovariants of *Chlamydia trachomatis*. *Infect Immun* 1993, 61:213-219.
[122] Suchland R, Stamm W: Simplified microtiter well cell culture method for rapid immunotyping of *Chlamydia trachomatis*. *J Clin Microbiol* 1991, 29:1333-1338.
[123] Grayston J: Infections cuased by *Chlamydia pneumonia* strain TWAR. *Clin Infect Dis* 1992, 15:757-763.
[124] Moss T, Darougar S, Woodlan R, Nathan M, Dine R, Cathrine V: Antibodies to Chlamydia species in patients attending a genitourinary clinic and the impact of antibodies to *C pneumoniae* and *C psittaci* on the sensitivity and the specificity of *C trachomatis* serology tests. *Sex Transm Dis* 1993, 20:61-65.
[125] Mohony J, Chernesky M, Bromberg K, Schachter J: Accuracy of immunoglobulin M immunoassay for diagnosis of chlamydial infections in infants and adults. *J Clin Microbiol* 1986, 24:731-735.
[126] Baud D, Regan L, Greub G: Comparison of five commercial serological tests for the detection of anti-Chlamydia trachomatis antibodies. *Eur J Clin Microbiol Infect Dis* 2010, 29:669-675.
[127] Schachter J, Stamm W, Chernesky M, Hook E, Jones R, Judson F, Kellogg J, LeBar B, Mardh P, McCormack W: Nonculture tests for genital tract chalmydial infection. What does the package insert mean, and will it mean the same thing tomorrow? *Sex Transm Dis* 1992, 19:243-244.
[128] Sackett D, Haynes R, Tugwell P: Clinical epidemiology. Boston: Little, Brown & Co; 1985.
[129] Hay P, Thomas B, Horner P, MacLeod E, Renton A, Taylor-Robinson D: *Chlamydia trachomatis* in women: the more you look, the more you find. *Genitourin Med* 1994, 70:97-100.
[130] Lin J, Jones W, Yan L, Wirthwin K, Flaherty E, Haivanis R, Rice P: Underdiagnosis of *Chlamydia trachomatis* infection. DIagnostic limitations in patients with low level infection. *Sex Transm Dis* 1992, 19:259-265.
[131] Magder L, Klontz K, Bush L, Barnes R: Effect of patient characteristics on performance of an enzyme immunoassay for detecting cervical *Chlamydia trachomatis* infection. *J Clin Microbiol* 1990, 28:781-784.
[132] Shrier L, Dean D, Klein E, Harter K, Rice P: Limitations of screening tests for the detection of *Chlamydia trachomatis* in asymptomatic adolescent and young adult women. *Am J Obstet Gynecol* 2004, 190(3):654-662.

[133] Gaydos C, Theodore M, Dalesio N, Wood B, Quinn T: Comparison of three nucleic acid amplification tests for detection of *Chlamydia trachomatis* in urine specimens. *J Clin Microbiol* 2004, 41:3041-3045.

[134] Lehmusvuori A, Juntunen E, Tapio A, Rantakokko-Jalava K, Soukka T, Lovgren T: Rapid homogenous PCR assay for the detection of *Chlamydia trachomatis* in urine samples. *J Microbiol Methods* 2010, 83:302-306.

[135] Gaydos C, Quinn T, Willis D, Weissfeld A, Hook E, Martin D, Ferrero D, Schachter J: Performance of the APTIMA Combo 2 assay for detecion of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in female urine and endocervical swab specimens. *J Clin Microbiol* 2003, 41:304-309.

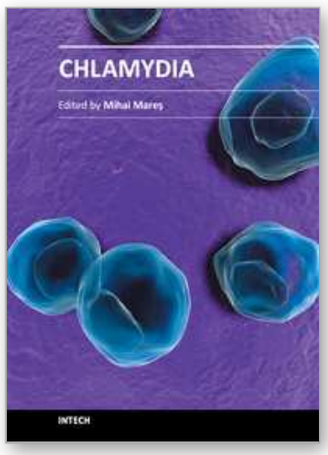
[136] Hadad R, Fredlund H, Unemo M: Evaluation of the new COBAS TaqMan CT test v2.0 and impact on the proportion of new variant *Chlamydia trachomatis* by the introduction of diagnostic detecting new variant C trachomatis in Orebro county, Sweden. *Sex Transm Infect* 2009, 85:190-193.

[137] Walsh A, Rourke F, Laoi B, Crowley B: Evaluation of the Abbott RealTime CT assay with the BD ProbeTec ET assay for the detection of *Chlamydia trachomatis* in a clinical microbiology laboratory. *Diagn Microbiol Infect Dis* 2009, 64:13-19.

[138] Whiley D, Sloots T: Comparison of three in-house multiplex PCR assays for the detection of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* using real-time and conventional detection methodologies. *Pathology* 2005, 37:364-370.

[139] Moller J, Pedersen L, Persson K: Comparison of the Abbott RealTime CT New Formulation Assay with Two Other Commercial Assays for Detection of Wild-Type and New Variant Strains of *Chlamydia trachomatis*. *J Clin Microbiol* 2010, 48(2):440-443.

[140] Ripa T, Nilsson P: A variant of *Chlamydia trachomatis* with deletion in cryptic plasmid: implications for use of PCR diagnostic tests. *Euro Surveill* 2006, 11:E061109.061102.




**Chlamydia**

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Nowadays, Chlamydia still represents a redoubtable pathogen. Among its consequences, the blindness in children and severe impairment of reproductive health in adults are the most mutilating. Worldwide, it is estimated that six million of people suffer from post-trachoma blindness and almost 90 million become sexually infected each year. Due to its silent evolution and sexually transmission, the chlamydial infection can occur in anyone. The book “Chlamydia - A Multifaceted Pathogen” contains an updated review of all-important issues concerning the chlamydial infection. It comprises 18 chapters grouped in four major parts dealing with etiology and pathogenicity, clinical aspects, diagnosis and prevention. The new molecular data about the pathogenicity and the exhaustive presentation of clinical findings bring novelty to the book and improve our knowledge about Chlamydia induced diseases.



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