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Chlamydia trachomatis Infections of the Adults

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1. Introduction

Chlamydiae are obligate intracellular bacteria and consist of four species, including *Chlamydia trachomatis*, *C. pneumoniae*, *C. psittaci* and *C. pecorum*, which cause many types of diseases. The word chlamys is Greek for „cloaked" or „draped", descriptive of the intracytoplasmic inclusion bodies that are „draped" around the host cell nucleus.

C. trachomatis is a Gram-negative bacteria, therefore its cell wall components retain the counter-stain safranin and appear pink under a light microscope. Identified in 1907, *C. trachomatis* was the first chlamydial agent discovered in humans.

Chlamydia trachomatis (CT) is one of the major bacterial agent of the sexually transmitted diseases (STDs) worldwide. It is a causative agent of urogenital, ocular and pneumonic infections, causing annually 92 million new infections worldwide. It is responsible for a wide range of infections, including trachoma (a chronic conjuctivitis, which is the leading preventable cause of blidness worldwide), newborn conjuctivitis, and genital infections in women and men. CT has a unique life cycle, dependent on the host cell's adenosine triphosphate (ATP) production, which differentiates it from all other microorganisms.

Chlamydial genital infection is the most frequently reported infectious disease in the United States, and prevalence is highest in persons aged ≤25 years (Centers for Disease Control and Prevention [CDC], 2009).

Asymptomatic infection is common among both, women and men. The fact is that as many as 70 to 80% of women and up to 50% of men who are infected do not experience any symptoms. The most serious sequelae as the CT infection in women include pelvic inflammatory disease- PID, tubal infertility, chronic pelvic pain and ectopic pregnancy.

In pregnant women, CT infection is associated with preterm birth and other complications such as stillbirth, premature rupture of membranes, and post-partum endometritis.

Since chlamydial infections first become a reportable disease in the United States in 1986, the number of reported cases in both men and women has increased each year. It is currently estimated that about 4 million new chlamydial infections occur each year in the United States at an estimated annual cost exceeding $ 2.4 billion (CDC, 2003).

Worldwide, it is estimated that there are more than 50 million new cases CT infection annually (CDC, 2003).

The prevalence of CT infection in sexually active adolescent women, the population considered most at risk, generally exceeds 10%, and in some adolescent and STD clinic populations of women, the prevalence can reach 40%.

The incidence of asymptomatic infection, it's impact on individuals, and it's influence on the prevalence of disease in the community has led multiple professional organizations to recommend that all sexually active women aged 25 years and younger and all asymptomatic women at risk infection be screened for CT genital infection. Chlamydial infections may increase susceptibility to and transmission of human immunodeficiency virus-HIV in both women and men (Westrom et al., 1999).

As far as Central and Eastern European ("CEE") countries are concerned, the epidemiological picture of chlamydial genital infections cannot be reliably estimated since there is no systematic registration, prevalence studies are sporadic and methodologically hardly comparable, and prevention programs focusing on asymptomatic population are scarce.

The incidence of chlamydial genital infections in CEE is estimated to be 21 to 276 cases per 100,000 inhabitants. The public health importance of chlamydial genital infections lies in the fact that their prevalence is the highest in young population, that they are mostly asymptomatic and that, if left untreated, they may later result in chronic pelvic infl ammatory disease, sterility or ectopic pregnancy.

Unfortunately, symptoms of genital infection are often completely absent or very mild among infected patients, especially women, creating a large reservoir of infected persons who continue transmission to new sexual partners. Because these infections are easy to diagnose and curable with a single dose of oral antibiotics, early detection and treatment are an important component of efforts to reduce the disease burden.

Chlamydia is often found as a co-infection with gonorrhea in both women and men. Between 30 and 50% of patients who have gonococcal infections also have infection with *C. trachomatis.* However, because the background incidence of gonorrhea is so much lower (<0.5%), it is far less likely that a person infected with *C. trachomatis* will also have gonoccocal infection. In the National Longitudinal Study, only 0.3% of young adults were co-infected (Miller et al., 2004). Although screening for *C. trachomatis* is widely recommended among young adult women, little information is available regarding the prevalence of chlamydial infections in the general young adult population. Screening programs have been demonstrated to reduce both the prevalence of *C. trachomatis* infection and rates of PID in women (Scholes et al., 1996).

Today chlamydial infections are diagnosed by simple, reliable and non-invasive tests, and the therapy of choice is a single dose of 1 g azithromycin, which has proven to be safe and effective, especially in acute infections. Azithromycin also proved to be the drug of choice in the treatment of chronic infections, chlamydial prostatitis, and in the treatment of major complications, such as pelvic inflammatory disease.

1.1 Facts

1. Chlamydia is the most commonly reported bacterial infection, with an estimated four million new cases each year.
2. Adolescents and adults are most commonly infected with *C. trachomatis.*
3. Asymptomatic infection is common among both, women and men.
4. Untreated chlamydial infections may lead to PID, ectopic pregnancy, and infertility.
5. The purpose of at least annually screening all sexually active women aged 25 years and younger is to reduce the incidence of upper tract infection.

2. Etiology

Because of their unique developmental life cycle, all chlamydiae were placed into their own order, *Chlamydiales*, family *Chlamydiaceae,* within one genus, *Chlamydia* (Pudjitamoko et al., 1997, as cited in Int J Syst Bacteriol, 1984). *C. trachomatis* is one of the four recognized species of the genus *Chlamydia*, with *C. pneumoniae*, *C. psittaci* and *C. pecorum. Chlamydia* species are readily identified and distinguished from other chlamydial species using DNA-based tests and on the basis unique growth cycle. *Chlamydia psitaci* is a common pathogen of avian species and domestic mammals, but only involves humans as a zoonosis. *Chlaymdia pneumoniae* is a common respiratory pathogen of humans that has been implicated as a possible cause of coronary artery disease. *Chlamydia pecorum* is a pathogen of domestic animals. Some *C. psitacci* strains are sexually transmitted in their natural hosts, and one-the guinea pig inclusion conjuctivitis (GPIC) agent –may offer a potenitially useful animal model for the study of sexually transmitted chlamydial infections. Molecular techniques such as PCR or DNA hybridization or the use of monoclonal antibodies are required to differentiate the species.

There are 15 serovars of *C. trachomatis*, which are divided into the trachoma serotypes A, B, Ba, and C, the oculogenital serovars, D-K, and the lymphogranuloma venereum (LGV) serovars L1-L3 (table 1.). Most strains of *C. trachomatis* are recognized by monoclonal antibodies (mAbs) to epitopes in the VS4 region of MOMP (major outer membrane protein). Serovars can be distinguished by serological typing using monoclonal antibodies or by molecular gene typing methods. Typing is useful for epidemiological studies, which focus on transmission and geographical differences. In the developed world, the oculogenital strains are predominantly the strains that are routinely prevalent, while trachoma is a sequelae of ocular disease in developing countries and countinues to be a leading cause of preventable blidness. LGV is sporadic in North America and Europe, and endemic in Africa, India, Southeast Asia, South America, and the Caribbean. Occasional cases or clusters of cases suggest ongoing low-level transmission in these areas. Few countries require official notification of LGV cases, and the lack of standard diagnostic criteria renders reported cases somewhat suspect. Likeother sexually transmitted diseases LGV is more common in urban than in rural areas, among the sexually active, and among the lower socioeconomic groups. Much of the reported epidemiology on LGV was based on cases diagnosed using clinical criteria or the results of serologic tests and/or Frei skin tests that were not specific for the disease.

Urogenital chlamydial infections occur primarily among young sexually active persons. Prevalence rates encompass all socioeconomic groups and geographical areas, and may range from 5-20% in various groups of young adults (Eng & Butler, 1997).

Disease/Syndrome	Biovar	Most frequent serovars
Trachoma	trachoma	A, B, Ba, C
Inclusion conjunctivits	trachoma	D, Da, E, F, G, H, I, Ia, J, K
Urethritis, cervicitis, salpingitis (pharyngitis, otitis media)	trachoma	B, C, D, E, F, G, H, I, K, L3
Lymphogranuloma venereum (syn. Lymphogranuloma inguinale, lymphopathia venerea, Favre-Durand-Nicolas disease)	lymphogranuloma venereum	L1, L2, L2a, L3

Table 1. Human infections caused by *Chlamydia trachomatis.*

3. Chlamydial biological cycle

Chlamydiae are obligate cell parasites and cannot be cultured on arteficial media. They have the ability to establish long-term associations with host cells. They are also restricted to an intracellular life style because chlamydiae lack the ability to synthesize high-energy compounds. When an infected host cell is starved for various nutrients such as amino acids (tryptophan) iron, or vitamins, this has a negative consequence for *Chlamydiae* since the organism is dependent on the host cell for these nutrients. They depend on the host cell to supply them with ATP and necessary nutrients.

It is developmental cycle of chlamydiae that sets them apart form all other bacteria. There are some differences in inclusion morphology within the chlamydiae, but all species appear to have essentially identical developmental cycles.

They go through two stages in their reproductive cycle; the elementary bodies (EBs) are optimized to survive outside of host cells. In the form of the reticular bodies (RBs), the chlamydiae reproduce inside the host cells. This cycle involves an alternation between two highly specialized morphologic forms, one adopted to an intracellular and the other to an extra cellular environment.

The cycle may be divided into several steps: (1) initial attachment of the infectious particle, or elementary body, to the host cell; (2) entry into the cell; (3) morphological change to the reticulate particle, with intracellular growth and replication; (4) morphologic change of reticulate particles to Ebs; and finally (5) release of the infectious particles (figure 1.).

The entire cycle takes place within a chlamydia –modified intracellular vacuole, which undergoes a large increase in size.

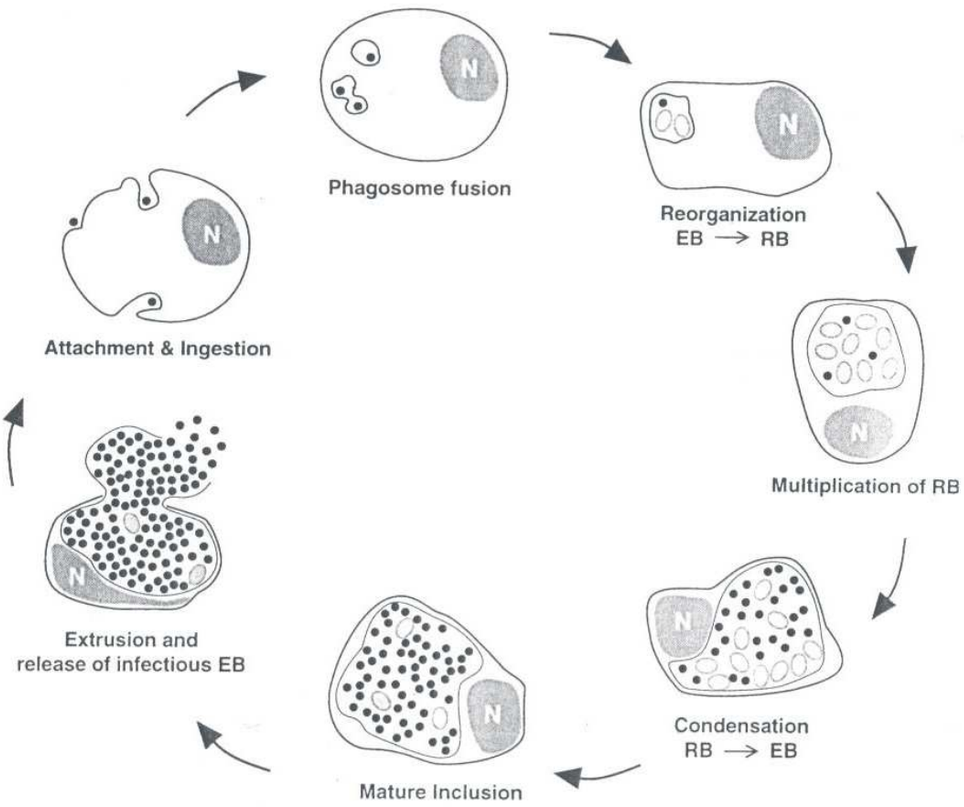

Fig. 1. Chlamydial Biological Cycle (Jones et al.,1994).

3.1 Elementary bodies

The round to oval, optically dense elementary bodies have a diameter 300 nm. Infection begins when EBs attach to specific receptors found on nonciliated columnar or cuboidal epithelium of the host. This type of epithelium is located in the endocervix, endometrium, fallopian tube, and urethra, making those sites vulnerable to infection.

3.2 Reticulate bodies

After phagocytosis, the EB exists within a cytoplasmic vacuole or phagosome, where it is protected from host defense systems. Within the phagosome, the EB transforms into a reticulate body in order to myltiply. It has a diameter of aproximately 1000 nm. At the end of the life cycle, RBs are transformed back into EBs. The cell breaks open and releases the EBs to continue the cycle by attaching themselves to new host cells.

4. Prevalence and Incidence

Chlamydial genital infection is the most frequently reported infectious disease in the United States, and prevalence is highest in persons aged ≤25 years (CDC, 2009). The Centers for Diseases Control and Prevention (CDC), Atlanta, GA, has not changed its age cutoff, and thus continues to recommend annual chlamydia screening of sexually active women aged ≤25 years. The CDC estimates that 2.8 million new cases occur in the United States each year

(CDC, 2005). Nearly 75% of cases occur in the 15-to 24-year-old age group (Grosecloseet et al., 1999). The World Heath Organization (WHO) estimated that 92 million new infections with *C. trachomatis* occured worldwide in 1999 (WHO, 2001). The prevalence of active infection in sexually active, asymptomatic, non-pregnant women in the general population is between 3 and 5% (Sweet & Gibbs, 2002). The highest age-specific rates were reported in women age 15-26. In the general population, men have the same prevalence of chalmydial infections as women (3-5%). Among men, the highest rates occurs in 20- to 24- year-old (CDC, 2005). However, accurate time trends in the incidence of chlamydia are difficult to define because of changes in reporting, increased detection due to improved laboratory tests and increasing laboratory surveillance. Gerbes et al. (Gerbes et al., 1998) estimated that the average annual incidence rates for people aged 15 to 49 years were similar in North America, Western Europe and Australasia at 2146/100,000 for males and 3073/100,000 for females in 1995.

Chlamydia causes more than 250,000 cases of epididymitis in the U.S. each year. Chlamydia causes 250,000 to 500,000 cases of PID every year in the United States. Women infected with chlamydia are up to five times more likely to become infected with human immunodeficiency virus (HIV), if exposed.

5. Risk factors

The risk factors for chlamydial infection include: age younger than 26, low socioeconomic status, minority group member, contraceptive use, age at first intercourse, multiple sexual partners and new partners, and other risk factors as well.

Younger age is shown consistently to be asociated with increased risk of chlaymdial infection among the sexually active population. Age is an important risk factor because *C. trachomatis* typically infects the columnar cells of the cervix; in younger women, columnar cells are more likely to be on the ectocervix (ectopy), where they can be exposed to semen carrying the organism. As women age, the columnar cells are located higher in the cervical canal. Combination hormonal contraceptive use apparently increases cervical ectopy and has been a proposed risk factor for chlamydial infection (Jocobson et al., 2000). The highest incidence rates of infection are reported in adolescents and young adults in Canada and the United States. Differences in the prevalence of infection between adolescents and adults are also often attributed to differences in sexual behaviours.

Race/ethnicity and socioeconomic status are often considered together because they are strongly interrealted (van de Hoek, 1999). Only 10 of 23 studies in females and one of four studies in males indicated a higher risk of chlamydial infection in nonwhite people compared with white people in multivariate analysis. Socioeconomic status was not associate with chlamydia in multivariate analysis using any measure for males and females, including employment status income level of parents education use of Medicaid or occupation.

Multiple partnerships may increase the likelihood of encountering a sexually transmitted pathogen through the increased probability of choosing a partner with infection, while having new or casual sexual contacts may be related to increased risk because of a reduced familiarity between partners.

The relationship between the use of condoms and other barrier contraceptives (diaphragm), and genital chlamydial infection is inconsistent across the studies. Use of a barrier method was shown to be associated with reduced risk of infection compared with the use of other methods of contraception in two of five studies in females.

Age at first intercourse may be casually related to sexually transmitted infections through the biological mechanisms affecting adolescents that and also be an indicator of other aspects of sexual activity that will directly increase risk, including multiple partnerships and the recruitment of nonregular partners.

6. Pathogenesis, infectivity and transmission

Although the pathologic consequences of infection are well established, the mechanism of chlamydia-induced tissue damage are not fully understood. Emerging knowledge of the immune response to infection suggests that many of the complications of chlamydial infection are accompanied by important alterations in immunoregulation; both antibody-mediated and cell-mediated immune effectors may be significant in eliminatory or limiting chlamydial infection.

The ways of spreading are different; sexually, perinatal, although are not exclusive the other ways of transmission through the chloride water of swimming pool, wet towel as well as the possibility of intrahospital infections, by gynecological exam, are not keep the necessary protection measures. It is supposed, statistically, that about 10% percent of women in reproductive age are infected with *C. trachomatis*.

C. trachomatis is the most common sexually transmitted bacterial agent, which infects only humans. The single exposure male-to-female transmission rate has been estimated to be 40%, and the female-to-male transmission rate has been estimated to be 32% (Sweet & Gibbs, 2002). Other investigators have found that transmission rates between sexes are equivalent (Quinn et al., 1996).

Vertical transmission of *C. trachomatis* is more efficient than horizontal transmission. More than 60% of newborns who delivered through a chlamydia-infected cervix will aquire the infection (Sweet & Gibbs, 2002).

As well as the infection with human papilloma virus, chlamydial infection is very important promoter of cervical intraepithelial neoplasm, which result with bad Papanicolaou test, with salpingitis with consequently opturation tuba incompletely or completely, which finally results as extrauterine pregnancy and sterility. During pregnancy, *C. trachomatis* causes disorders and ruptures of the fertile membranes with consequent delayed spontaneous abortion or the earlier delivery.

7. Clinical manifestations

Genital infections caused by *C. trachomatis* closely parallel those due to *N. gonorrhoeae* in terms of clinical manifestations. Both preferentially infect columnar or transitional epithelium of the urethra, with extension to the epididymis; the endocervix, with extension to the endometrium, salpinx, and peritoneum; and the rectum. *C. trachomatis* are naturally found living only inside human cells. Chlamydia can be transmitted during vaginal, anal, or

oral sex, and can be passed from an infected mother to her baby during vaginal childbirth. Between half and three-quarters of all women who have a chlamydia infection of the neck of the womb (cervicitis) have no symptoms and do not know that they are infected.

C. trachomatis serovars A, B, Ba, and C are associated with endemic trachoma, the most common preventable form of blidness, while serovars L1, L2, and L3 are associated with LGV. Serovars D through K are the major causes of nongonococcal urethritis and epididymitis in men and may induce Reiter's syndrome, proctitis, and conjuctivitis in both men and women and cervicitis, urethritis, endometritis, with salpingitis with tubal obstruction which could be complete or incomplete, and perihepatitis in women. During pregnancy CT can cause „premature" rupture of membranes, spontaneous abortions and preterm delivery.

7.1 Trachoma

Trachoma is a follicular keratoconjuctivitis. The disease occurs in all climatic zones, although it is more frequent in warmer, less-developed countries. The pathogen is transmitted by direct contact and indirectly via objects in daily use. Untreated, the initially acute inflammation could develop a chronic course lasting months or years and leading to formation of a corneal scar, which can than cause blidness.

The laboratory diagnostics procedure involves detection of *C. trachomatis* in conjuctival smears using direct immunofluorescence microscopy. The fluorochrome-marked monoclonal antibodies are directed against the MOMP of *C. trachomatis*.

The pathogen can also be grown in cell cultures. The therapeutic method of choice is systemic and local application of tetracyclines over a period of several weeks.

Chlamydia conjunctivitis or trachoma is a common cause of blindness worldwide. The WHO estimates that it accounted for 15% of blindness cases in 1995, but only 3.6% in 2002 (WHO, 2002).

7.2 Inclusion conjuctivitis

This is an acute, purulent papillary conjuctivits that may affect neonates, children, and adults (swiming-pool conjuctivitis). Newborn children are infected during birth by pathogenes colonizing the birth canal. Untreated, a pannus may form as in trachoma, followed by corneal scarring. Laboratory diagnosis and therapy as in trachoma.

7.3 Genital infections

Chlamydial infections of the genital tract have a worldwide distribution and are prevalent both in the industrialized countries and in the developing world. C. *trachomatis* as the bacterial agent is responsible for the huge number of genital infections, which is spreading especially among younger (table 2.). Adults are defined as persons between 15 and 49 years of age. Almost four million new cases of chlamydial infections on genital plane are registrated every year in the United States, and three million in Europe (CDC, 1997). Epidemiological investigations of a large number of women in the United States and Scandinavia confirm chlamydiae as the most prevalent STDs for developed countries. Considered the prevalence infections, hard consequences and huge bills for the treatment in the United States is implement screening methods, which include persons with high risk:

- Persons with anamnestic history of STDs;
- Young persons sexually active;
- Promiscuity persons;
- Male with lymphogranuloma infection;
- Newborns,
- Reiter was diagnosed in younger males.

Women		
Cervicitis	Perihepatitis	Preterm labor
Urethritis	Conjunctivitis	Preterm delivery
Acute urethral syndrome	Ectopic pregnancy	Premature rupture of membranes
Proctitis	Infertility	Postpartum endometritis
Endometritis	Chronic pelvic pain	
Salpingitis	Reiter' s syndrome	
Men		
Urethritis	Proctitis	
Epididymitis	Infertility	
Prostatitis	Conjunctivitis	
Reiter' s syndrome		
Newborns		
Conjunctivitis	Pneumonia	
Otitis media		

Table 2. Clinical manifestations of *Chlamydia trachomatis.*

In women, *C. trachomatis* can cause urethritis, proctitis, or infections of the genital organs. It has even been known to cause pelvioperitonitis and perihepatitis. Massive perinatal infection of a neonate may lead to an interstitial chlamydial pneumonia.

C. trachomatis is responsible for 30 to 60% of cases of nongonococcal urethritis (NGU) in men. Possible complications include prostatitis and epididymitis. The pathogens are communicated by venereal transmission. The source of infection is the female sexual partner, who often shows no clinical symptoms.

Urogenital chlamydial infections occur primarily among young sexually active persons. Prevalence rates encompass all socioeconomic groups and geographical areas, and more range from 5-20% in various groups of young adults (Eng & Butler, 1997; Tamm, 1999). Because symptoms are absent in most infected individuals, the prevalence in population groups may be severely underestimated. So, widespread screening of individuals at greatest risk, e.g. those individuals who are young, sexually active, and have new or multiple partners, has been recommended.

7.3.1 Genital infections in women

Genital infections caused by the *C. trachomatis* is the most frequently reported STD's worldwide, with the highest prevalence in aged category of ≤25 years (CDC, 2009). In women, *C. trachomatis* has been shown to cause both lower and upper genital tract

infections. Untreated, chlamydial infection can lead to severe reproductive complications. Chlamydia is known as the "silent epidemic" because in women, it may not cause any symptoms in 75% of cases, and can linger for months or years before being discovered. Symptoms that may occur include unusual vaginal bleeding or discharge, pain in the abdomen, painful sexual intercourse (dyspareunia), fever, painful urination or the urge to urinate more frequently than usual (urinary urgency).

C trachomatis is an important causal agent in pelvic inflammatory disease, with sequelae including infertility, ectopic pregnancy, and chronic pelvic pain. Up to two thirds of cases of tubal-factor infertility and one third of cases of ectopic pregnancy may be attributable to *C. trachomatis* infection.

Chlamydial infection during pregnancy is associated with a number of adverse outcomes of pregnancy including preterm labor, premature rupture of the membranes, low birth weight, neonatal death, and postpartum endometritis. Chlamydial infection during pregnancy may be transmitted to the infant during delivery.

An infant born to a mother with active infection has a risk of acquiring infection at any anatomical site of 50 to 75%. Approximately 30 to 50% of infants born to chlamydia-positive mothers will have conjunctivitis, and at least 50 percent of infants with chlamydial conjunctivitis will also have nasopharyngeal infection. Chlamydial pneumonia develops in about 30% of infants with nasopharyngeal infection.

7.3.2 Genital infections in men

In men, the most common clinical manifestation of *C. trachomatis* infection is nongonococcal urethritis. In fact, *C. trachomatis* causes approximately 35 to 50 % of all cases of nongonococcal urethritis in heterosexual men. Symptoms of nongonococcal urethritis may develop after an incubation period of 7 to 21 days and include dysuria and mild-to-moderate whitish or clear urethral discharge. In most cases, physical examination reveals no abnormalities other than the discharge. Other clinical syndromes in men include acute epididymitis, acute proctitis, acute proctocolitis, conjunctivitis, and Reiter's syndrome. Male infertility, chronic prostatitis, and urethral strictures are possible results of infection. Both Reiter's syndrome (urethritis, conjunctivitis, arthritis, and mucocutaneous lesions) and reactive tenosynovitis or arthritis (without the other components of Reiter's syndrome) have been associated with genital *C. trachomatis* infection. Infection with *C. trachomatis* is also believed to be a cofactor for the transmission of human immunodeficiency virus in both men and women (Nelson & Helfand, 2001).

If left untreated, it is possible for chlamydia in men to spread to the testicles causing epididymitis, which in rare cases can cause sterility if not treated within 6 to 8 weeks. Chlamydia is also a potential cause of prostatitis in men, although the exact relevance in prostatitis is difficult to ascertain due to possible contamination from urethritis.

7.4 Lymphogranuloma venereum

Lymphogranuloma venereum-LGV is distinct venereal disease caused by three serotypes of *C. trachomatis* that are not associated with other chlamydial infections.

Lymphogranuloma venereum is frequently observed in the inhabitants of warm climatic zones and occurs principally in South America and Africa. The disease is uncommon in

North America, but outbreaks have occurred. A herpetiform primary lesion develops at the site of invasion in the genital area, which then becomes an ulcus with accompanying lymphadenitis. Laboratory diagnosis is based on isolating the proliferating pathogen in cell cultures from purulent material obtained from the ulcus or from matted lymph nodes. The antibodies can be identified using the complement binding reaction or the microimmunofluorescence test.

Tetracyclines and macrolides are the potentially useful antibiotic types.

8. Laboratory diagnostics of *Chlamydia trachomatis*

C. trachomatis is a biosafety level 2 agent and should be handled appropriately, although it is not considered a particularly dangerous pathogen. *C. trachomatis* urogenital infection in women can be diagnosed by testing urine or by collecting swab specimens from the endocervix or vagina. Diagnosis of *C. trachomatis* urethral infection in men can be made by testing a urethral swab or urine specimen. Rectal *C. trachomatis* infections in persons that engage in receptive anal intercourse can be diagnosed by testing a rectal swab specimen.

Today, culture-independent tests have revolutionized chlamydia diagnostics. Comercially available antigen detection methods and nucleic acid hybridization tests, when introduced in the 1980s, largely replaced the technically more demanding isolation procedures (table 3.).

8.1 Culture

Although originally chlamydia was grown in embroyonated chicken eggs, growth and detection of chlamydia is now accomplished by staining of chlamydial inclusions grown in tissue culture cells. The cell line the most commonly used is McCoy cells**.** The other cell lines have been used as well as monkey kidney, HeLa, and HEp-2. It is confirmed that the culture is technically difficult and has been shown to be not as sensitive as previously thought**.** Recent studies have indicated that culture sensitivity compared to molecular techniques can range from 50-100%, while specificity is considered to be nearly 100% (Van Der Pol et al., 2001).

8.2 Non-culture diagnostic test

Other non-culture diagnostic tests include: direct cytological examination, direct fluorescent antibody (DFA) test and antigen detection using the enzyme immunoassay (EIA).

Cytology was used to detect chlamydial infections before more sensitive tests were developed. Specimens obtained from the genital tract were diagnosed for the presence/absence of inclusion bodies. The sensitivity of cytology testing is very low with only 20% cases being detected.

DFA using commercial monoclonal antibodies which detect the major outer membrane protein (MOMP) of *C. trachomatis*, which stains only this organism. The test involves the specimen swab being rolled onto a glass slide air dried and fixed with methanol. Fluorescein-conjugated monoclonal antibody is applied to the slide, which after incubation is mounted in mounting medium, coverslipped and read for the presence of EBs with a

fluorescent microscope under 1,000 x. The test requires the experience of a trained microscopist and has a sensitivity of 80-85% with specificity of 98-99% compared to culture (Mahoney &Chernesky, 2003).

Diagnostic method	Sensitivity	Specificity
Tissue Culture	70-85%	100%
Direct Fluorescence Assay	80-85%	>99%
Enzyme Immunoassay	53-76%	95%
Hybridization (Pace 2)	65-83%	99%
Ligase Chain Reaction		
Cervical	94.4-96.4%	99.5-100%
Female Urine	93-98%	99-100%
Male Urine	96.4%	94-100%
Polymerase Chain Reaction (COBAS)		
Cervical	89.7%	99.4%
Female Urine	89.2%	99.0%
Male Urine	90.3%	98.4%
Strand Displacement Amplification		
Cervical	92.8%	98.1%
Female Urine	80.5%	98.4%
Male Urine	93.1%	93.8%
Transcriptional Mediated Amplification		
Cervical	94.2%	97.6%
Female Urine	94.7%	98.9%
Male Urine	97%	99.1%
Male Urethral	95.2%	98.2%

Table 3. Sensitivity and specificity of diagnostic tests for the detection of *Chlamydia trachomatis.*

EIA was the one of the earliest non-culture developed tests. EIA was widely used before the advent of molecular tests and is still used as the most prevalent non-culture detection test for chlamydia (Gaydos et al., 1990).There are several EIAs commercially available using either polyclonal or monoclonal antibodies to detect chlamydia LPS. The sensitivity of the EIAs range from approximately 53-76%, with specificities of about 95%, especially when antibody blocking confirmatory assays is used to confirm the positive EIA result.

Because older non-culture tests, such as DFA and EIA, were traditionally compared to culture as a gold standard, the sensitivities reported in the older literature can no longer be viewed as accurate. The antigen detection techniques are generally less expensive and easier to perform than newer molecular tests.

8.3 Serology

The microimmunofluorescence test (MIF) has been the gold standard test for the detection of antibody for Chlamydia (Wang et al., 1985). The assay is useful for population studies but is not useful for the diagnosis of active *C. trachomatis* ocular or urogenital disease.

8.4 New molecular diagnostic tests for detection of *C. trachomatis*

The diagnosis of genital chlamydial infections evolved rapidly from the 1990s. The most important advance came from the introduction of nucleic acid amplification tests (NAATs), such as polymerase chain reaction (PCR), transcription mediated amplification (TMA), and the DNA strand displacement amplification (SDA). NAATs for chlamydia may be performed on swab specimens collected from the cervix (women) or urethra (men), on self-collected vaginal swabs, or on voided urine. Urine and self-collected swab testing facilitates the performance of screening tests in settings where genital examination is impractical. At present, the NAATs have regulatory approval only for testing urogenital specimens, although rapidly evolving research indicates that they may give reliable results on rectal specimens.The most sensitive and accurate of the non-culture tests are the NAATs and are highly specific, as well. Because they can be used with noninvasively collected specimens such as first catch urines from either sex, or vaginal swabs, NAATs are well suited for screening as well as diagnosis. There are several types of NAATs. The two most commonly used tests are the PCR and LCR tests. These tests offer greatly expanded sensitivities of detection, usually well above 90%, while maintaining very high specificity. Choice of test is mainly dependent upon cost and preference of the laboratory, as all of these NAATs are closely comparable in sensitivity and specificity (Gaydos et al., 2004).

Because NAATs detect DNA and RNA targets, they do not require viable organisms to detect infection.

9. Diagnosis and treatment

Chlamydial infections are often asymptomatic, so diagnosis generally requires chlamydia-specific laboratory test identification or confirmation. Treating infected patients prevents sexual transmission of the disease, and treating all sexual partners of those testing positive for Chlamydia can prevent reinfection of the index patient and infection of other partners. There is no universally accepted protocol for testing the antibiotic susceptibility of *C. trachomatis*. Because of the unique intracellular characteristics of *C. trachomatis*, only certain antibiotics are effective in treatment. The CDC treatment guidelines for chlamydial infections are summarized in tables 4. and 5. (CDC, 2009).

Recommended Regimens
Azithromycin 1 g orally in a single dose
or
Doxycycline 100 mg orally twice a day for 7 days
Alternative Regimens
Erythromycin base 500 mg orally four times a day for 7 days
Or
Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days
Or
Levofloxacin 500 mg orally once a day for 7 days
Or
Ofloxacin 300 mg orally twice a day for 7 days

Table 4. Recommended regimens (CDC, 2009).

Recommended regimens
Azithromycin 1 g orally in a single dose
Or
Amoxicillin 500 mg orally three times a doa for 7 days
Alternative regimens
Erythromycin base 500 mg orally four times a day for 7 days
Or
Erythromycin base 250 mg orally four times a day for 14 days
Or
Erythromycin ethylsuccinate 800 mg orally four times a day for 7 daysbase 500 mg orally four times a day for 7 days
Or
Erythromycin ethylsuccinate 400 mg orally four times a day for 14 days

Table 5. Recommended regimens in pregnancy (CDC, 2009**).**

10. Follow-up

The validity of chlamydial diagnostic testing at <3 weeks after completion of therapy has not been established. False-negative results might occur in the presence of persistent infections involving limited numbers of chlamydial organisms, as well as false-positive results because of the continued presence of nonviable organisms.

In addition, NAATs conducted at <3 weeks after completion of therapy in persons who were treated successfully could yield false-positive results because oh the continued presence of nonviable organisms (CDC, 2009). Routine repeat testing is also encouraged at every other examination done 3-12 months after treatment regardless of whether the patient believes that her sex partner(s) was treated.

11. Recommendations for chlamydial screening and re-screening

In the United States, the CDC recommends that all sexually active adolescent women should be screened for chlamydia infection at least annually, even if symptoms are not present. Also recommended is annually screening of sexually active women 20-25 years of age and older women with risk factors such as a new sex partner or multiple sex partners.

Since the risk of re-infections is very high, especially in women, the CDC recommends that previously infected women are at a high risk and constitute a priority for repeat testing and should be re-screened 3-4 months after treatment.

12. Conclusion

Chlamydia trachomatis has been recognized as a genital pathogen responsible for an increasing variety of clinical syndromes. CT infection is the STD most strongly associated with adolescents. Adolescents, young women and men are consistently at higher risk of being infected with chlamydia than others. The high level of asymptomaticity and the low

levels of testing among females and males make an important reservoir for chlamydial infection. Immunity induced by chlamydial infection is not well understood.

It is clear that single infections will not result in solid immunity to reinfection. Multiple infections, homo- or heterotypic, are common.

Unfortunately, the natural infection is not readily quantifiable in terms of inoculum size, and thus relative degrees of immunity may exist which are overcome with a sufficiently large challenge.

In screening studies, younger women are found to have higher cervical infection rates than older women, who often have higher antibody levels. In addition, many isolate-negative individuals attending STD clinics have IgM to the organism. This antibody may result from recent exposure and rapid resolution of the infection or its ablation by an immune response.

Having in mind that many chlamydial infections are asymptomatic, it has become clear that effective control must involve periodic testing of individuals at risk.

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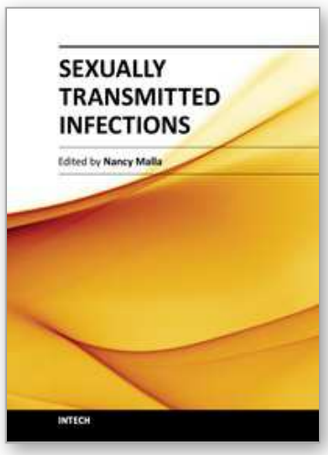

Sexually Transmitted Infections

Edited by Prof. Nancy Malla

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Sexually transmitted infections (STIs) are infections that are spread primarily through person to person sexual contact. There are more than 30 different sexually transmissible bacteria, viruses and parasites. STIs lead to high morbidity and complications. This book entitled as Sexually Transmitted Infections is not a text book but provides useful information for general reference work for physicians, researchers and students interested in the subject. Each chapter is abundant in tips useful to general readers as well. It also includes the Introductory chapter providing an overview with special emphasis on syndromic approach to the management of STIs in clinical setting.

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