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Review on Chlamydia Trachomatis

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ABSTRACT

Chlamydia trachomatis infections affect young, sexually active persons. Risk factors include multiple partners and failure to use condoms. The incidence of infection has increased in the past 10 years. Untreated C. trachomatis infections are responsible for a large proportion of salpingitis, ectopic pregnancy, infertility and, to a lesser extent, epididymitis. This review summarizes C. trachomatis infection in the male genitourinary tract, including urethritis, epididymitis, orchitis, and its complications, and addresses the microbiology, epidemiology, screening, clinical manifestations, diagnosis, and treatment.

Screening is a possible intervention to control the infection, which is often asymptomatic. The emergence of lymphogranuloma venereum proctitis in men who have sex with men, in Europe, and of a variant with a deletion in the cryptic plasmid, in Sweden, are new features of C. trachomatis infections in the last years. A diagnosis is best made by using nucleic acid amplification tests, because they perform well and do not require invasive procedures for specimen collection. Single-dose therapy has been a significant development for treatment of an uncomplicated infection of the patient and his or her sexual partner.

Antigen detection, the enzyme immunoassay test and nucleic acid hybridization tests remain important challenges. Nucleic acid amplification technologies make non-invasive urine testing cost effective and easily performed in primary care. Historically the diagnosis of C. Trachoma infections has been difficult, but newer chlamydia diagnostic tests have become clinically available in the past decade.

Keywords: Chlamydia; Chronic prostatitis; Infertility orchitis; Diagnosis; Clinical signs.

INTRODUCTION

According to the WHO, in 2020, 129 million new infections of Chlamydia trachomatis (CT) were estimated. Chlamydosis is one of the most common sexually transmitted infections (STIs) worldwide. It is caused by the pathogen Chlamydia trachomatis, which can be found in the mouth, penis, vagina, or anus [1]. This gram-negative bacterium is associated with 19 serovars (A, B/Ba, C, D/Da, E, F, G/Ga, H, I/Ia, J, K, L1, L2, L2a, and L3) and variants that are classified according to genotyping. In detail, serovars A–C are associated with trachoma; serovars D–K are associated with oculo genital infections; and serovars L1–L3 are related to lymphogranuloma venereum [2].

This diversity, concomitantly with the genetic variability of the infected individuals, may lead to different clinical symptoms of infection [3,4,5,6]. Chlamydia trachomatis is an obligate intracellular bacterium. During its unique developmental cycle, two different forms are observed, elementary bodies (EBs), which are infectious but not able to divide, and reticulate bodies (RBs), which are metabolically active and able to multiply. Persistent forms can also be present under particular conditions [7].

Serovars A, B, Ba and C are the agents of trachoma, a major cause of blindness in Africa, the Middle East, Asia and South America. Serovars D–K, including D, Da, E, F, G, Ga, H, I, Ia, J and K, are the most common sexually transmitted bacteria, and serovars L1, L2, L2a and L3 are the agents of transmission of lymphogranuloma venereum (LGV). C. trachomatis, a bacterium specifically found in humans, is currently divided into 19 serovars, according to the specificity of major outer membrane protein (MOMP) epitopes [8].

EPIDEMIOLOGY

In the USA in 2006, more than one million cases of chlamydial infection, which is a notifiable disease, were reported to the CDC, corresponding to a rate of 347.8 cases/ 100 000, an increase of 5.6% as compared with the rate in 2005 .In Europe also, the incidence of chlamydial infections has increased in the past 10 years. In 2005, over 200 000 cases were reportedin17 European countries this is probably an underestimate. Prevalence rates have been shown to range from 2% to 17% in asymptomatic women, depending on the setting, population and country. In Denmark, the overall prevalence rate

of infection was 456 cases/100 000 in 2007. In the UK, it has been reported that 10.3% of women and 13.3% of men. The number of diagnosed infections has been increasing steadily since 1995, partly owing to increased numbers of people being tested: nearly 700,000 genital infections and sexually transmitted infections were diagnosed in genitourinary clinics in 2003 compared with 442,000 in 1995. The National Chlamydia Screening Programme reported that the prevalence in 16 to 24-year-olds was 6.2% in women and 5.3% in men in 2007 [9].

According to the Centres for Disease Control and Prevention (CDC) 2009, the last 5 years have seen an increasing rate of infection (43.5%) and it is more common in women than in men (3:1) in United States (US) [62]. In Korean J Urol 2013;54:73-77 74 Lee and Lee United Kingdom in 2004, 104,155 cases of chlamydia were diagnosed in genitourinary medicine clinics [63]. The number of diagnosed infections has been increasing steadily since 1995, partly owing to increased numbers of people being tested: nearly 700,000 genital infections and sexually transmitted infections were diagnosed in genitourinary clinics in 2003 compared with 442,000 in 1995.

The National Chlamydia Screening Programme reported that the prevalence in 16 to 24-year-olds was 6.2% in women and 5.3% in men in 2007 [63]. The prevalence in young men was the same as in young women. The examination of risk factors for chlamydia in the prevalence and case-control studies did not find any factors, other than young age. The number of new partners in the past 12 months was the strongest predictor of infection [63].

	Univariate Analysis				Multivariate Analysis	
Variables	*C trachomatis* Positive,† % n = 137	*C trachomatis* Negative,† % n = 547	OR (95% CI)	*P* Value	Adjusted OR (95% CI) n = 684	*P* Value
Reason for clinic visit						
STD contact	12.4	5.9	2.5 (1.3-4.8)	.003	1.7 (0.8-3.3)	.16
STD symptoms	26.3	24.1	1.3 (0.8-2.0)	.24	0.8 (0.5-1.4)	.49
Other	10.2	8.8	1.4 (0.7-2.7)	.31	1.6 (0.8-3.1)	.22
Screening	51.1	61.2	1	. . .	1	. . .
Clinic type						
Family planning	29.9	41.1	1.1 (0.6-2.1)	.70	1.3 (0.7-2.5)	.42
STD	57.7	39.7	2.2 (1.3-4.0)	.005	2.5 (1.3-4.8)	.006
School	12.4	19.2	1	. . .	1	. . .
Risk behaviors						
Inconsistent condom use	81.8	73.7	1.6 (1.0-2.6)	.05	1.2 (0.7-2.1)	.42
>1 Sex partner	13.9	12.8	1.1 (0.6-1.9)	.74	. . .	. . .
New sex partner	19.0	15.0	1.3 (0.8-2.2)	.25	. . .	. . .
Self-reported STD history						
Prior syphilis infection	3.7	2.6	1.4 (0.5-3.9)	.56	. . .	. . .

*Repeat infection model includes all 684 repeat visits more than 30 days apart made by 277 adolescent females who have had at least 1 prior positive test result during the study period. OR indicates odds ratio; CI, confidence interval; STD, sexually transmitted disease; and ellipses, data not applicable.

†*C trachomatis* was tested by polymerase reaction chlamydia cervix or urine tests.

Fig .1 Univariate and Multivariate Analysis

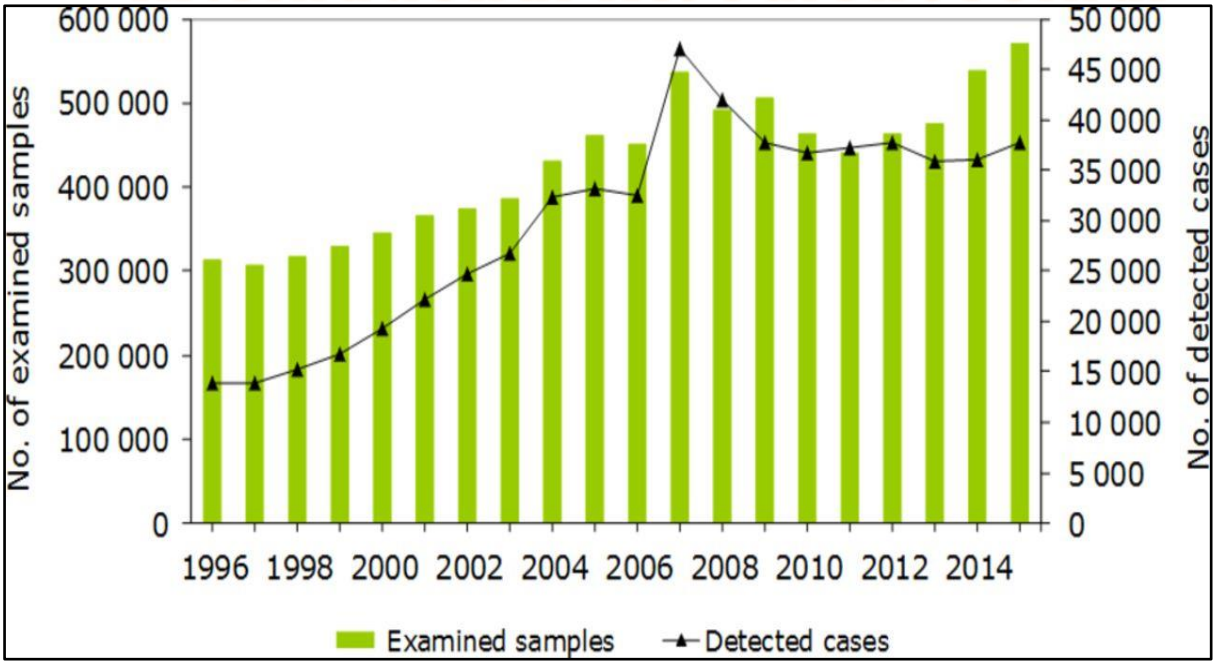

Fig .2 . 10 years of transmission of the new variant of chalmadiya trachomatis

CLINICAL SIGNS

If not adequately treated, women develop PID. Scarring sequelae of PID will cause involuntary infertility in 20% of women, ectopic pregnancy in 9%, and chronic pelvic pain in 18% of women [10].

Chlamydial infection can cause cervicitis in women and urethritis in men **[Fig.3]**. However, these infections produce few or no symptoms in approximately 70% of women and 50% of men and thus remain undetected [11].

Serovar	Clinical Manifestation	Complication
A-C	Keratoconjunctivitis	Scarring trachoma, blindness
D-K	Males: urethritis, proctitis Females: cervicitis, urethritis, proctitis	Epididymitis Endometritis, salpingitis, pelvic pain, ectopic pregnancy, perihepatitis (Fitz-Hugh–Curtis syndrome), infertility Reiter's syndrome, reactive arthritis.
L1-L3	Lymphogranuloma venereum: inguinal syndrome, proctitis.	Fibrosis, rectal stricture

Fig.3 Complications of Serovar

Infections in men

C. trachomatis is the major cause of non-gonococcal urethritis and post-gonococcal urethritis. Urethritis can be complicated by acute epididymitis in young men. After 7–21 days of incubation, the symptoms include dysuria, and a moderate clear or whitish urethral discharge [12]. Acute proctitis can be associated with oculo-genital serovars, but is usually milder than that associated with LGV serovars. There is no evidence of the role of C. trachomatis in prostatitis [13], and chlamydial infection does not significantly contribute to male infertility [14]. Reiter's syndrome (urethritis, conjunctivitis, arthritis and mucocutaneous lesions) or reactive arthritis have also been associated with genital C. trachomatis infections, with a high male/female ratio [13].

Infections in women

Women with cervicitis can be asymptomatic or may complain of mucopurulent vaginal discharge or postcoital bleeding. Oedema, congestion and bleeding of the cervix have been observed. Urethral infection can be associated with cervicitis. A culture-negative leukocyturia finding is suggestive of C. trachomatis infection. Ascending infections can result from cervicitis.

Endometritis is frequently associated with this and may produce irregular uterine bleeding. Salpingitis or pelvic inflammatory disease (PID) is often subclinical. It seems possible that, in Europe, C. trachomatis is the cause of at least 60% of cases of acute PID [15]. Salpingitis may lead to tubal scarring and sever reproductive complications. Two-thirds of all cases of tubal factor infertility and one-third of all cases of ectopic pregnancy could be due to chlamydial infection [12,15]. Chronic pelvic pain linked to the presence of peritoneal adhesions may occur in more than 15% of women with previous episodes of PID [16].

Pelvic inflammatory disease.

The rate at which chlamydia! organisms have been recovered from patients with symptoms of PID has varied widely, probably because of differences in the populations being studied and in the methods used to recover the organisms. Investigators from Europe and North America have found a higher proportion of C trachoma/is than Neisseria gonorrhoeae in women treated for PID [17,18,19,20].

The role of asymptomatic or subclinical chlamydia! PID in the development of reproductive problems has assumed greater importance. Colonization of the fallopian tube by C. trachomatis has been found in infertile women who have no clinical symptoms of PID and no laparoscopic signs of active pelvic infection. Ectopic pregnancy may result from prior chlamydial tubal damage [21].

Neonatal infections

Infants of mothers with chlamydial infections can be infected at delivery. The transmission rate via infected vaginal secretions is high (50–70%). Approximately 30–50% of infants of infected mothers will have conjunctivitis 5–10 days after delivery. At least 50% of infants with conjunctivitis will have nasopharyngeal infection [22]. Chlamydial pneumonia develops in c. 30% of these cases, after 2–3 weeks of incubation. The untreated infection acquired at birth can persist for months or years [23,24].

DEVELOPMENT AND IMMUNE RESPONSE

Chlamydia trachomatis has a particular development biphasic cycle, as shown in **Fig 4** . Briefly, this pathogen alternates between two distinct forms. Firstly, the infectious form, named the elementary body (EB), which when in contact with a host cell, can be internalized into the cell cytoplasm by cell adhesion through the major out member protein (MOMP), localized into the bacterium's envelop, and subsequent actin remodelling processes then facilitate the entry [25,26].

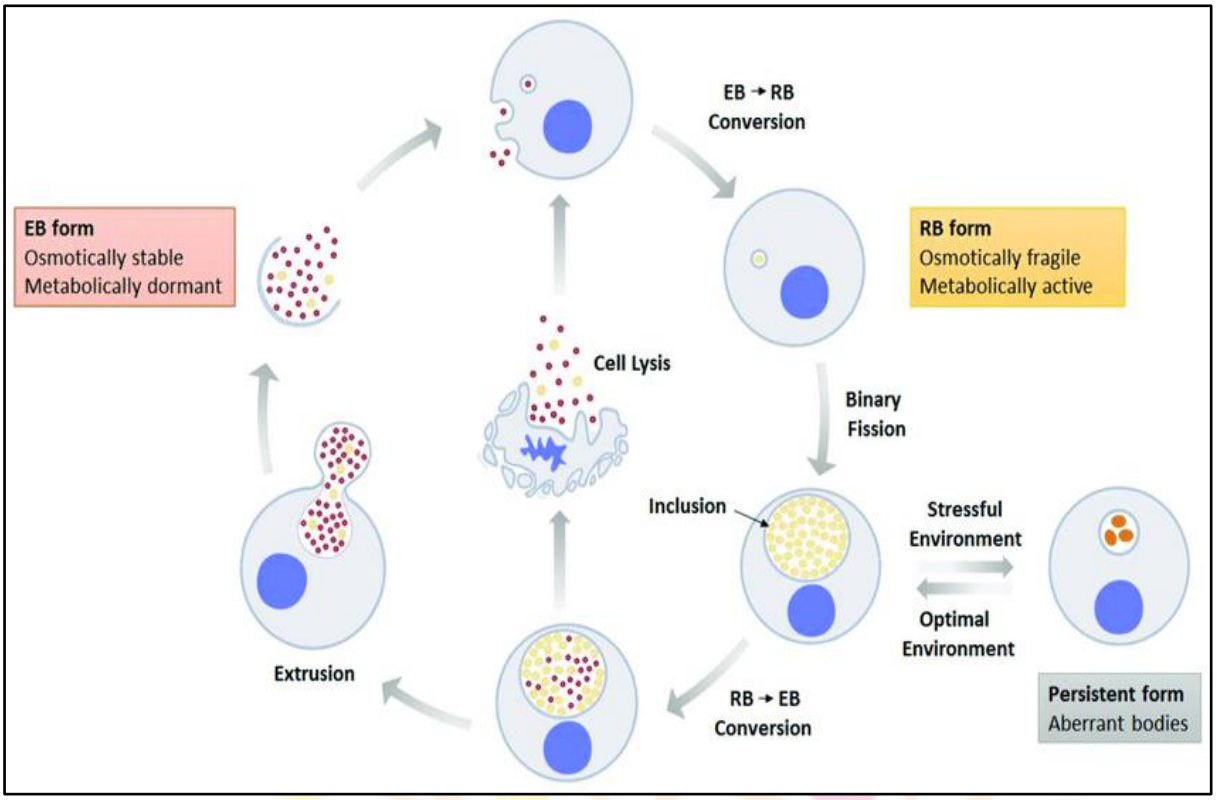

Fig.4 Development of Chlamydia trachomatis

Thus, this infection stimulates an immunogenic environment establishment. Notwithstanding, Chlamydia trachomatis has developed immune escape/evasion mechanisms. For example, it down-regulates the major histocompatibility complexes—I and II (impeding T-cell immune recognition), the modulation of specific cytokines that have pleiotropic roles (interleukin 18, beta interferon, type I interferons), and apoptosis inhibition (increasing cell survival signals and the release of Chlamydial protease-like activity factor proteins), creating a chronic inflammation with infection persistence [34,25,28,29].

In order to start the reproductive cycle, EBs are converted into the metabolic active and non-infectious form, designated as the reticulate body (RB). These can go through the replication process by using the host's resources when ATP and nutrients are available in the cell microenvironment. Otherwise, under cellular stress conditions, RBs are maintained in a reversible state of persistence. Of note, after the replication process, RBs differentiate into the previous form, EBs. For the ultimate process, the extracellular EBs are released, possibly by (1) lysis inducing apoptosis signals or (2) extrusion through exocytosis mechanisms. This cycle occurs repeatedly in the adjacent cells of the host [34,27]. Therefore, the several previously mentioned factors, mostly the adapted mechanisms of replication through the biphasic development cycle and the evolutionary protection mechanisms to surpass the milieu stress and to avoid the immune system, are the major barriers that are responsible for the challenging process of a vaccine development [26].

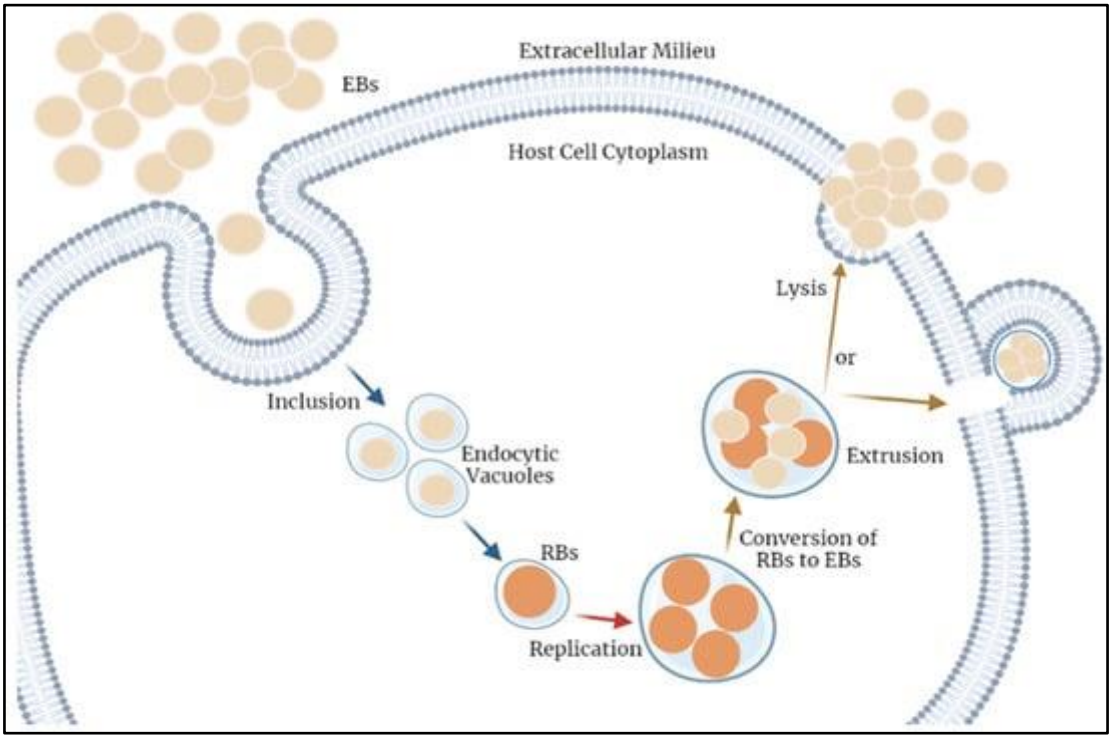

Fig.5. Chlamydia trachomatis cell cycle of infection

This pathogen alternates between two distinct forms. The infectious form, named elementary body (EB), when in contact with a host cell, can reach the cell cytoplasm by adhesion and internalization into a vacuole. Herein, EBs are converted into the alternative non-infectious form, the reticulate body (RB).

These are capable of going through the replication process, using the host's resources, and spending the cell's energy and nutrients; concomitantly, it reaches a critical volume, thus, the RBs must transform into the previous form, EBs. Finally, there are two possible mechanisms for the extracellular EB release, (1) lysis of the host cell or (2) extrusion. This cycle occurs repeatedly in the adjacent cells. The Figure was created with Bio Render.

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Nonetheless, with the improvements of the in silico studies using bioinformatic tools and machine learning predicted models, Shiragannavar and colleagues have designed a candidate vaccine that could potentially stimulate T- and B-cells for a long-term immunity establishment [31]. In detail, this is possible due to the pathogen–host cell interactions that occur within the cytoplasm of this same cell, as well as through the modifications that this microorganism induces within its inclusion vesicles [28]. Furthermore, other immune system evasion mechanisms are well-described by Bastidas et al. 2013 [30]. Therefore, the several previously mentioned factors, mostly the adapted mechanisms of replication through the biphasic development cycle and the evolutionary protection mechanisms to surpass the milieu stress and to avoid the immune system, are the major barriers that are responsible for the challenging process of a vaccine development [26].

In addition, studies covering in silico methods, as well as immune and proteomic approaches, have been developed and have resulted in more candidate vaccines that are capable of triggering a humoral and cell response [32]. Currently, some of these studies still need in vitro and pharmacological validation, highlighting the urgent need to screen this infection in the population, aiming to eradicate it [31,33].

LABORATORY DIAGNOSIS

Because chlamydia are obligate intracellular organisms that infect the columnar epithelium, the objective of good specimen collection should be to obtain columnar epithelial cells from the endocervix or urethra. The diagnosis of chlamydia! STDs generally has been difficult and remains a challenge, but newer chlamydia diagnostic tests have been clinically available in the past decade [34,35,36,37].

Antigen Detection.

New nonculture diagnostic tests, each with their own utility and limitation, were introduced in the 1980s. The direct fluorescent antibody (DF A) test is based on detection of elementary bodies (EB) in patient specimens using a fluorescein - labelled monoclonal antibody that is specific for either the major outer membrane protein of C. trachomatis or the lipopolysaccharide (LPS) moiety of the EB. A distinct advantage of DFA is that the quality of the specimen can be assessed. when it is applied to a slide, the direct visualization of epithelial cells in the specimen under fluorescent microscopy indicates an adequate specimen is obtained. Slides can be restored at 4°C for a few months or at -80°C indefinitely. The sensitivity, specificity, and positive predictive values for DF A have been assessed by comparison with culture. In high prevalence populations (>5%), sensitivity varies from 70 % to 90 % depending on the quality of the specimen collected, patients characteristics including age and STD risk factors, and the technical reliability of the laboratory performing cultures. The specificity is from 96% to 99% in the same high prevalence populations [39,40,41]. False negative and false positive results can occur but are more of a problem in low prevalence groups (<5%).

Cell culture

The isolation of C. trachomatis in tissue culture was first developed in the 1970s and has been refined over the years. The sensitivity is 70% to 90%, with a specificity of close to I 00% [51,52,53]. Tissue culture remains the gold standard, yet its application in clinical settings ranging from university hospital to local family medicine office and public health clinics is limited by a lack of appropriate reference laboratories, technical expertise, funds or recognition of chlamydiae as important STD pathogens. The requirement of at least 3 to 7 days for optimal chlamydia! growth diminishes the utility of cell culture. Once the specimen is collected, it must be kept refrigerated for no longer than 24 hours before inoculation onto McCoy cells. The preferred method for detection of chlamydia in tissue culture is with a fluorescein labelled antibody that is specific for C trachoma/is and reacts with the inclusion body formed inside the cell. Since tissue culture amplifies small numbers of organisms, it is also preferred for specimens in which low numbers of organisms are expected [38,37].

Leukocyte esterase screening.

The leukocyte esterase test (LET) detects enzymes that are released by polymorphonuclear leukocytes. LET only confirms a diagnosis of urethritis; it fails to determine the specific causative agent of urethral inflammation. The test comes in the form of a dipstick on which a purple colour is produced when indoxyl carbonate ester is hydrolysed by leukocyte esterase's. At present, LET is recommended only as a screening test for urethritis in adolescent boys. Because further studies are required to assess its usefulness, LET is not recommended for use in older men or in women as a chlamydia screening test [45,46,34,41,47].

The enzyme immunoassay test (EIA).

This test employs polyclonal or monoclonal antibodies that detect chlamydia LPS. The antibodies are conjugated with an enzyme that reacts with a substrate to produce a coloured product if chlamydiae are present. A spectrophotometer is required to detect the intensity of the coloured product. A major disadvantage of this assay is that the antibodies with the LPS of other bacterial species found in the vagina or urinary tract can produce a false positive result. This · is also not species specific for C. trachoma/is. Most EIA tests contain a blocking antibody that can be used to confirm a positive test. The sensitivities, specificities, and positive predictive values for EIA are similar to those for DFA [35,41,42].

Nucleic acid hybridization.

Nucleic acid hybridization (gen-probe) tests use chemiluminescent type DNA probe that is complementary to a sequence of ribosomal RNA in the chlamydia] genome of the patient sample. A distinct advantage of this assay is that it is specific for C. trachomatis and does not cross react with other bacteria. Specimens can be stored at room temperature in special transport material and processed within 7 days. The sensitivity and specificity rates are similar to those for DF A and EIA. The availability of nucleic acid amplification technologies may make non-invasive urine testing available for young men and for young women when a gynaecologic examination is not otherwise required. Accurate detection of asymptomatic chlamydia] disease in a timely, cost effective, and non-invasive manner as well as the development of effective partner treatment strategies remain important challenges. This review provides a clinical update on office based testing for C. trachoma/is, management and treatment options for the adolescent and young adult population [43,42].

Two additional nucleic acid type assays recently developed were: ligase chain reaction (LCR) and polymerase chain reaction (PCR). With these tests, detection is achieved by exponential amplification of a specific DNA target sequence. Studies suggested that LCR and PCR in the urine of both men and women are more sensitive than culture; sensitivities for the nucleic acid tests reach 95% compared with 85% for cultures. A major problem, however, is the interpretation of positive tests in asymptomatic individuals in low prevalence populations; in this situation, the assay may represent residual DNA but non-viable organisms [35,44].

SEROLOGY

Two serologic tests, micro-immunofluorescence and complement fixation are available for serological diagnosis of chlamydia] infection. Both require a high level of technical expertise, and have little value in the routine clinical care of patients with possible chlamydia! genital infections [48,49,40,47,50].

TREATMENT

Chlamydia trachomatis is treated with antibiotics. You might receive a one-time dose, or you might need to take the medication daily or multiple times a day for seven days [64].

In most cases, the infection clears up within 1 to 2 weeks after you take the antibiotic. But you can still spread the infection at first. So avoid sexual activity from when you start treatment until all your symptoms are gone. Your sexual partner or partners from the last 60 days also need screening and treatment even if they don't have symptoms. Otherwise, the infection can be passed back and forth between sexual partners. Make sure to avoid sexual contact until all exposed partners are treated [64]. Having chlamydia or having been treated for it in the past doesn't prevent you from getting it again.

Antibiotics can get rid of your infection, but they can’t reverse any harm the bacteria may have caused to your body before treatment. This is why it’s so important to get screened regularly for chlamydia, to see your provider at the first sign of symptoms, and get treatment immediately if you’re infected [65].

The most common antibiotics used to treat chlamydia infections are:

- **Doxycycline.** Usually taken over seven days, is preferred.
- **Azithromycin.** Usually taken as a single dose, is recommended as the first choice in pregnancy [65].

HOME REMEDIES FOR CHLAMYDIA

Certain home remedies with antibacterial properties might be useful while dealing with the initial stages of the infection. If you doubt something is off, you can start with the below home remedies to get rid of chlamydia while you wait to consult your doctor.

1. Garlic

Garlic contains active compounds such as allicin which is known to have antibacterial and anti-inflammatory effects [64].

Garlic when crushed or chopped and left for 10 minutes lets the enzymes form the antibacterial allicin.

Garlic also has proven antifungal properties and has been shown to be effective against yeast infection that might be beneficial during antibiotic treatment for chlamydia as antibiotics increase the risk of yeast infections.

2. Echinacea

Echinacea is a flowering plant best known to be used as a natural remedy for snake bites, cold, cough, flu, pain, and intestinal upset [66].

Echinacea has also been found to be effective against STDs, a natural cure for chlamydia and gonorrhea symptoms [67].

Echinacea extract has been shown to boost immunity and help fight certain bacterial and viral infections. While it might help you calm certain symptoms of chlamydia, it is best done in conjunction with antibiotics.

3. Turmeric

Turmeric with its natural antioxidant and anti-inflammatory properties has been shown to provide numerous health benefits. Curcumin, a plant chemical in turmeric, has many therapeutic properties [68].

Studies have found that a topical ointment containing curcumin along with a few other plant compounds has inhibitory effects on chlamydia in lab tests [69]. Hence, it can be used safely to relieve initial symptoms at home.

CHLAMYDIA RISK FACTORS

Since chlamydia has no specific symptoms, it often goes unnoticed and might lead to further complications [70]. When left undiagnosed and untreated for a long time, it might lead to the following potentially serious conditions:

- Cervicitis: Painful inflammation of the cervix resulting in abdominal pain, vaginal discharge, and bleeding.
- Urethritis: Inflammation of the urethra that can be painful and cause abnormal discharge, pain during urination or intercourse, and occasionally blood in seen or urine.
- Salpingitis Inflammation of the fallopian tubes that might lead to infertility.
- Proctitis: Inflammation of the lining of the anus or rectum.
- Pelvic Inflammatory Disease (PID): Infection in the reproductive organs of women.
- Tubal Factor Infertility: PID or endometriosis can often lead to tubal factor infertility that is caused due to fallopian tube obstruction. Surgery or IVF treatments might be required to get conceive thereof.
- Ectopic Pregnancy: A fatal pregnancy that occurs outside the uterus, mostly in the fallopian tubes.

PROBLEMS REGARDING VACCINE DEVELOPMENT

There have been no studies that have examined the effects of vaccine administration during an acute chlamydial genital infection. Therefore, it is unknown whether any experimental chlamydial vaccine candidates could have a therapeutic effect, whether they might reduce or enhance pathological sequelae, or whether they could cause chronic, persistent infections, when administered during an infection. Knowing that Chlamydia can enter a persistent state when put under various pressures, including cytokine production, it is plausible that enhancement of infection-induced immune responses by vaccination may cause the Chlamydia to enter this state and promote both pathology development and future reactivation of infection [52,54,55-57].

It is also unknown whether any vaccine candidates administered after resolution of a previous genital infection will further boost the individual's infection-induced immune response, provide a greater level of protection and prevent further pathology development. Herpes simplex virus-2 (HSV-2) vaccine trials in women revealed that those who were HSV-1 seropositive at the time of vaccination did not mount an effective immune response. However, women who were

seronegative for HSV-1 and 2 mounted strong anti-HSV-2 immune responses [58]. With genital tract Chlamydia infection rates on the continual rise and the asymptomatic nature of infections, these are important aspects that have yet to be examined in any way.

A vaccine designed to target the mucosal surfaces of the female reproductive tract could also be affected by reproductive cycle-associated changes in female sex hormones. Studies on animal models have shown that progesterone and estradiol can affect many components of the immune response, including antigen presentation by DCs and macrophages, production and transport of antibody into the female reproductive tract (FRT) and also the induction of cell-mediated immunity [59,60,61].

CONCLUSION

The prevalence and financial impact of C. trachomatis infection in Turkey requires that family physicians and gynaecologist stay alert for this disease, especially in women, where the sequelae of untreated chlamydia infection are significant. Also, C. trachomatis can cause chronic prostatitis and infertility. Ascending chlamydial infections have been thought to be an infective cause of prostatitis. To reduce the morbidity and subsequent complications associated with C. trachomatis infection in Turkey, effective control and prevention strategies must be implemented.

Selective screening to detect asymptomatic infection is an essential component of all control programs. Without effective screening programs, women will continue to become infertile and to seek expensive surgery; ectopic pregnancies will occur endangering the mother's life; and new-borns will be at increased risk for exposure and will have a greater chance of developing pneumonia and eye infection. Clinical trials continue to demonstrate equivalent efficacy and tolerability of azithromycin and doxycycline regimens, and both remain recommended as first-line therapy. Further evaluation of chlamydial etiology of prostatitis and infertility is required to make definitive statement on the association between isolation of this organism and the diseases.

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