Review Article:
THE EFFECTS OF *CHLAMYDIA TRACHOMATIS* INFECTION ON WOMEN'S REPRODUCTION SYSTEM

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ABSTRACT

Chlamydia, a genus of bacterial parasites, is composed of three species: C. psittaci, which causes psittacosis; C. trachomatis, whose some of its strains cause trachoma, lymphogranuloma venereum, and conjunctivitis; and C. pneumoniae, which causes respiratory-tract infections. C. trachomatis also causes several sexually transmitted diseases, primarily nongonococcal urethritis (infection of the urethra) in males and females and epididymitis (infection of the epididymus) in males. In women, a chlamydial infection ordinarily produces few if any symptoms. There may be a slight vaginal discharge and pelvic pain. If untreated, C. trachomatis can seriously infect the cervix and causing cervicitis, the urethra to cause urethritis, or the fallopian tubes to cause salpingitis. It can also cause pelvic inflammatory disease. Infection of the fallopian tubes can cause sterility, and a chlamydial infection also leads to a higher risk of premature births, ectopic pregnancies, and postpartum infections. A woman with an infected cervix may give birth to infected newborns who can develop pneumonia or the eye disease known as neonatal conjuctivitis.

Keywords: *Chlamydia trachomatis, women's reproduction, genital tract*

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INTRODUCTION

Chlamydia trachomatis is one of the bacterial infections that have a significant impact on community's health. *Chlamydia trachomatis* can cause trachoma (serovars A, B, Ba dan C), lymphogranuloma venereum (serovars L1, L2 dan L3) and genital infections (serovars D-K). *Chlamydia trachomatis*-caused genital infection can lead to pelvic inflammatory disease (PID), which is the main problem in women's reproduction health, both in developing and developed countries.

World Health Organization (WHO) estimates that 89 million new cases of *Chlamydia trachomatis* infection on genitalia will happen every year; there were 877.478 "Chlamydial genital infection" cases which are recorded by the CDC (Centre of Disease Control) in 2003 and this by far is the number one bacterial infection among the ten most common bacterial infections in the US. Considering the significance of *Chlamydia trachomatis* infection in genitalia, we need to know the microbiological aspects of *Chlamydia trachomatis*, its pathogenesis, early detection, and the therapy.

MICROBIOLOGICAL ASPECTS OF *CHLAMYDIA TRACHOMATIS*

Chlamydiae are intracellular-obligate bacteria. They do not have the ability to produce enough energy for their own growth. Therefore, the can only reproduce in a host cell. However, they are different with virus because they have both nucleic acids, RNA and DNA. They have rigid cell wall, but do not have peptidoglican layer. The cell wall is similar to those of gram negative bacteria, but lacks muramic acid. Chlamydiae have different reproduction cycle with other bacteria. The cycle begins with the formation of an elementary body (EB), infectious but "metabolically inert", from extracellular into the host cell and forms a reticulate body (RB) which is "metabolically active". RB will replicate through "binary fission" and produce a large amount of EBs, which are then released into the cell to infect other cells.

Soon after Chlamydiae enter the host cell, they will stay in "phagocytic vesicle" during the next growth cycle. Chlamydiae specifically inhibit fusion from phagosome and lysosome. The phagolysosomal fusion will not happen until the death of this particular cell. Fusion inhibition is made possible because there is a surface

antigen from Chlamydiae. Therefore, phagolysosomal fusion inhibition does not happen in a cell which has been given an antibody therapy. In the host cell, EB form will convert into RB in the first 6-8 hours after entering. There is not detailed explanation of the conversion factor, but it is clear that the protein synthesis reaches its peak at 10-15 hours after infection, that is during multiplication of Chlamydia particles. Chlamydia cannot synthesis high energy compounds for themselves because Chlamydia is an intracellular-obligate parasite. Although the protein synthesis of the host cell is not inhibited by Chlamydia infection, there will be nutrient competition between the host cell and Chlamydia cell. In phagosome cell, Chlamydia which stays in "inclusion bodies" will replicate through "binary fission" from about 8 hours after entering the host cell to about 18-24 after. This is the best time for antimicrobes, such as antimicrobes which inhibit cell wall synthesis and those which inhibit bacteria metabolism activity. After those 18-24 hours, some RBs will transform into EBs, which will replicate and fill "inclusion bodies". This whole cycle happens in the phagosome so that the cell will expand in size. Mature "inclusion bodies" will fill ¾ of the host cell volume and contain more than 10.000 Chlamydia particles. At one time, between 48-72 hours, the cell will rupture and release many infectious EBs which are ready to infect other cells.

PATOPHYSIOLOGY AND ITS COMPLICATION IN WOMEN'S GENITAL TRACT

Chlamydia trachomatis infection in women's genital tract is varied, from asymptomatic cases (70%) to cases which cause permanent damage with serious complications in women's reproductive organs. *Chlamydia trachomatis* usually enter through sexual intercourse because they accumulate and colonize in urethra, vagina and endocervix. Ascending infection may happen through uterus, Fallopian tube and cause "silent/overt Pelvic Inflammatory Disease" (PID) with its complications. The infection may spread to liver (perihepatitis) which symptom is pain at the upper right quadrant of the abdomen. The autoimmune response to these bacteria will worsen PID and may cause a reactive arthritis. If it happens to a pregnant woman, Chlamydia will cause infections in the neonatus and a post-partum complication in the mother.

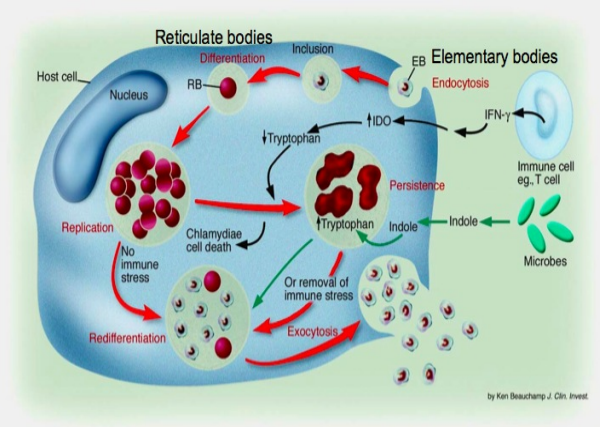

Figure 1. Microbiological aspect of *C. trachomatis*

C. trachomatis enters into the epithelial columnar cell or transitional from genital tract, rectum and perineum. EB from Chlamydia will enter the cell, infect it, change into RB which will then replicate, and finally cause the cell's death. At the Fallopian tube, there will be subepithelial inflammation, epithelial ulceration and scar formation. These damages are initiated by the cell death and are supported by the repeated slow hypersensitivity reaction to the heat shock from Chlamydia 60kDa (HSP-60). The table below shows possible complications which are triggered by *Chlamydia trachomatis* infections in women's genital tract:

Table 1. Complications triggered by *Chlamydia trachomatis* infections in women's genital tract

Site	Disease	Symptoms And Signs
Urethra	urethritis	Frequency/dysuria
Cervix	cervicitis	Mucopurulent
		Vaginal discharge
Uterus	endometritis	Vaginal discharge
		Irregular bleeding
		Post coital bleeding
Fallopian tubes	salpingitis	Pelvic Inflammatory Disease
		Ectopic pregnancy
		Tubal infertility
		Chronic pelvic pain
Bartholins glands	bartholinitis	Swelling and pain of vulva
Pregnancy/Neonate	Pneumonitis	
	Conjunctivitis	
	Post partum endometritis	

EARLY DETECTION OF *CHLAMYDIA TRACHOMATIS* INFECTION

The specimens which may be collected for diagnosing *Chlamydia trachomatis* genitalia infections are:

1. Cervical Swab.
   This method must be done with extra care because it is very manipulative and may cause bleeding.
2. Urethral Swab.
   This method requires a relatively deep insertion into the patient's urethra, therefore it is painful. This is also a manipulative step.
3. First Catch Urine.
   This is an alternative specimen which is very suitable for genital infection filter test because it is not manipulative. It also shows accurate results.

Some of the methods used to diagnose *Chlamydia trachomatis* infections are as follows :

1. Culture is not performed in most modern laboratories for routine diagnosis of *Chlamydia trachomatis* infection because it requires a complex facility, high costs and well-trained technicians. Furthermore, culture method can only detect living elementary body form. However, this method is still used in sexual violence cases because culture is a "gold standard: of 100% specificity.
2. Conventional Enzyme-linked Immunoassays (EIA). There are some EIA methods performed to detect Chlamydial lipopolysaccharide through antigen-capturing method using monoclonal or polyclonal antobodies. However, the sensitivities are varied and therefore a confirmation is needed.
3. Amplified Enzyme-linked Immunoassays. In this test, antigen is captures normally and the doubling indication is ampified through two ways. First, the antibody is conjugated with a linker just as each antibody molecule carries several enzyme molecules. Second, an enzyme is added into the reaction as a coloring agent through substrate regeneration. While this test has good sensitivity an specificity, it still requires a confirmation.
4. Direct Immunofluorescense. The quality of the result of this test depends on the experience of the technician.
5. Nucleic Acid Amplification Test (NAAT). NAAT test includes polymerase chain reaction (PCR), ligase chain reaction (LCR), both needs heat denaturizing at a thermocycler to separate DNA chain for the following reactions. While with transcript mediated amplification (TMA) and strand displacement amplification (SDA), the reactions are performed in a fixed temperature. NAAT test has the highest sensitivity and specificity, but needs a spacious laboratory with sufficient facility so that it is quite costly. However, considering the excellent specificity and sensitivity, this test could be a filter test for *Chlamydia trachomatis* genital infection. To suppress the cost, a "pooling specimen" can be done at several big laboratories around the world.

THERAPY OF *CHLAMYDIA TRACHOMATIS* INFECTION

Table 2 shows medicines which can be taken by patients with *Chlamydia trachomatis* genital infection, along with the advantages and the disadvantages.

Table 2. Medicines for patients with *Chlamydia trachomatis* genital infection

Medicines	Advantages	Disadvantages
Doxycycline 100 mg, 2X/day for 7 days	Affectivity >95% Relatively cheap	Contraindicate pregnancy, photosensitive, side effects in 20% of the cases (disturbance at the GI Tract)
Deteclo (Triple tetracycline) 300mg, 2X/day for 7 days	Cheap Affectivity >95%	Should not be taken with milk, contraindicate pregnancy, photosensitive
Azithromycin1g	Affectivity >95% Single dose Preferred by patients	Expensive, no available data on long-term usage and pregnancy
Erythromycin 500 mg, 4X/day for 7 days or 500mg, 2X/day for14 days	Cheap Safe for pregnancy	4X/day, varied medication time, affectivity <95%, significant side effects on 25% of the cases
Ofloxacin 400 mg, 2X/day for 7 days	Affectivity > 95% No side effect	Expensive Contraindicate pregnancy and youngsters (<12 years old)
Amoxicillin 500 mg, 3X/day for 7 days	Safe for pregnancy No side effect	Low affectivity, a risk to latent infection, dosage of 3X/day

By understanding the microbiological aspects, pathogenesis, early detection and therapy of *Chlamydia trachomatis* infection, we expect to be able o suppress the incidents of *Chlamydia trachomatis* genital infection in Indonesia, so that finally it will improve women's reproductive health in Indonesia.

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