

Pathogenesis and virulence of *Chlamydia trachomatis*

Abstract:

The pathogenesis of *C. trachomatis* disease is a multi-step process that includes: (1) infectivity and exposure to the organism (2) Susceptibility to infection and sickness related to the host's genetic makeup. In at-risk teenage and young adult groups, recurrence and chronic infections are also common. Antibiotic resistance to the primary medications used to treat *C. trachomatis* is becoming increasingly widespread, even with correct diagnosis. A chlamydial infection can prevent tumour necrosis factor (TNF)- α -induced physiological apoptosis. Failure to adequately prevent, identify, treat, and remove infection increases the risk of pathogenicity and illness. The plasmid glycoproteins 1–8 (pGP1–8) encodes eight open reading frames and is found in most *Chlamydia* species. In the United Kingdom, there has been a recent increase in the prevalence of such illnesses, whereas in the Scandinavian nations, there has been a drop, albeit there has been a minor increase in recent years (owing to the development of nucleic acid testing technologies, to some extent). However, it should be noted that reliable monitoring systems and population-based data are *Chlamydia trachomatis* 4 gitis. *Chlamydia trachomatis* is made plasmator free moreover it's weakened in the vaginal canal of the mouse and nonhuman primate ocular tissue. The plasmid-free organisms 'which are in vivo but not in vitro traits were completely mimeographs when pGP3 was inadequate, demonstrating that plasmid encoded pGP3 is an important virulence factor in vivo. Moreover, leading to a shortage on cost-effective moment in time tests including methodologies that consistent strain typing during therapeutic, overall degree underlying therapeutic failure is totally foreign. Those disadvantages were exacerbated by the found that the rest of genders infestations were undiagnosed, allowing both continuous silence propagation and developmental defects. The popular medications *C. trachomatis* is becoming more prevalent, also with proper identification.

Keywords

Innate along with acquired immunity, Reiter's syndrome, 7.5 kilobyte plasmid, *Chlamydia muridarum*, pGP4, pGP3

Objective- Review of *Chlamydia trachomatis* pathogenesis and virulence

Introduction:

Humans are infected with *Chlamydia trachomatis* and *C. pneumonia*, pigs with *Chlamydia suis*, and mice with *Chlamydia muridarum*, and other species are for colonising various host species in the Chlamydiaceae family of obligate intracellular bacteria. Guinea pigs and cats, are poisoned by *Chlamydia caviae* and *Chlamydia felis* respectively psittaci bacteria-carrying bugs can infect the person's respiratory tract, producing dreadful septicemia. Humans, on other hand, are mostly concerned with *Chlamydia trachomatis*, a sexually transmitted infection. The genus *Chlamydia*, it involves *Chlamydia trachomatis*, *Chlamydia psittaci*, *Chlamydia pneumoniae*, along with, *Chlamydia pecorum* is most recent addition to the *Chlamydia* subfamily. The homology of DNA between Chlamydial species has been approximated not as much as 10%. *Chlamydia trachomatis* is the world's majority customary infection transmitted through sexual intercourse (STD). The real prevalence and incidence of this disease are unknown. World Health Organization (WHO) says that every year, almost 100 million new instances of lower genital tract infections are reported, according to them. However the most off females in the company of these infections have no symptoms, hence they go unobtrusive. According to A systematic review says that according to them, In symptomless women of Europe continent, the pervasiveness of *C. trachomatis* fluctuated from 1.70 to 17.0%. The prevalence of STD among young women who have taken part in clinics for STD is quite higher than 10%, and in studies based on population, the prevalence among under 30-year-olds in the Netherlands, Denmark, and the United Kingdom was in between 2 and 6%. The figure of infections caused by chlamydia in the genital region was recorded and it is on the ascent, though it's indistinct either it is related to escalated rate otherwise an escalation in the number of cases.[1]

The cryptic plasmid is detected in maximum clinical isolates and is extensively disseminated among many distinct strains of chlamydia, this fact suggests that the plasmid comes up with advantages for plasmid-rich chlamydial organisms. Furthermore, the homology of the plasmid sequence closely bears a resemblance to that of the genome of chlamydia which implies that the plasmid was chosen for its ability to adapt to a variety of hosts of chlamydia.[2]

During the time of chlamydial infection, all 8 transcripts from plasmids are translated into proteins. In spite of the fact that precise functions of these proteins have yet to be resolved, it is possible that the plasmid is maintained to complete functions which are essential for chlamydial

infection advancement. There was no detectable difference in in vitro growth in cultured cells between the plasmid-inadequate *Chlamydia trachomatis* L2 strain acquired from inflammation of rectum and colon outpatient and L2 strain of a wild type, which implies that the plasmid isn't necessary in favour of maturation of chlamydia ex vivo. A recent study found that a *Chlamydia trachomatis* urethra isolate (aa serovar B variation) could be cultivated and recovered successfully without the plasmid aided this conclusion. Trachoma, lymphogranuloma venereum, along with murine pneumonitis emissary, these are the three biovariants (biovars) of *C. trachomatis*. Homology of the DNA analyses the three *C. trachomatis*, as well as direct comparisons of sequences of DNA of determined nucleic acids, experienced let fall in such a manner that the trachoma and lymphogranuloma venereum (LGV) group of micro organisms are almost equivalent, the murine biovar, on the other hand, is more distantly connected.[3]

Biology of Chlamydia

A chlamydial infection can cause the development of proinflammatory cytokines, as well as an immunological response to the agent and antibodies to heat shock proteins (hsp). For example, to hsp60 (Witkin et al. 1996). *Chlamydia* is a sexually transmitted disease. It has been discovered that human hsps and other bacteria share epitopes. It's been suggested that chlamydial infections could cause elicit an immunological reaction. The manufacture of hsp60 is possible, produce localised inflammatory reactions, such as in the gastrointestinal tract RBs may be able to evade the immune reaction by passing through the uterine tubes. As a result, persistent infections can be explained. The creation of new EBs derived from RBs can elicit an immunological response. Inflammatory responses that lead to a cyclic phase of the diseased tissue is scarred. This is an example. The elementary body (EB) is extracellular, and is a transmissible form which is characterized by an osmotically resistant outer membrane and a highly condensed chromosome.[4]

The reticulate body (RB) is a chlamydiae replicative intracellular form. Chlamydiae are classified as energy parasites because they are unable to generate a net gain of ATP and hence rely on the host for energy. Because of this, *Chlamydia*'s cell-free development has been abandoned, and in vitro growth requires the use of cell culture methods or yolk sacs. The envelope structure is another distinguishing feature of Chlamydiae. [5]

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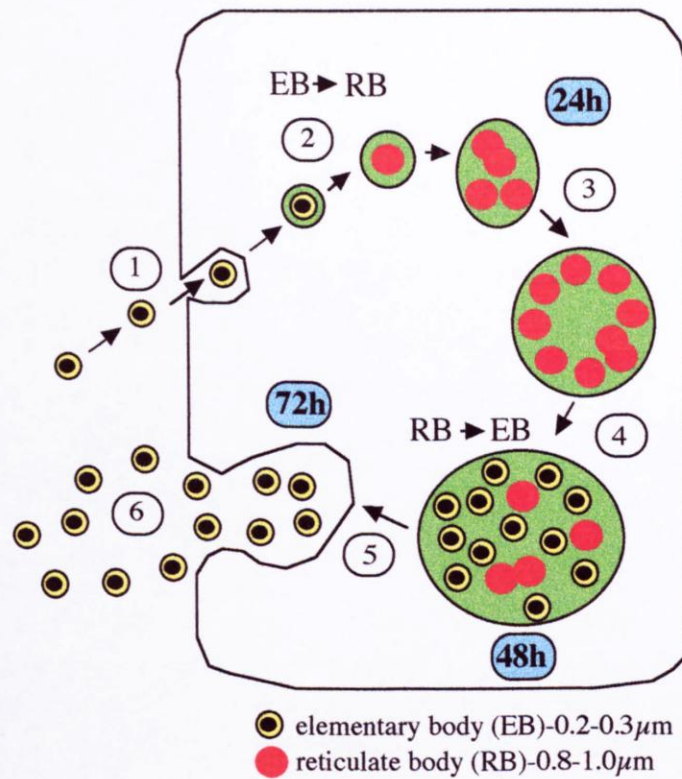


Figure 1. Schematic representation of the chlamydial developmental cycle.

- 1) EB adherence/attachment to the host cell, followed by internalization.
- 2) Inhibition of phagolysosomal fusion, and primary differentiation EB->RB.
- 3) RB multiplication by binary fission.
- 4) Asynchronous re-differentiation RB->EB.
- 5) EB release from host cell.
- 6) Continuation of chlamydial developmental cycle.

Developmental cycle of Chlamydia

Several ligands of bacterial and host receptors are involved in engaging to the host cell [16–18] (FIG. 1). When T3SS effectors come in proximity with the elementary body, the elementary body is internalised into the inclusion. Early genes are translated and the shift to the reticulate body takes only a few hours (6–8 hours post-infection for *C. trachomatis*). The term "nongonococcal urethritis" (NGU) was coined to describe urethral discharge that was not caused by gonorrhoea (Dunlop et al. 1972). The true aetiology of these cases was uncovered after procedures to diagnosis *C. trachomatis* infection were established. NGU cases exceeded gonococcal urethritis cases by the end of the 1970s, a trend that has continued in most nations. This is also true for urethritis that remains after gonorrhoea has been cured microbiologically but not clinically, i.e. postgonococcal urethritis (PGU). PGU is frequently caused by a *C. trachomatis* infection that has not responded to traditional gonorrhoea treatment. Exocytic vesicles are guided to the inclusion, and host–pathogen interactivities are ameliorated [6]

Genes of mid-cycle are then subsequently produced (8–16 hours after *C. trachomatis* infection) and hold effectors that arbitrate nutrition for the survival of the host. The bacteria carves up via binary fission, which gives rise to the inclusion to grow remarkably. Individual inclusions are generated when many elementary bodies contaminate a single cell in some species, such as *C. trachomatis*, and they homotypically put together with each other. During this stage, some late-cycle receptors are bundled in progeny elementary bodies, ready to be allowed to leave during the successive infection cycle. Toxic factors of chlamydia in governing the morbid consequence of chlamydial infection in the catarrhine female genital tract representation. [7]

Implementation of attachment and entry

When the elementary body (EB) of chlamydial gets into deal with the epithelial cell membrane of the anchor, the infectious operation starts. The recognition of adhesins (i.e. the predictor of initial elementary body (EB /cell interconnections) of chlamydia is not studied, but a number of acknowledged adhesins have been put further, as well as the outer membrane protein (MOMP) of chlamydia, chlamydial cytoadhesin (CCA), a heparan sulphate-like glycosaminoglycan (GAG), and chlamydial heat shock protein (CH). In spite of the fact that the precise technique of elementary body (EB) engrossment is not calculated, conjectures consist of receptor-mediated

endocytosis in trenches carpeted with clathrin, pinocytosis in non-carpeted trenches, and bloodsucker-specific internalization.[8]

Multiplication and growth

Because of the early start, production of proteins of chlamydia, the chlamydiae remain within an inclusion that does not merge with lysosomes once they have entered the host cell. The fundamental divergence of elementary body (EB) to reticulate body (RB) calls for the diminutive splitting of MOMP and supplementary proteins of outer membrane, as well as the unfastening of the nucleic acid of chlamydia. Sphingomyelin is carried to the inclusion membrane originating at the trans-Golgi network of the host, and it has even been found in chlamydiae. Proteins of Chlamydia are thrust into the inclusion membrane. It appears that the inclusion membrane should be remodelled in chlamydia. Reticulate body(RB) replicates within the inclusion by binary fission, accompanied by the offspring still alive intimately linked until later along with the cytoplasmic insertion layer in the embryonic revolution, implying that sort of close contact is essential for intracellular growth.[9]

Ejection from the host cell

The RB to EB differentiation pathway starts asynchronously. 48-72 hours after infection. The detachment of RB from the inclusion membrane has been suggested as a signal for differentiation. [10]

Antigens of Chlamydia

Proteins high in cysteine

The proteins OMP2 and OMP3 are cysteine-rich. found solely in elementary bodies that are specific to developmental stages. MOMP, OMP2, and OMP3 are thought to be substantially disulfide cross-linked, mediating the chlamydial elementary body's structural and osmotic resilience. OMP2 has different pI values than the trachoma biovars, which is single enzymatic distinction between , lymphogranuloma venereum (LGV) and the biovars of trachoma[11]

Heat shock proteins

Proteins that are activated by heat. When *C. trachomatis*-poisoned cells are cultured, exposed to warmth, stress. During the in vitro chlamydial developmental cycle, the pair cHSP60 together with cHSP70 stay contained within the inclusion.[12]

Glycoprotein

LPS (lipopolysaccharide polysaccharide) of chlamydia is an antigen which is group specific. that should be demonstrated to have a 3-deoxy-2-keto sugar that is comparable, 3-deoxy-octulosonic acid is similar, but not identical (Kdo) as an immunodominant group. The two terminal chlamydial Kdo units are joined by a unique 2.8 linkage (coded by the *gseA* gene), forming a chlamydial distinctive epitope. According to research, chlamydiae produce both a smooth and a rough LPS version.[13]

The outer membrane compound of chlamydia of elementary bodies is manufactured of about 60% major protein of outer membrane (MOMP). Major protein of outer membrane (*omp1*), a single-copy gene that was originally ordered from LGV2 and comprised of 1,182-bp which encodes 394 albuminoid.[14]

Pathogenicity

pGP4's Role in Chlamydial Pathogenicity

The discovery came up with the molecular foundation for the Caldwell group's early conclusion that the *Chlamydia trachomatis* plasmid DNA is a transcriptional selector. When the chromosome outlines of plasmid-free L2R life forms supplemented with the out-and-out plasmid as opposed to a plasmid diminished of *pgp4* were compared, *pgp3* impression shranked by four folds, while 9 chromosomal nucleic acids, together with *glgA*, declined by two to twenty-three folds together with 5 supplementary chromosomal genes escalated by two folds in non-attendance of *pgp4*. In addition, plasmid-deficient creatures' chromosomal gene expression trended in the same direction as *pgp4* struck-out life forms, implying that pGP4 is substantially in the wrong for plasmid-arbitrated gene control.[15]

Immune defence mechanisms

Innate reaction

It is only recently that the significance of the host's reaction to chlamydial infection has been examined. In acute chlamydial infection, an early entrance of white blood corpuscles (perhaps controlled by CD 18, convoluted in lipopolysaccharide binding) was shown to have a substantial role in reducing early illness phases.[16]

The action of pro-inflammatory cytokines could be another simplification for the intrusion of white blood corpuscles to the infection area. The production of pro-inflammatory cytokines may have a role in recruitment of white blood cells and other corpuscles of inflammation to infection area preliminary to lymphocytes arrive. Persistent stimulation of epithelial cells following re-infection or the commencement of an immune response may increase the local inflammatory response, and IFN- γ has been hypothesised to have such an effect during recurrent infections. IFN- γ has been found to stimulate the synthesis and secretion of IL-8 in chlamydial infected epithelial cell lines. As a result, greater inflammation may be caused by the synthesis of IFN- γ as part of a Th 1 response. In spontaneous infection, such an increased cytokine response has been observed.[17]

Humoral reaction

According to studies, antibodies aid in protection against *C. trachomatis* MOMP in mouse models, but they aren't essential. In vitro, however, antibodies have been demonstrated to neutralise *C. trachomatis* infection. In the presence and absence of complement, neutralisation occurs by either blocking the attachment of chlamydial elementary bodies to the cell or allowing chlamydial internalisation but inhibiting/preventing multiplication. Lymphocytic proliferation experiments revealed that humans produce cell-mediated immune responses to chlamydial genital tract infection. According to animal and human research, the protective response against chlamydial infection is predominantly T_H1 related. People who have a poor cell-mediated immune system. Immune responses and powerful antibody responses have been demonstrated to be susceptible to reinfection, slow to heal infection, and have significant levels of clinical inflammation and sickness in scarring disease.[18]

Non-gonococcal bacteria causing Urethritis.

Non-gonococcal urethritis (NGU) is urethritis that is caused by a bacteria other than *Neisseria gonorrhoeae*. *C. trachomatis* has been detected in the urethral samples of close to 13 percent to 50 percent of NGU patients, with the remaining cases attributed to *Trichomonas vaginalis*, Herpes simplex virus, and *Mycoplasma genitalium*. There is no variation in clinical outcomes among chlamydial and non-chlamydial NGU.[19]

Venereal lymphogranuloma

Lymphocytic granuloma venereum (LGV) is a systemic, transmissible disorders which we get through sexual contact are caused by *C. trachomatis* serovars L 1 to L3. The countries of East and West Africa, India, Southeast Asia, and South America are all affected. LGV causes an ulcer that appears 3–12 days after infection and affects the coronal, sulcus, inner foreskin, or glans penis in male and the rear vaginal wall, fourchette, or posterior cervical line in females.[20].

Diagnosis in Lab

Specimens

As we know Chlamydia is an intracellular organism, the most vital goal is that the specimen should obtain from host cells that contain the microorganism. A well designed media is used for the collection of specimen, such as 0.2Molarity sucrose in phosphate buffered saline (2SP). [21]

Method used for the preservation of tissue is known as Tissue culture. Many scientists worked on it and used different technique for tissue culture for example –Gordon used irradiated McCoy cells to demonstrate and distinguish the first cell culture for *C. trachomatis* in vitro growth. Immunizing or Inoculating patient specimens onto cell monolayers is how culture is done. While the technique has a high particularity and explicitness of 100 percent, it has a lesser sensitivity (70-85 percent) than DNA amplification techniques. There are few of the cell lines such as BGMK and McCoy cells that have been used to propagate *C. trachomatis*. A high frequency sound waves sonicate the bacterial cells to destroy cellular components and free chlamydial elementary bodies are done prior to the cultivation or development.[22]

Conclusion:

COVID is pandemic situation in whole world which goes through trouble and due to these condition economic status of most of the countries is decreases due to lockdown\ shutdown in economically stable countries . Wuhan in china is origin of COVID – 19 pandemic , death rate of COVID patient is gradually increases due to incomplete availability of hospitalization ,and decreases in oxygen supply in hospital , COVID patient follows the symptoms like coughing ,pneumonia, double pneumonia, chest pain , low oxygen supply to patient suffering from covid situation ,dosage vaccine and amount of availability of vaccine controls the situation (patients health, and economic control . KOH technique is expensive screening test. Candida is often cause fungal infection. Overgrowth of fungi can result from drug overuse which can harm basic vaginal enviornment, loss of immune system. [23]

Among the eight pGPs identified by chlamydial plasmids, only pGP3 is both localised in the outer membrane complex and liberated into the cytoplasm of the host cell. Medical negligence (carelessness , non performance ,laxness) is at peak to concern about pubic health among public health care provider as it effect public health and safety and also not only helth also wealth . Or any dis ability which Is permanent to subject or patient .the patient safety is depend on doctors skill and experience that how he \she is gone treat the subject. Because Chlamydia can finish its manufacture inside an inclusion, the chlamydial proteins it produces can interact with host cells. The immunodominant pGP3 protein has been linked to illnesses in infected patients. Due to its C-terminal trimerization dominion (pGP3c), which is comparable to TNF's receptor binding dominion, it is a well-constructed trimer [24-29]

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