ROLE OF CHLAMYDIAE IN INFERTILITY

THESIS

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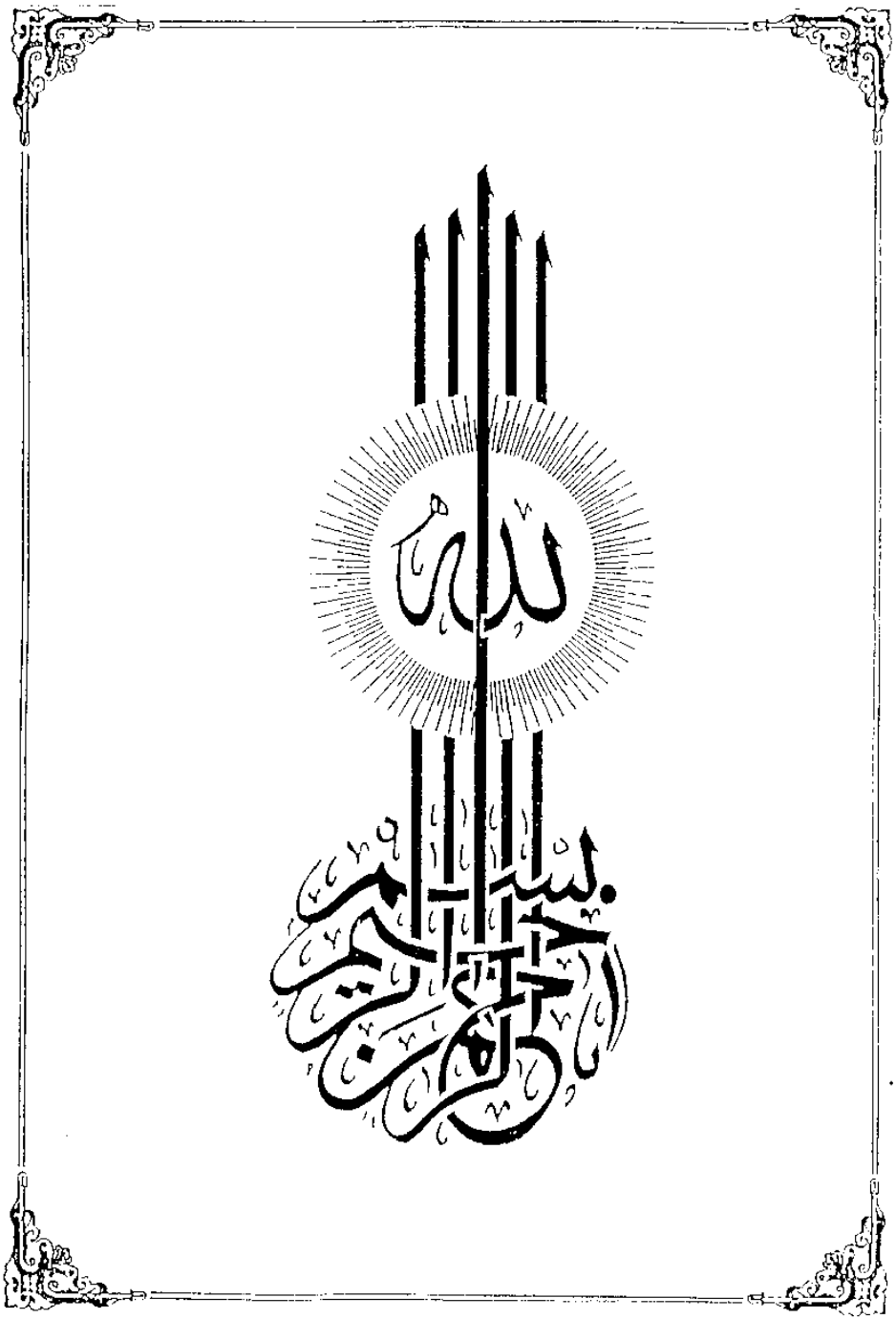

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Introduction:

The chalmydiae are obligatory intracellular parasites once considered to be large viruses senstive to the action of some antimicrobial agents or antibiotics However a more sophisticated defenition of viruses and bacteria has allowed the recognition that the chlamydiae are bacteria - like and definitely not viruses. The sole feature that chlamydiae share with viruses is the obligatory intracellular nature of their parasitism. Genital chlamydiae are commonly found in the genital tract in promiscuous populations. When the incidence of these organisms in groups of women was compared with the incidence of other recognised sexually transmitted pathogens as Nisseria gonorrhea, Trichomonas vaginalis and herpes simplex type 2, chlamydiae were usually the most frequently isolated organism.

There is now good evidence that chlamydiae cause salpingitis and this suggests that tubal infertility

may sometimes be of chlamydial origin. Whether active chlamydial infection, for example cervicitis, might be related to infertillity is unknown. Since chlamydiae cause urethritis and epididymo-orchitis in men, it is possible that infertility or subfertility in some men might be caused by chlamydiae, although this has never been studied.

This work investigates the prevalence of chlamydia trachomatis infection in 25 infertile women as an attempt to establish a +ve relation between tubal aetiology in infertile women and chlamydial infection.

MICROBIOLOGY OF CHLAMYDIAE

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The chlamydiae are obligatory intracellular parasites once considered to be large viruses sensitive to the action of some antimicrobial or antibiotics. However, a more sophiticated definition of viruses and bacteria has allowed the recognition that the chlamydiae are bacteria-like and definitely not viruses. They differ from viruses in having two nucleic acids, DNA and RNA, multiply by binary fission rather than by self-assembly and in having a discrete cell wall, quite analogus in structure and content to those of the gram-negative bacteria. The sole feature that chlamydiae share with viruses is the obligatory intracellular nature of their parasitism.

Chlamydiae are restricted to an intracellular milieu because they are incapable of synthesizing high energy compounds such as adenosine triphosphate (ATP) and guanosine triphosphate (GTP). These compounds which are essential for metabolism and respiration must be provided by the infected host cell leading "Moulder" [75] (1974) to coin the term "energy parasites". The host cell in addition to being the sole source of the ATP & GTP required for the chlamydial metabolic reactions, it supplies metabolites from its pool rather than

by degradation. Some of these metabolites such as isolucine may be growth restricting. When chlamydiae infect the host cell, they direct their synthetic capabilities to their own metabolic requirements. The infected cell ceases to multiply and though its metabolic capabilities remain equal to the normal metabolic capabilities of an uninfected multiplying cell, they are directed toward the production of more chlamydiae rather than of more cells. Because chlamydiae are obligatory intracellular parasites, it is high advantageous for them to induce phaocytosis by host cell. Comparative uptake studies using other bacteria showed that chlamydiae were able specifically to induce their own phagocytosis by nonprofessionally phagocytic host cells. The chlamydiae share with many obligatory intracellular parasites the ability to resist or escape the normal defence mechanisms of the cell. They entre the cell through a phogocytic process and are present within a phagosome through their developmental cycle. However, this phagosome does not fuse with lysosomes until very late in the developmental cycle. The prevention of lysosomal fusion is directed by chalmydial antigens and is dependent upon live chlamydiae. Chlamydiae could be distinguished from the other group of intracellular bacteria, the rickettsiae, by their inability to synthesize compounds for high-energy storage and utilizations (Weiss & Wilson[124] 1969; Hatch[47] 1975), by their lack of cytochromes and other

compounds of the respiratory electron chain, and by their developmental cycle.

CLASSIFICATION:

Because of a unique developmental cycle that differentiate them from all other micro-organisms, the chlamydiae have benn place in their own order, the chlamydiales. There is one genus chlamydia, and two species - Chlamydia psittaci and C. trachomatis. All members of the genus are clearly related by their common-developmental cycle, common antigens and similar biological and metabolic activities. Some of the features distinguishing the two chlamydial species are summerized in the following table.

FEATURES	C.TRACHOMATIS	C. PSITTACI
Natural infections	Principaly human ocular & urogenital disease.	Respiratory-urogenital & systemic infections in a wide variety of animals. Man is incidentally infected.
Inclusions	Compact glycogen-containing stain with iodine.	Diffuse non-glycogen containing, do not stain with iodine.
Nucleic acid	Guanosine+cytosine (G+C)44/, little homology on hybridization between C-trachomatis & C-psittaci DNA.	G + C 41.2/
Antibiotic sensitivity	Sulphadiazine sensitive	Sulphadiazine resistant
Laboratory growth	With exception of LGV, gents require centifugation on to specially prepared tissue-culture cells.	Grow readily in tissue culture without centrifugation or special cell treatment.

Table (1)

The terms "Chlamydia subgroup A" and "Chlamydia subgroup B" for C. trachomatis & C. psittaci introduced by Gordon & Quan (1965), although still used in the literature, are absolute and must be abondoned to avoid confusion with alphabetically

designated C. trachomatis serotypes and serogroups.

Classification according to micro-immunofluorescence (micro-IF) technique:

It is classified according to type-specific antigens. By this technique, C. trachomatis has been shown to have at least 15 serotypes found in lymphogranuloma venereum, A-C in trachoma and C-K in oculogenital infections.

Development:

Chlamydiae have responded to the specialized demands of obligate intracellular life by evolving a developmental cycle that is unique amongest prokaryotic organisms.

Two main structures in the chlamydial growth.

Characteristic	Elementary body (EB)	Reticulat body (RB)
Size	0.2 - 0.3 um	1.0 um
Morphology	Electron-dense core rigid	Pleomorphic Gram-negative coccus
Infectivity to host cell	Infectious	Non infectious
RNA : DNA ratio	1 : 1	3 : 1
Metabolic activity	Inactive	Active
Trypsin digestion	Resistant	Sensitive
Haemagglutinin	Present in some strains	Absent
Envelop subunits	Present in some strains	Absent

Table (2)

Infection of the host cell is initiated by the close adhesion of EB to the host cell surface. It is highly likely that chlamydiae have evolved specific mechanisms for attachment and penetration into the host cell, but no specific chlamydial adhesion or host cell receptor has yet been characterized. Entery of the attached EB into the host cell is by endocytosis, the invading organisms lying within a tight vacuole formed by the host cell membrane. Paradoxically chlamydial uptake, unlike classic phagocytosis, does not involve microfilament - dependent cell surface movement. Protaglandins and other compounds known to alter cyclic nucleotide levels in the cell affected the susceptibility of the cell to chlamydial infection. This observation may be of clinical importance, given the modulating effect of sex hormonal changes during the menstrual cycle on the cyclic nucleotide levels in the cells lining the genital tract.

Within 6 - 9 hrs. after ingestion, the EB enlarge, synthesize ribosomes and forms RB, with a diameter of about 1 um. The RB are metabolically active and multiply by binary fission.

By 20 hrs. after infection some of RB undergo reorganization within the expanding inclusion to form infectious EB. These reorganizing RB are frequently termed "intermediate

bodies". Release of these infectious EB in these circumstances is by host cell lysis.

A clinical characteristic of infection with chlamydiae is the tendency to produce persistant infection. At low multiplicity of infection, chlamydiae compete with the host cell for nutrients (Hatch, 47 1975). The host cell is not killed and the infected cells can divide giving rise to infected progeny. Limitation of the essential nutrients may greatly extend the chlamydial growth cycle giving rise to persistently infected host cells (Hatch, 47 1975). Such a mechanism might explain the frequent relapse of chlamydial infection following apparently adequate chemotherapy.