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INTRODUCTION TO PHARMACEUTICAL MICROBIOLOGY (PMB 271)
CHLAMYDIA

Introduction

The Chlamydiae are small, ovoid and colligate intracellular pathogens with peptidoglycan-free cell wall and can only grow by infecting eukaryotic host cells they cannot be grown in culture media. They lack several metabolic and biosynthetic pathways and depend on the host cell for intermediates, including ATP.

Chlamydial are classified according to their pathogenic potential, host range, antigenic differences, etc.

The chlamydiae consist of three species, ***C trachomatis, C psittaci,*** and ***C pneumonia.*** The first two contain many serovars based on differences in cell wall and outer membrane proteins. Chlamydia pneumoniae contains one serovar - the TWAR organism.

Chlamydia trachomatis: This species produces compact intracytoplasmic inclusions that contain glycogen; it is usually inhibited by sulfonamides. It includes agents of human disorders such as trachoma inclusion conjunctivitis, nongonococcal urethritis, salpingitis, cervicitis, pneumonitis of infants, and Lymphogranuloma Venerum (LGV)

Chlamydia pneumoniae : This species produces intracytoplasmic inclusions that lack glycogen; it is usually resistant to sulfonamides. It causes respiratory tract infections in humans.

Chlamydia psittaci : This species produces diffuse intracytoplasmic inclusions that lack glycogen; it is usually resistant to sulfonamides. It includes agents of psittacosis in humans, ornithosis in birds, feline pneumonitis, and other animal diseases. Three species that infect only humans have been characterized.

Characteristics of the three species of Chlamydiae

	C. trachomatis	C. Pneumoniae	C. Psittaci
Inclusion morphology	Round, vacuolar	Round, dense	Large, variable shape, dense
Glycogen in inclusions	yes	No	No
Elementary body morphology	Round	Pear shaped, Round	Round
Susceptible to sulphonamides	Yes	No	No
plasmid	Yes	No	YES
Serovar	15	1	>/ 4
Natural host	Humans	Humans, Animals	Birds
Mode of transmission	Person to Person, Mother to Infant	Airborne, Person to Person	Airborne, bird excreta to humans
Major Diseases	Tracoma, STDs, Infant Pneumonia, LGV	Pneumonia, Bronchitis, Pharyngitis, Sinusitis	Psittacosis, Pneumonia, fever of unexplained origin

Infectivity: *Chlamydia trachomatis* is a much dreaded sexually transmitted infection known. Chlamydia infection is passed from one person to another during vaginal, oral, or anal sex. It can also be passed from an infected mother to her baby during vaginal delivery and result in eye infection, blindness, and pneumonia in the newborn. This infection causes varieties of infections in humans including urogenital infections (urethritis, cervicitis, pelvic inflammatory disease, endometritis), conjunctivitis, ocular trachoma and abscess of gland.

Chlamydia trachomatis is a bacterium that causes varieties of infections in humans including urogenital infections (urethritis, cervicitis, pelvic inflammatory disease, endometritis), conjunctivitis, ocular trachoma and abscess of batholin gland. Of all the urogenital *Chlamydia* infections studied, 50-60% presented with cervical and urethral problems, 30% are single cervical infections while 5-30% are single uretheral infections (Isiabor *et at.*, (2005). The differences in the presenting symptoms are due to the different serovars and numerous variants of antigens which the organism posses. Serovars A, B/Ba, C, D/Da/E, F, G, Ga, H, I/Ia, J. K, L1, L2,, L2a and L3 have been identified using polyclonal and monoclonal antibodies against their major antigens, (major outer-membranes proteins-momp). Serovars A-C are associated with trachoma, serovars D-K, with urogenital and conjunctival cases while serovars: LI-L3 are associated with lymphogranuloma venereum. C. trachomatis is an obligate intracellular parasite. The obligate intracellular nature is a barrier to its study. Most isolates carry a piasmid which encodes eight proteins. The plasmid is a transcriptional regulator and a virulence factor. Plasmid-free isolates do exist in nature and these isolates do not spread in the population which indicates reduced biological fitness. One of these proteins called the outer membrane protein 1 (omp l) has five regions of conserved sequences that alternate with four variable regions which have high genetic variations, .and can therefore be used in genotyping of isolates. These variable domains are thought to be responsible for the bacteria's survival in their environments. The human immune response is directed towards these variable domains and the monoclonal antibodies mounted on these domains are able to destroy the bacteria in a cell culture. The T-cell epitopes .are also coded for in these variable domains; therefore any change in the epitopes that are coded for (which often happens) will enable the bacteria to escape monoclonal antibody detection. Efforts are then directed at sequencing these regions to determine which

serovars are present in a particular case of an infection, at a given time and in a given location.

Associated gynaecological problems:

C. trachomatis urogenital infections are associated with severe gyneacological condition, and present with such symptoms as urethritis and occasionally epididymits in men, and miscarriage and/or ectopic pregnancy or tubal infertility in women, resulting from the blockade of fallopian tubes and a complex immunological reaction emanating from autoimmune inflammatory damage of the bacterial 60-kD heat-shock protein-10. However, most infections by this organism remain asymptomatic; and this accounts for many untreated cases that often lead to complications, which' pose a great public health problem. The consequence of untreated cases is migration of the bacterium to the upper genital tract of women; which often .result in tubal dysfunction including tubal blockage and consequently ectopic pregnancy.

Active *C. trachomatis* infection has been shown to be an important risk factor for other STIs including HIV and syphilis, and this is due primarily to the mutual beneficial outcomes of the two infections to the infectious agents and their common portal of entry (urogenital tracts).

Other diseases

Psittacosis in birds and in humans is caused by *C. psittaci*, spread by wild and domestic birds, including poultry.

Chlamydia pneumonia is humans causes atypical pneumonia in hospitalized patients as well as in young individuals with an acute respiratory disease

Forms of Chlamydia:

Chlamydiae exist as two forms: (1) infectious particles called elementary bodies and (2) intracytoplasmic, reproductive forms called reticulate bodies.

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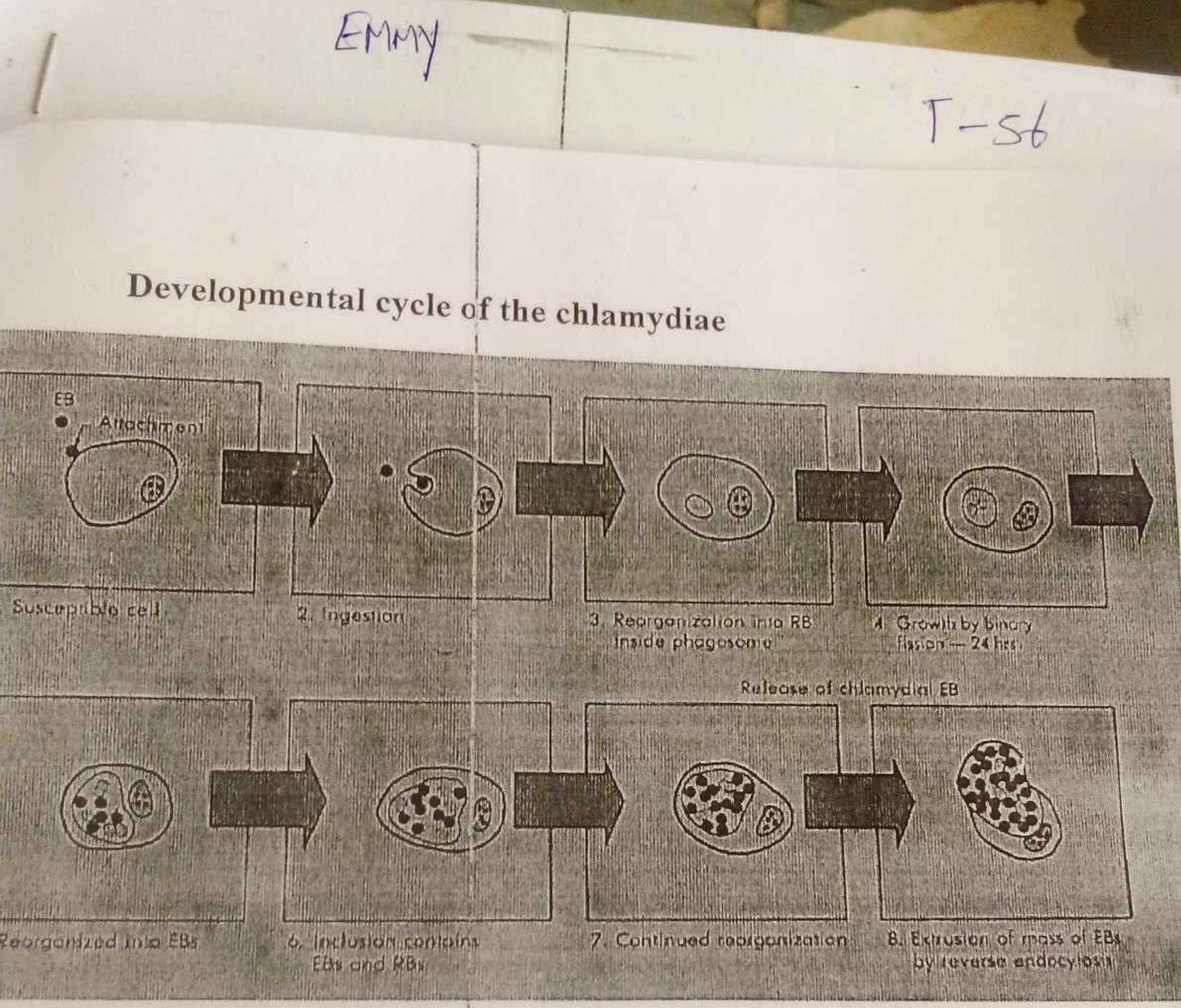
Developmental cycle of the chlamydiae



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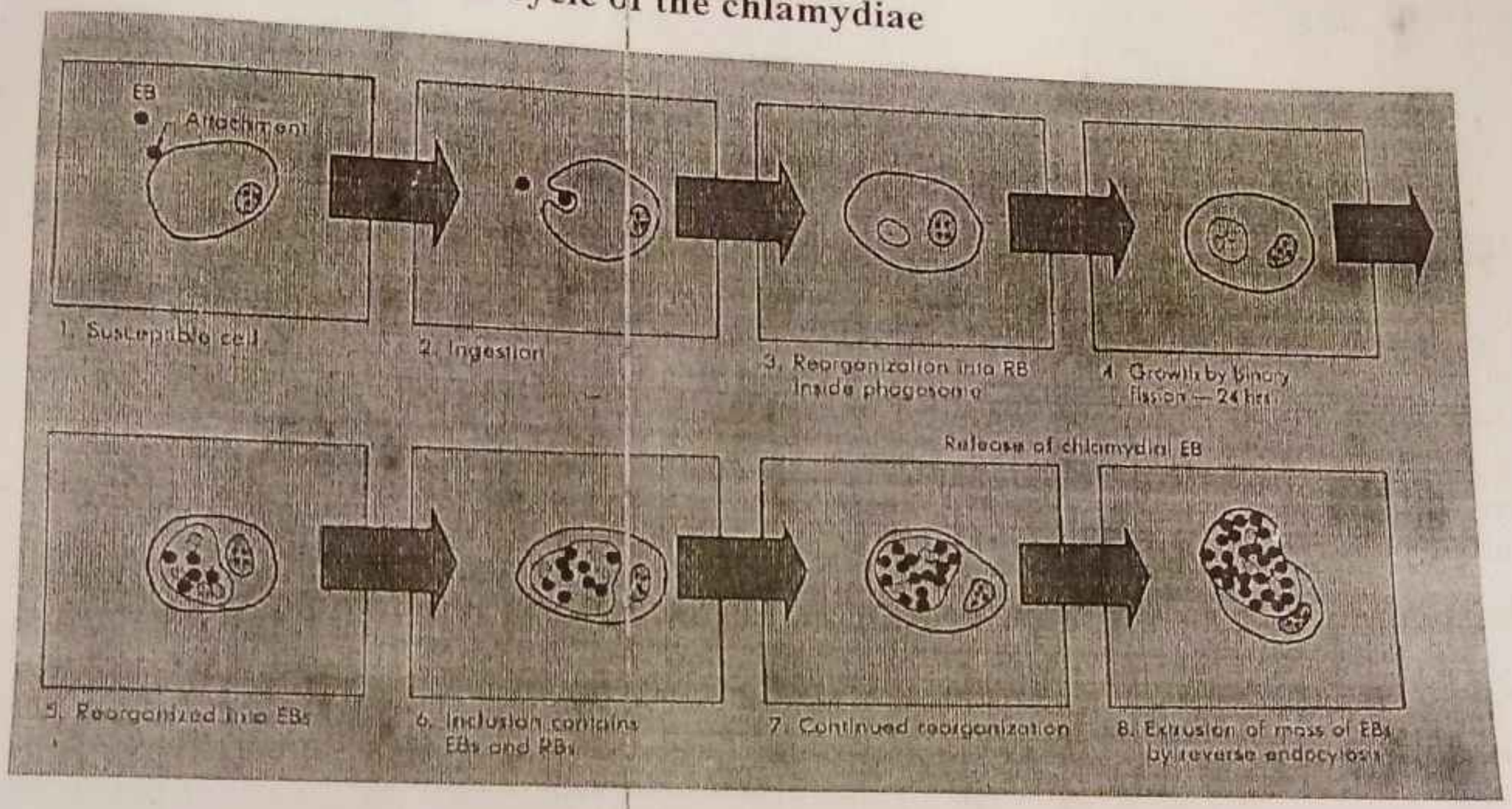

STAGES IN THE DEVELOPMENT CYCLE

Step 1: Attatchment : The infective particle, the elementary body attatches to the susceptible / eukaryotic cell. The elementary body acts like viruses.

Step 2: Ingestion : they guide the host cell to engulf them by endocytosis pathway

Step 3: The elementary bodies grows and divides several times inside the vesicle or cytoplasm. After which ,they are internalized and converted into reticulate bodies. there is increase in structure as well as the ability to grow and divide rapidly.

Step 4: Growth by binary fission of the reticulate bodies for 24 hrs

Step 5: More reticulate bodies are produced and few elementary bodies.

Step 6: Inclusion contains EB's and RB's

Step 7: Continued reorganization.

Step 8: vesicle is open for release or Extrusion of mass of EBs to attack another host cell and the cycle continues.

Pathology and Pathogenesis

Chlamydiae have a hemagglutinin that may facilitate attachment to cells. The cell-mediated immune response is largely responsible for tissue damage during inflammation, although an endotoxin-like toxin is also involved. The elementary bodies are infectious particles that can be transmitted from the infected tissues to uninfected tissues in the same person (transfer of *C. trachomatis* elementary bodies from an infected genital tract to the eyes and vice versa) or from a person with atypical pneumonia (caused by *C. psittaci* or *C. pneumoniae*) to healthy individuals (respiratory release of elementary bodies). In the infected individuals the chlamydial agent causes tissue damage and induction of interleukin-Iα, interleukin-Iβ, and tumor necrosis factor alpha, which are cytokines involved in the inflammation process. Neonatal infection by *C. pneumoniae* strains can also occur during passage through the birth canal, resulting to acute purulent conjunctivitis or blindness, either due to infection of the neonate during passage through the birth canal. In the presence of urethritis or cervicitis, *Chlamydia trachomatis* infection can also be further spread through sexual contact. The genital tract infection serves as a source of infectious elementary bodies for the eyes.

Epidemiology

Trachoma infection is a global problem, though prevalent in Africa and Asia. Trachoma occurs more in hot, dry areas with shortage of water and poor standard of living. The organism is spread to the eyes by flies, dirty towels, fingers, or cosmetic eye pencils. The initial infection usually occurs in childhood, and the active disease eventually appears (mostly by 10 to 15 years of age). Trachoma may leave a residuum of permanent lesions that can lead to blindness. *Chlamydia trachomatis* also resides in the genital tract. cervix and uretnra of adults, and genital infection is spread sexually. Lymphograrmloma venereum persists in the genital tract of infected persons.

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Treatment

The first step in the treatment of chlamydia infection is prevention. Prevention of chlamydia infection is best accomplished by abstaining from sexual activity or having sex only within a mutually monogamous relationship in which neither partner is infected with a sexually transmitted disease. Latex condoms also provide some protection when used properly.

Treatment of an uncomplicated chlamydia infection includes antibiotic therapy. Tetracycline and erythromycin, rifampin, sulfonamides, chloramphenicol, are in common use, but-control measures are better options. Hospitalization may be necessary if the woman is acutely ill with such complications as pelvic inflammatory disease, abscess or high fever. Prompt diagnosis and treatment increases the chances of preserving fertility in both men and women.

Laboratory Diagnosis

Culture: One involves collecting a specimen from an infected site (cervix or penis) to detect the bacterium directly. Another test that is becoming widely available can accurately detect chlamydia bacteria in a urine sample.

The organism is first grown in irradiated McCoy cells; homogenates that contain the chlamydial elementary bodies are centrifuged onto the' culture cells incubated. Isolates are then stained Giemsa stain or iodine and examined for typical cytoplasmic inclusions bodies. Fluorescent monoclonal antibodies are used to stain *C. trachomatis* elementary bodies in urethral and cervical exudates.

Serology and PCR: DNA hybridization can also identify and distinguish between species .