Case Scenario

A 25-year-old woman who presented to OBG clinic with spotting between the menstrual cycles. On examination she gave the H/O multiple sexual partners in the past 2 years without using any protective barriers. On examination no vaginal discharge, genital lesions or sores. Vital signs normal. The genital exam reveals normal vulva and vagina. Cervix appears inflamed, bleeds easily with a purulent discharge from the cervical os. Bimanual examination is normal. Cervical swab for Gram staining was not informative, KOH mount negative for fungal elements. HIV test, pregnancy tests were negative. Lugol's iodine stain shows reniform inclusions inside the infected cells. What is the possible diagnosis and treatment?

CHLAMYDIAE

species and their IMPORTANCE

General properties

- Obligate ***intracellular*** bacteria… produces number of diseases
- **Earlier names :**
  - PLT agent (Psittacosis Lymphogranuloma Trachoma)
  - TRIC agents (Trachoma-Inclusion Conjunctivitis)

Takes on two forms in it's life cycle:

– Elementary body (EB) : Extracellular and infective form.

Cell wall possesses Rigid trilaminar structure

– Reticulate body (RB): Multiplying form within the cell.

Were thought to be Viruses….but why bacteria?

Viruses

- Obligate intracellular
- No growth on artificial medium
- Pass through bacterial filters
- Intracytoplasmic inclusion bodies

Bacteria

- Both DNA & RNA
- Gram negative cell wall
- Mutiply by binary fission
- Synthesize their own nucleic acid
- Killed by antibacterial agents

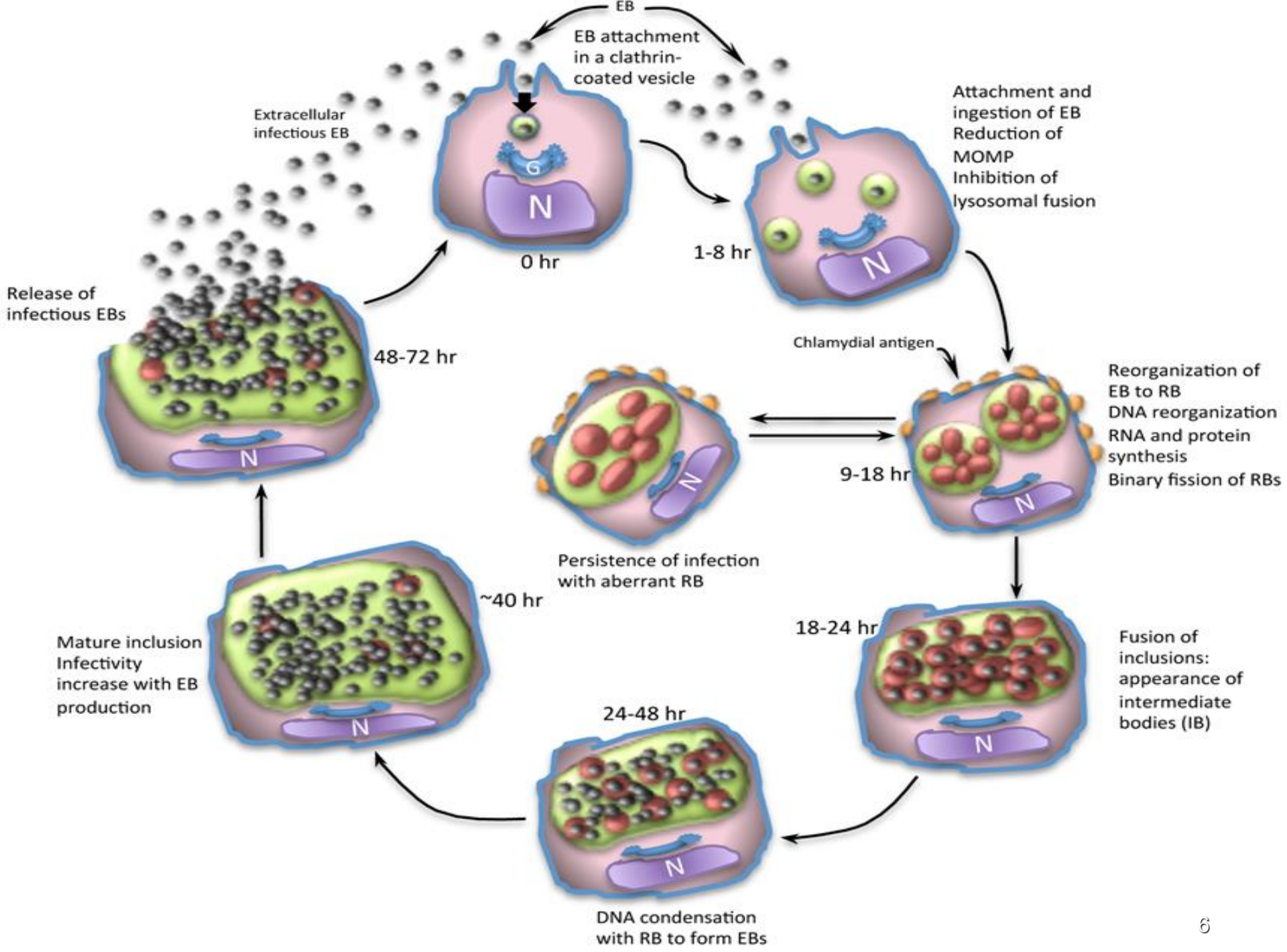
Growth and multiplication

- Growth initiated *by the attachment of* ***Elimentary Body*** to specific receptors on host cells (respiratory epithelia cells and macrophages) and endocytosed.

- Prevent the fusion of phagolysosome with cellular liposomes.

- In the phagosome **EB** transform into reticulate bodies **(RB)→ EB;** called inclusion bodies. (Round/pear shaped)

- **EB** released from the host cell by 48 hours.


EB
EB attachment in a clathrin-coated vesicle
Extracellular infectious EB
G
N
0 hr
Attachment and ingestion of EB
Reduction of MOMP
Inhibition of lysosomal fusion
1-8 hr
Release of infectious EBs
48-72 hr
Chlamydial antigen
Reorganization of EB to RB
DNA reorganization
RNA and protein synthesis
Binary fission of RBs
9-18 hr
Persistence of infection with aberrant RB
Mature inclusion
Infectivity increase with EB production
~40 hr
18-24 hr
Fusion of inclusions: appearance of intermediate bodies (IB)
24-48 hr
DNA condensation with RB to form EBs

Pathogenesis

- **EB** attached to receptors on *non ciliated columnar, cuboidal or transitional* epithelial cells on mucus membranes of the conjunctiva and genitourinary system

- Pocess LPS- protein complex

- LGV biovar mutiplies in mononuclear phagocytes seen in lymphatic system and produces *granulomatous lesion*

Chlamydiaceae Family
(Species, which cause human disease)

Species (genus)	Disease
C. trachomatis	
Trachoma biovar TRIC agents (A,B,Ba,C)	Trachoma, NGU, Adult Inclusion conjunctivitis,
Trachoma biovar TRIC agents D,E,F,G,H,I,Ia,J,K)	Genital chlamydiasis Neonatal conjunctivitis Infant pneumonia,
LGV biovar (L1,L2,L3 and L4)	LGV
C. pneumoniae	Pharyngitis, bronchitis, **CA pneumonia**
C. psittaci	Psittacosis

Chlamydia trachomatis

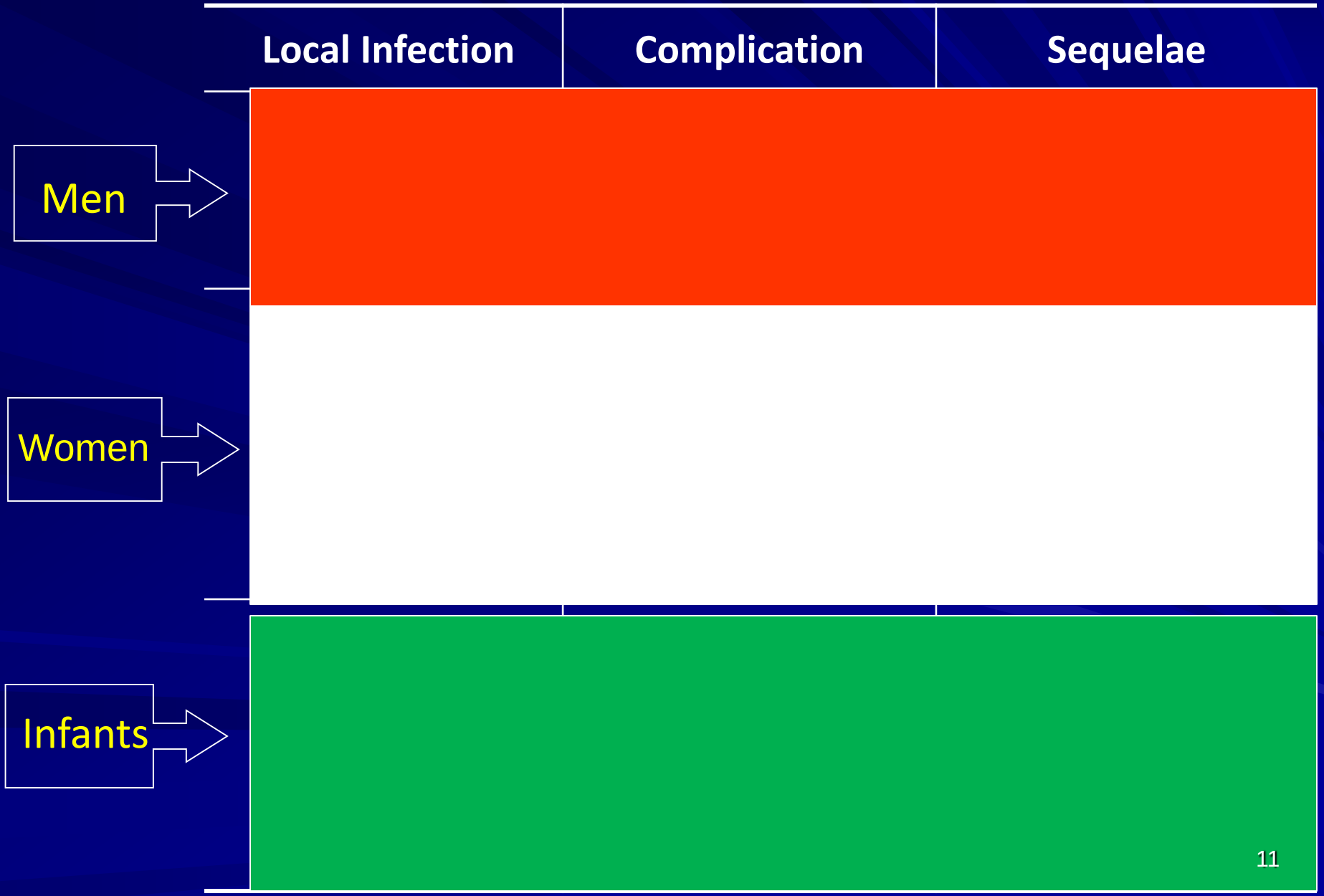
Mode of transmission

- Direct contact
  - Fingers and fomites (eye discharges)
- Perinatal transmission
- Sexual transmission
- Incubation period is 7-21 days
- Asymptomatic reservoirs more in population

Chlamydial infections: Occurrence

- Ocular infections
  - 2-3 yrs and young children
- Genital infections
  - Adolescent age
  - Multiple, abnormal sex partners
  - Presence of another STD
  - Oral contraceptive user

Clinical Syndromes Caused by *C. trachomatis*



C. trachomatis infection in Men (serovars D-K)

- **Non-gonococcal urethritis (NGU)**
  - Majority (>50%) asymptomatic
  - Symptoms/signs if present:
    Dysuria, urethral irritation, watery discharge
  - Incubation period : 7-10 days

- **Post-gonococcal urethritis (PGU)**
  - 2-3 weeks after recovery from gonococcal urethritis
- **Epididymitis & Proctitis**
  - Most common cause in male

C. trachomatis infection in Women

Mucopurulent Cervicitis

- Common;
- Majority (70%-80%) are asymptomatic
  - Mucopurulent endocervical discharge
  - Edematous cervix with erythema and friability

Urethritis

- Usually asymptomatic
- If symptomatic; dysuria, frequency, pyuria

Endometritis,Salpingitis,(PID)

Perihepatitis (Fitz-Hugh-Curtis Syndrome)

Adult inclusion conjunctivitis

(Swimming pool conjunctivitis ,Acute follicular conjunctivitis)

C.trachomatis serovars ***D-K***

- Bilateral red eye
- Ocular discharge, marked hyperemia

Neonatal conjunctivitis

(Inclusion blenorrhoea, Opthalmia neonatorum)

- Common than gonococci
- 3 weeks to 3 months after birth.
- *Swelling of eye lids with purulent discharge and severe hyperemia*

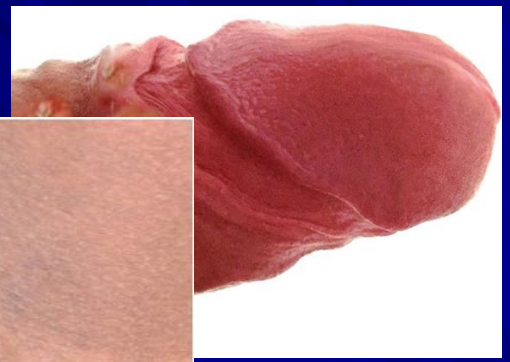
Trachoma *C.trachomatis serovars A,B,Ba,C.*

(Chronic keratoconjunctivitis)

- Acute infection:
  - Starts as follicular conjunctivitis advanced to papillary hyperplasia
- Late stages:
  - Pannus formation; cicatrization.
  - Limbal or palpebral conjuctival scarring
  - Entropian (Eye lashes inward)
  - Repeated rubbing on cornea (opacity,blindness)
- Corneal scrapings: Inclusion bodies *(Halberstaedter- Prowazek bodies)*

Lymphogranuloma venereum (LGV)

C.trachomatis **serovars L1,L2,L3**



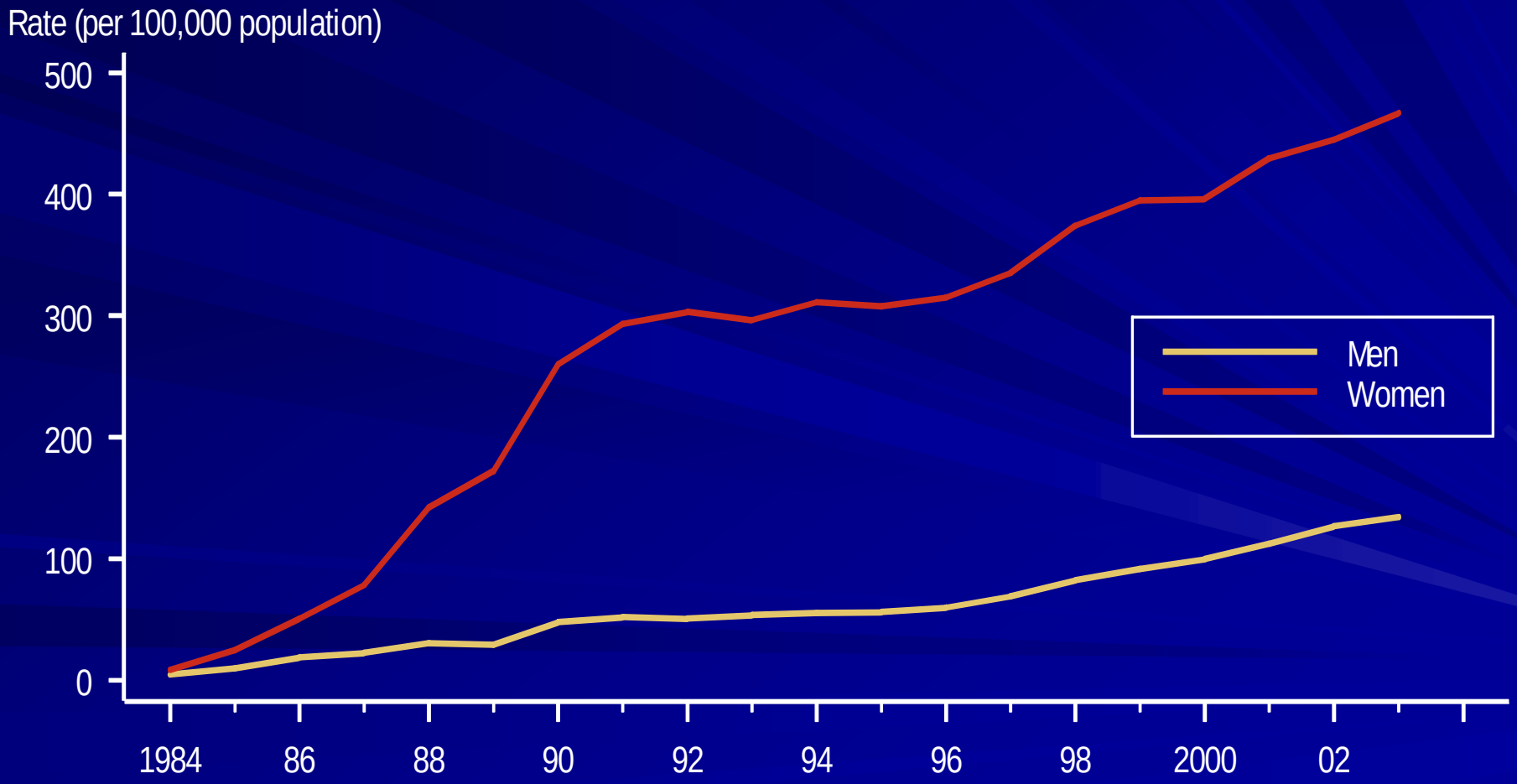
- Early stag
  - Painle
- Later sta
  - Inguin soft **(Bubo**
- Final sta
  - Rectal
  - Esthimene
    (edematous ,granulomatous hypertrophy of penis/scrotum/**vulva**)

- Parinaud's oculogenital conjunctivitis

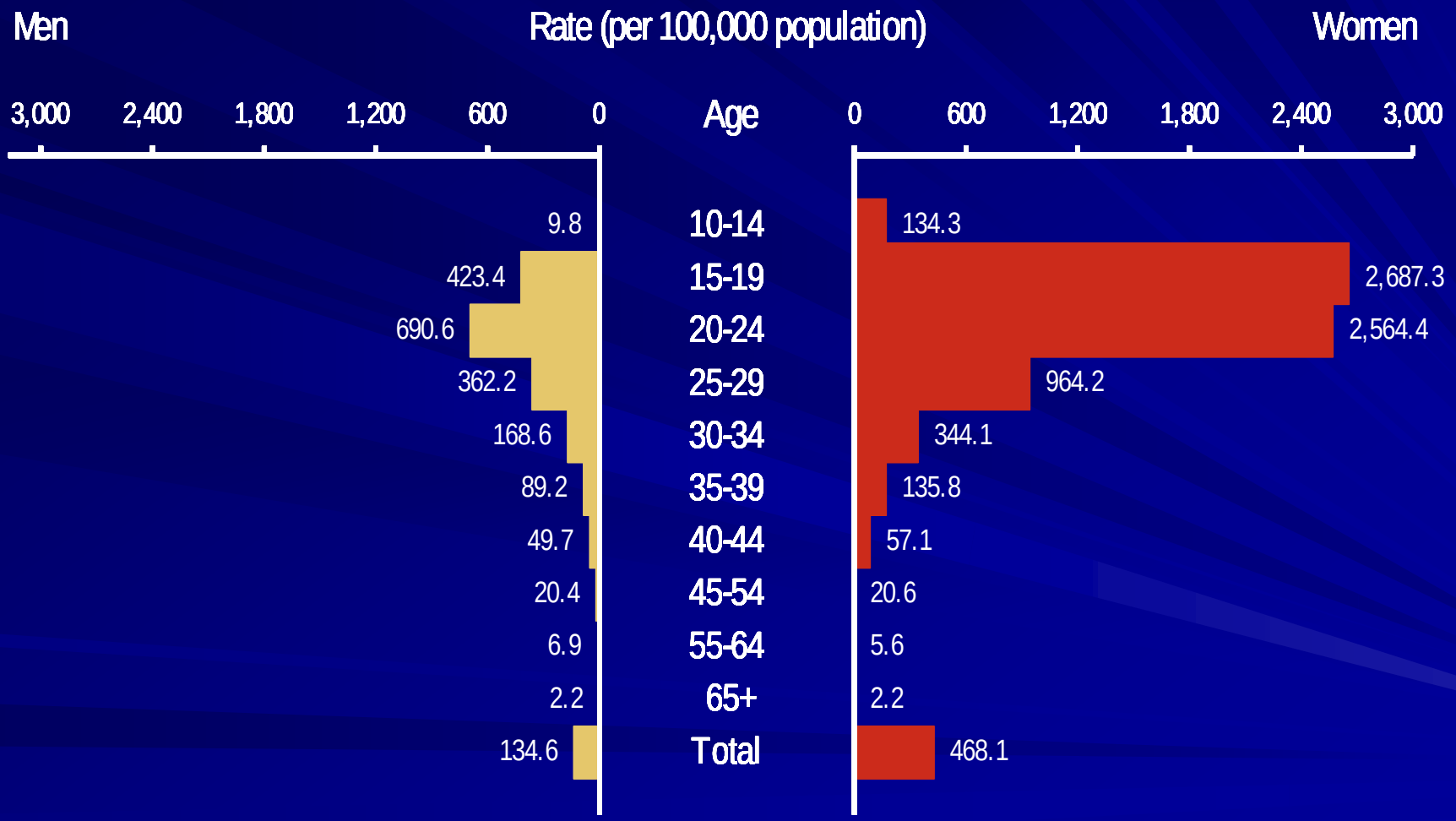
Conjunctivitis with periauricular, submandibular and cervical lymphadenopathy

Epidemiology

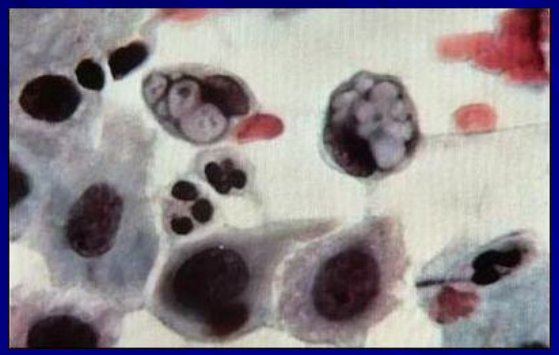
- Trachoma seen in sub-saharan Africa,Middle East,SEA (India also)
- *Leading cause of blindness in 5 -6 million patients per year*



Chlamydial infections: Age and Sex relation



Diagnosis of Chlamydial infections



- Samples: Endo Cervical swab,
  Urethral swab
  Corneal scrappings
- Microscopy: Lugol's iodine staining

(C.trachomatis only); reniform inclusion bodies

Giemsa stain:

Trachoma Halbertstaedter-Prowazek bodies ;

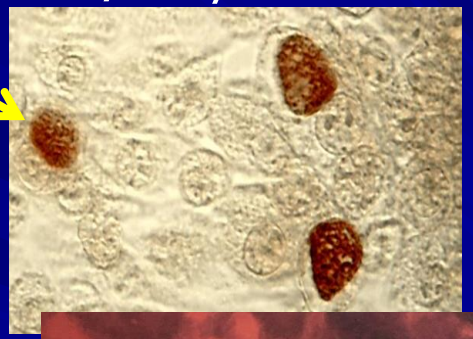
Miyagawa corpuscle ; LGV

LCL bodies; psittacosis

- **Nucleic Acid Amplification Tests (Test of choice CDC)**
- Serological test (Antibody detection) Many NOT in use

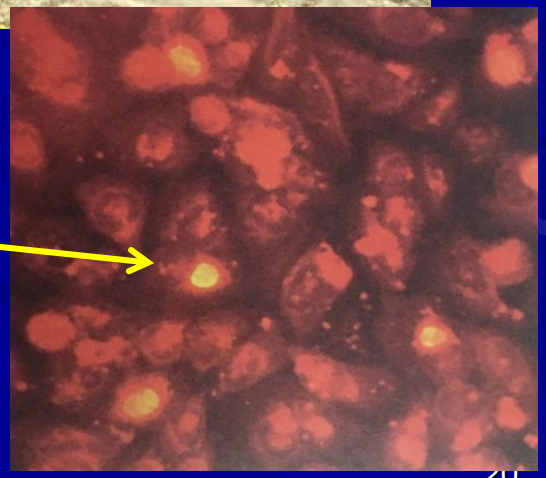
Culture of Clinical specimen

- Variable sensitivity (50%-90%),High specificity(99%)
- ***Mc Coy cell*** line cultures with cyclohexamide.
  - Presence of inclusion bodies..... 2- 7 days of incubation.



Others

- HEp2 cell lines
- **HeLa-229**
- BHK-21
- Yolk sac of 6-8 days embryonated egg



Other rapid tests

- *Direct fluorescent antibody (DFA)*
  - To detect bacteria with a fluorescent antibody
- *Enzyme immunoassay (EIA)*
  - To detect bacterial antigens
- **Serology:** *Microimmunofluorescence test (MIF)*
  - To detect serovar specific MOMP antibodies (Significant titer $\geq$ 1:512)
- *Nucleic acid hybridization (NA probe)*
  - Detects specific DNA or RNA sequences of *C. trachomatis.*

Treatment:
(Uncomplicated Genital Chlamydial Infections)

- **CDC-recommended regimens**
  - Azithromycin- 1 g orally in a ***single dose,*** OR
  - Doxycycline- 100 mg orally BID for 7 days (21 for LGV)

Pregnant: *Ampicillin, 500 mg TID*

- **Alternative regimens**
  - Erythromycin -500 mg orally TID for 7 days
  - Ofloxacin -300 mg orally BID for 7 days

- ***Neonatal Pneumonia (CDC):***
  Erythromycin *50 mg/kg/day orally* in 4 divided doses for 14 days.
  - Azithromycin - 1 gm as ***single dose*** (if >45kgs)

Why & for whom Screening tests for Chlamydia?

Why

- Reduce the incidence of PID by >50%.
- To identify the asymptomatic individuals.
- Decreases the prevalence and reduces the transmission of disease.

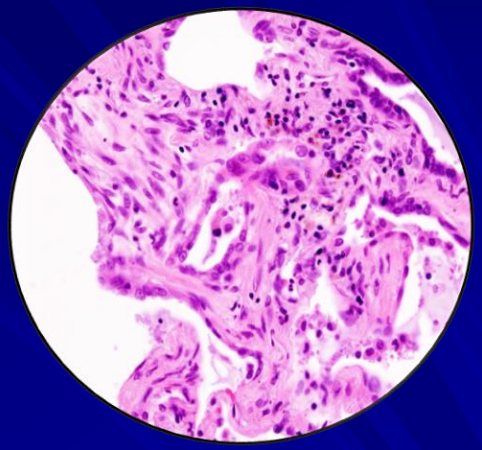
Whom

- Young women with multiple sex partners
- Pregnant women in the first and third trimester

Chlamydophila

- Isolated from conjuntiva of a child from Taiwan in 1965 named as *TW-183*, isolate from pharyngitis as named as *AR-9.*
- Previously it was believed as C.psittasi due to production of inclusion bodies.
- Later these two were named as Chlamydia pneumoniae *(TWAR agent) , finally reclassified* under a *new genus Chlamydophila*

Chlamydiphila pneumoniae



- Exclusively human pathogen
- Person-person by inhalation
- Atypical pneumonia *(M.pneumoniae)*
  - Fever,non-productive cough
  - No leucocytosis
- Atherosclerosis (OMP may cross-react with human protein: Autoimmune process)
- Exacerbations of bronchial asthma and COPD
- Diagnosis: MIF, ELISA,PCR
- Treatment: Doxycycline/Azithromycin (10-14 days)

Chlamydophila psittaci

- Pathogen of parrots, macaws, poultry (turkeys, ducks) and reservoirs for human

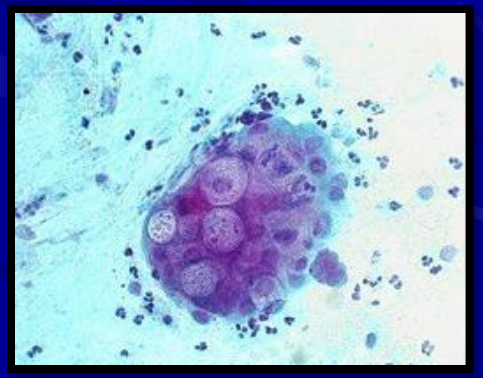
- Inhalation of aerosols from birds
- Direct contact with pet birds

- No person to person transmission
- Incubation period **5-19 days**

Psittacosis

- Mild 'Flu' like symptoms to fatal pneumonia
- Septicemia (spread to many organs)
- Typhoid like illness
  - Fever, spleenomagay
  - Harder's spots (Rash)

- **Broncho-alveolar Lavage Fluid**
  - MIF more sensitive
  - Giemsa stain:
    - Levinthal-Cole-Lillie (LCL) bodies



Happy Learning