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INFECTIILE UROGENITALE CU

CHLAMYDIA TRACHOMATIS

TAXONOMIE

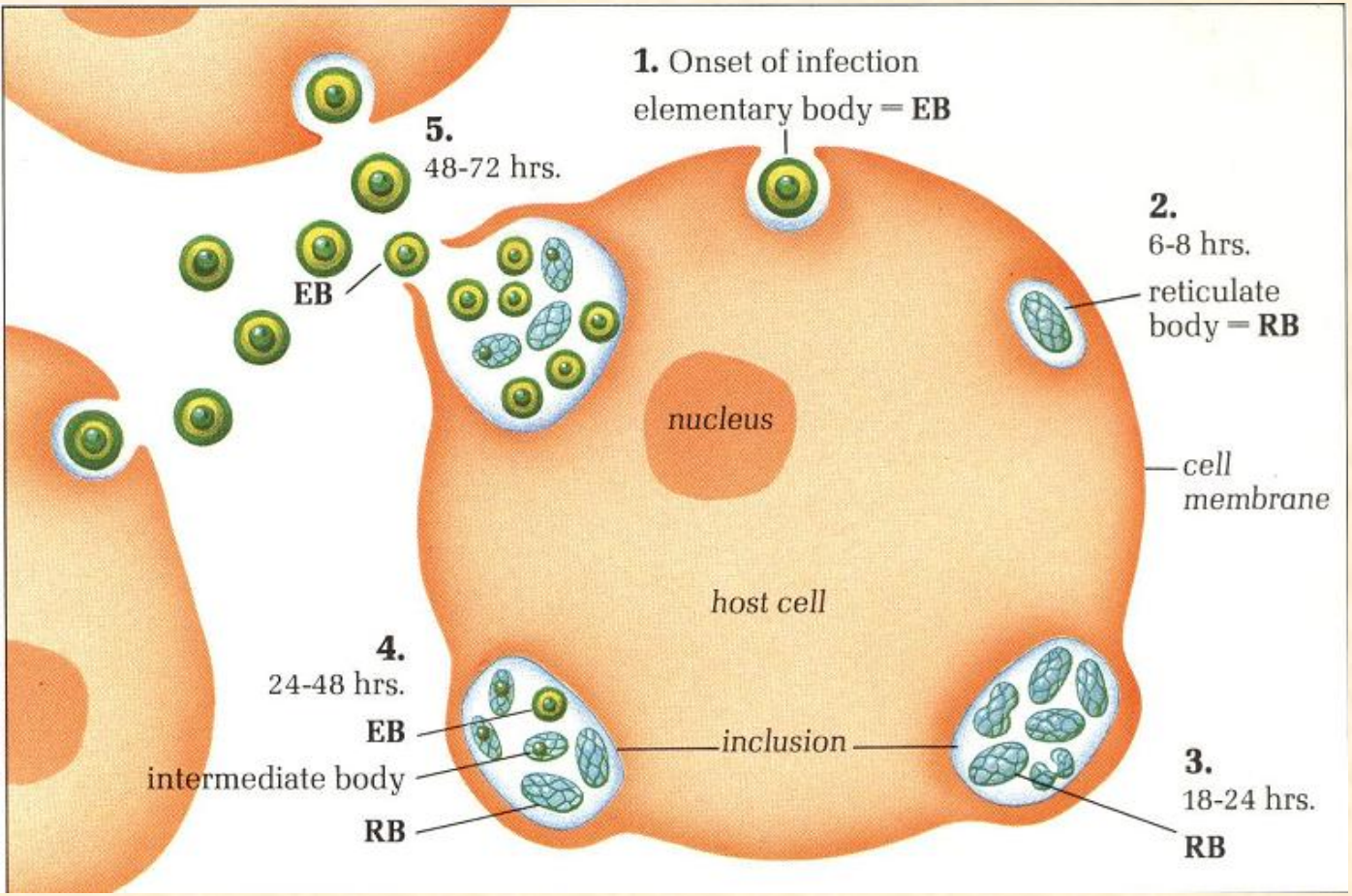
	Anterioara	Everett (Helsinki, 2000)	
Fam	• Chlamydiaceae	• Chlamydiaceae	
Gen	• Chlamydia	• Chlamydia	• Chlamydophila
Spec	• ***C. trachomatis*** • ***C. psittaci*** • ***C. pneumoniae*** • *C. pecorum*	• ***C. trachomatis*** • *C. suis* • *C. muridarum*	• ***C. psittaci*** • ***C. pneumoniae*** • *C. pecorum* • *C. felis* • *C. caviae* • *C. abortus*

C. trahomatis
Biologie

- Patogen cu genom minimal: 1 Mbp
- Replicare intracelulara:
  - ✓ Nu sintetizeaza aminoacizi
  - ✓ Produce ATP (glicoliza, pentoze, Krebs)
- Membrana celulara tip G (-), fara peptidoglican
- **RB** si **EB** protejate de osmolaritatea mare intracelulara si mica extracelulara de catre proteine membranare cu multiple legaturi S-S:
  - ✓ **MOMP** (major outer membrane protein),
  - ✓ **POMP** (polimorphic outer membrane protein),
  - ✓ **CRP** (cysteine rich protein)
- Marele mister: de ce este susceptibila la ß lactamice ?
  - ✓ Prezent peptidoglicanul, dar nedetctabil cu metodele actuale.
  - ✓ Efecte secundare ale Penicilinei pe metabolismul celular.

EB = elementary body RB = reticulate body

Bacteriile din genul Chlamydia sunt paraziti intracelulari obligatorii care se multiplica in 48-72 ore printr-un singur ciclu



1. Particulele elementare infectante (EB) sunt endocitate

2. Reorganizarea in particule reticulate neinfectioase (RB)

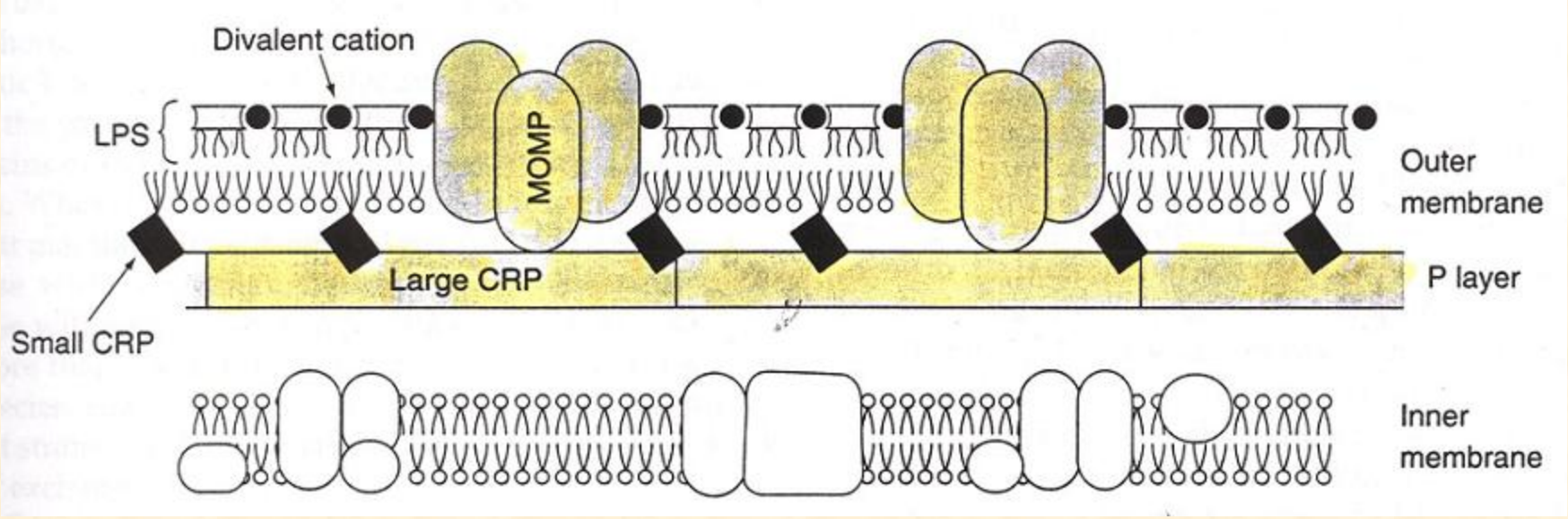
3. Particulele reticulate se multiplica in incluziile citoplasmatice pe seama gazdei

4. Particulele reticulate devin intermediare si contina formarea de particule elementare

5. Incluziile citoplasmatice cresc, se sparg si elibereaza particule elmentare, care infecteaza alte celule

EB = elementary body RB = reticulate body

Structura membranei particulei elementare (EB)



LPS = Lipopolysaccharide (genus specific)
MOMP = Major Outer Membrane Protein (secies specific)
CRP = Cysteine Rich Protein

A Salyers & D Whitt - Bacterial Pathogenesis- 2002

C. trachomatis
Factori de virulenta

- **EB intra in celula prin:**
  - ✓ **endocitoza mediata de receptori (clathrin – coated pits)**
  - ✓ **pinocitoza**
  - ✓ **fagocitoza normala**
- **Nu se produce fuzionarea cu lizozomii celulari**
- **Ag bacteriene expuse in mica masura pe suprafata celulei infectate: limfocitele T citotoxice slab efective**
- **"Stealth pathogen" : multiplicarea in endozom nu produce distrugerea celulei**
- **Atunci cum apar simptomele cervicitei, artritei, trahomului etc.?**
  - ✓ **prin raspunsul inflamator la proteinele EB sau alte componente de pe suprafata celulara, caruia i se adauga si raspunsul imun specific.**
- **Citotoxina ?**

C. trachomatis
Patogenie

- **Infectia acuta evolueaza frecvent spre infectia cronica asimptomatica**
- **Alternanta intre fazele active/pasive (persistenta) in care se schimba expresia profilului antigenic**
- **In cursul inf. persistente, Ag MOMP, produse continuu, stimuleaza sistemul imun, promovand inflamatia cronica**
- **Sinteza continua de HSP60 chlamydial sub actiunea IFNγ, TNFα, produse de raspunsul imun celular, conduce spre cronicizare cu sechele**
- **IgG anti HSP60 propusi ca markeri de cronicizare**
- **MΦ infectate cu C. trachomatis produc TNFα cu inducerea Tcell apoptosis, supravietuire intracelulara si persistenta infectiei cronice**

MC Jandro & col. Med Microbiol Immunol 2004, 193, 45

Manifestarile clinice ale infectiilor cu *C. trachomatis* (asimptomatice 70% femei si 50% barbati) prevalenta 700 milioane / glob

19 Serotipuri (epitopi MOMP)	Manifestare clinica	Complicatii
A - C	Keratoconjunctivita	Trahom - orbire
D - K	b : Uretrita Proctita	Epididimita
	f : Uretrita Cervicita Proctita	Endometrita Salpingita Sarcina ectopica Nastere prematura Sterilitate Infectie pelvina (PID)
	b + f : Conjunctivita Uretrita	Sindrom Reiter Artrita reactiva
	nn : Conjunctivita Pneumonie	
L1 – L3	LGV Proctita	Fibroza Stricturi rectale

Adaptare dupa Bébéar & de Barbeyrac, Clin Microbiol Infect Dis 15,1,2009

C. trachomatis
Diagnostic de laborator

Diagnostic direct – dg. certitudine

Metoda	Avantaje	Limite
Culturi celulare	Specificitate, tulpina	Sensibilitate 80-85%
Detectie Ag prin DFA	Simpla	Sensibilitate 75-80% Subiectiva
ELISA	Automatizata	Sensibilitate 75-80%
NAAT =nucleic acid amplification test (PCR, RT-PCR etc)	Specificitate 99% Sensibilitate > 95%	Contaminare Cost

2006 – Suedia - tulpini serovar E – cu deletie 377 bp plasmida criptica
- 10-65% infectii nedetectabile in zona deletiei.
- varianta detectabila prin amplif. gena cromozomala ompA sau rRNA

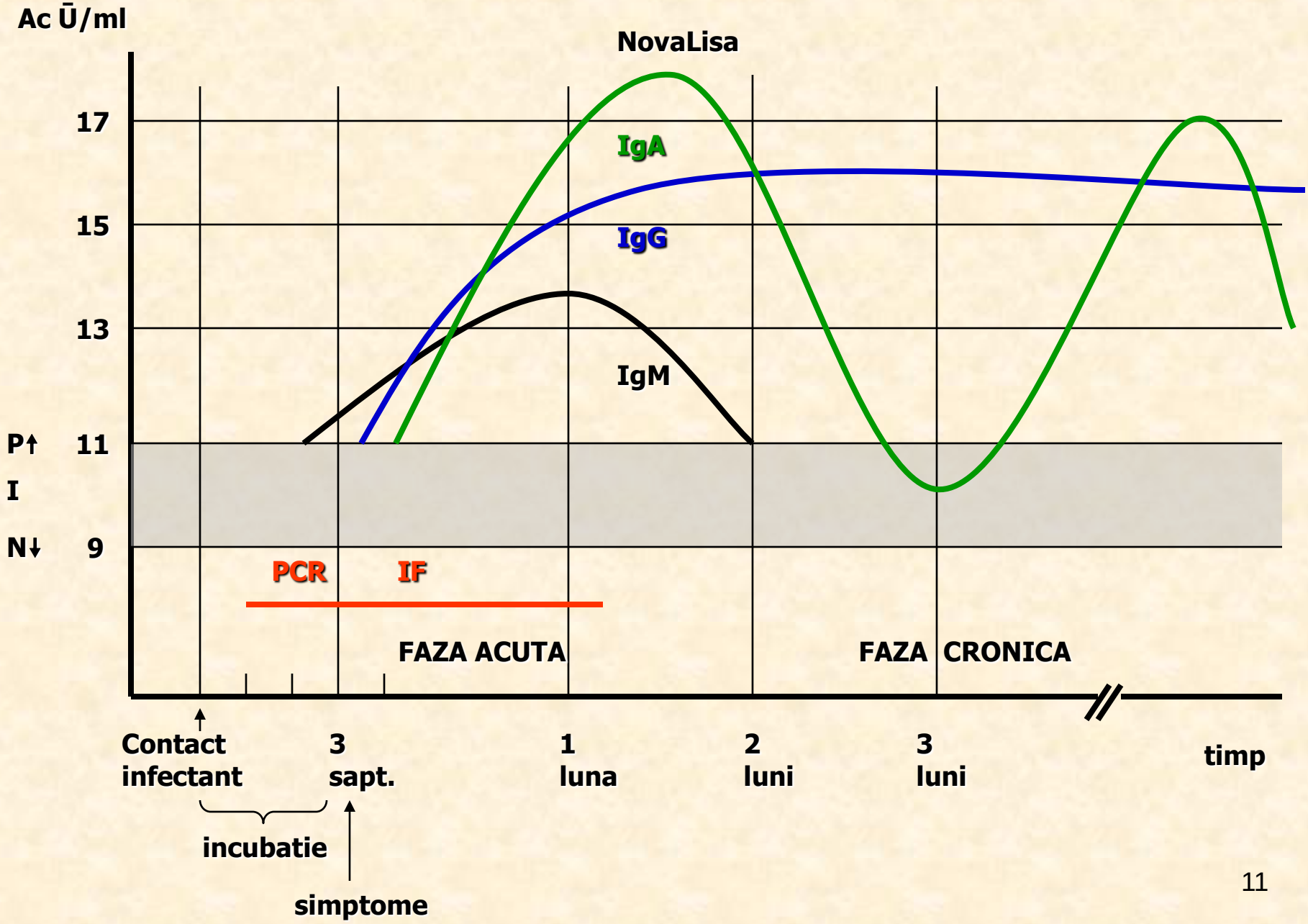
C. trachomatis
Diagnostic serologic

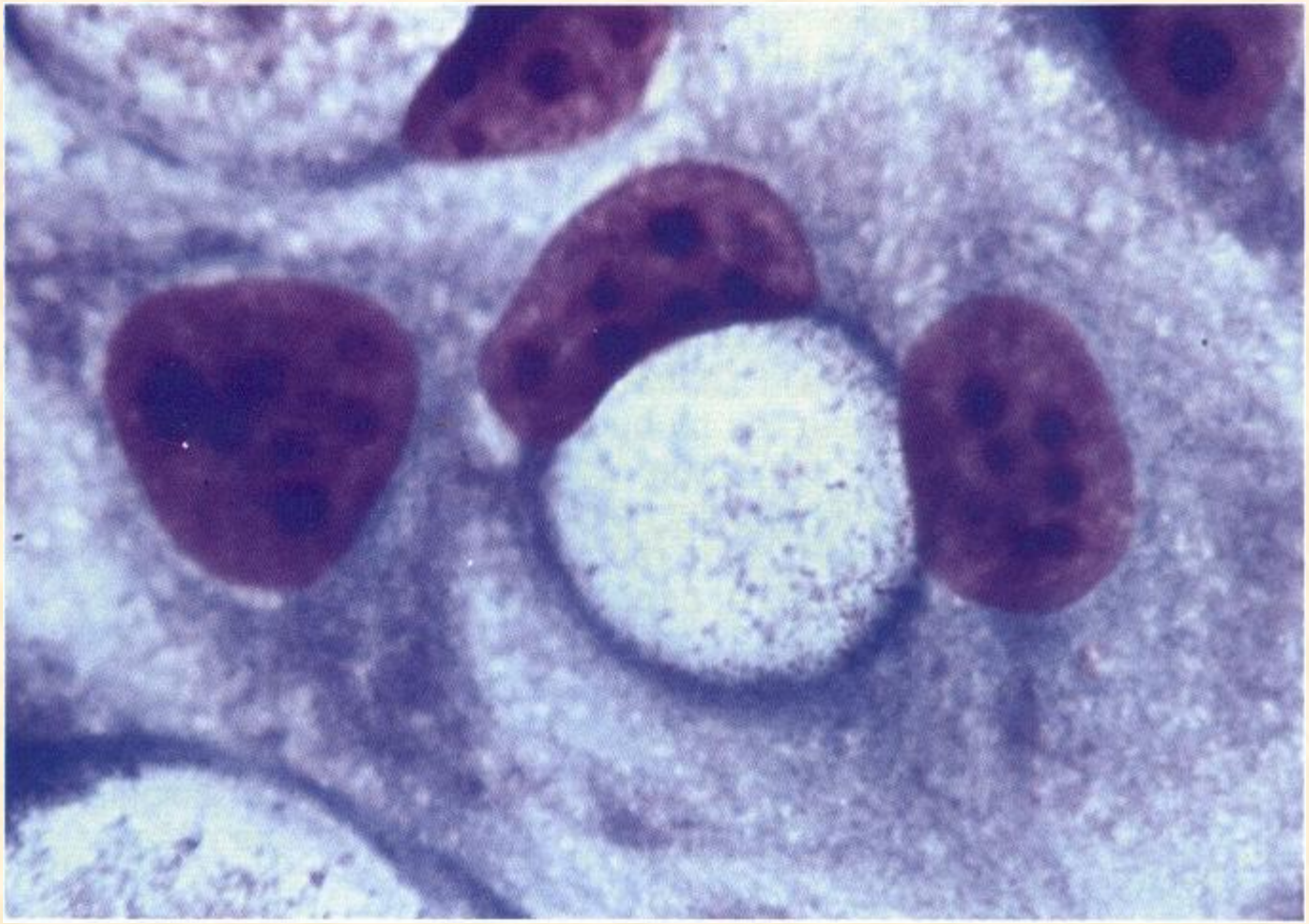
- **MIF** – species specific (Ac monoclonali) – metoda de referinta

- **ELISA** – **IgG, IgA, IgM** - in paralel pe aceeasi proba
  Ag: **r LPS, r MOMP** – domeniul IV variabil:
  - ✓ durata si activitatea infectiei

- **ELISA – IgG – c HSP60**:
  - ✓ Infectie cronica activa sau latenta tract genital superior
  - ✓ Sensibilizare, autoimunitate
  - ✓ Identificare infertilitate tubara

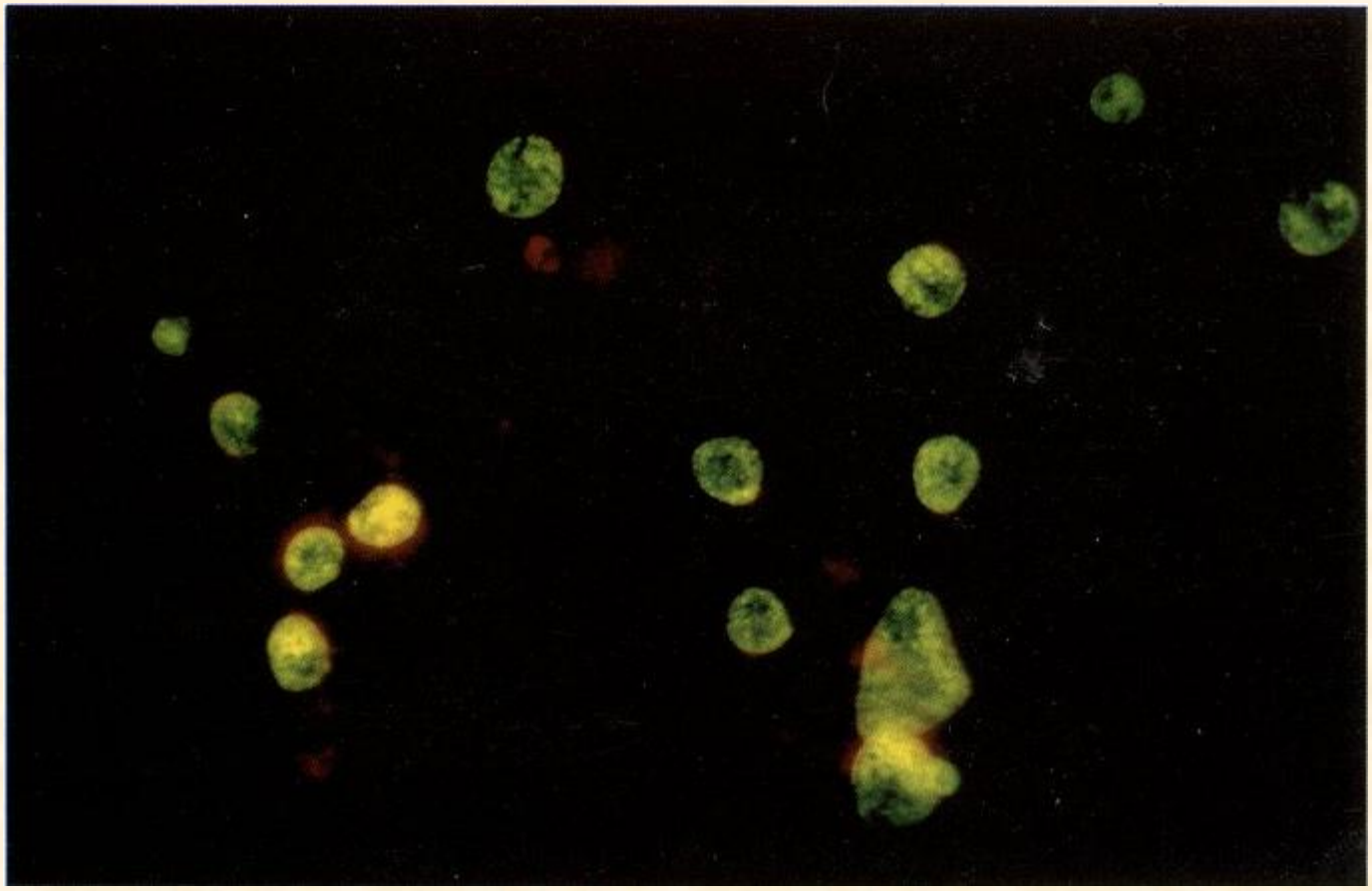
Dinamica Ac in infectia cu *C. trachomatis*





***C. trachomatis*: incluzii in celule Hela 229**

J. Orfila - Diagnostic d'une infection à Chlamydia – Laborama Diagnostics Pasteur- 1991



Detectare *C. trachomatis* secretie genitala
prin IF directa (conjugat policlonal)
Rezultat pozitiv: incluzii citoplasmatice (EB florescente)

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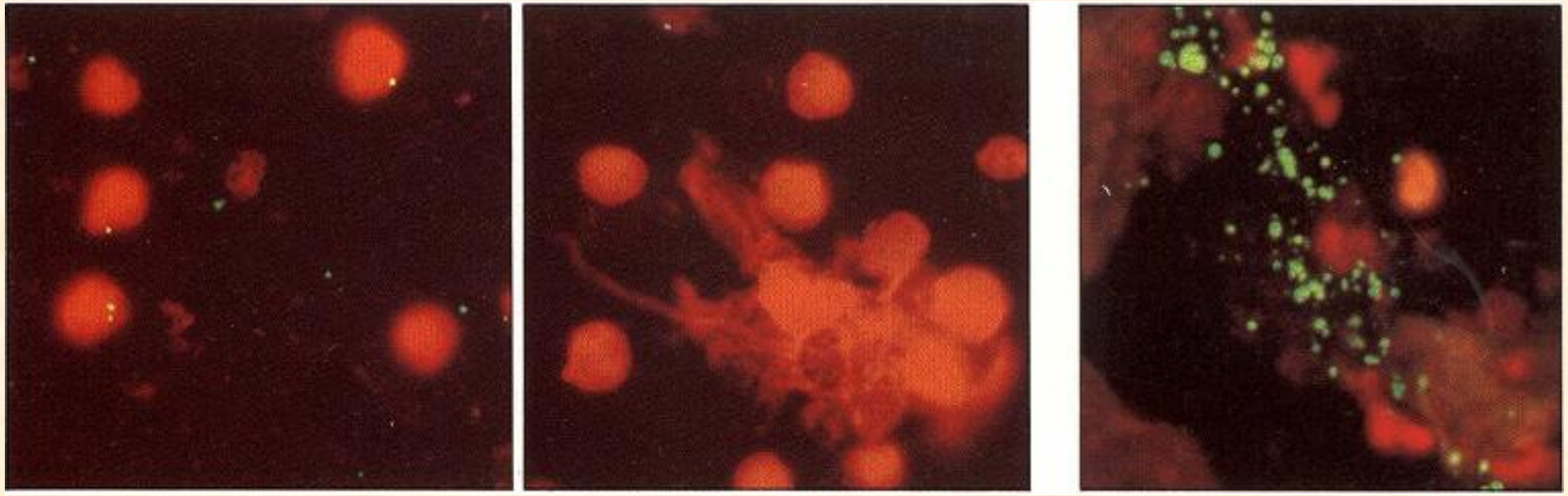
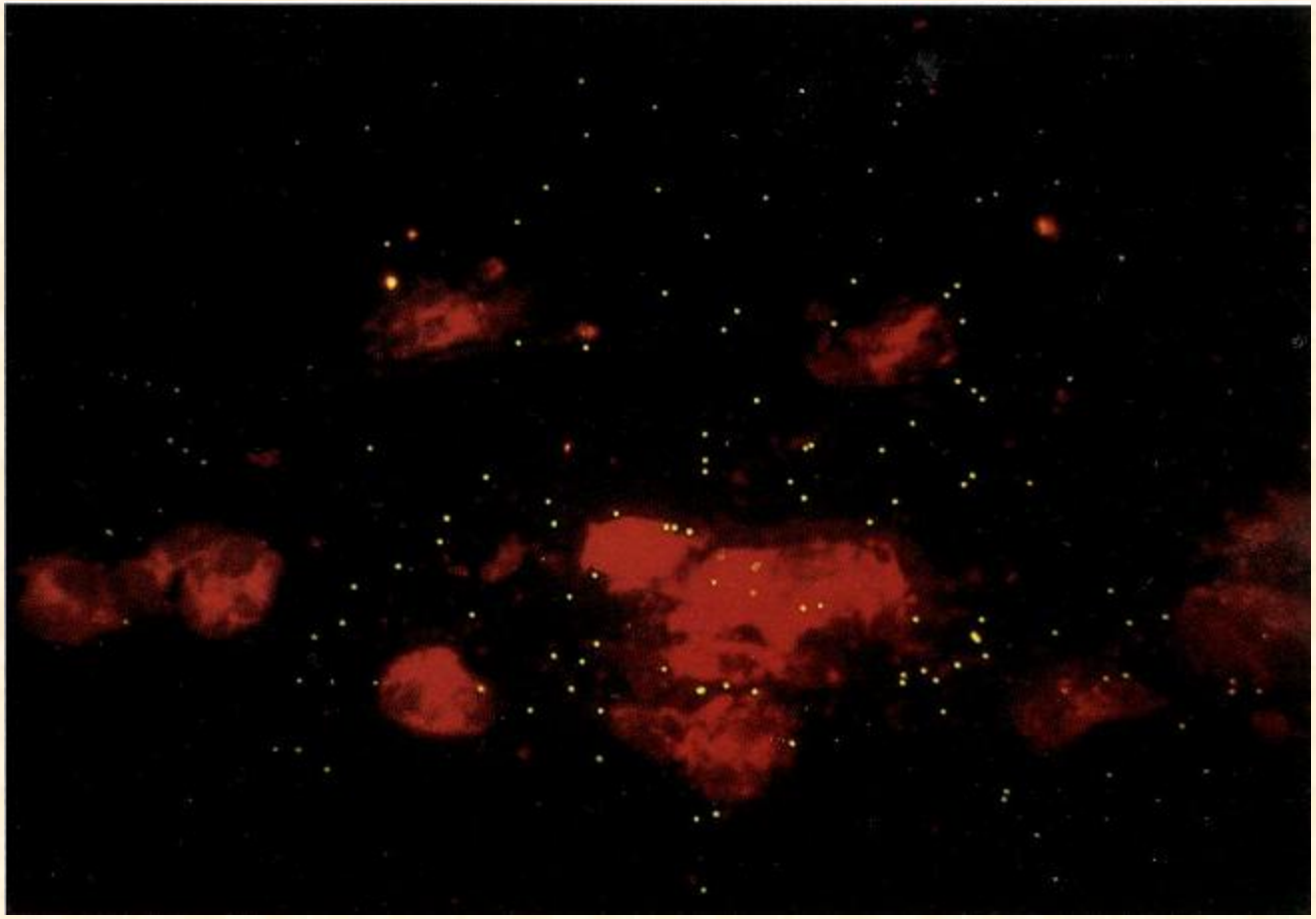


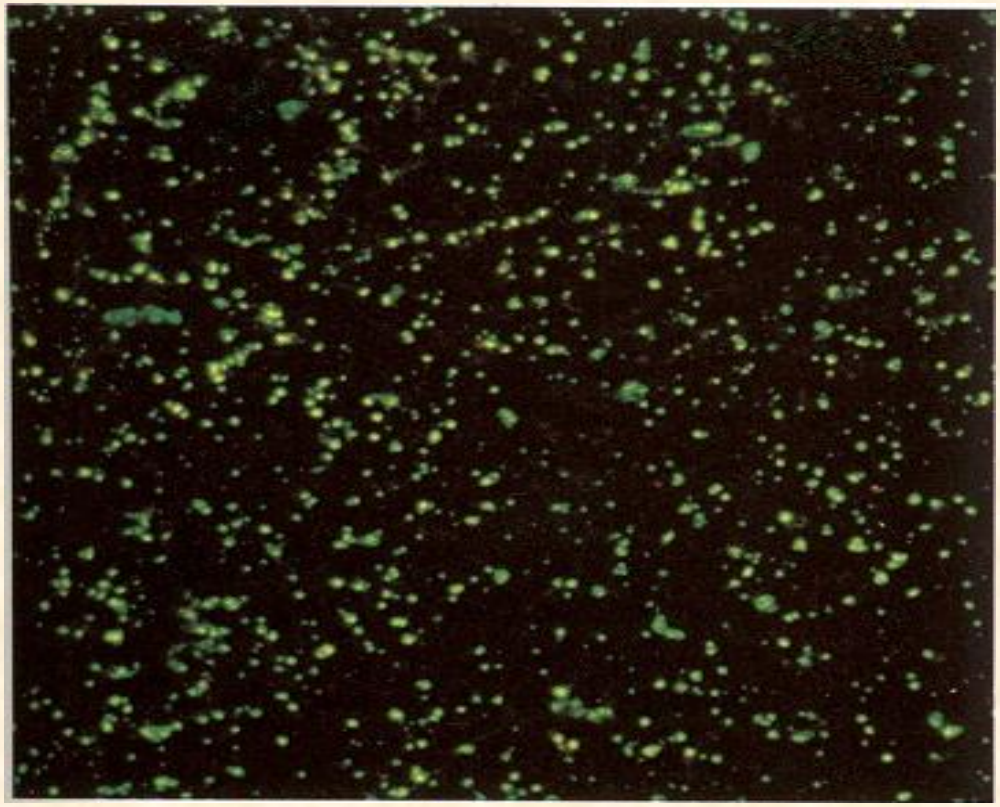
Control pozitiv **Control negativ** **Proba pozitiva**

Identificarea C. trachomatis prin IF directa
(conjugat cu Ac. monoclonali anti MOMP)



IF indirecta (EB fluorescente, PMN colorate rosu): rezultat pozitiv

J. Orfila - Diagnostic d'une infection à Chlamydia – Laborama Diagnostics Pasteur- 1991



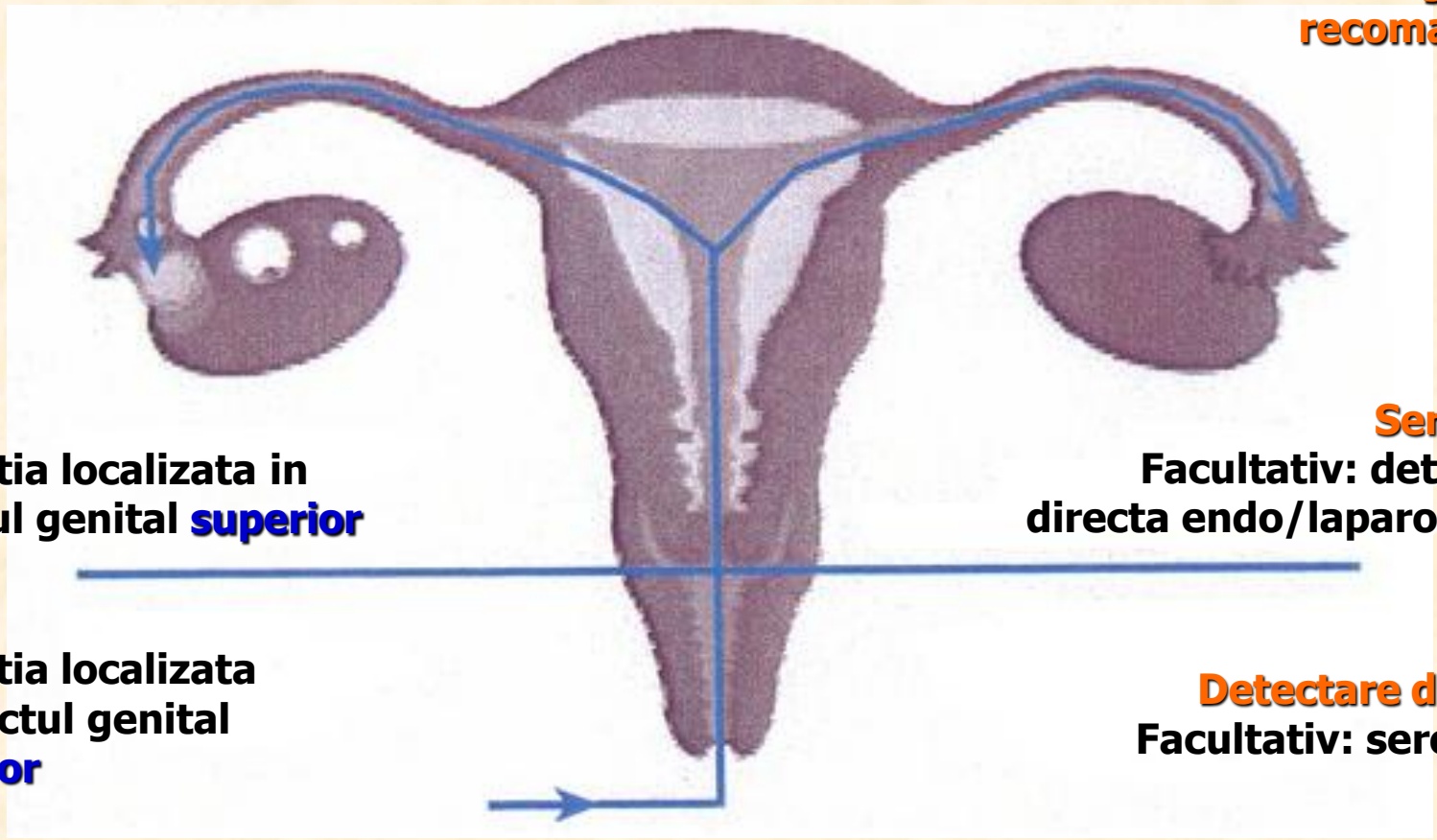
Imunoflorescenta indirecta: pozitiv "cer instelat"
(Ag: EB din sac vitelin ou embrionat)

- *C. Trachomatis* colonizeaza mucoasa tractului genital inferior.
- Simptomele, in special la femei, sunt discrete sau chiar absente.
- Infectia urca spre tractul genital superior si persista acolo luni - ani.

Procedura de diagnostic depinde de localizarea infectiei

Locul infectiei

Metoda de diagnostic recomandata



Infectia localizata in tractul genital superior

Serologie
Facultativ: detectare directa endo/laparoscopie

Infectia localizata in tractul genital inferior

Detectare directa
Facultativ: serologie

Adaptat dupa M. Böttcher-Chlamydia trachomatis-MEDAC Diagnostica-2003