

Chlamydial Infections

Pathogenesis • morphology • clinical correlation

Elementary body $\rightleftharpoons$ Reticulate body

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Learning outcomes

- Explain the elementary-body $\rightleftharpoons$ reticulate-body cycle and the role of the inclusion
- Associate serovars with anatomic disease patterns
- Recognize urethritis and lymphogranuloma venereum morphology
- Connect mucosal and ocular inflammation to long-term structural complications

Organism

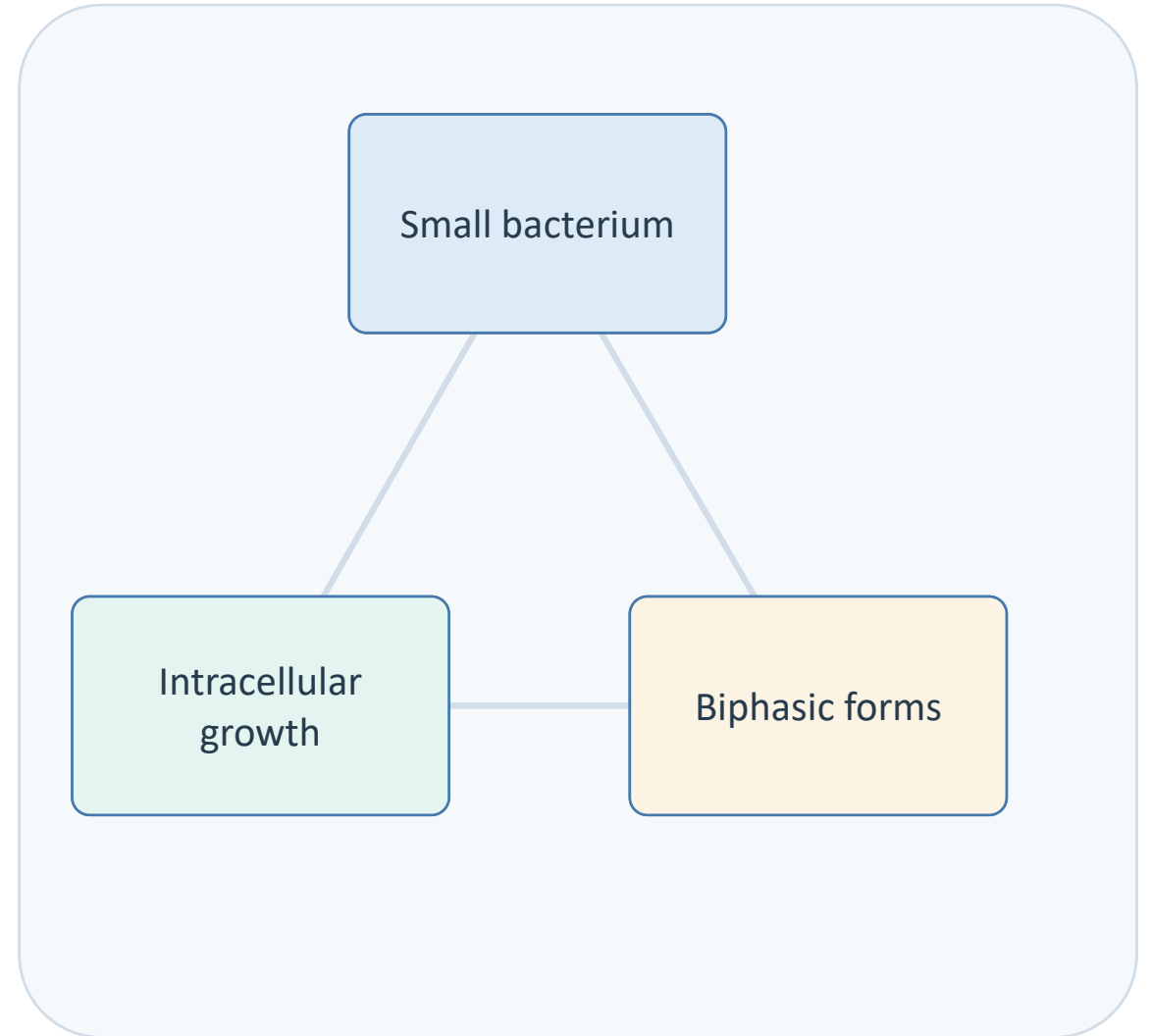
Pathogenesis

Morphology

Clinical impact

Chlamydia trachomatis: Defining properties

- Small bacterium with a gram-negative cell organization
- Obligate intracellular pathogen: Replication occurs inside a host cell
- Infection couples specialized entry, protected intracellular growth, and release



What “obligate intracellular” means

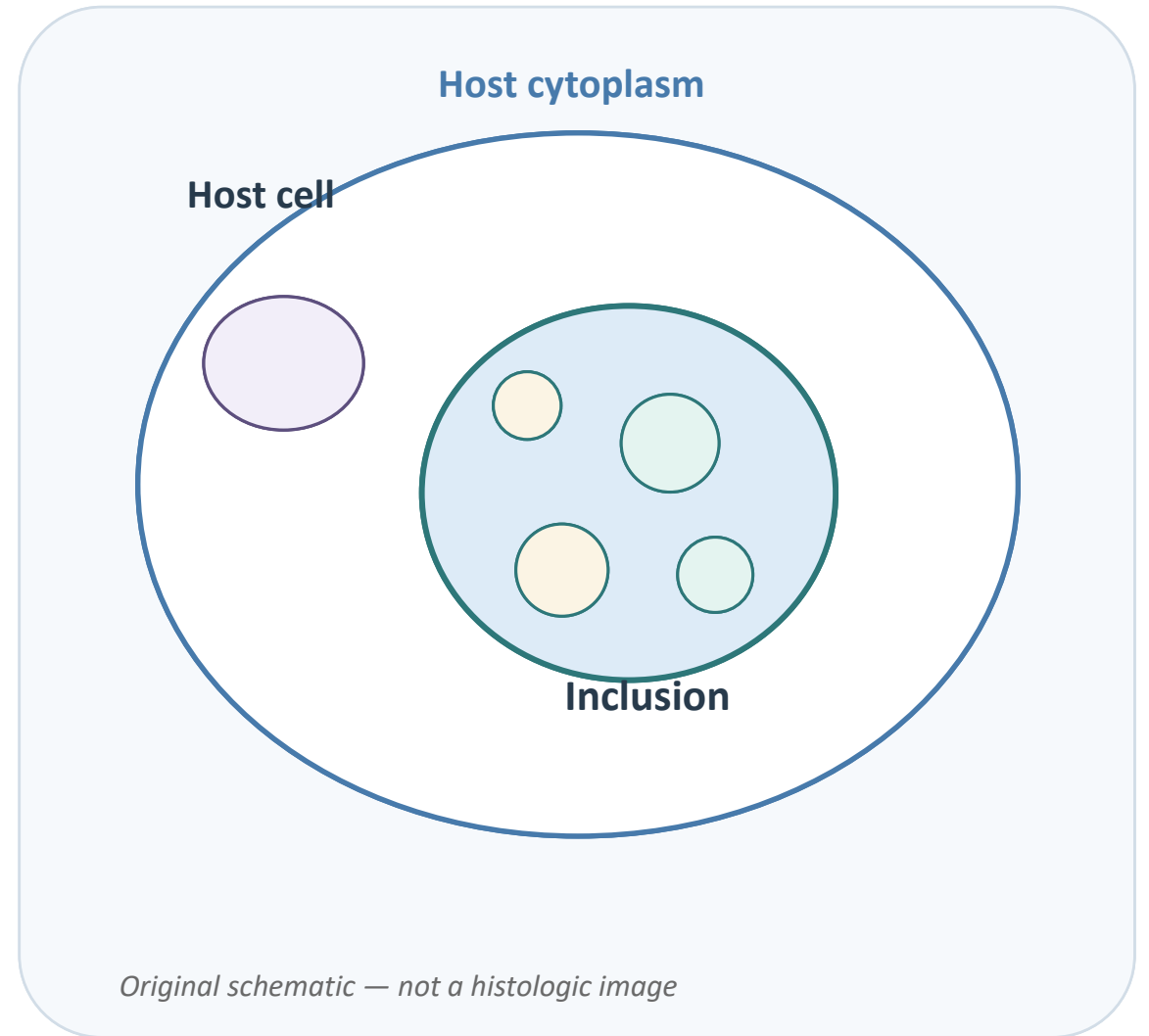
- A permissive host cell is needed for organism proliferation
- The intracellular niche supplies metabolites and protects the growth phase
- The infectious form and the replicating form perform different tasks

**Outside host cell:
Transmission**

**Inside host cell:
Multiplication**

Host cell as a metabolic resource

- The pathogen draws nutrients from the intracellular environment
- Glucose-6-phosphate and glutamine support differentiation to the replicative form
- A membrane-bound inclusion enables an adapted intracellular compartment



Two forms, two biological functions

- Elementary body: Infectious and comparatively metabolically inactive
- Reticulate body: Metabolically active, intracellular, replicating
- Conversion between forms separates transmission from amplification

Elementary body

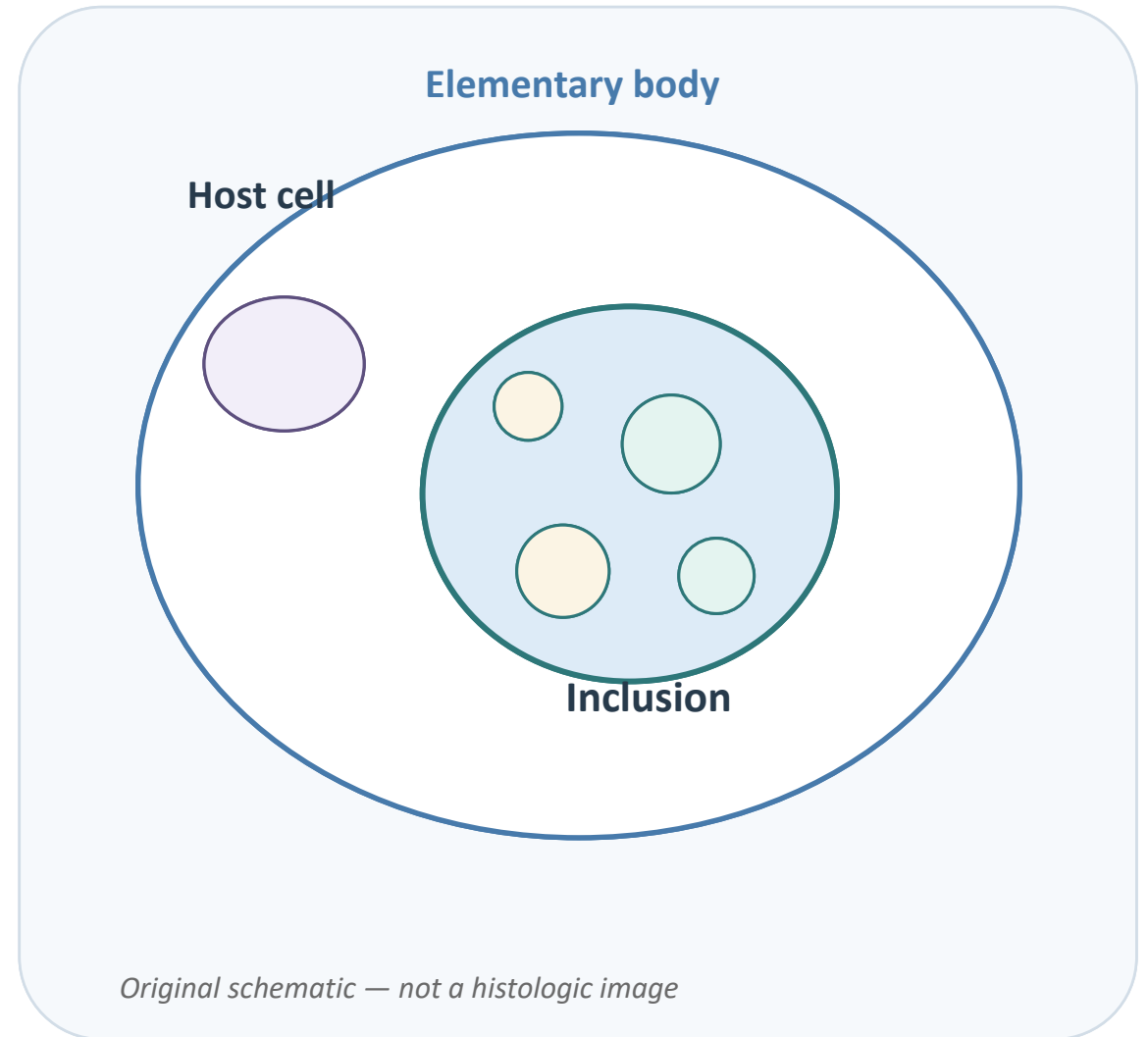
Infectivity •
reduced
metabolism

Reticulate body

Replication •
active
metabolism

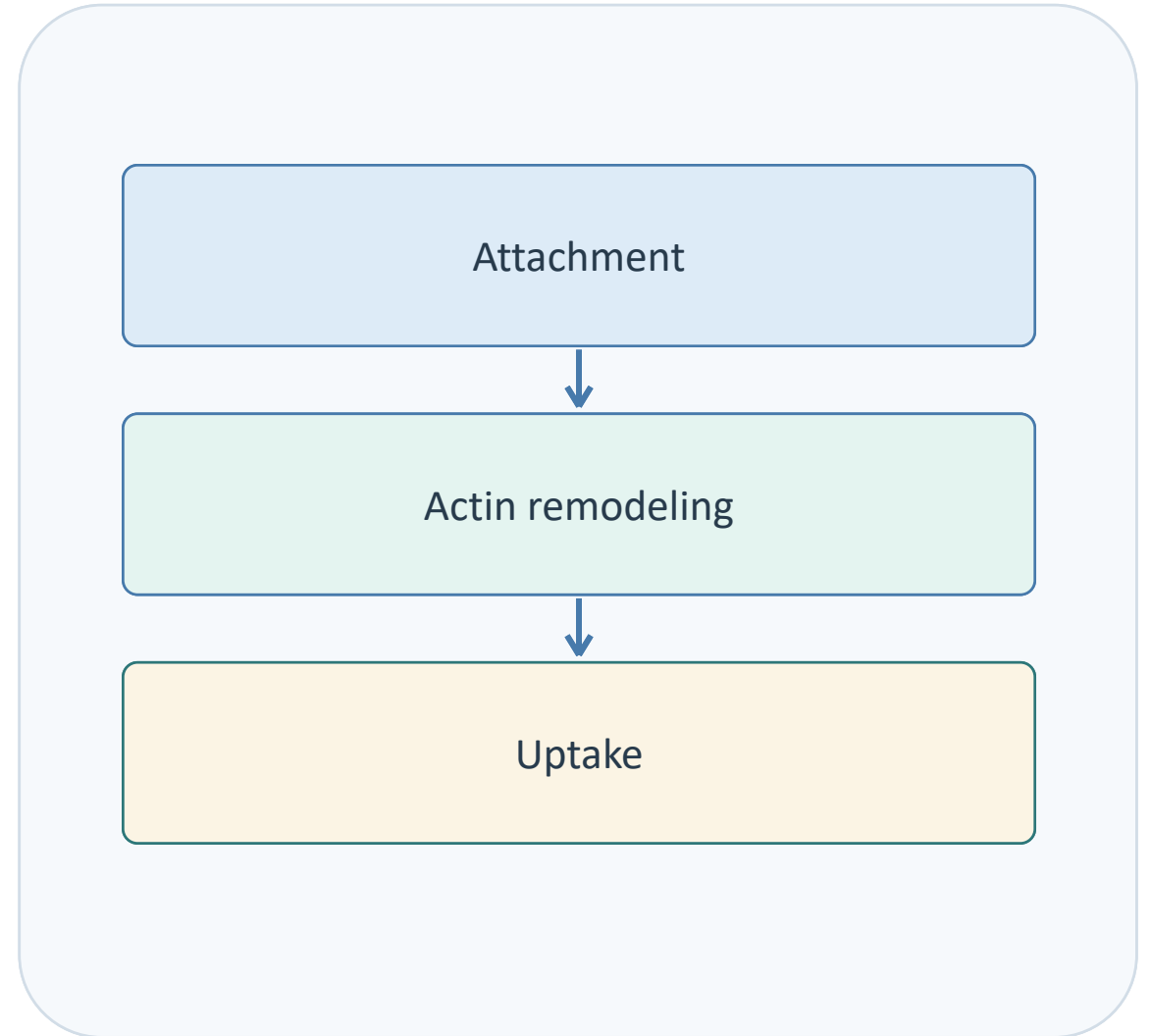
Elementary body: The infectious stage

- Infectious elementary bodies bind susceptible host cells
- They initiate entry rather than extensive extracellular replication
- Their low metabolic activity contrasts with the reticulate form



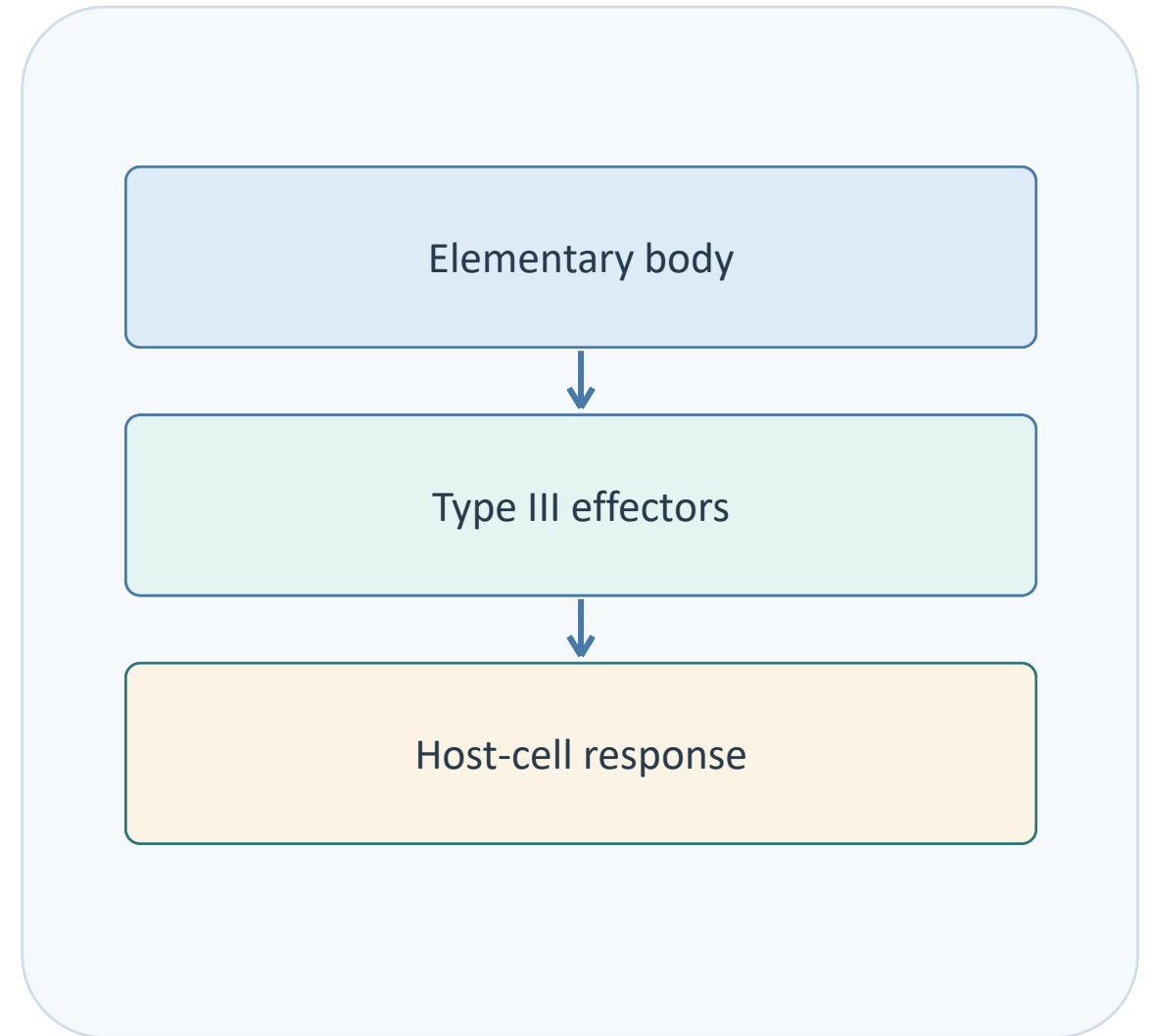
Host cell attachment precedes uptake

- Elementary bodies first contact and bind the host-cell surface
- Attachment is followed by bacterial manipulation of host actin
- Entry culminates in uptake into a membrane-bounded compartment



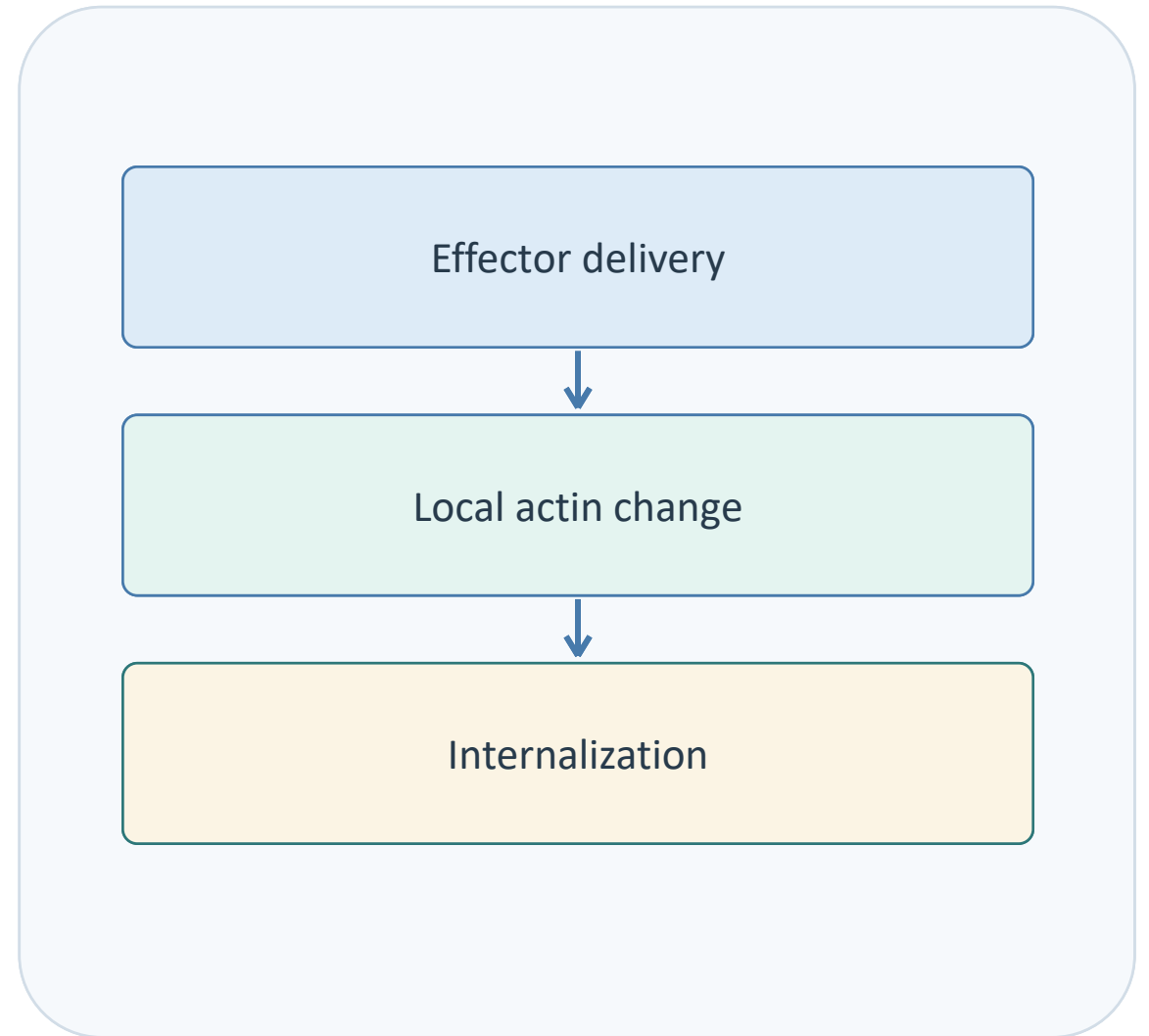
Type III secretion during entry

- An elementary body injects effector molecules into the host cell using a type III secretion system
- The injected effectors alter host-cell processes at the attachment site
- This is an active pathogen-driven entry mechanism



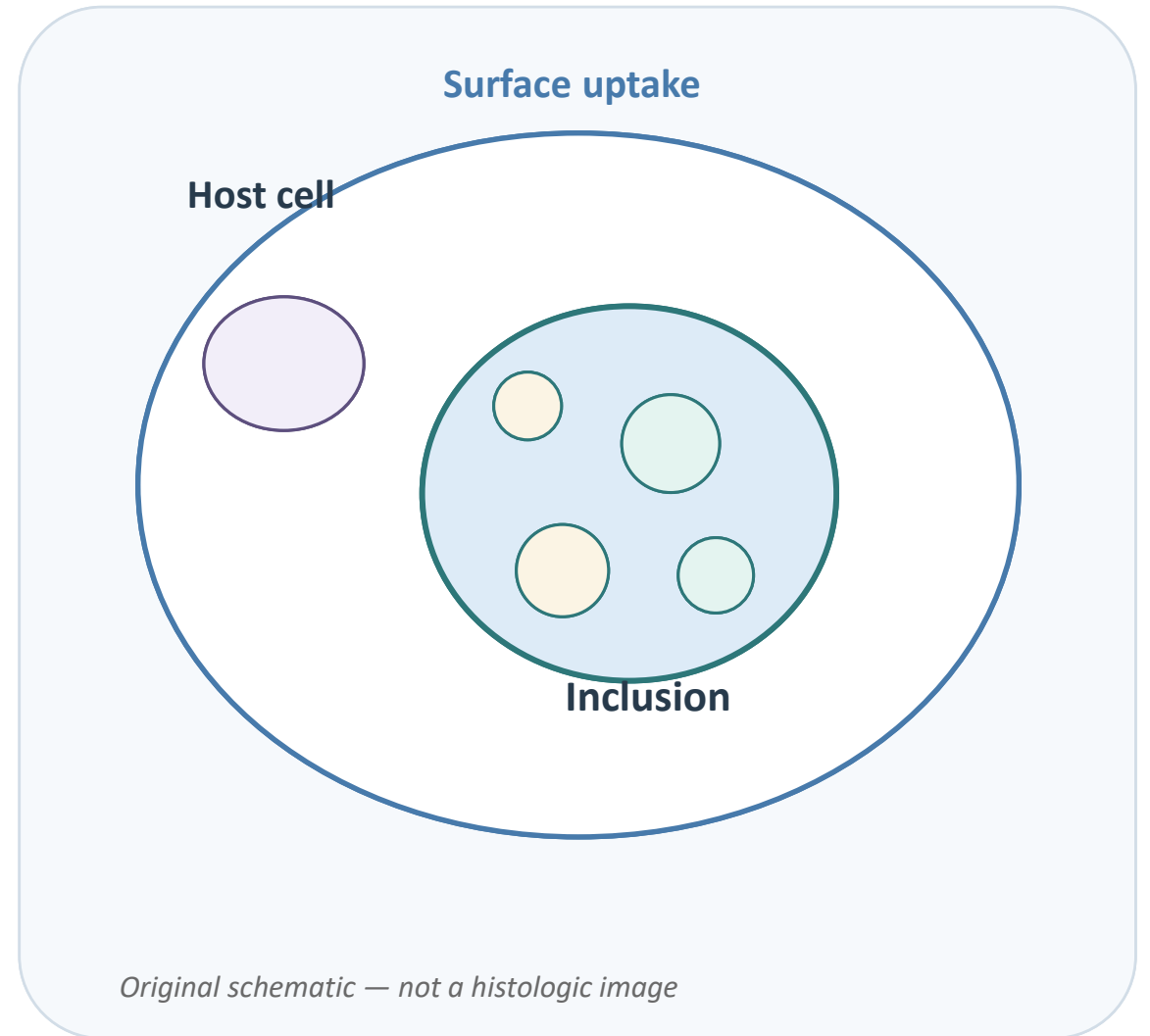
Actin remodeling facilitates entry

- Secreted effectors trigger local changes in the host actin cytoskeleton
- Remodeling occurs where the elementary body enters
- The resulting cytoskeletal rearrangement supports phagocytic uptake



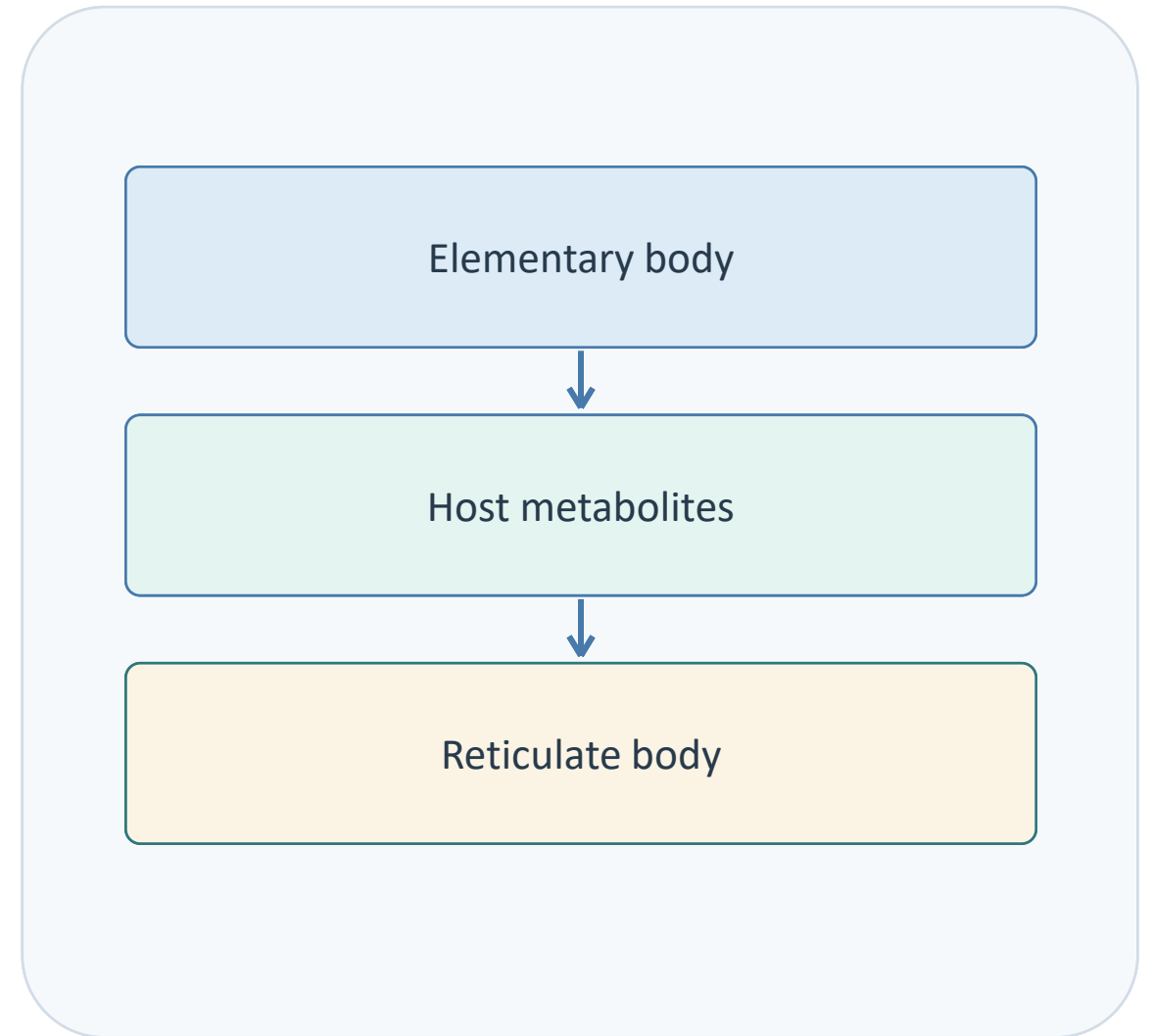
Internalization creates a protected niche

- The organism is taken into the cell by a phagocytic process
- A membrane-bound inclusion originates from an endosomal compartment
- The pathogen subsequently modifies this compartment for survival



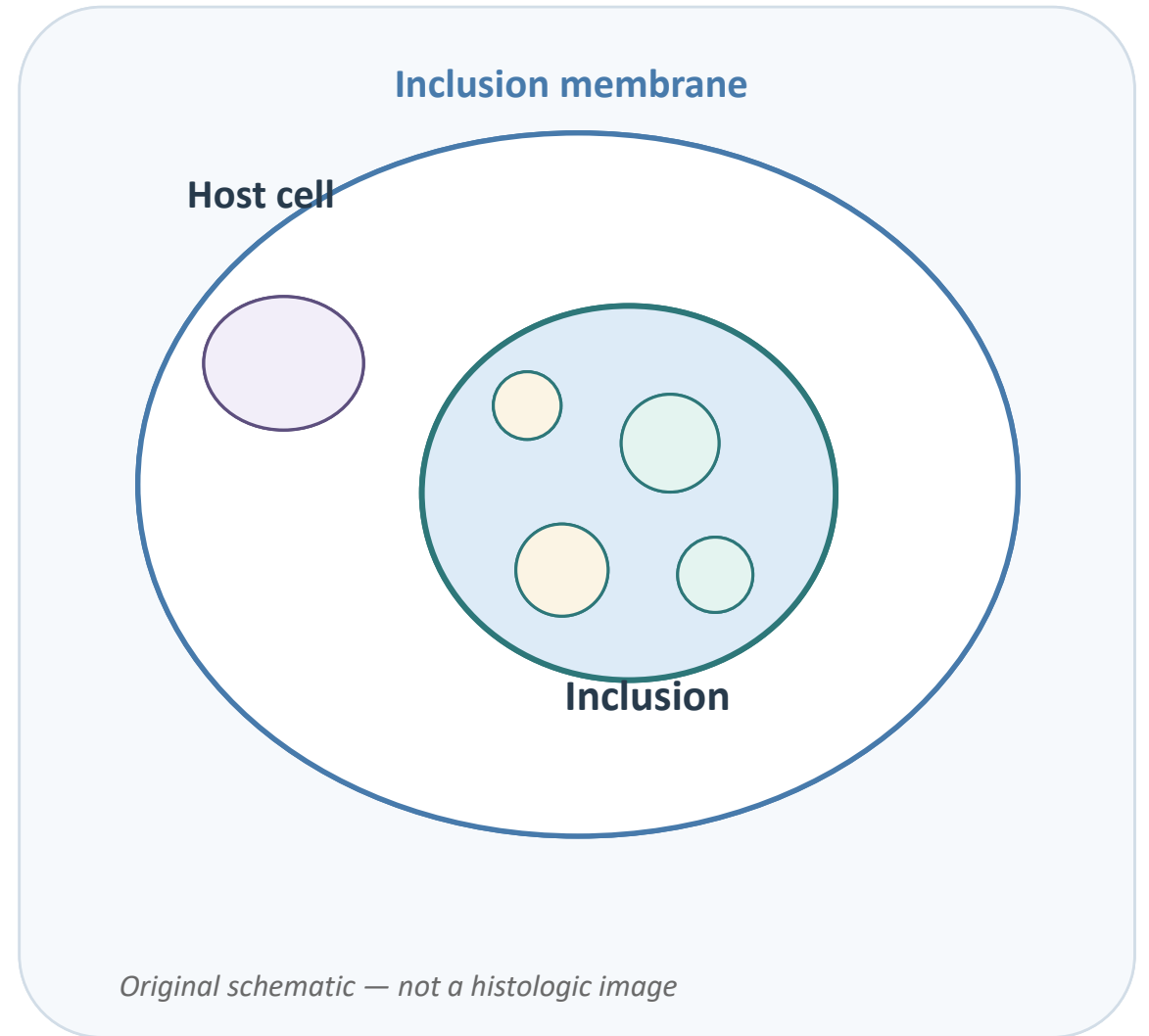
Elementary-to-reticulate transition

- Intracellular host metabolites permit differentiation of the elementary body
- The resulting reticulate body becomes metabolically active
- This transition precedes intracellular replication



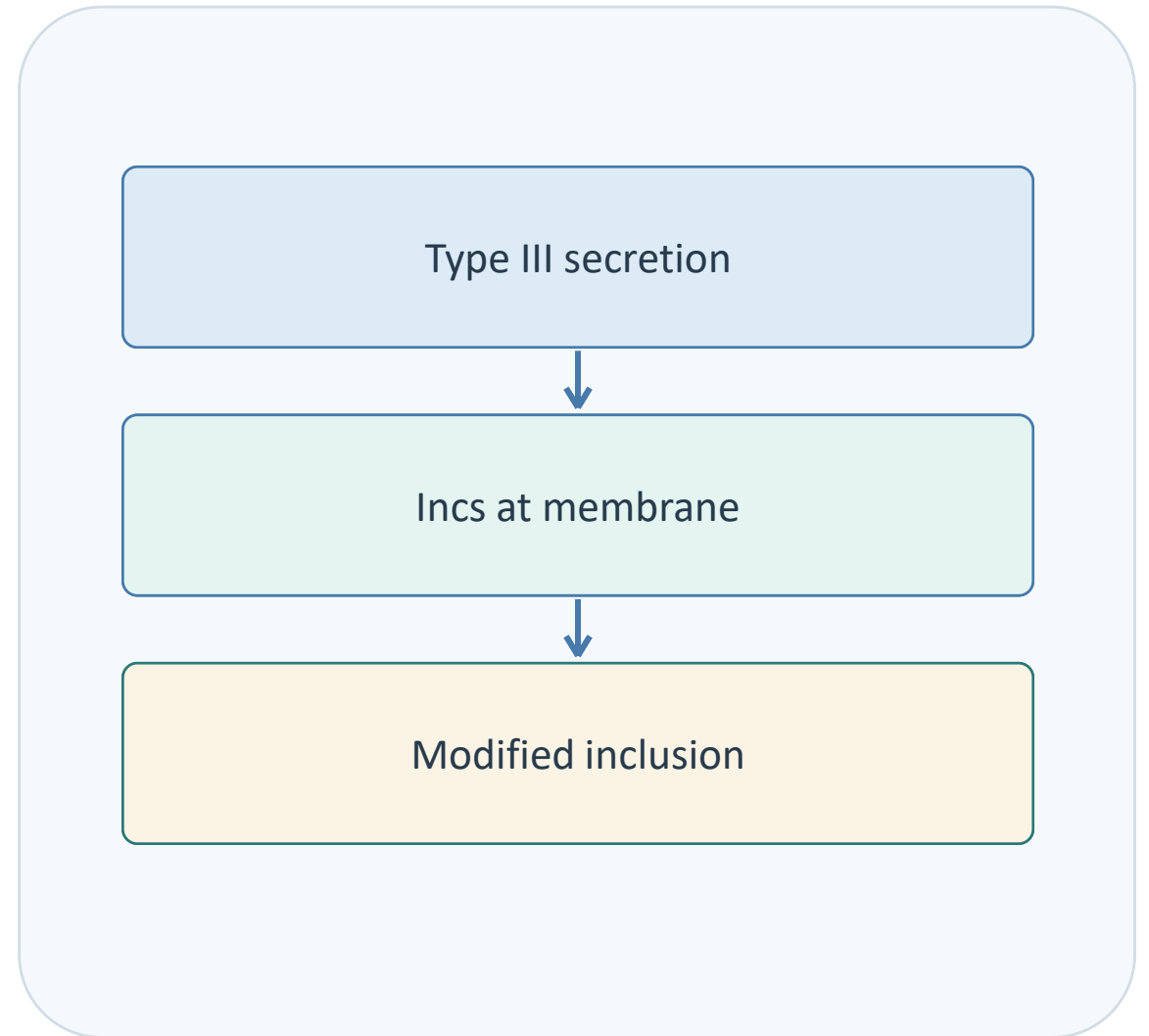
The inclusion is more than a vacuole

- Reticulate bodies persist within a membrane-bound inclusion
- The inclusion is derived from an endosomal membrane
- Its membrane is actively remodeled by bacterial products



Inclusion membrane proteins: “Incs”

- Type III secretion delivers proteins that alter the inclusion membrane
- These inclusion membrane proteins are termed Incs
- They help create a compartment favorable for chlamydial growth



Escape from phagolysosomal destruction

- A conventional endocytic compartment can mature toward a degradative phagolysosome
- Incs and other bacterial molecules obstruct that maturation
- The protected inclusion permits survival of intracellular reticulate bodies

Unmodified vesicle

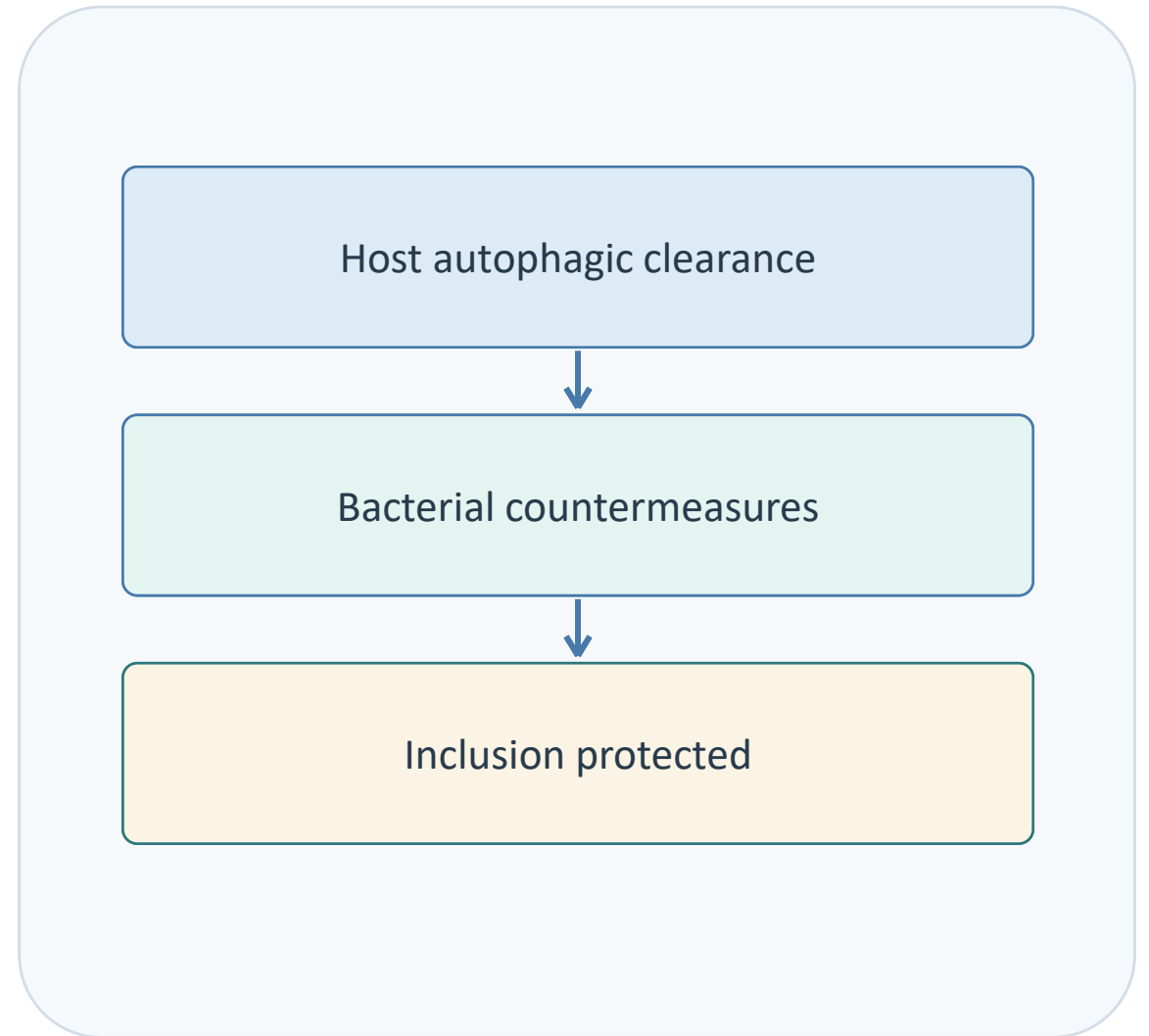
Phagolysosomal
maturation

Chlamydial inclusion

Maturation
prevented

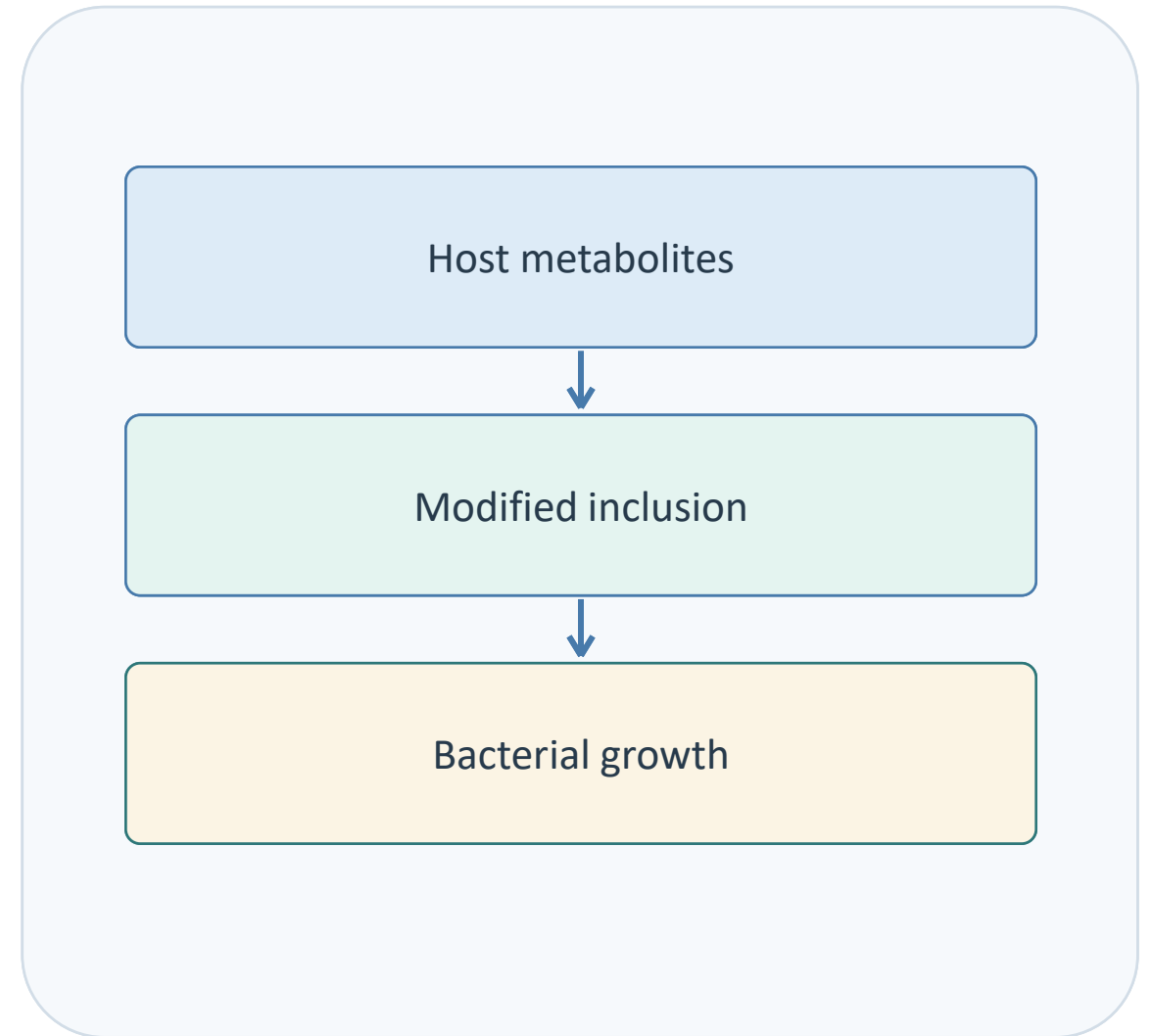
Protection against autophagy

- The intracellular inclusion is also protected from host autophagic clearance
- Incs and additional bacterial molecules contribute to this protection
- Avoiding degradative pathways favors persistence of the replicative niche



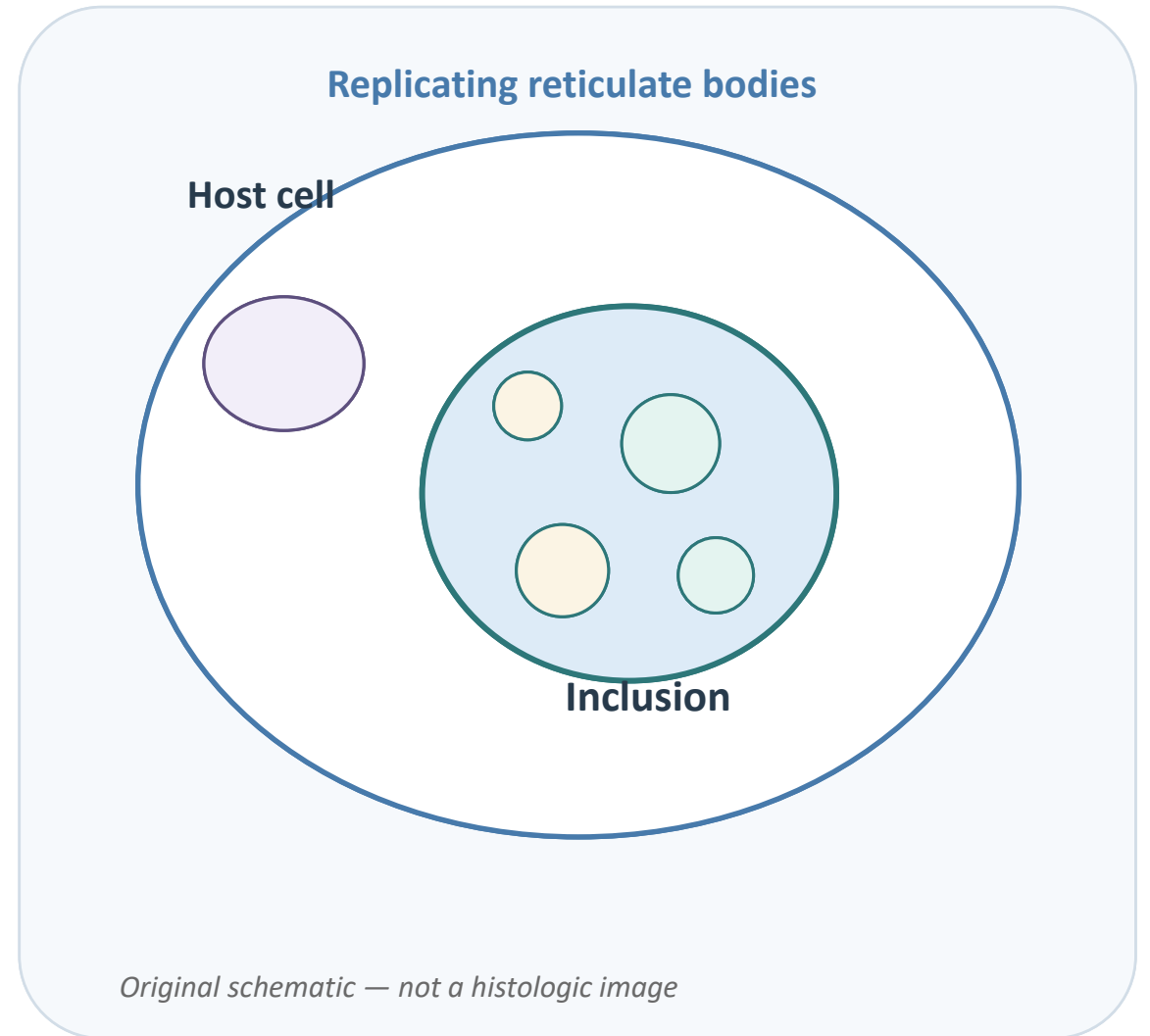
Nutrient acquisition across the inclusion

- Reticulate bodies require access to host-cell nutrients
- The modified inclusion facilitates nutrient entry
- Nutrient use supports bacterial metabolism and reproduction



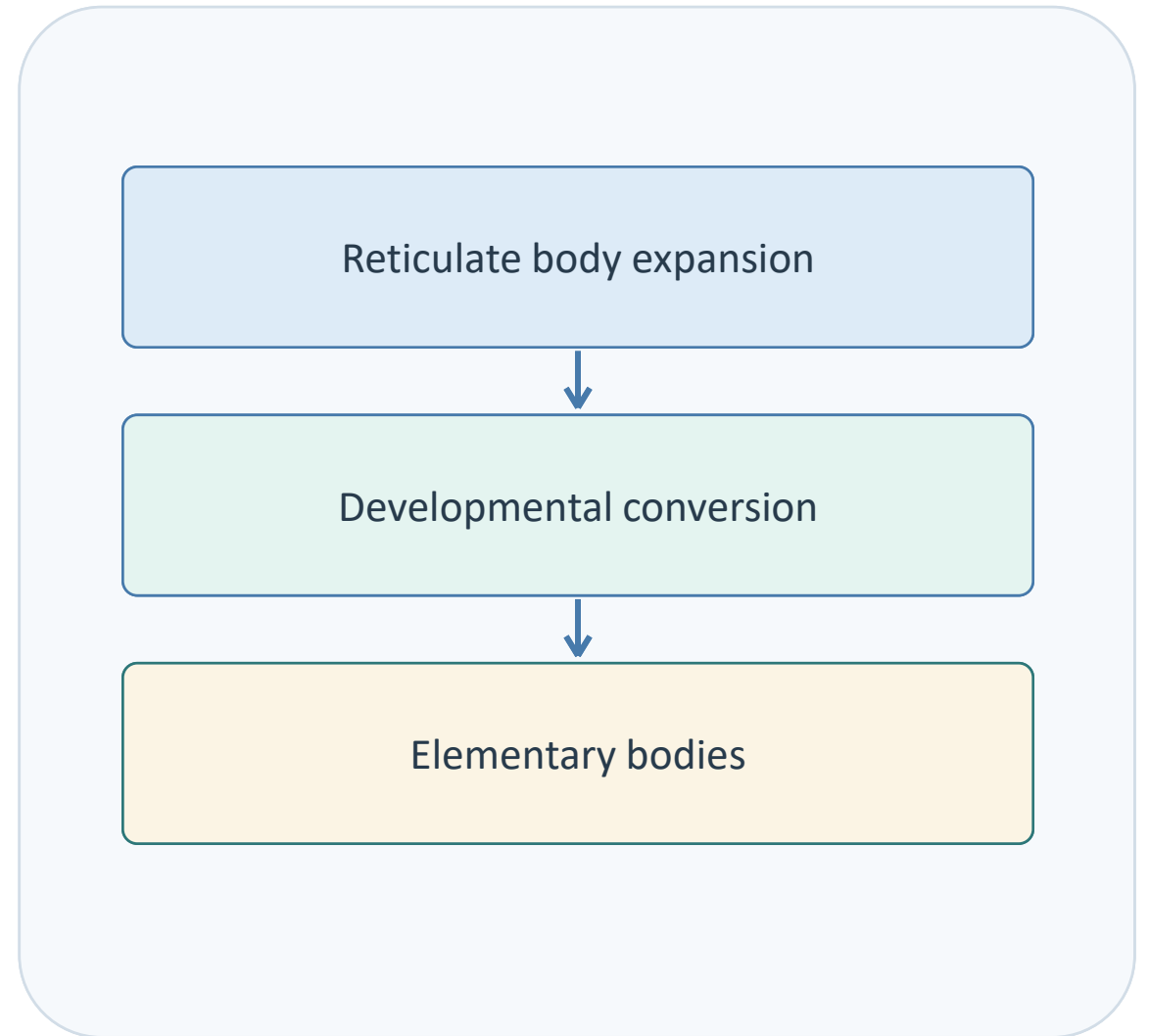
Reticulate body: Intracellular amplification

- Reticulate bodies use host-derived nutrients to replicate
- Replication increases the number of organisms within the inclusion
- This is the active multiplication stage of the cycle



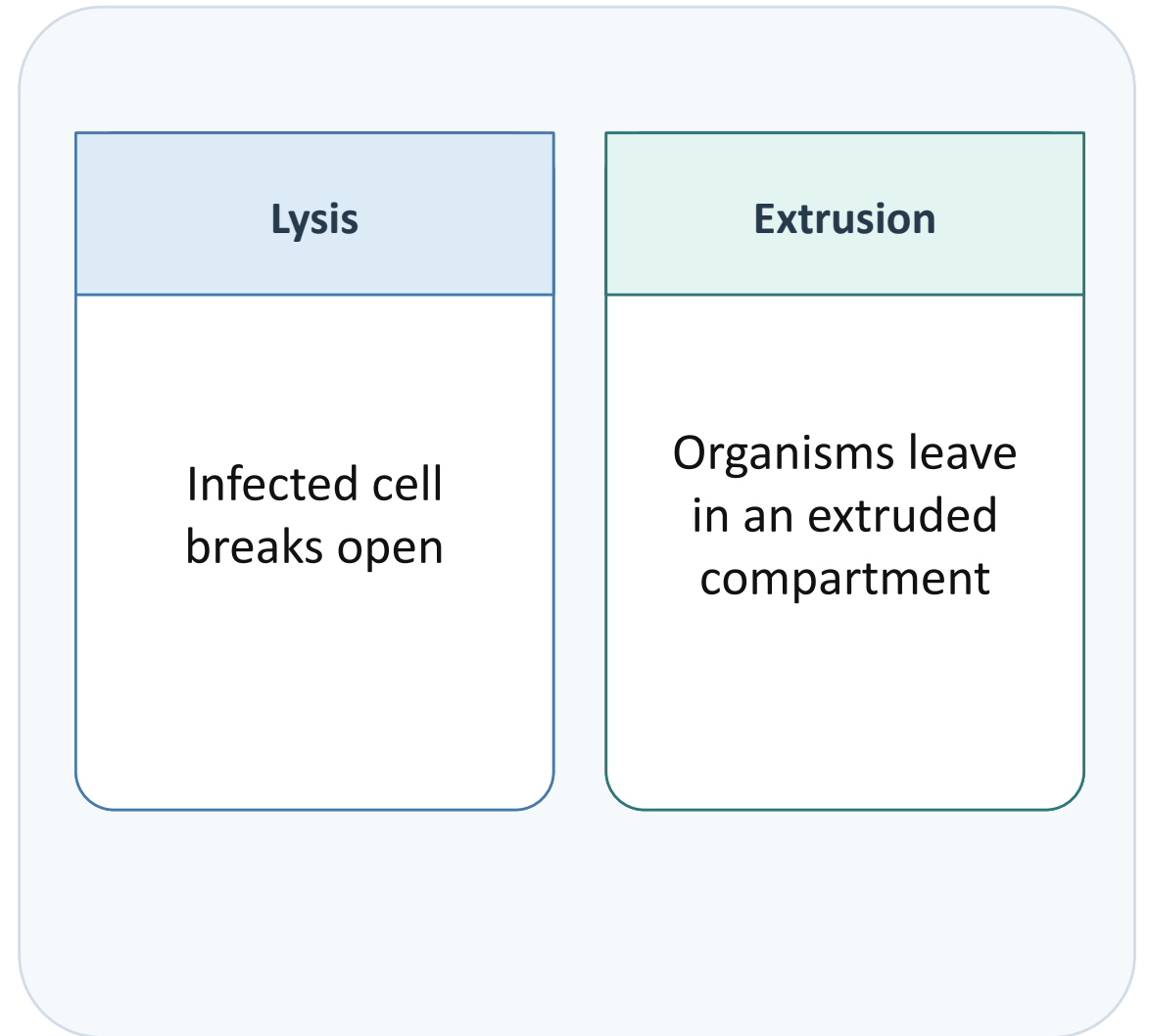
Reappearance of infectious elementary bodies

- After reticulate-body replication, newly infectious elementary bodies form
- Differentiation prepares progeny organisms for transmission to additional cells
- An infected inclusion may therefore contain successive developmental stages



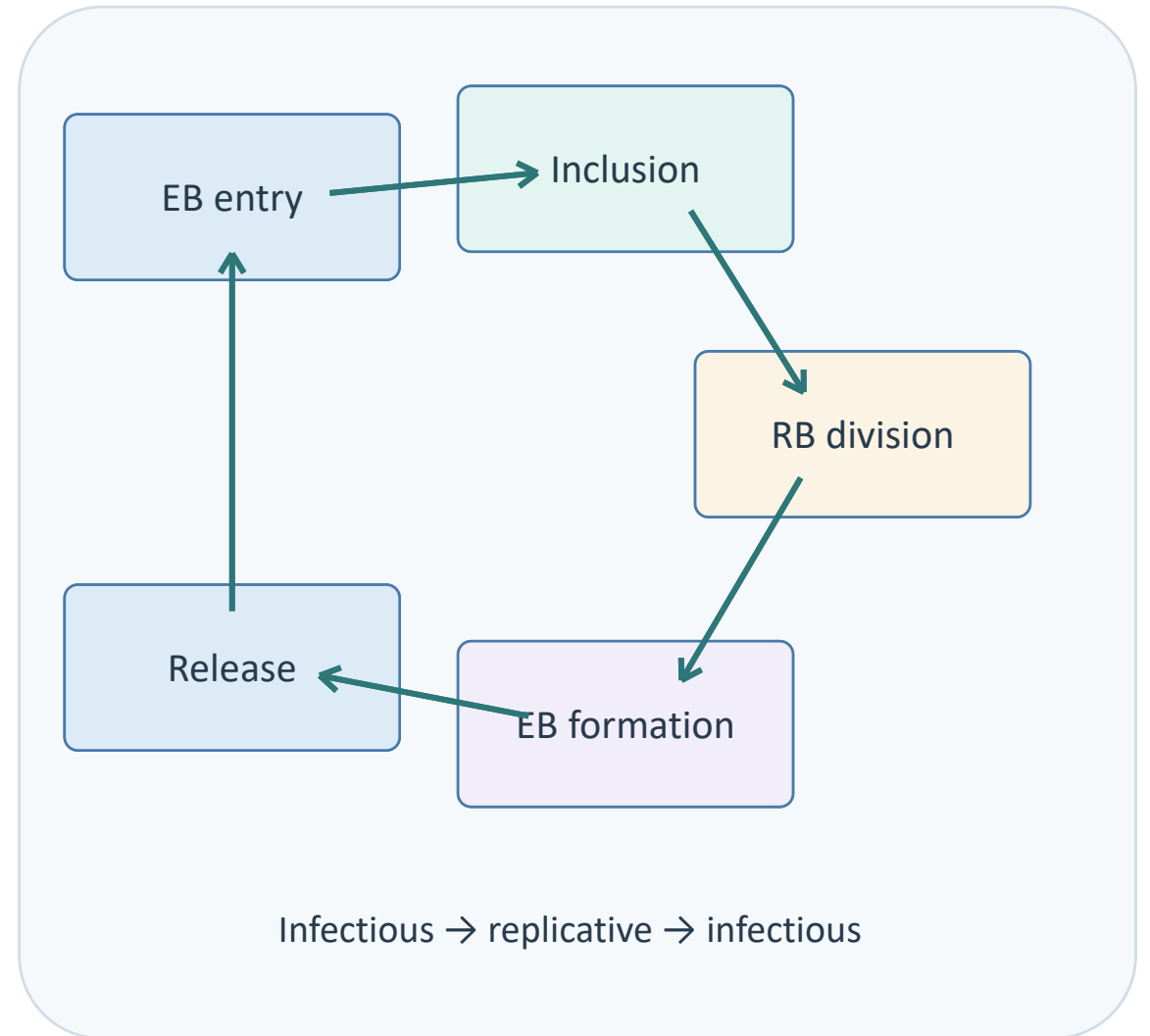
Two routes of exit

- New infectious organisms are released by lysis of the infected host cell or by extrusion
- Either route delivers elementary bodies to the extracellular environment
- Released elementary bodies can initiate another host-cell infection



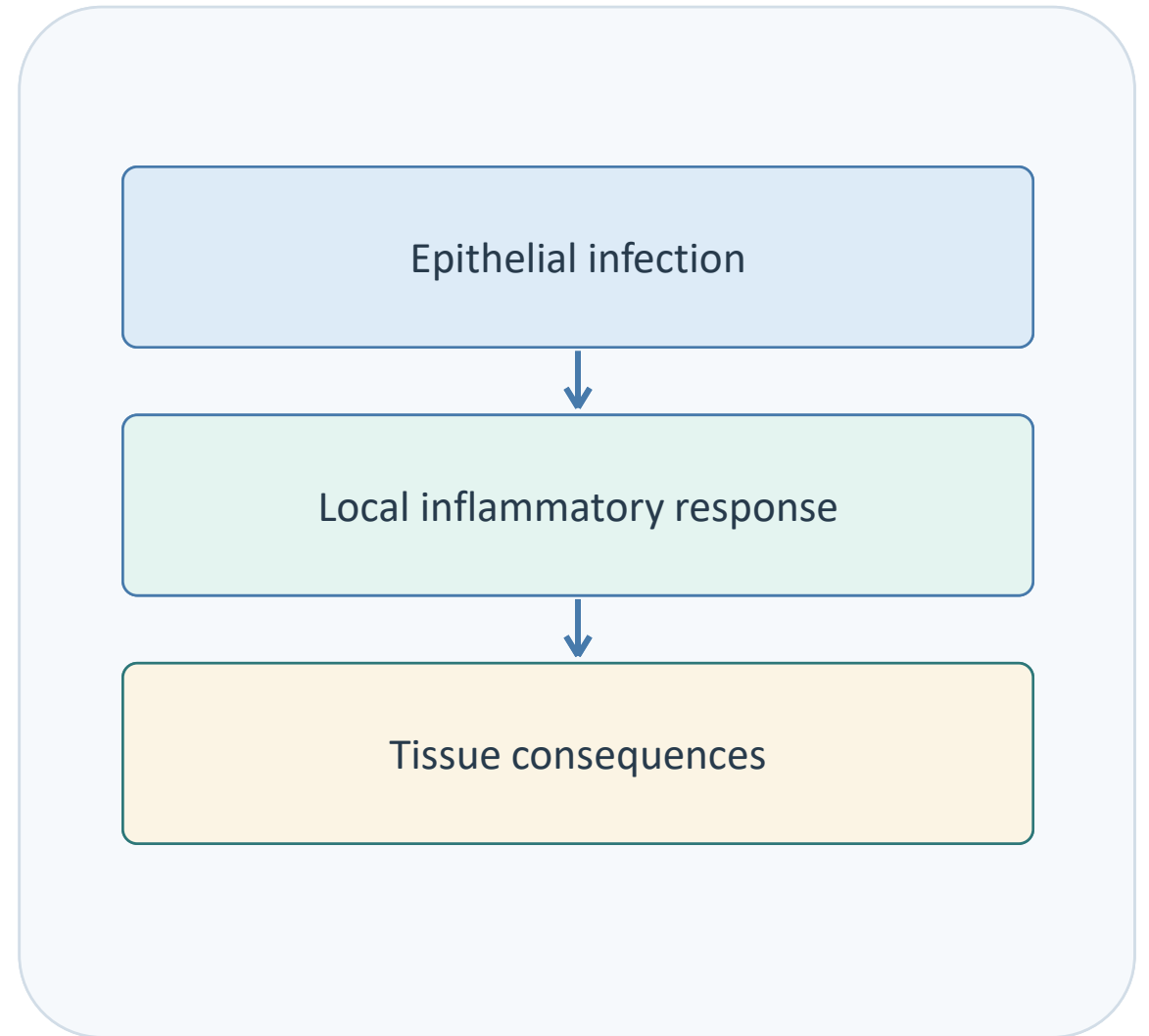
Life cycle: One integrated sequence

- Elementary body → attachment and type III-dependent entry
- Inclusion formation → differentiation to reticulate body → replication
- Elementary body re-formation → lysis or extrusion



Why the cycle matters for tissue injury

- Intracellular growth permits organism multiplication in epithelial cells
- Release enables involvement of additional host cells and sites
- The host inflammatory response contributes to mucosal lesions and their sequelae



Serovar–syndrome map

- Different *C. Trachomatis* serovars preferentially produce different disease syndromes
- A–C: Trachoma; D–K: Genital infection and inclusion conjunctivitis
- L1–L3: Lymphogranuloma venereum

A–C

Trachoma

D–K

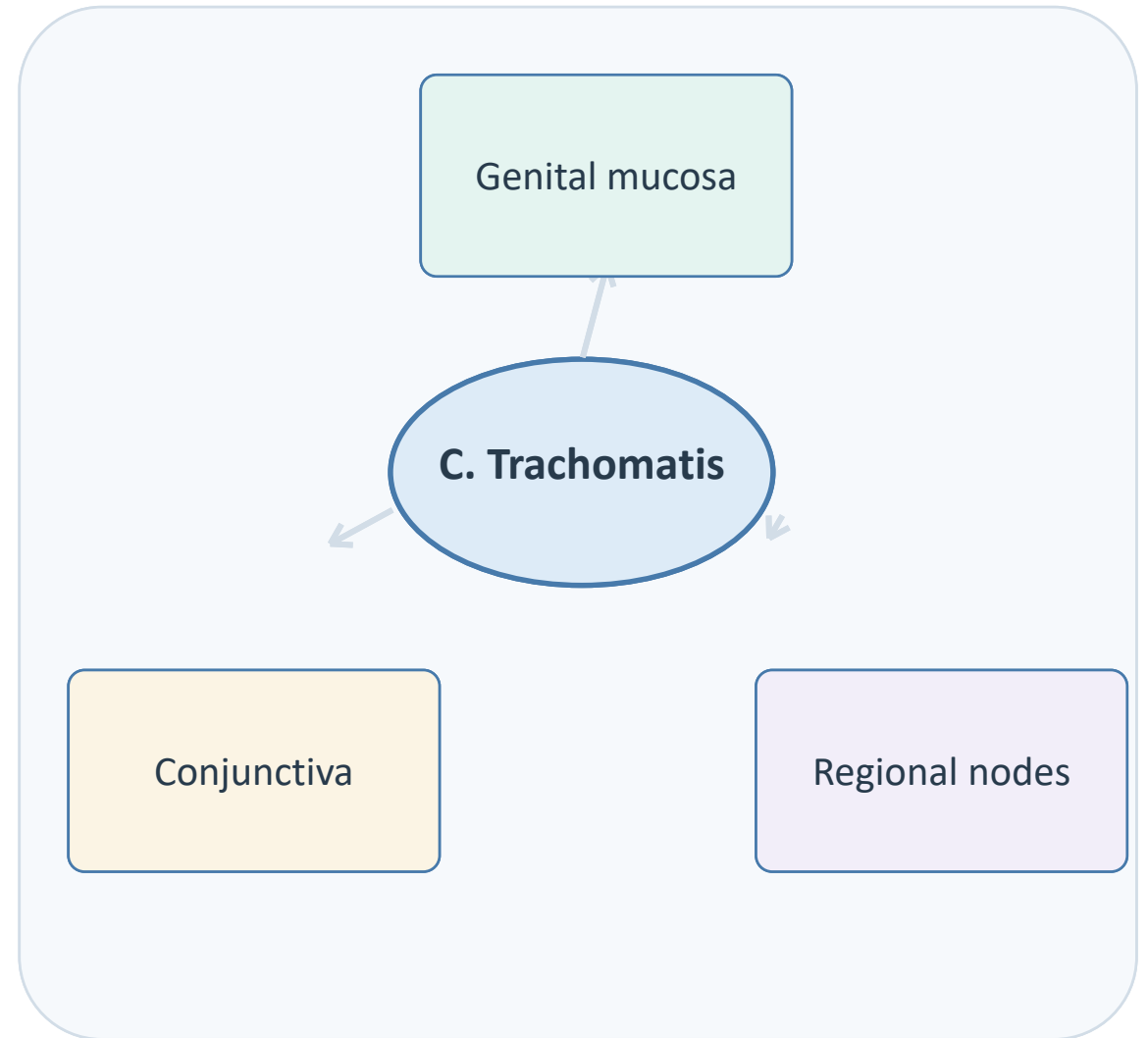
Genital infection • inclusion conjunctivitis

L1–L3

Lymphogranuloma venereum

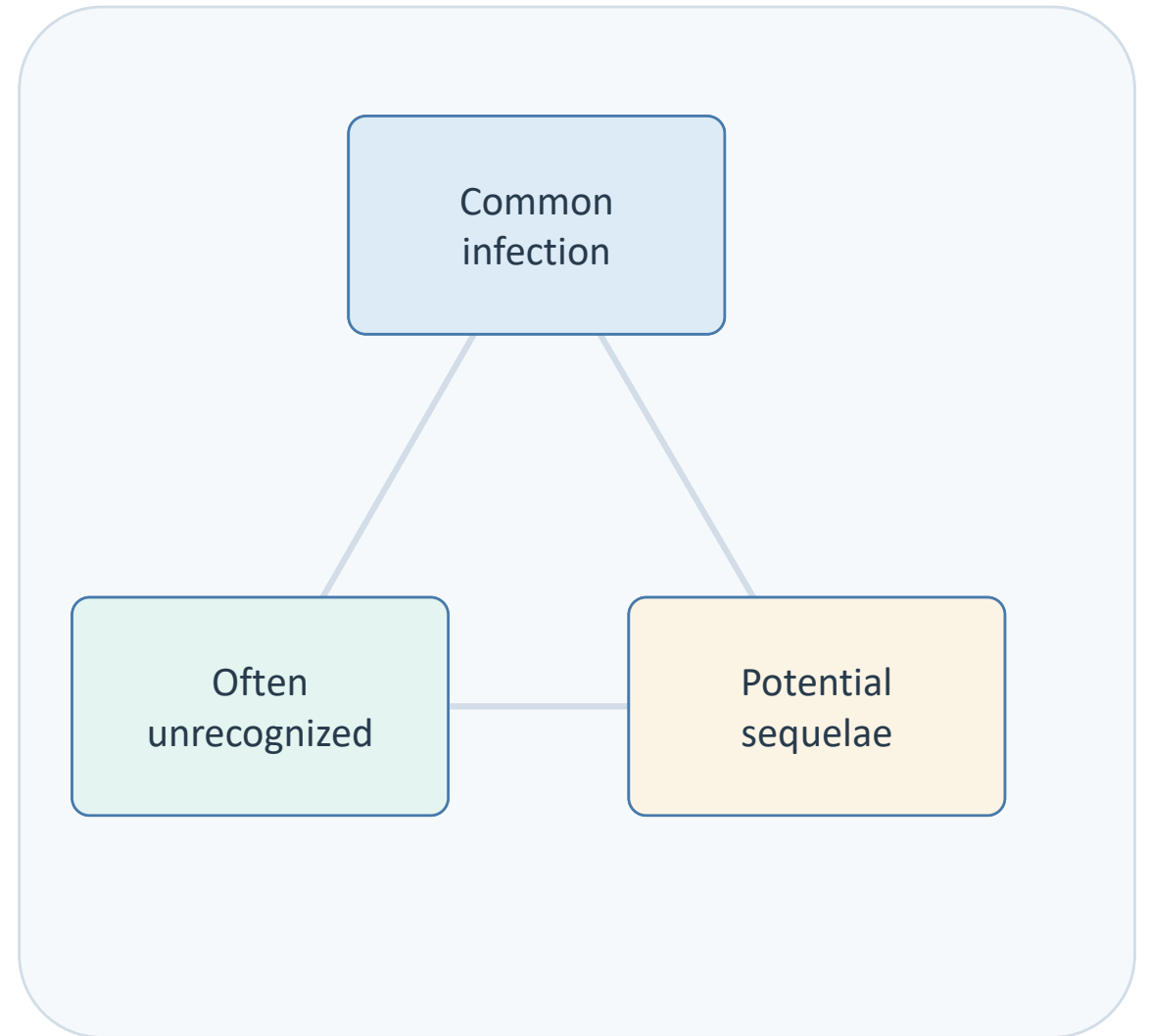
Different sites, one pathogen species

- The same species is associated with ocular, urogenital, and lymphatic manifestations
- Serovar identity is linked to the characteristic clinical syndrome
- Organism identification alone does not specify the full extent of tissue injury



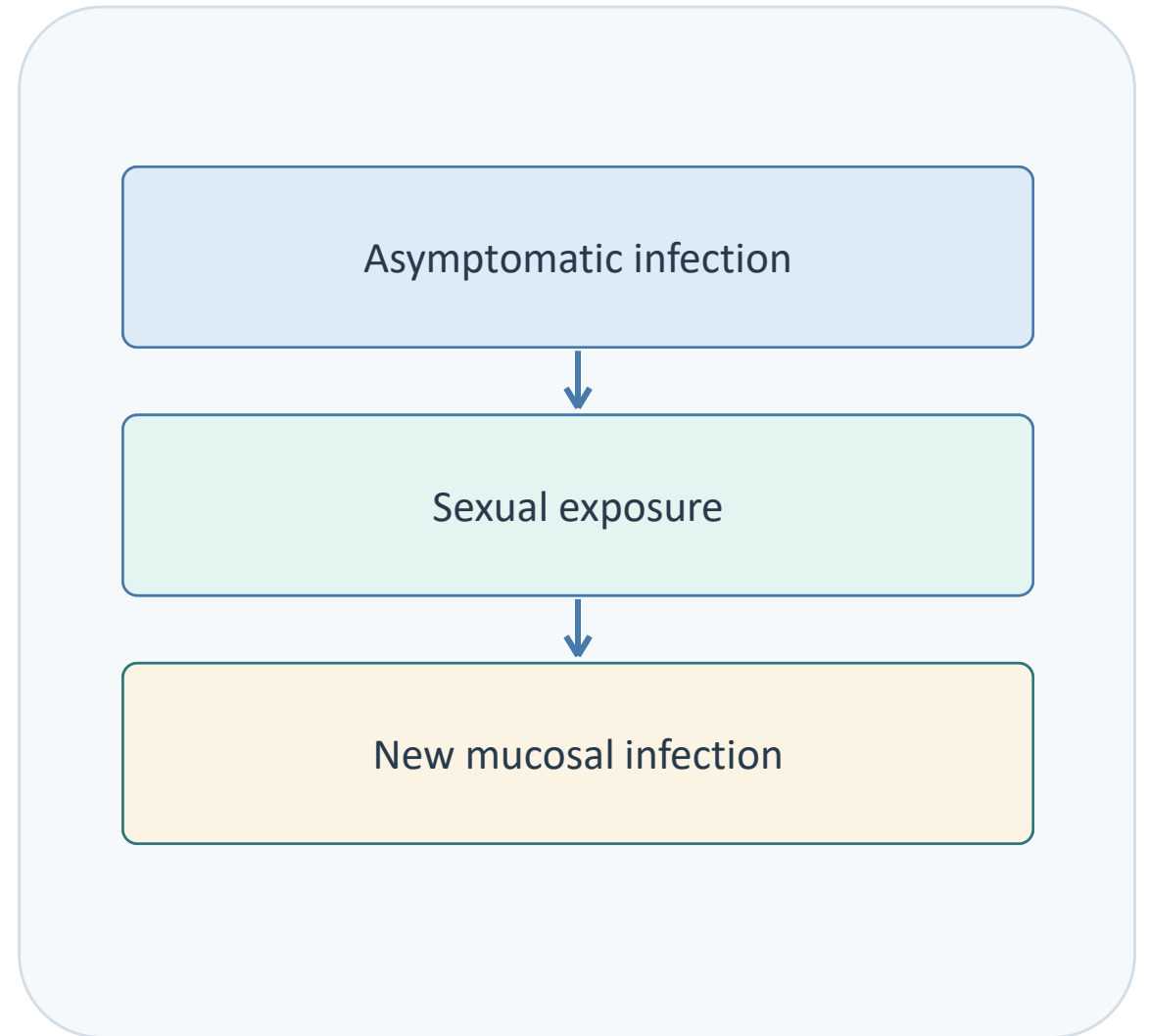
Genital infection: Population relevance

- C. Trachomatis as a leading bacterial sexually transmitted infection
- Infections may be clinically silent and remain untreated
- Silent infection is important because complications may occur beyond the initial mucosal site



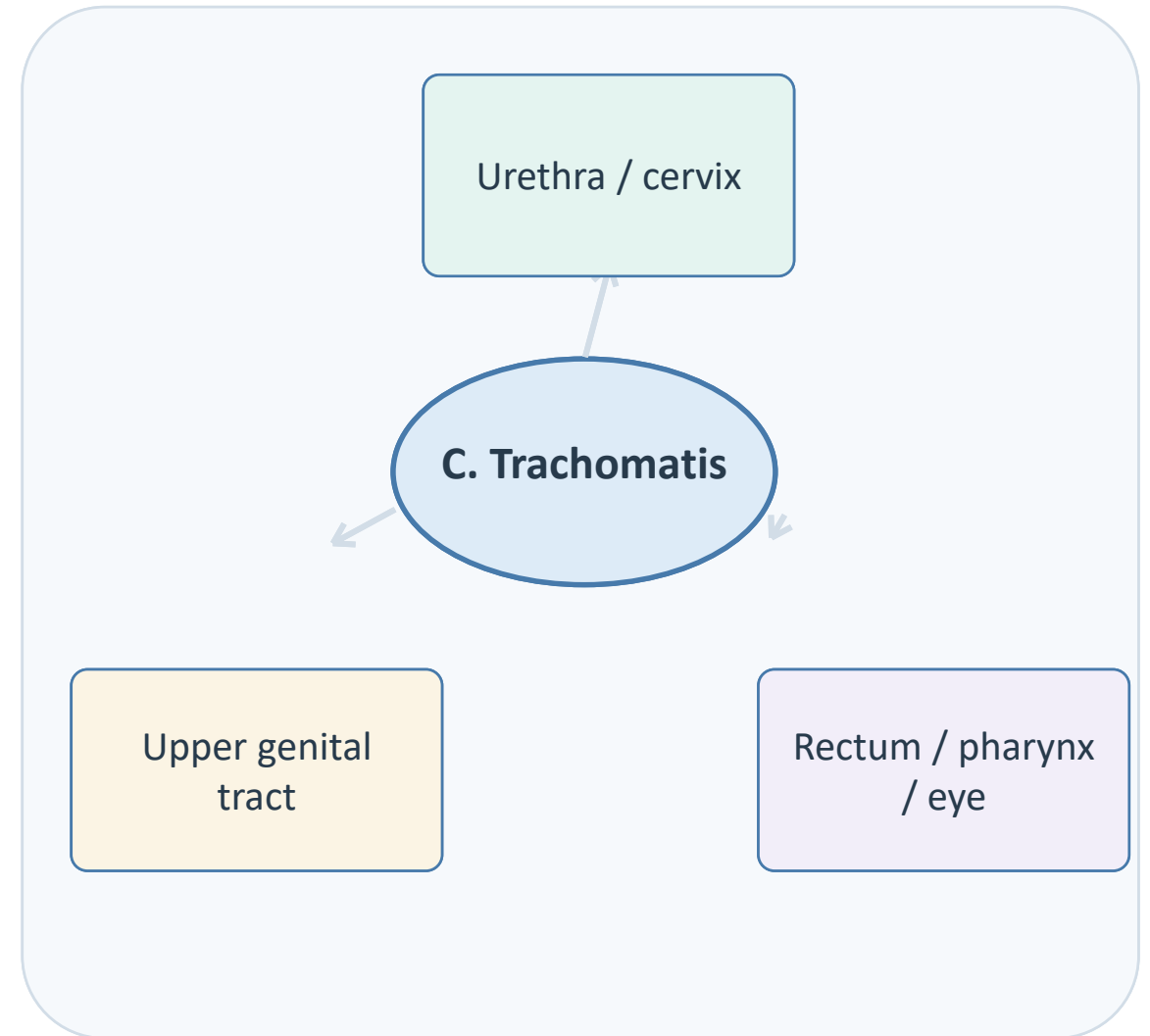
Sexual transmission and silent reservoirs

- Chlamydial genital infection is primarily transmitted through sexual contact
- Transmission may occur from a person without recognized symptoms
- The absence of symptoms does not imply absence of infection



Anatomic spectrum of genital infection

- Lower genital tract: Urethritis and cervicitis
- Adjacent or ascending involvement: Epididymitis, prostatitis, endometritis, salpingitis
- Extragenital mucosa or surfaces: Proctitis, pharyngitis, conjunctivitis



Chlamydial urethritis: Clinical presentation

- Urethral infection may cause local symptoms or remain asymptomatic
- Commonly silent chlamydial urethritis with gonococcal urethritis in men
- Unrecognized urethritis can delay testing and treatment

Symptomatic

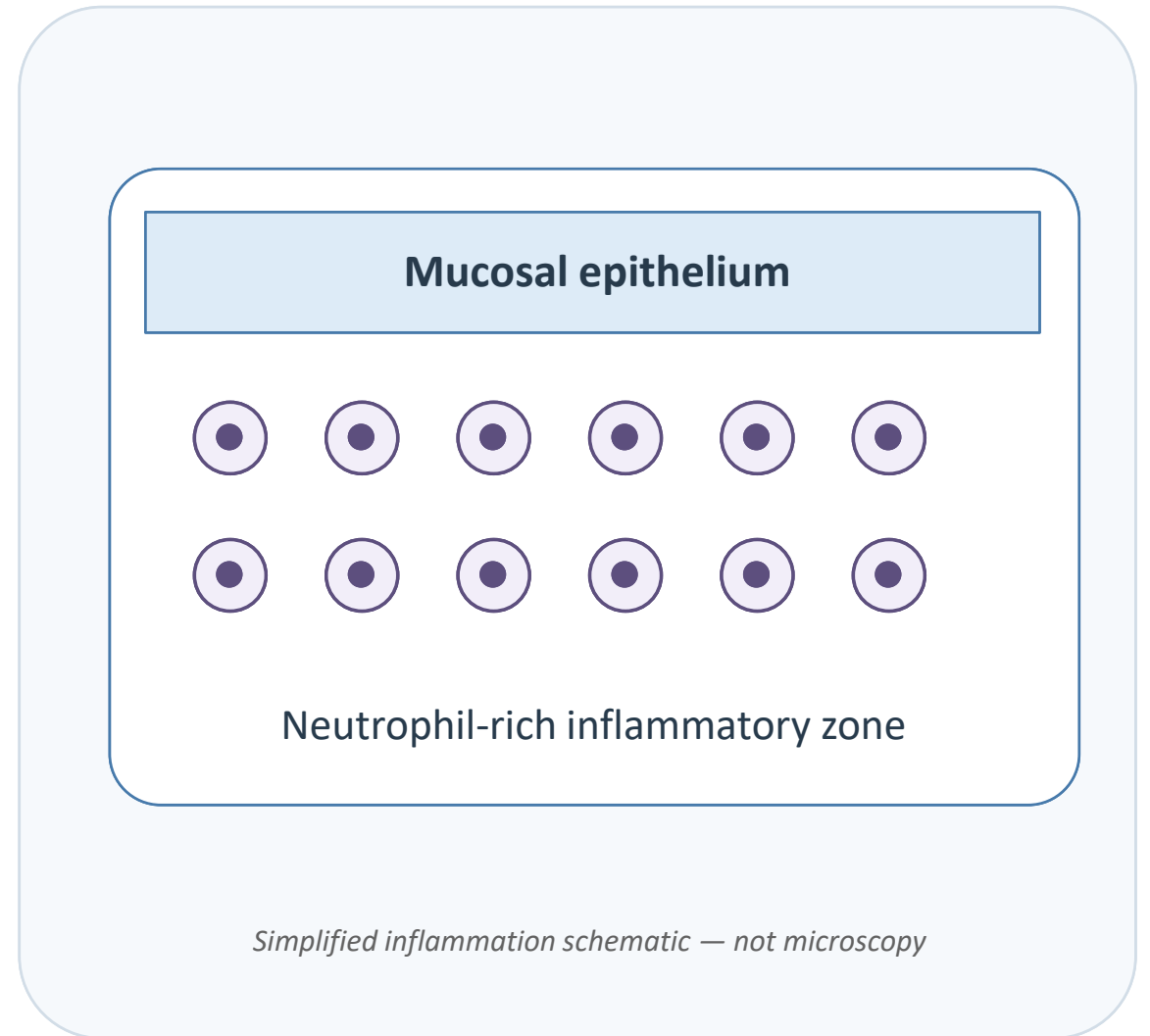
Discharge and
local irritation

Asymptomatic

No obvious
warning signs

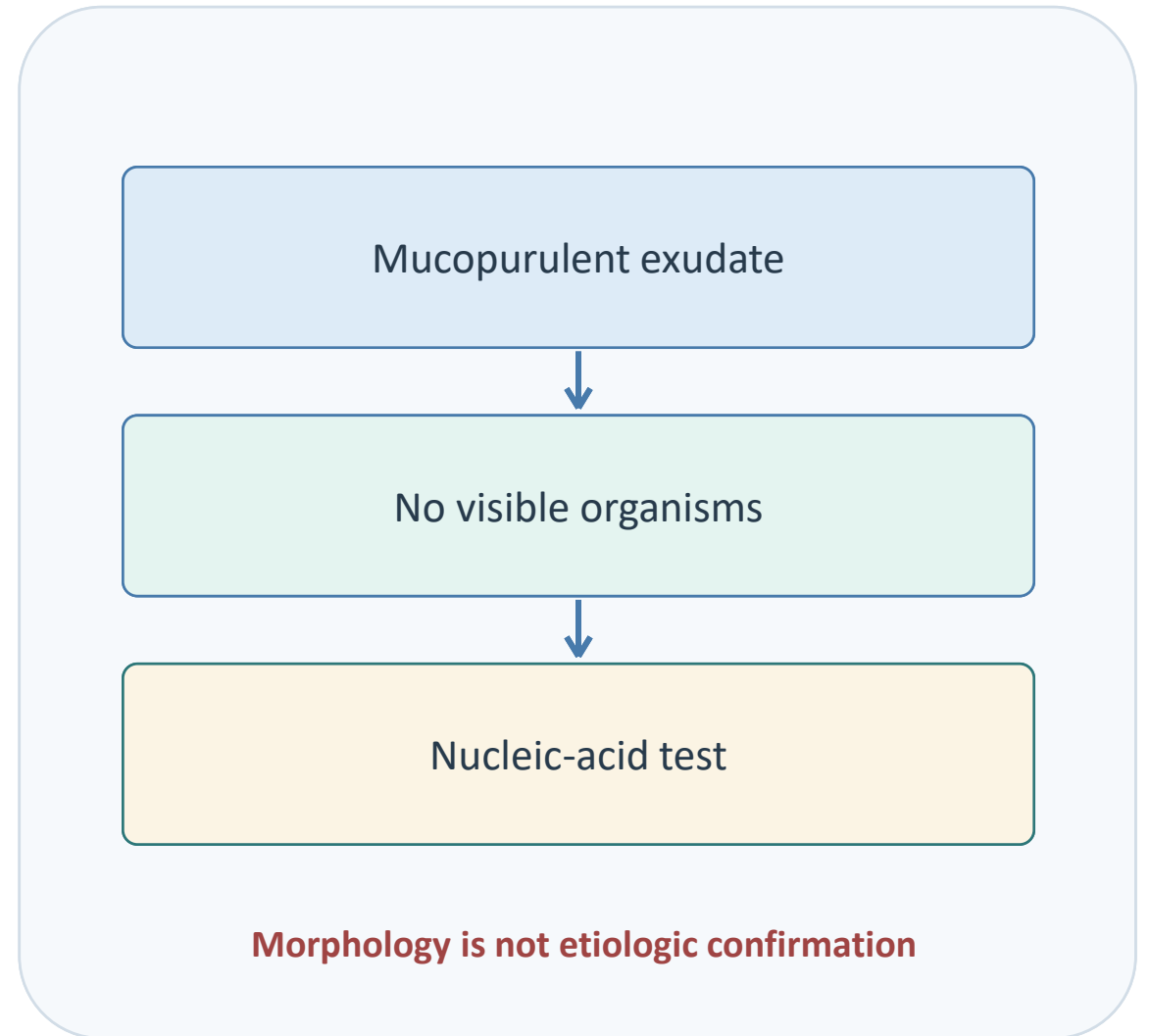
Urethritis: Predominant exudate

- Acute chlamydial urethritis may produce a mucopurulent discharge
- Neutrophils predominate in the inflammatory exudate
- This inflammatory pattern is not unique to Chlamydia



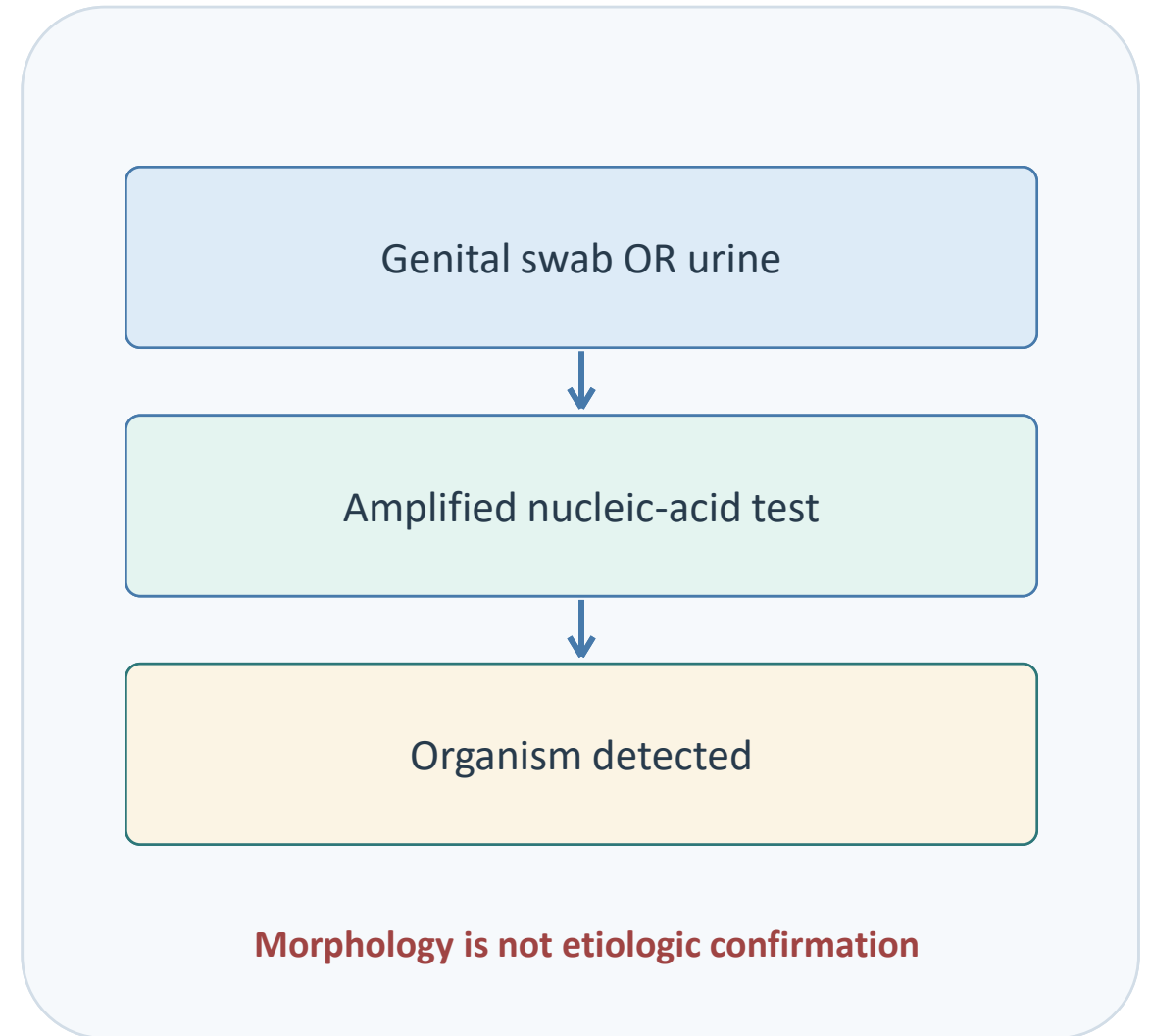
Why a Gram stain can mislead

- Chlamydial organisms are not visible in routine Gram-stained smears or sections
- Neutrophil-rich discharge indicates inflammation rather than a specific cause
- A negative organism finding on Gram stain does not exclude chlamydial urethritis



Nucleic-acid amplification: Diagnostic principle

- Amplified nucleic-acid testing for C. Trachomatis urethritis
- Acceptable specimen categories in the text include genital swabs and urine
- The diagnostic target is microbial nucleic acid rather than visually detectable bacteria



Gonorrhea and chlamydia: Overlapping phenotype

- Both may cause urethritis and genital mucosal infection
- Their urethritis morphology is virtually identical
- Clinical symptoms and neutrophils alone cannot reliably separate the two infections

Chlamydial urethritis

Neutrophilic
mucosal exudate

Gonococcal urethritis

Similar
inflammatory
phenotype

The discriminating value of organism visibility

- Gonococci may appear as gram-negative diplococci within neutrophils in exudate
- Chlamydiae are not visualized on routine Gram-stained sections or smears
- Microbiological testing, rather than appearance alone, determines the etiology

Gonorrhea

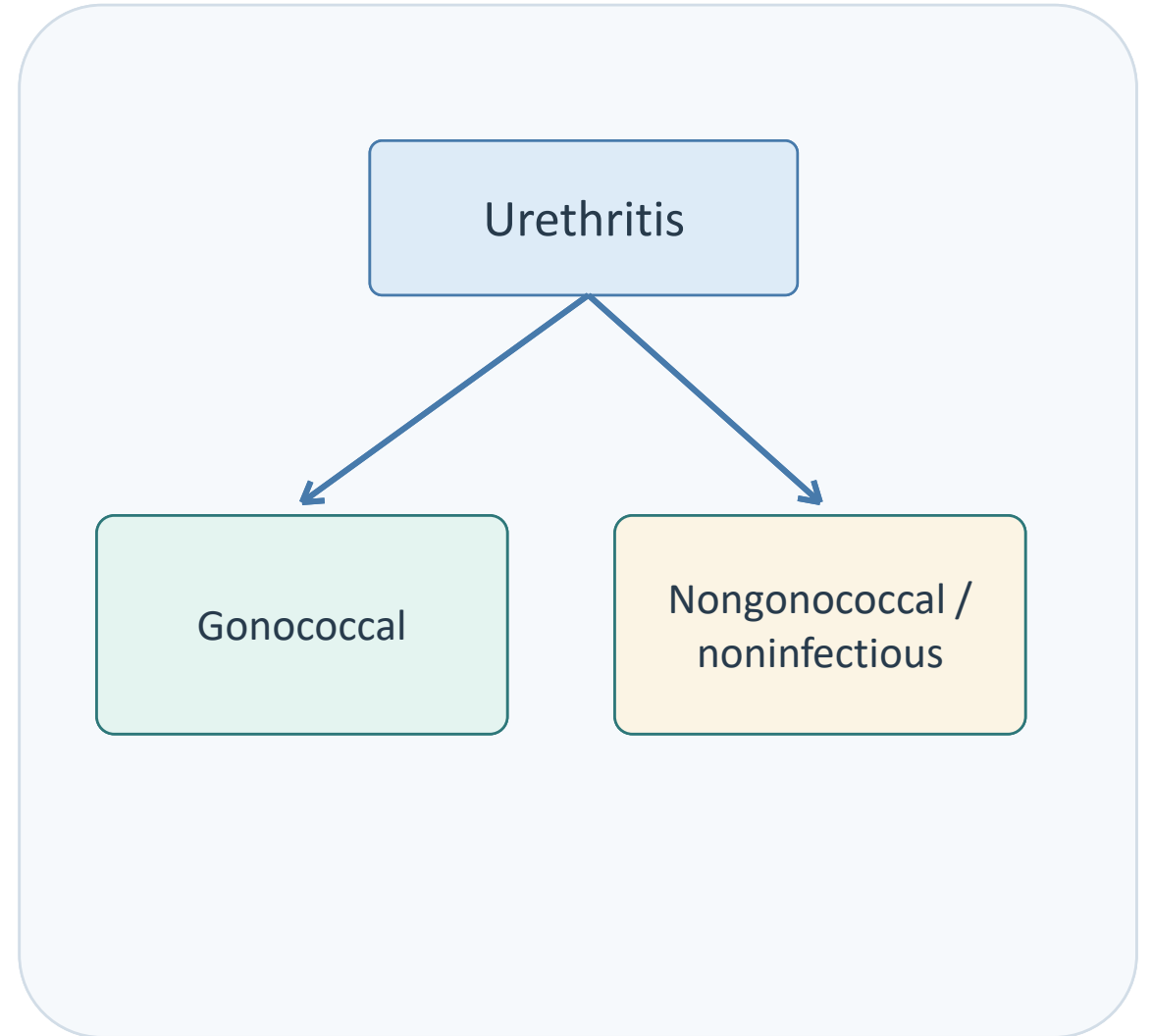
Diplococci may be seen

Chlamydia

Organisms not seen by Gram stain

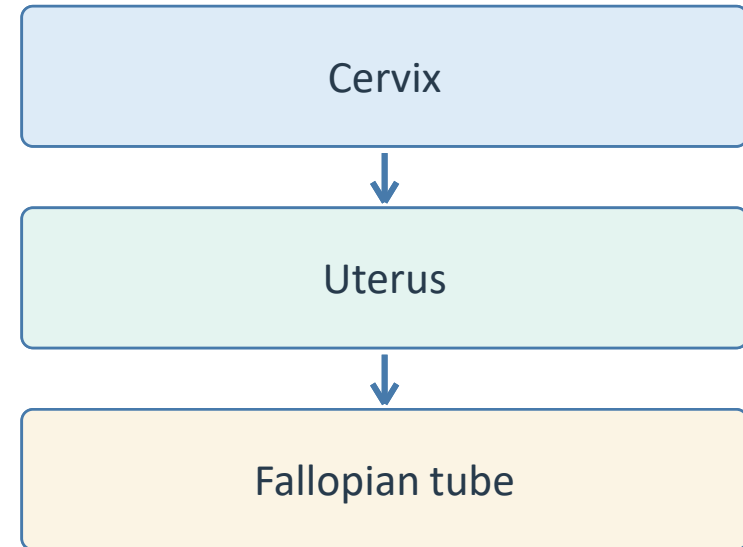
The broad differential of nongonococcal urethritis

- Chlamydia is one important cause of nongonococcal urethritis
- Robbins also describes Ureaplasma and noninfectious urethritis
- The morphologic label “urethritis” is not a microbiologic diagnosis



Female genital infection: Cervicitis

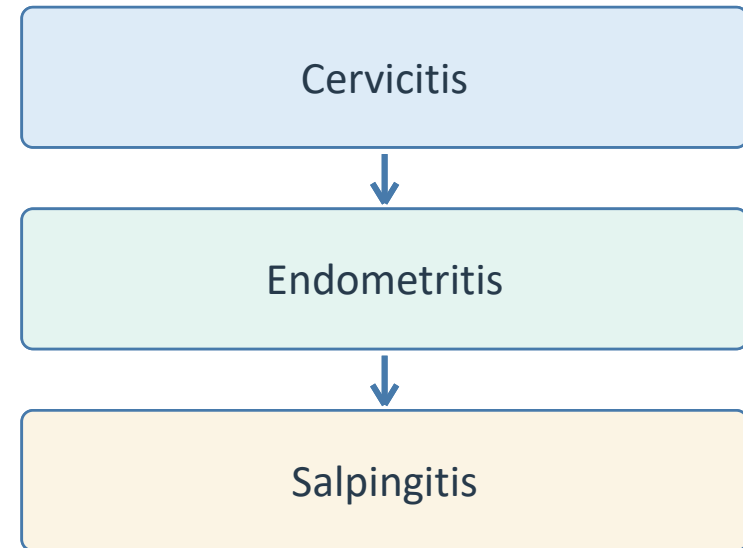
- The female genital tract chapter describes cervicitis as the predominant presentation
- Chlamydial infection in females is frequently asymptomatic
- Cervical involvement can be a starting point for ascending infection



Schematic of anatomic relationships / consequences

Ascending chlamydial infection

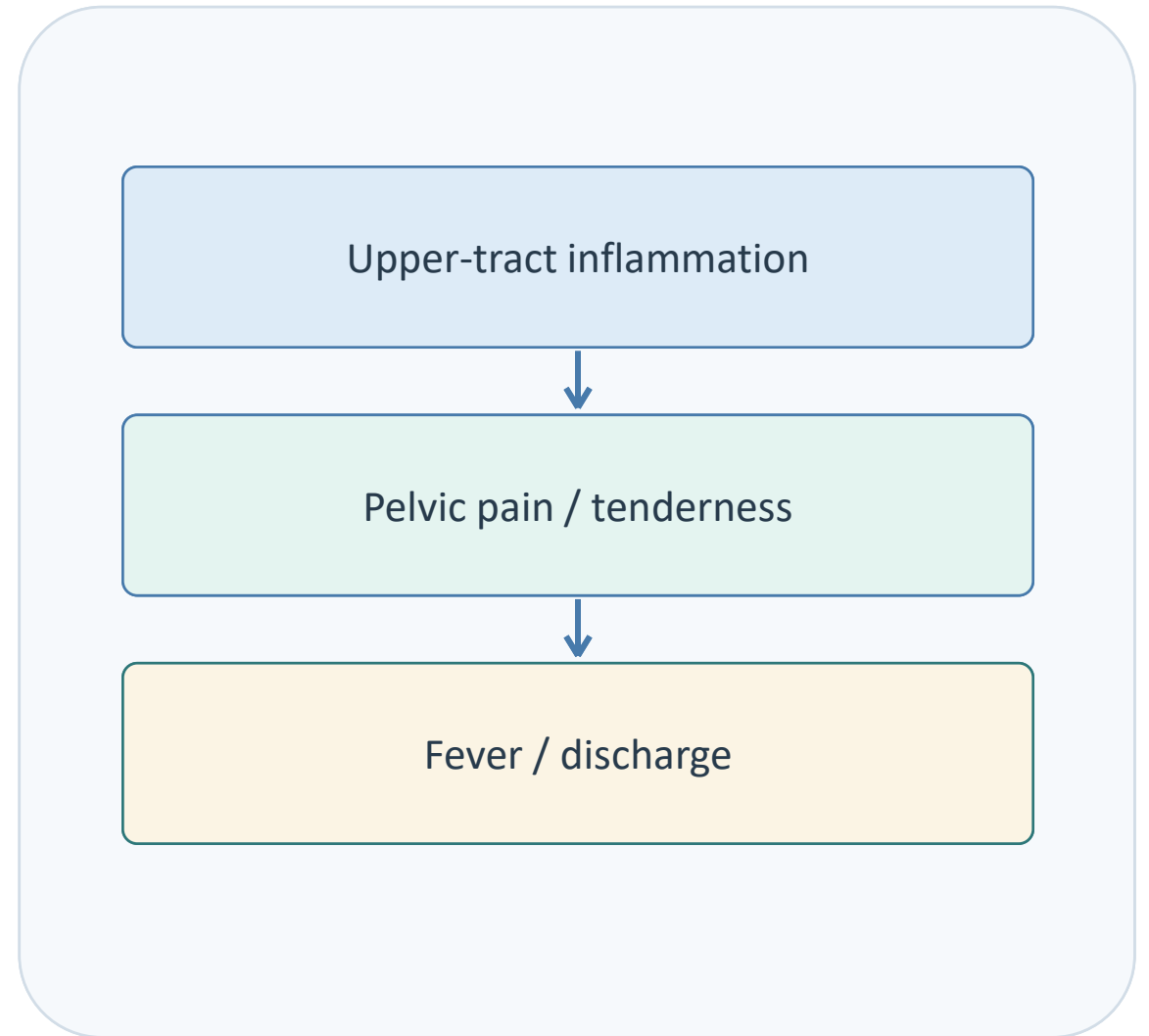
- In some patients infection ascends from the cervix
- Endometritis and salpingitis may develop as infection involves the upper genital tract
- This places Chlamydia among recognized causes of pelvic inflammatory disease



Schematic of anatomic relationships / consequences

Pelvic inflammatory disease: Clinical picture

- PID is infection and inflammation involving upper female genital structures
- The source associates PID with pelvic pain, adnexal tenderness, fever, and discharge
- This is a syndrome with multiple possible microbial causes



PID has multiple etiologies

- Chlamydia and gonorrhea are both established causes of PID
- Other pelvic infections may be polymicrobial, including postprocedural or puerperal disease
- A diagnosis of PID does not by itself identify the organism

STI-associated

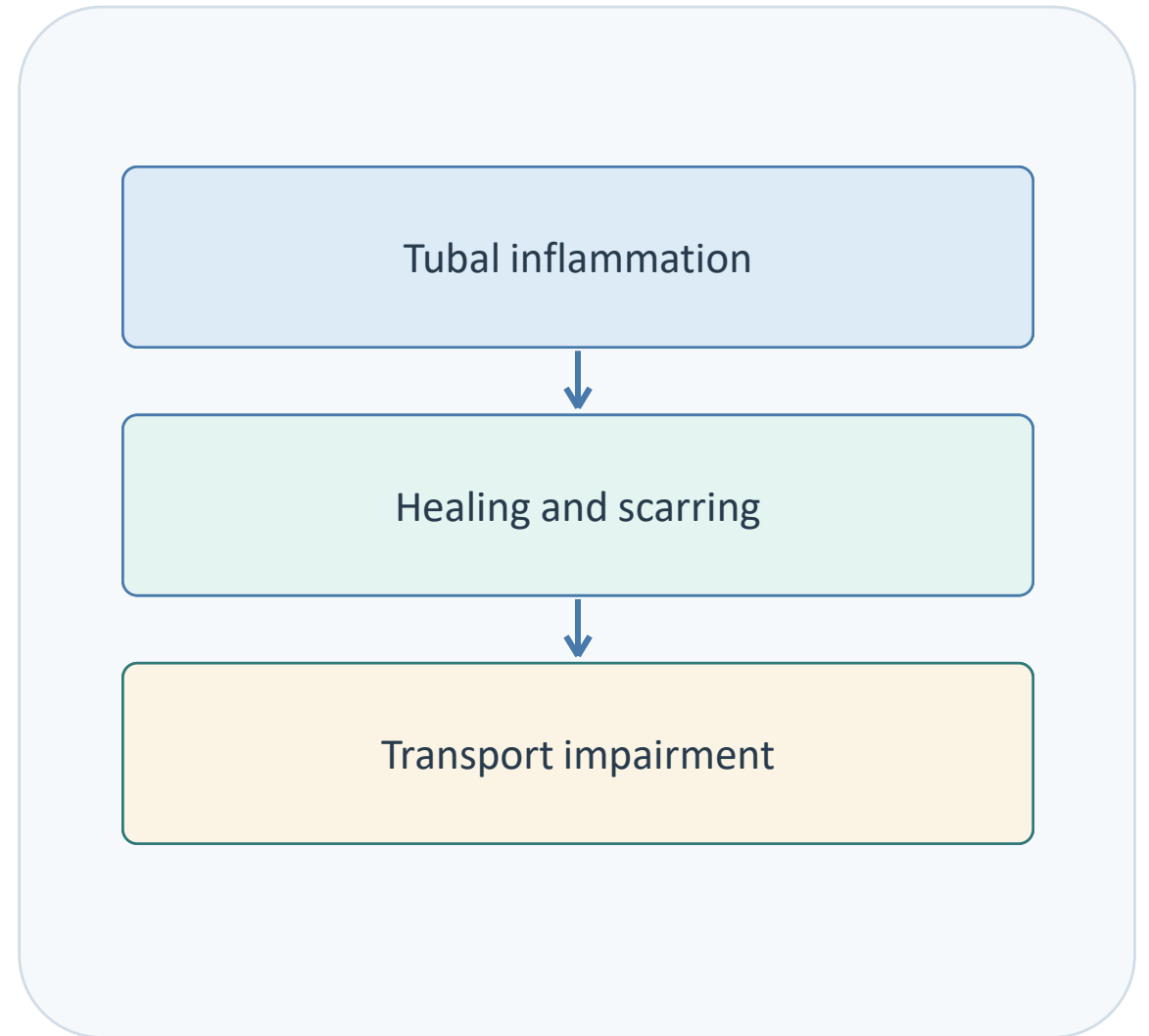
Chlamydia •
gonorrhea

Other contexts

Mixed
postprocedural or
puerperal
infection

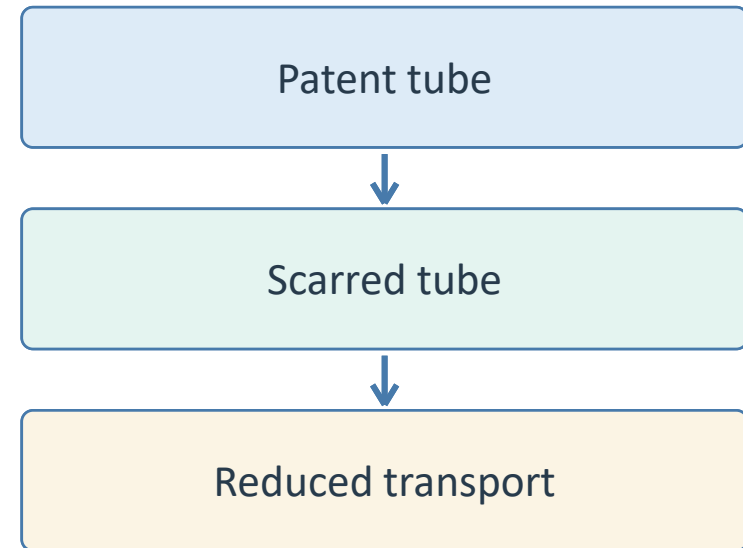
From tubal inflammation to impaired function

- Inflammation of the fallopian tubes may lead to healing with scarring
- Distortion of the tube and fimbriae can impair oocyte capture or passage
- Infertility and ectopic pregnancy are recognized sequelae of PID in the source



Why infertility can follow PID

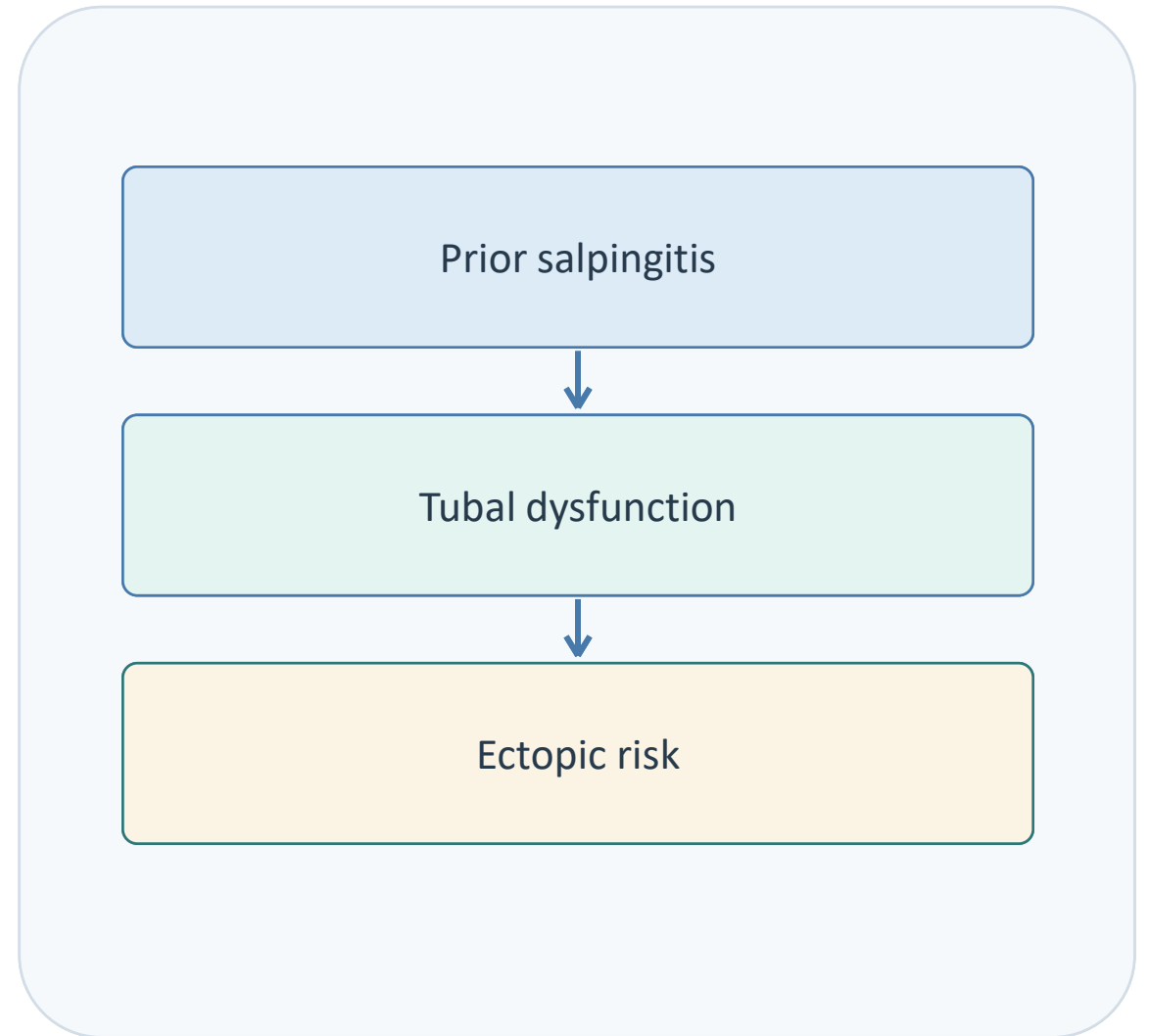
- Normal tubal architecture matters for transport of the oocyte
- PID-related scarring may obstruct the lumen or alter fimbrial function
- Structural damage may persist after the active infection has resolved



Schematic of anatomic relationships / consequences

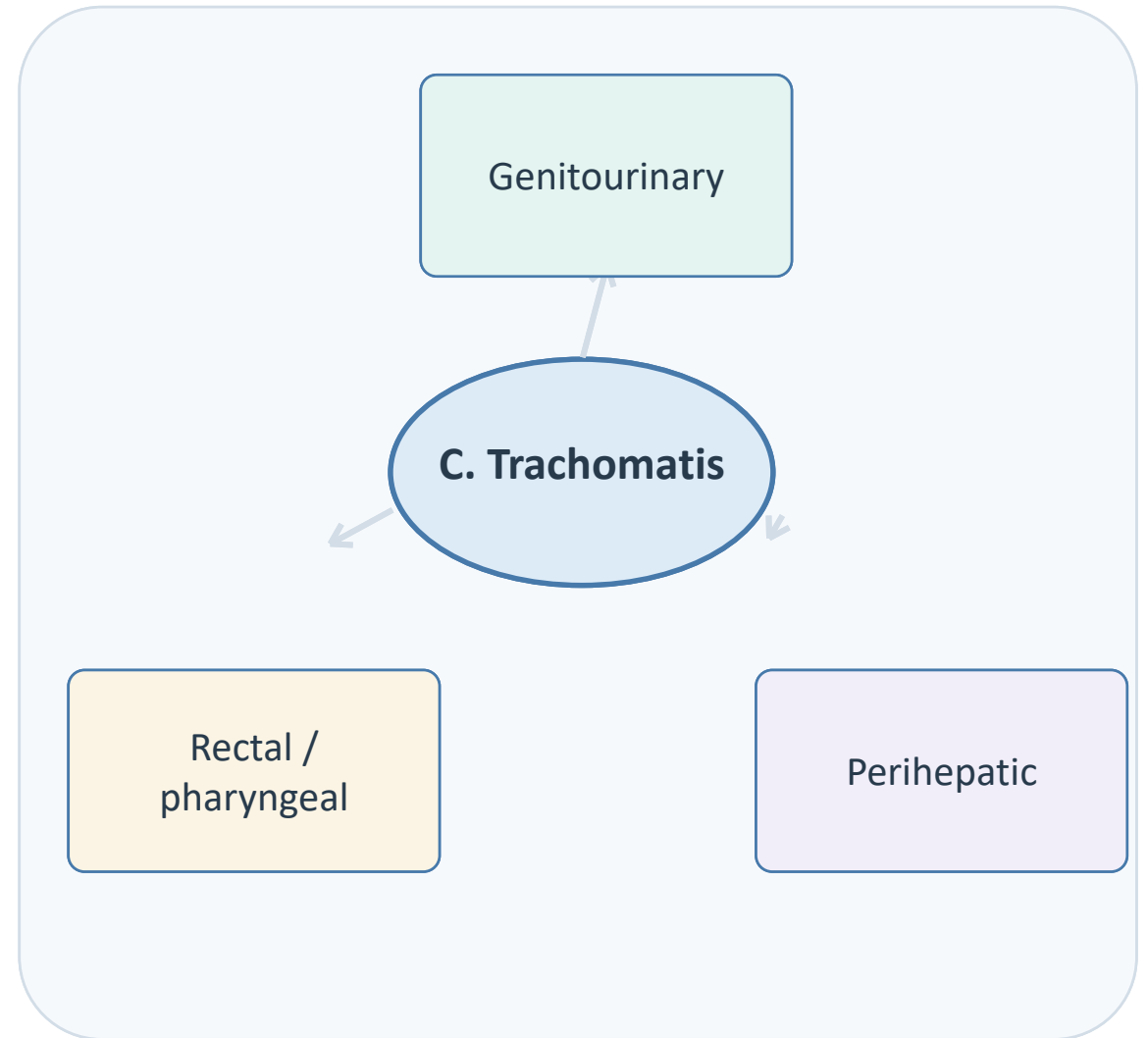
Ectopic pregnancy: The pathological link

- Tubal damage can interfere with orderly passage of the conceptus
- The female genital tract chapter lists ectopic pregnancy among PID sequelae
- The relationship is a complication of tubal injury, not a diagnostic sign of active Chlamydia



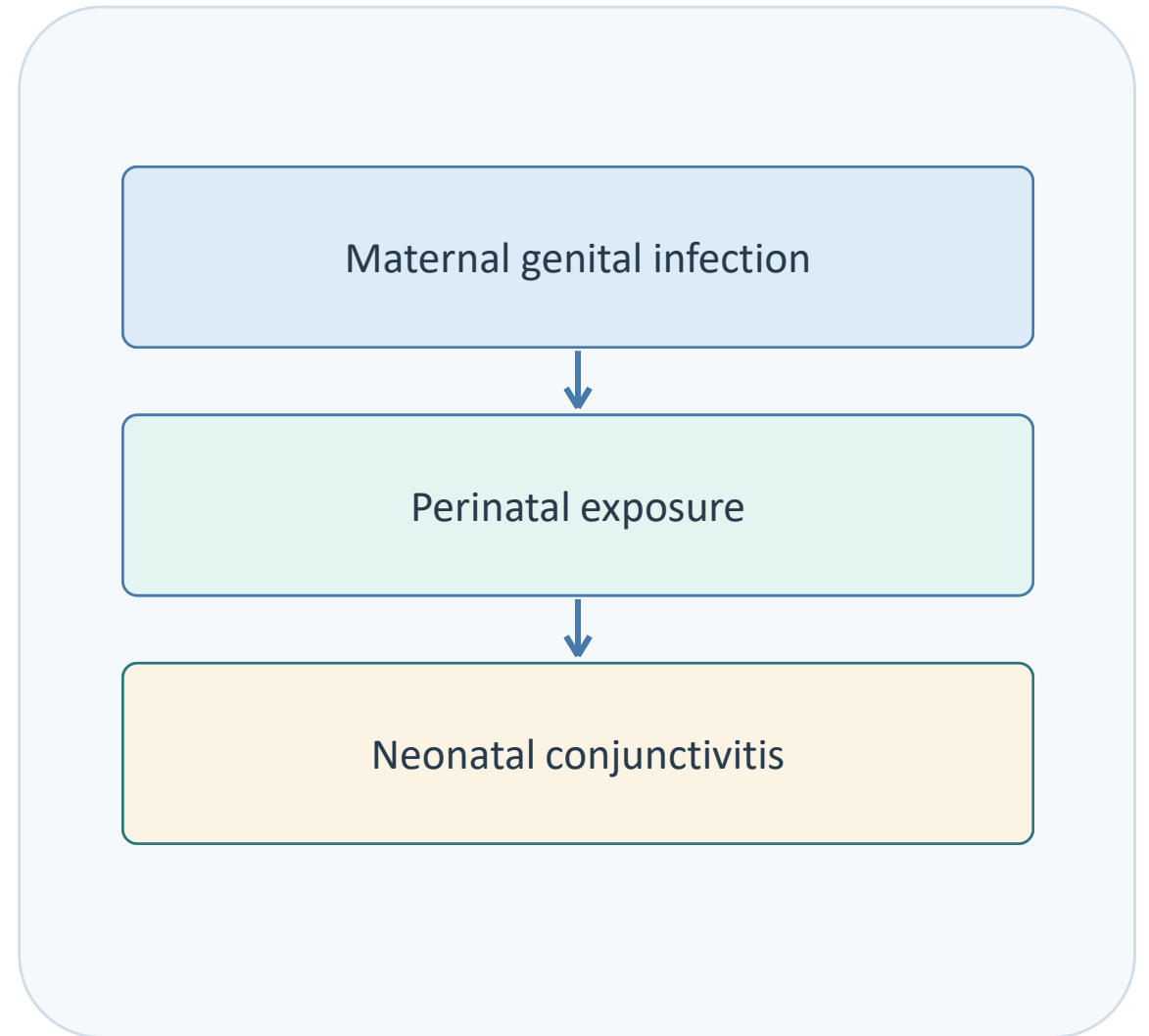
Other sites of chlamydial inflammation

- The infectious-diseases chapter lists epididymitis and prostatitis among associated syndromes
- Pharyngitis, proctitis, and perihepatic inflammation are also described
- Clinical evaluation depends on the affected anatomic site



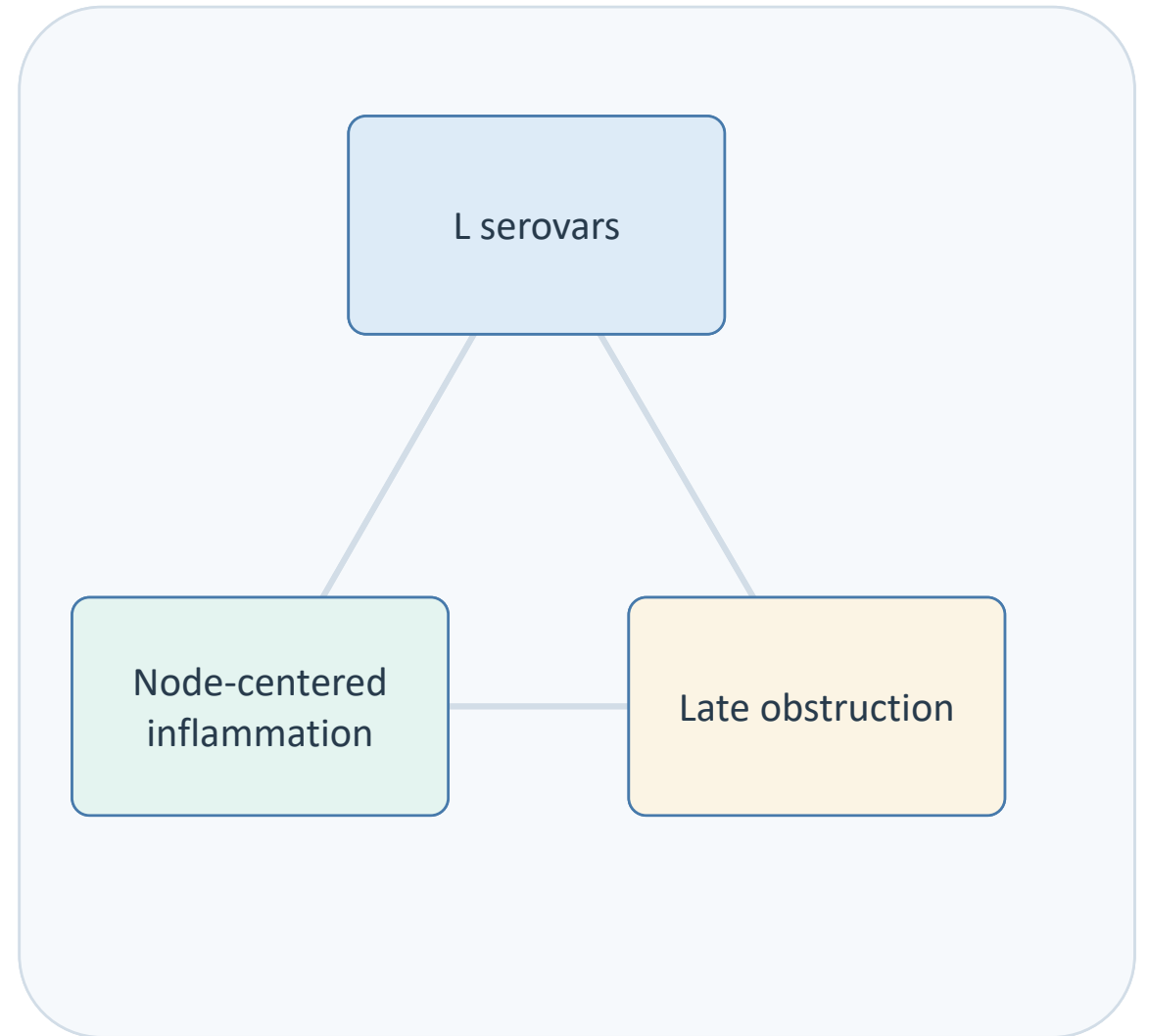
Perinatal acquisition and conjunctivitis

- The general STI section describes perinatal *C. Trachomatis* as a cause of neonatal conjunctivitis
- The maternal genital infection may be clinically silent
- Neonatal conjunctivitis is distinct from serovar A–C trachoma



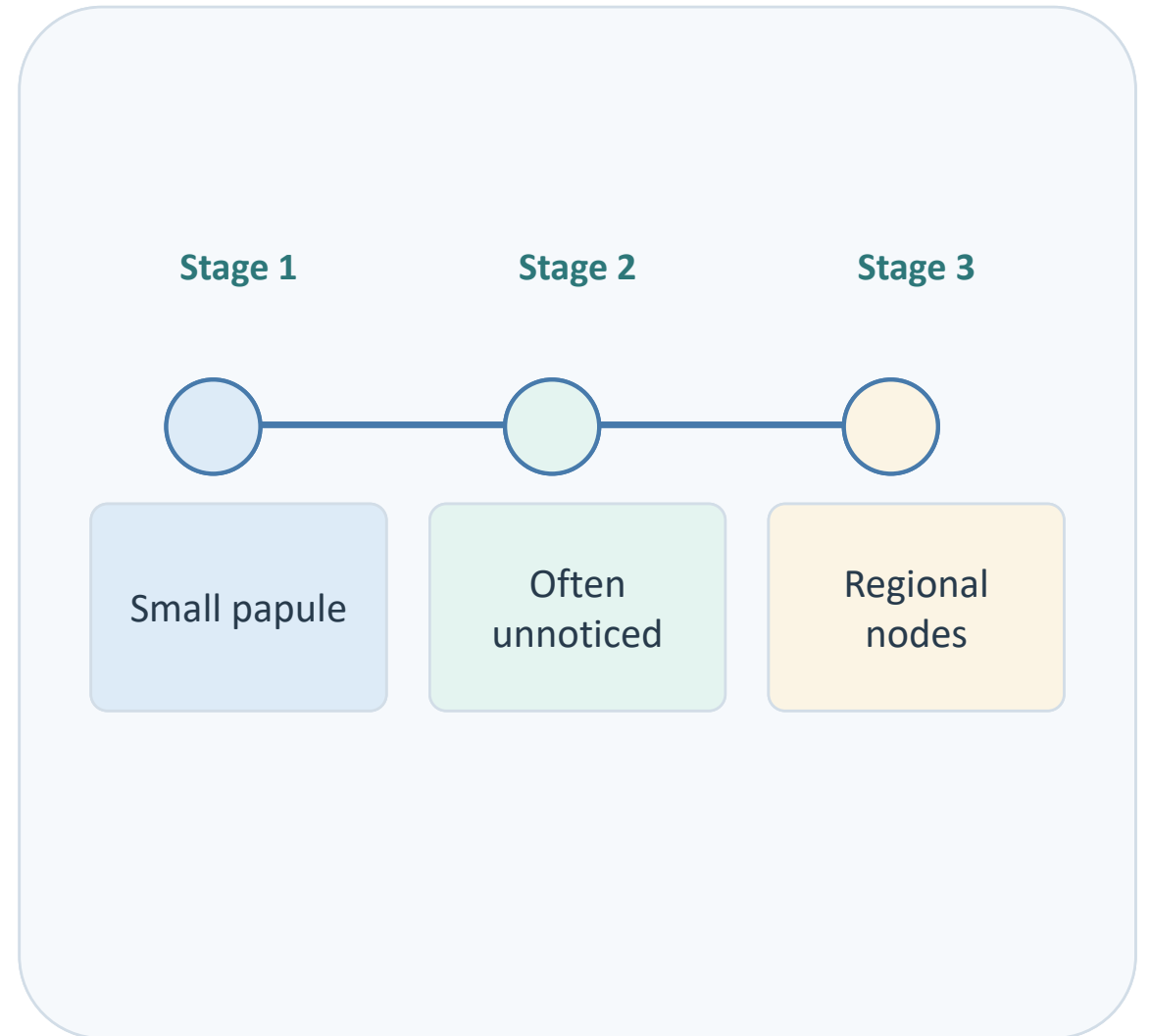
Lymphogranuloma venereum: Distinct serovars

- L1, L2, and L3 cause lymphogranuloma venereum (LGV)
- Unlike uncomplicated mucosal infection, LGV features ulcerative lesions and regional lymph node disease
- The course can proceed from acute inflammation to fibrosis and strictures



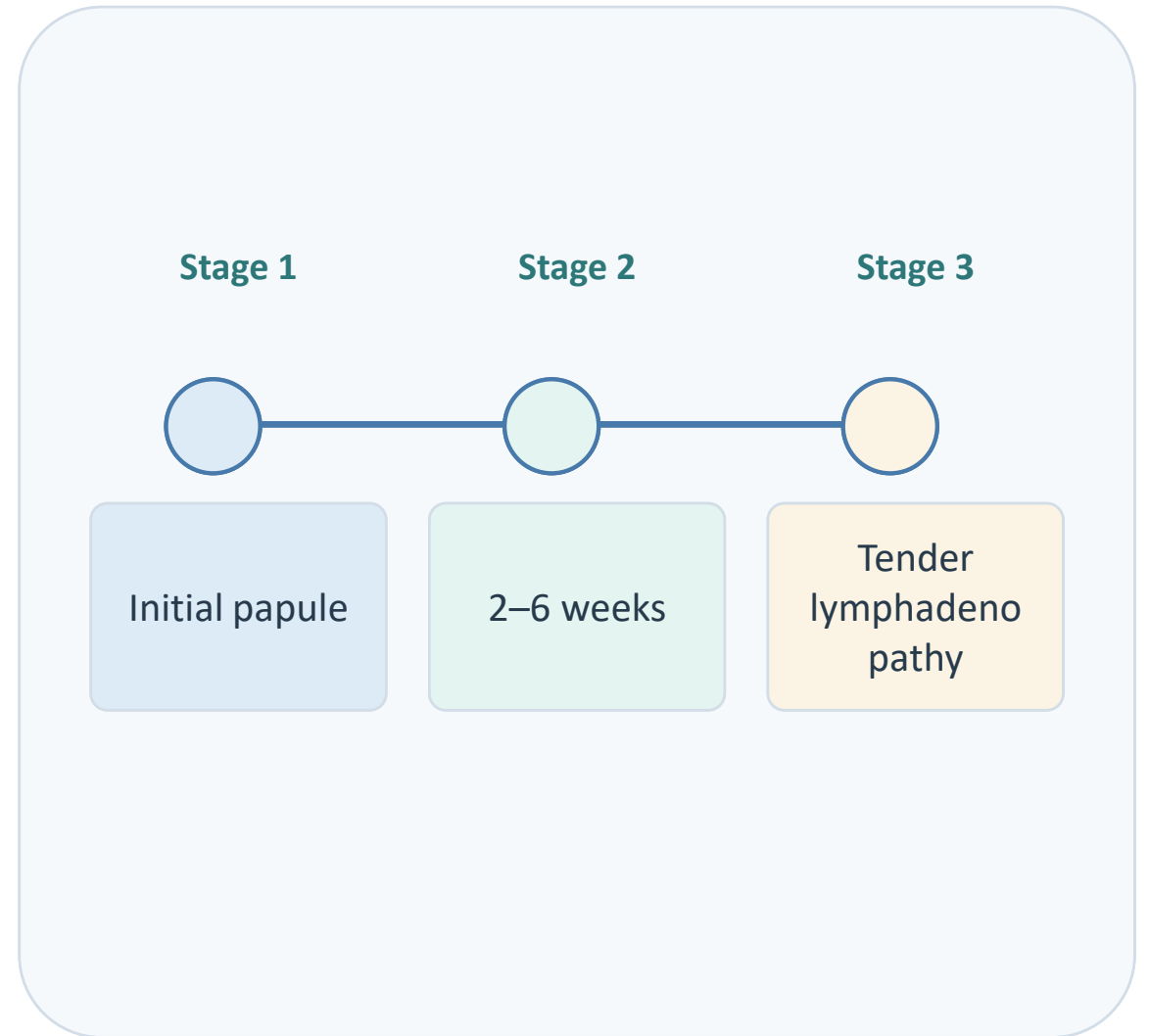
The early LGV lesion may be missed

- LGV may begin with a small papule on genital mucosa or nearby skin
- The initial lesion is often inconspicuous
- Subsequent lymphadenopathy may dominate the clinical presentation



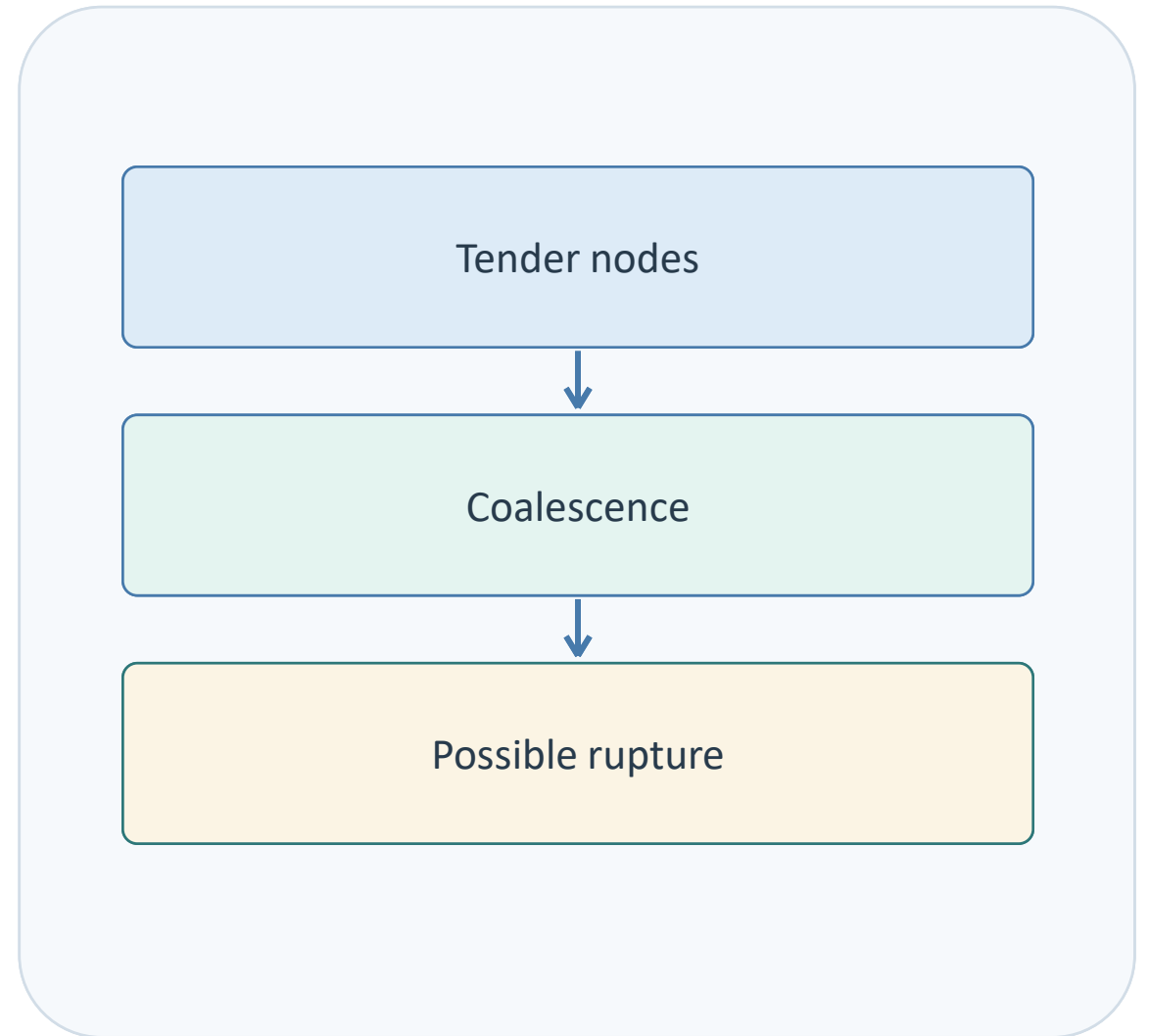
The lymph-node phase develops over weeks

- A 2–6 week interval after the primary lesion
- Bacterial growth and host response develop in draining regional nodes
- Nodes become enlarged and tender



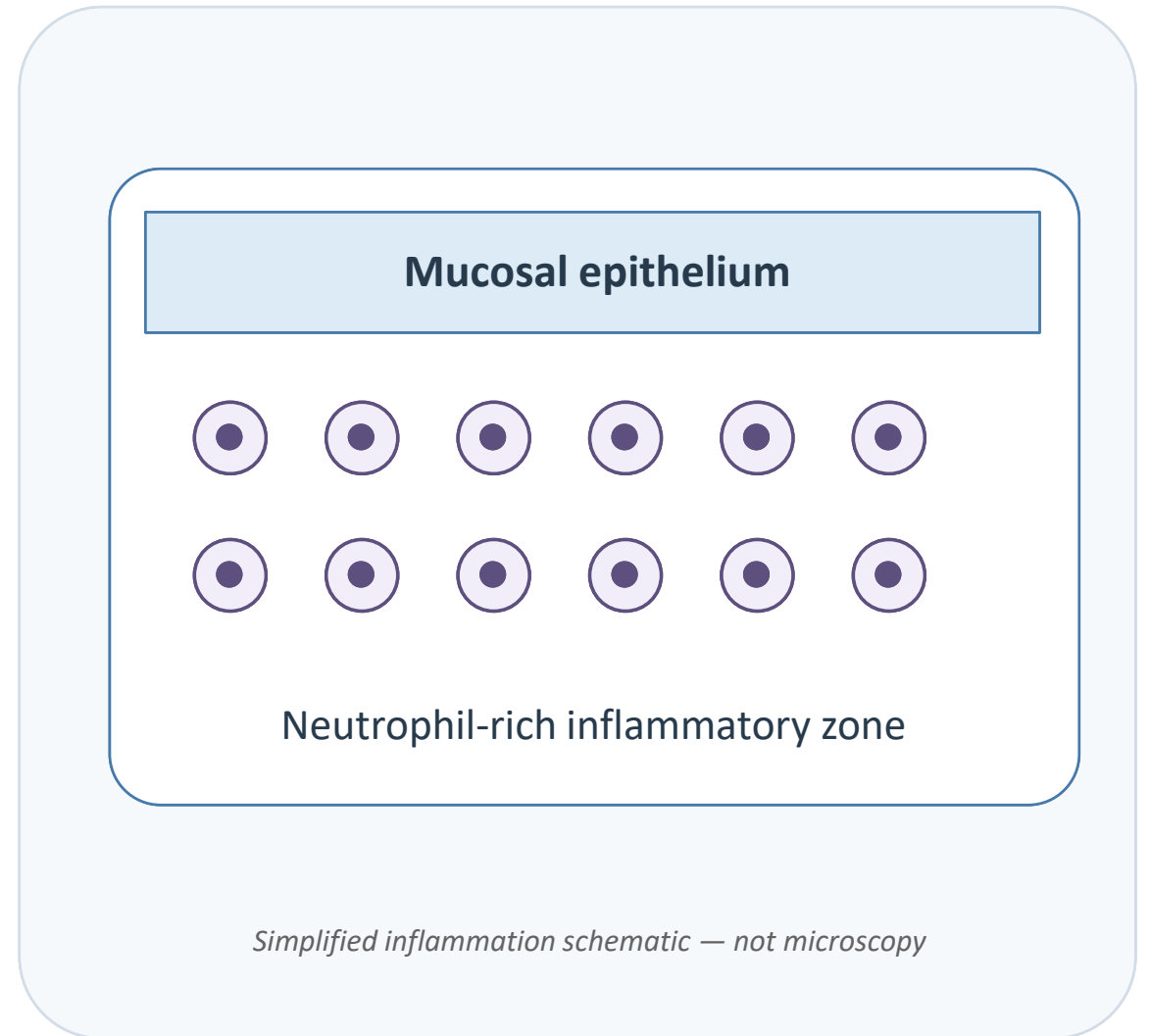
Coalescent nodes and rupture in LGV

- Regional lymph nodes may coalesce as inflammation progresses
- Advanced inflamed nodes may rupture
- This clinical progression reflects intense destructive lymphadenitis



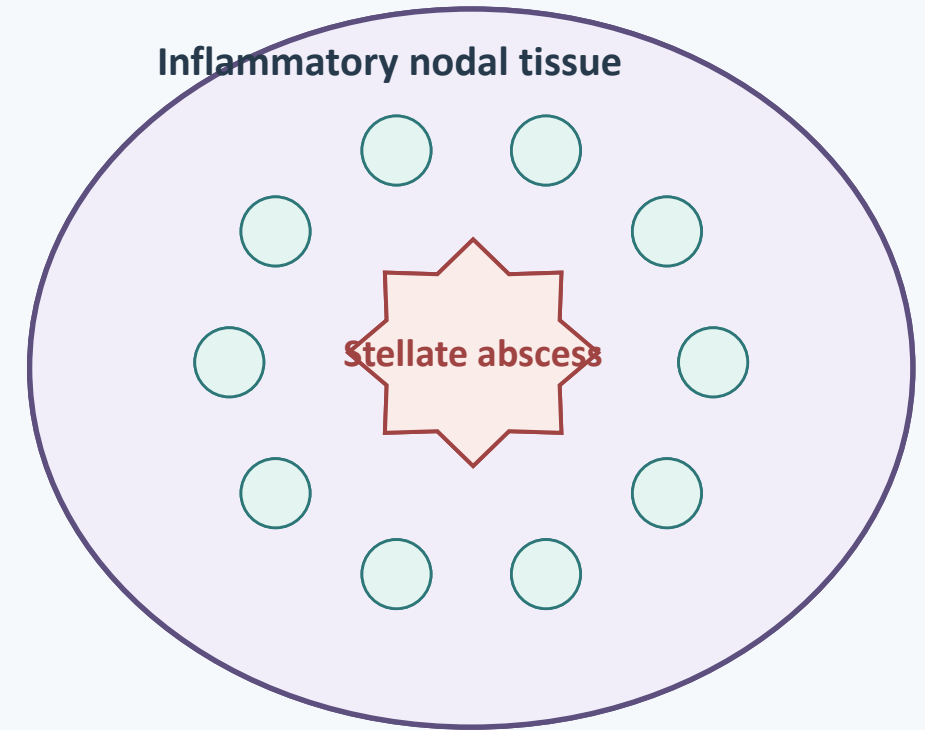
Mixed inflammatory pattern in LGV lesions

- The source describes both granulomatous and neutrophilic inflammation
- The mixture suggests an ongoing inflammatory response with focal tissue destruction
- LGV is therefore not appropriately characterized as purely granulomatous



LGV lymphadenitis: Stellate abscesses

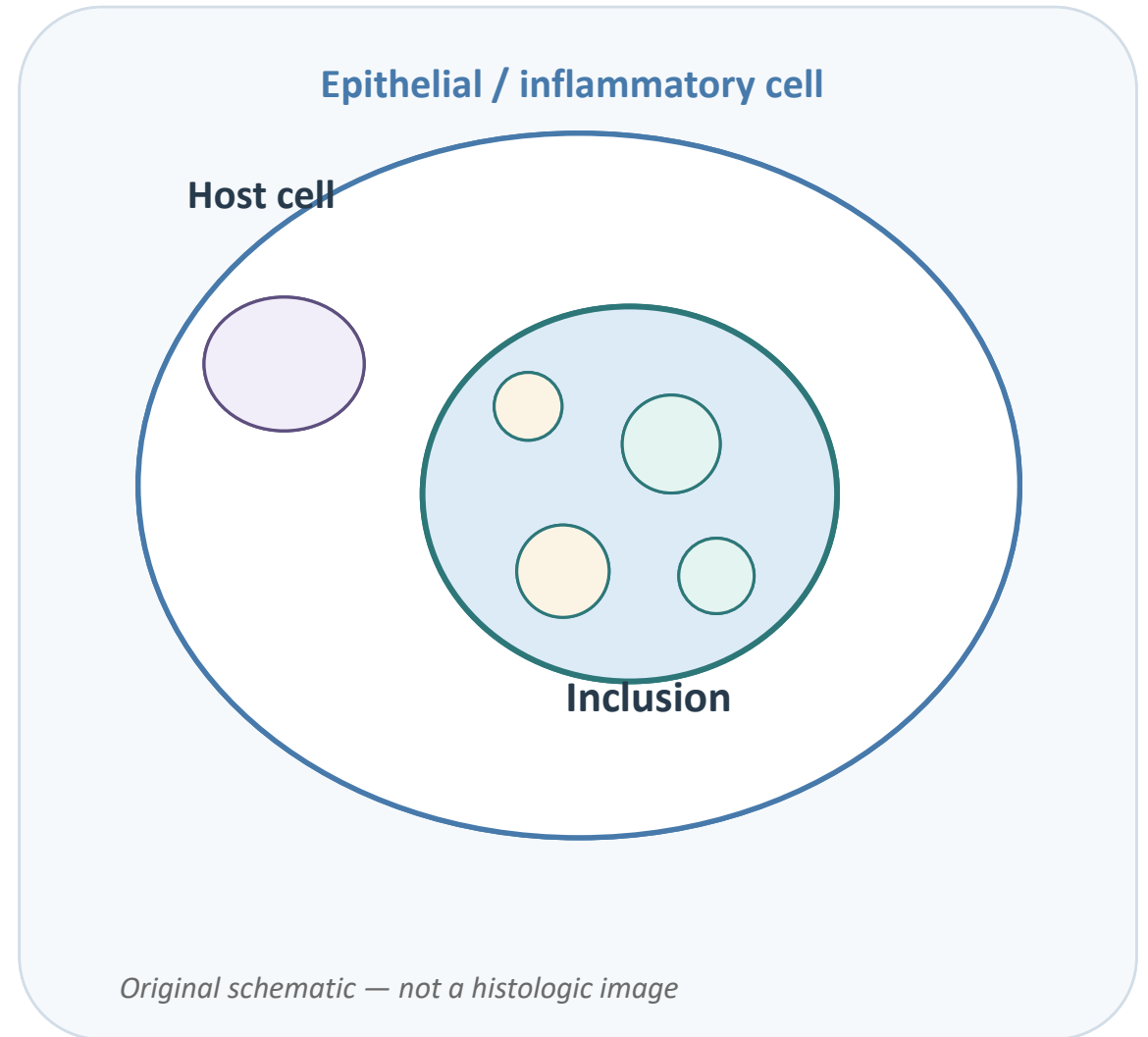
- Affected nodes contain irregular foci of necrosis populated by neutrophils
- The source names these lesions stellate abscesses
- Granulomatous inflammation surrounds or accompanies the necrotic foci



Schematic only; No specimen image supplied

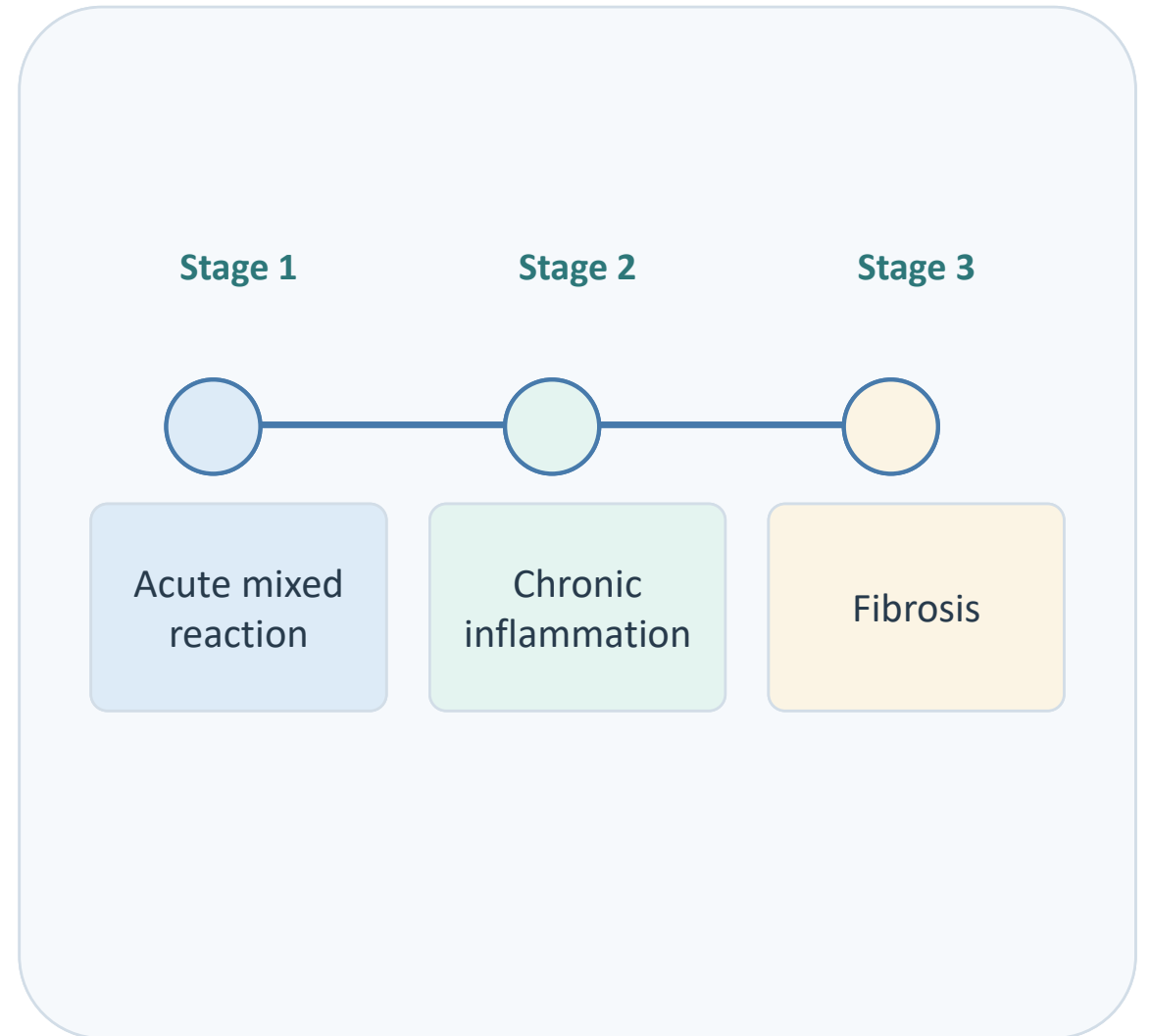
Intracytoplasmic inclusions may be present

- Variable numbers of chlamydial inclusions may be seen in epithelial or inflammatory cells
- This finding corresponds to the intracellular phase of the organism
- Inclusions are variable: Absence in a particular section is not definitive exclusion



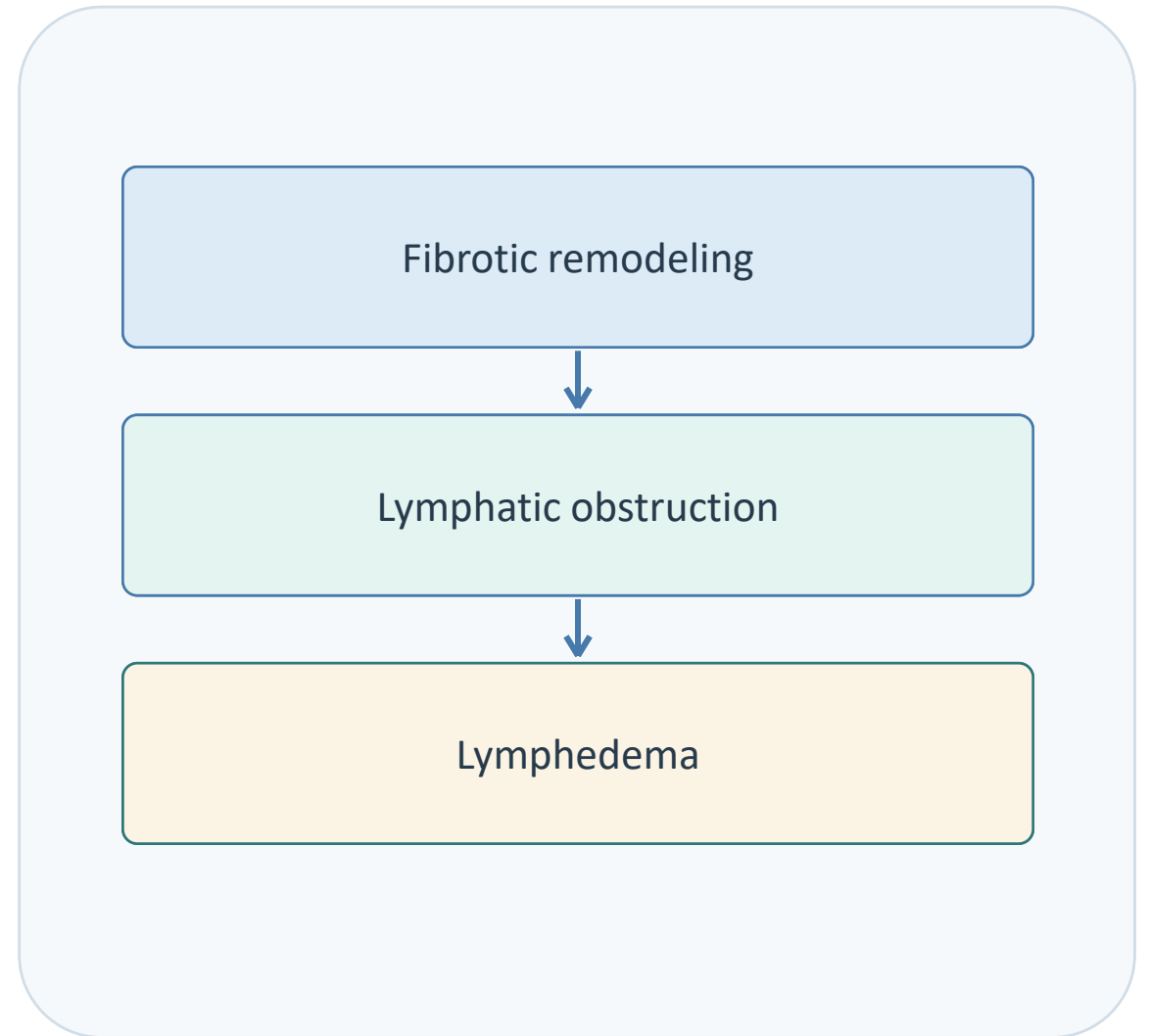
Chronic LGV: Inflammatory remodeling

- With time, chronic inflammatory cells and fibrosis predominate
- Destructive inflammation can be replaced by scar tissue
- Late pathological findings may differ markedly from active suppurative lymphadenitis



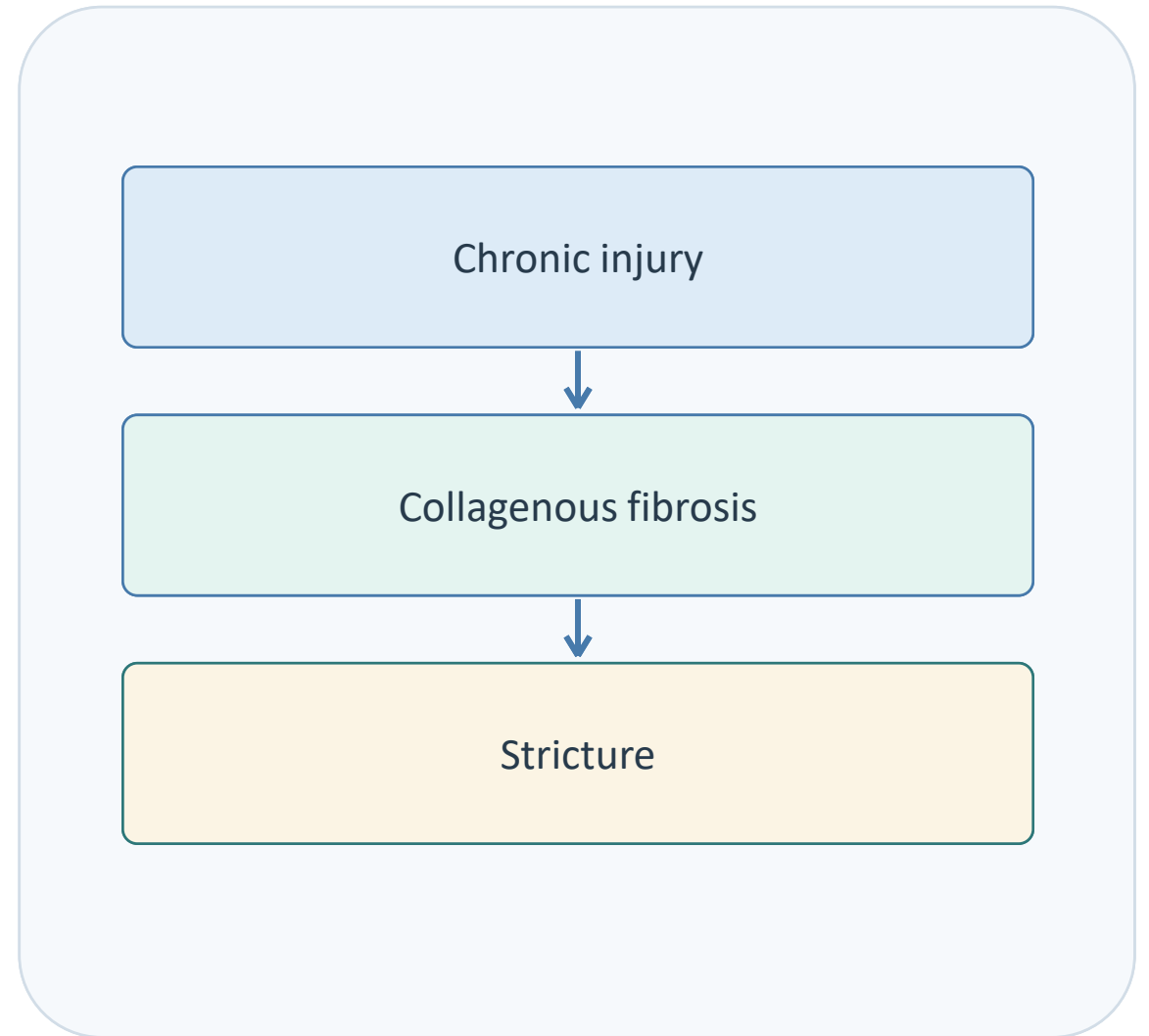
Lymphatic obstruction and lymphedema

- Fibrosis from chronic LGV can obstruct local lymphatic channels
- Impaired lymph drainage can produce lymphedema
- The obstructive consequence is explained by tissue remodeling, not merely organism burden



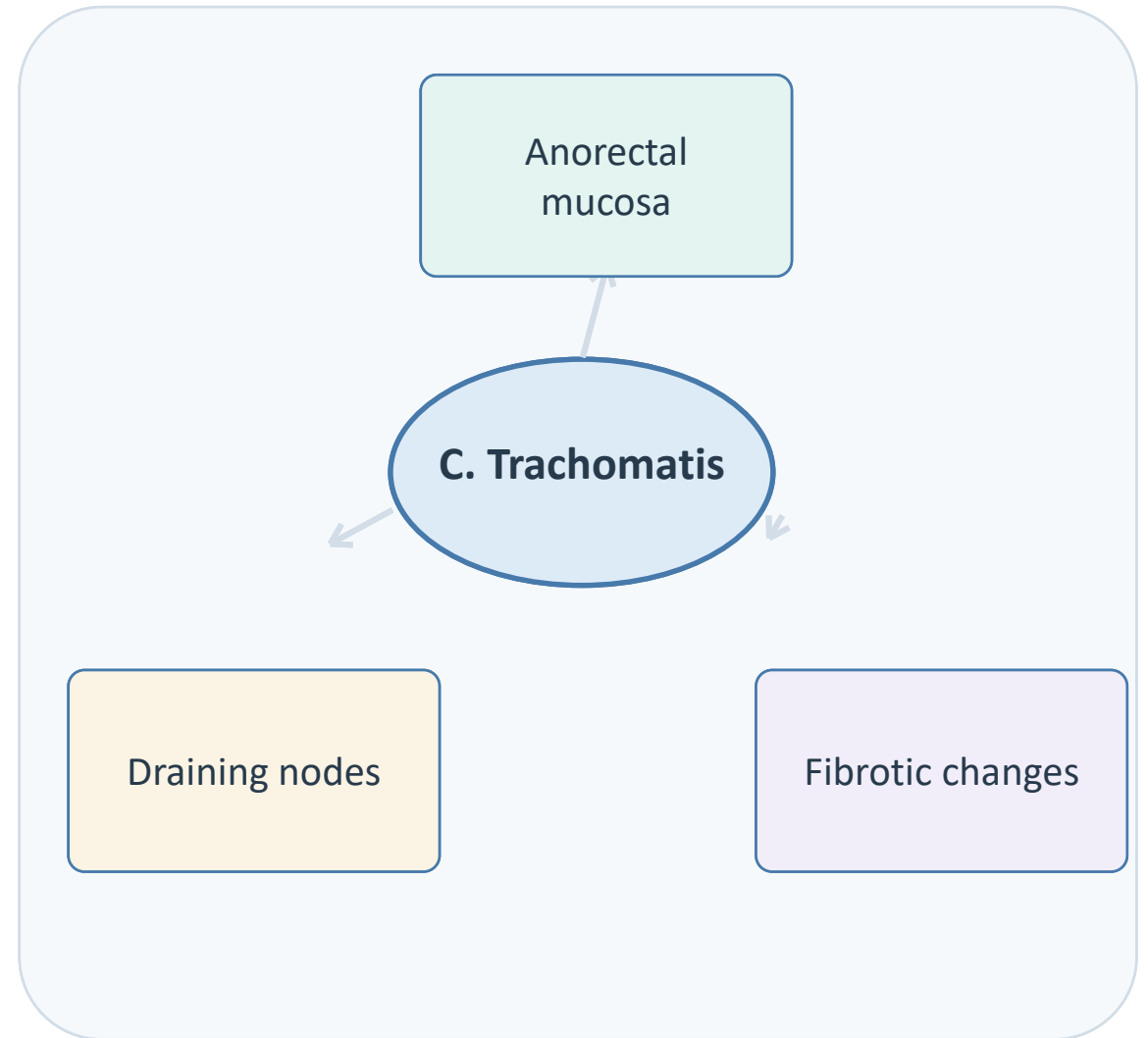
Anogenital strictures: Late complications

- Anogenital fibrosis can narrow luminal structures
- The source particularly emphasizes rectal strictures in females
- Stricture represents a chronic structural endpoint of untreated infection



LGV proctitis: An important syndrome

- Robbins records LGV as a cause of proctitis in men who have sex with men
- It describes sporadic cases in the United States and Western Europe
- The anatomic presentation can draw attention to lymphatic and rectal complications



Active versus chronic LGV diagnosis

- Detection of organisms in biopsy or exudate during active disease
- For chronic cases, it discusses antibodies directed at the relevant serovars
- These statements report the supplied textbook, not an independently updated diagnostic guideline

Active lesion

Organism
demonstration

Chronic lesion

Serotype
antibody
approach in
textbook

Non-LGV and LGV: Pathological contrast

- D–K genital infection: Often silent mucosal disease with neutrophilic urethral discharge
- L serovars: Ulcerative disease, regional lymphadenitis, stellate abscesses
- Late LGV may progress to lymphatic obstruction, lymphedema, and strictures

D–K infection

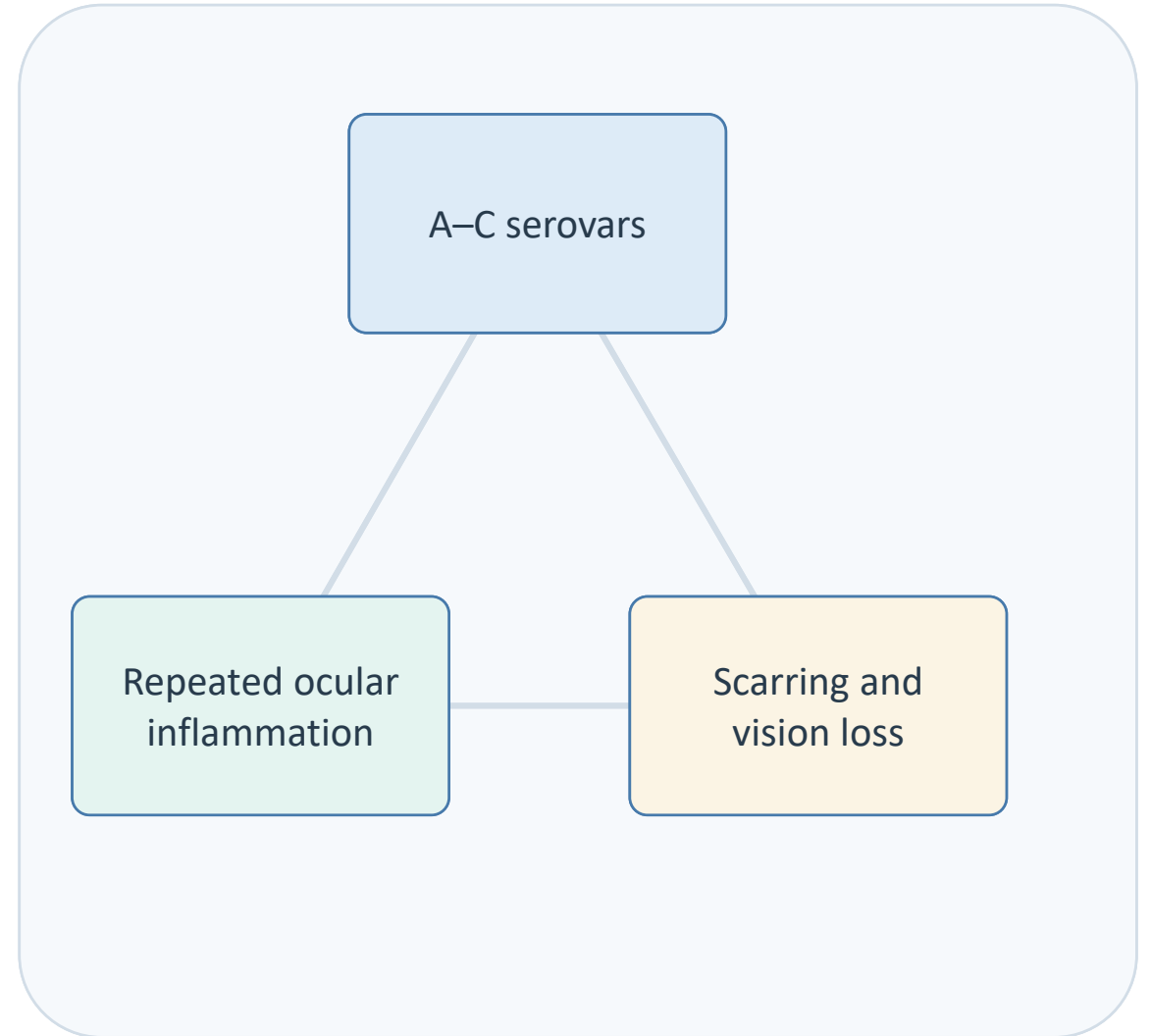
Mucosal-centered
inflammation

L1–L3 infection

Ulcerative • nodal
• fibrosing
disease

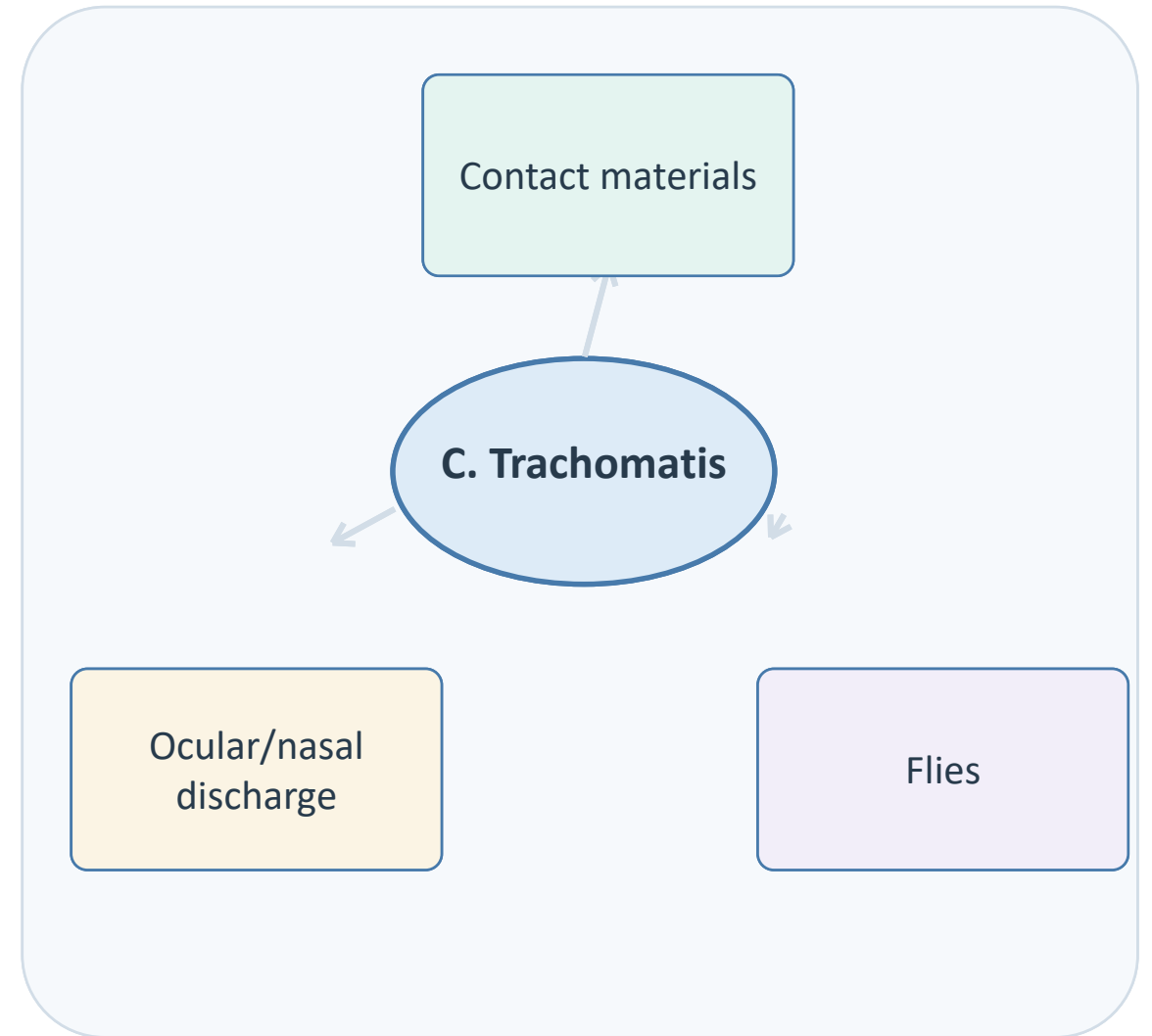
Trachoma: The ocular serovar group

- Serovars A, B, and C produce trachoma, particularly an ocular infection of children
- The eye chapter identifies trachoma as an important preventable cause of blindness
- Chronic injury involves the conjunctival surface and tear-producing apparatus



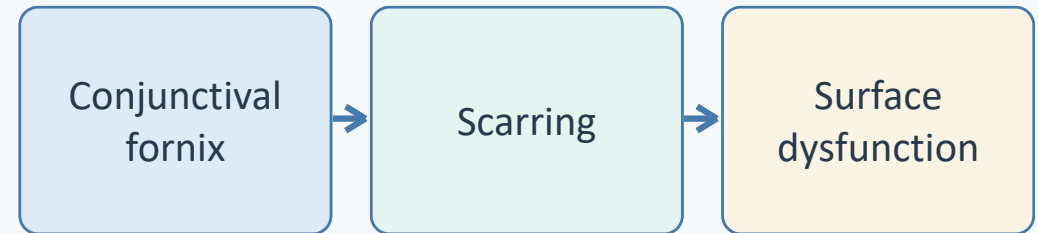
How trachoma spreads

- The eye chapter describes contact transmission involving hands, clothing, bedding, and surfaces
- Flies contaminated by ocular or nasal discharge can contribute to spread
- This differs from the primary sexual-transmission context of genital serovars



Conjunctival scarring is the critical lesion

- Untreated trachoma and conjunctivitis may cause progressive conjunctival scarring
- Severe scarring can obliterate the conjunctival fornix
- Loss of normal ocular surface structures contributes to functional impairment

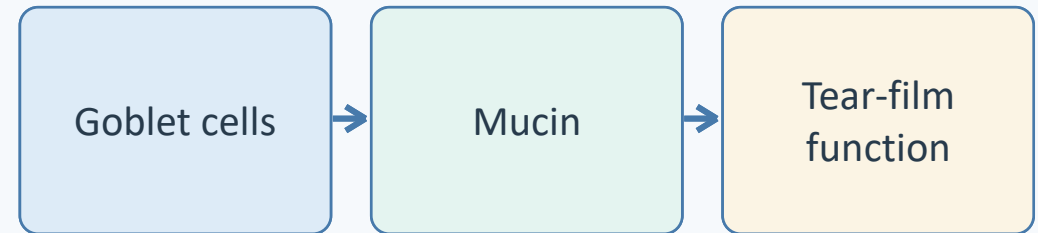


Ocular-surface function

Scarring can produce dryness, irritation, and visual loss

Loss of goblet cells reduces mucin

- The normal fornix contains goblet cells
- Scarring and fornix obliteration can remove these mucin-producing cells
- Reduced mucin compromises the protective tear-film surface

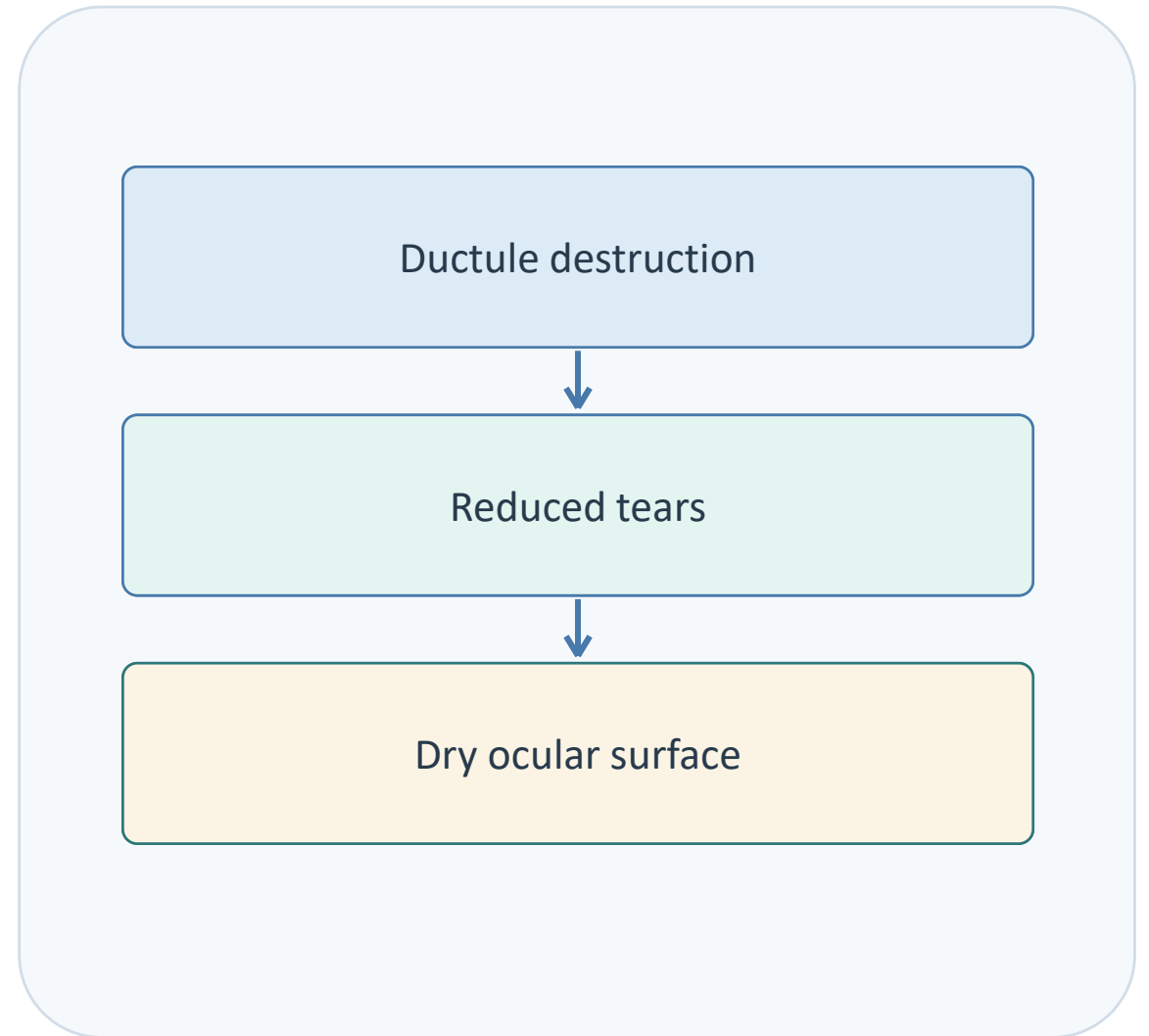


Ocular-surface function

Scarring can produce dryness, irritation, and visual loss

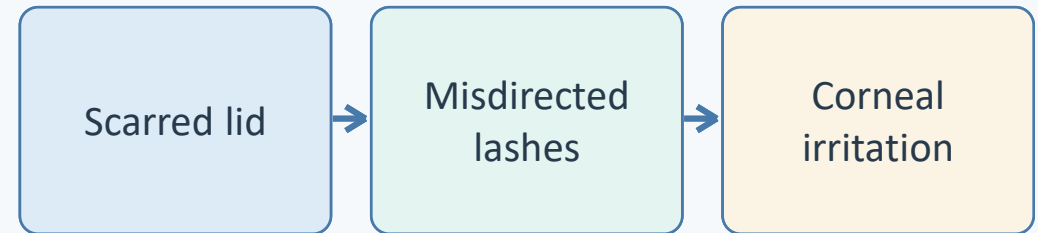
Lacrimal ductule injury reduces tears

- Ocular scarring can damage or obliterate lacrimal ductules
- Less tear delivery aggravates dryness of the ocular surface
- Mucin loss and tear insufficiency act together in the severe end-stage eye



Trichiasis adds mechanical corneal injury

- Trachoma-associated scarring can misdirect eyelashes toward the cornea
- This condition is termed trichiasis
- Mechanical irritation compounds the damage from chronic dryness

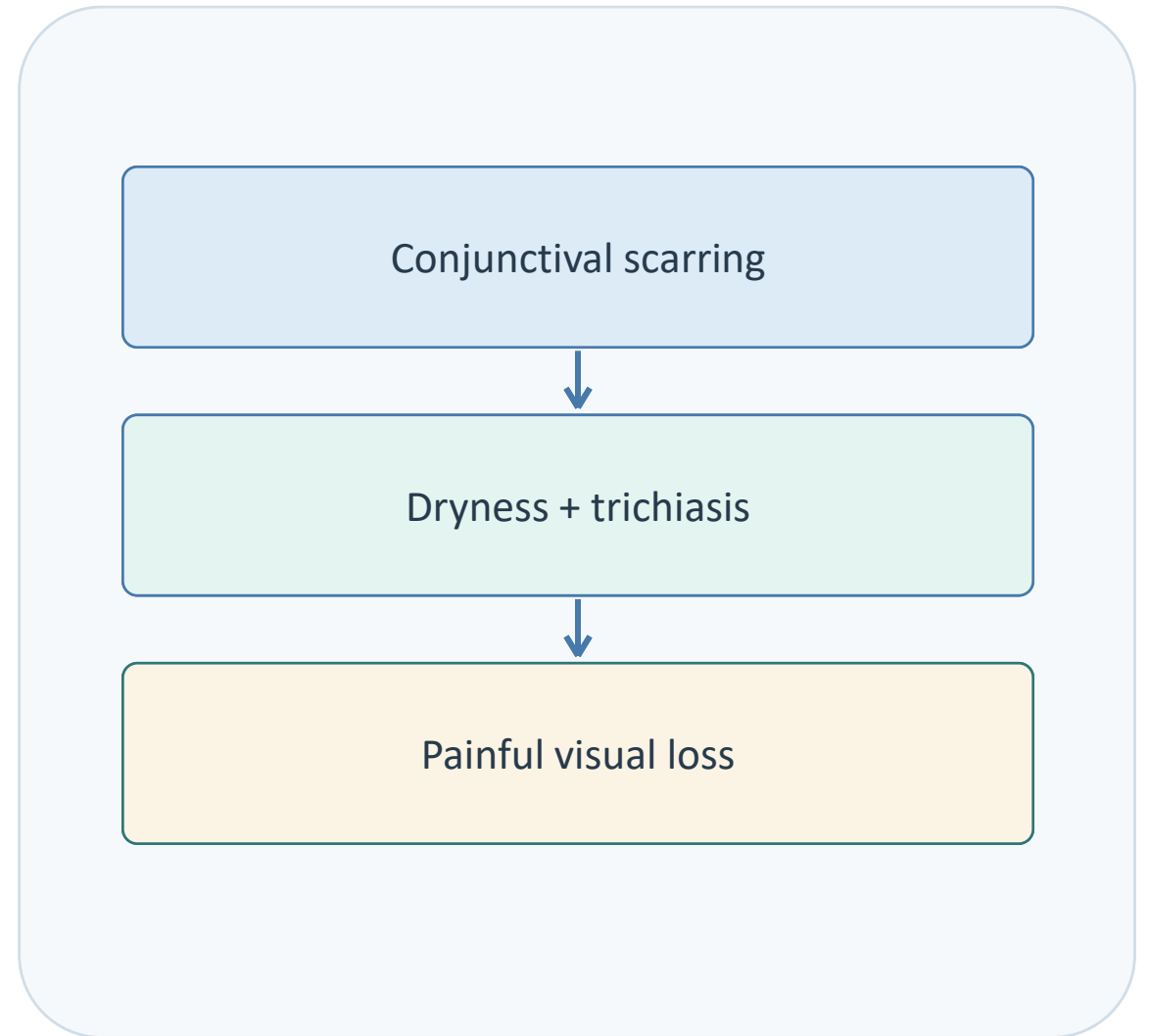


Ocular-surface function

Scarring can produce dryness, irritation, and visual loss

The pathway to painful blindness

- Severe conjunctival scarring leads to mucin and tear deficiency
- Trichiasis adds persistent corneal irritation
- The combination may culminate in a very dry, painful eye with blindness



Case: Inflammatory discharge without visible bacteria

- A patient has urethral discharge rich in neutrophils, but no organisms are identifiable by Gram stain
- The result is compatible with chlamydial urethritis but is not organism-specific
- The supported next diagnostic principle is an amplified nucleic-acid test on an appropriate sample

1

Neutrophil-rich

2

Gram stain negative for organisms

3

NAAT needed

Case: New tender nodes after a small papule

- A small genital papule was barely noticed several weeks earlier
- Tender, enlarging regional nodes now dominate the presentation
- This temporal pattern supports consideration of LGV caused by L serovars

1

Unnoticed papule

2

2–6 weeks

3

Tender lymphadenopathy

Case: An unusual nodal abscess pattern

- A lymph-node specimen contains granulomatous inflammation and irregular neutrophil-rich necrotic foci
- The combination resembles the stellate-abscess morphology described in LGV
- Clinical history and organism-specific investigation remain necessary

1

Granulomatous nodes

2

Stellate abscesses

3

Correlate with infection

Case: Infertility following pelvic infection

- A prior episode of pelvic inflammatory disease is followed by infertility
- Tubal scarring can disrupt passage of an oocyte or conceptus
- This is a downstream PID complication and does not alone establish a particular pathogen

1

Prior PID

2

Possible tubal scar

3

Infertility

Case: Ocular dryness and inward lashes

- Longstanding conjunctival inflammation is followed by scarring, dryness, and eyelashes directed toward the cornea
- Loss of mucin and tear delivery plus trichiasis provide a coherent mechanism
- This pattern is consistent with advanced trachomatous damage

1

Scarred fornix

2

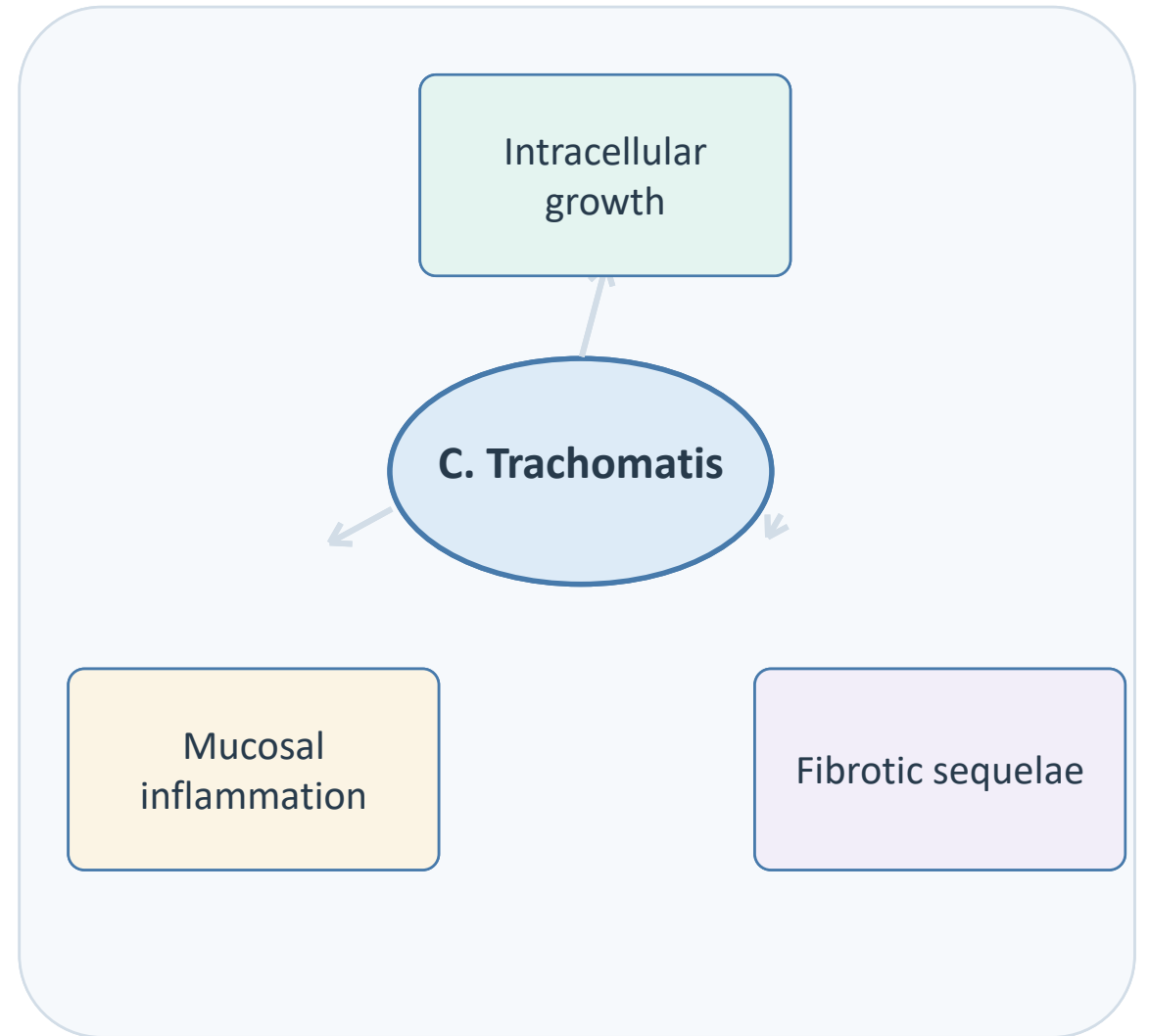
Reduced tears

3

Trichiasis

Integrative pathology map

- Intracellular survival depends on inclusion remodeling, nutrient acquisition, and cycle switching
- Mucosal infection may be silent yet ascend or produce extragenital manifestations
- LGV and trachoma illustrate long-term consequences of chronic inflammation and fibrosis



Three distinctions that prevent diagnostic error

- Elementary bodies transmit infection;
Reticulate bodies multiply inside cells
- A neutrophil-rich smear cannot establish
chlamydial etiology by morphology alone
- LGV nodal abscesses and trachomatous
ocular scarring have different anatomic
consequences

Question	Correct distinction
Infectious form?	Elementary body
Gram-stained organism?	Usually not visible
LGV lesion?	Stellate abscess + fibrosis
Trachoma endpoint?	Conjunctival scar + painful blindness

Source readings

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th ed. (2026)
- Source sections: chlamydial infections, sexually transmitted infections, and Neisseria for differential comparison
- Related pathology: urethral inflammation, female genital infections, and pelvic inflammatory disease
- Related eye pathology: trachoma and ocular-surface scarring

Disease mechanism

Genital pathology

Ocular pathology