

Sexually Transmitted Infections

Pathogenesis, morphology and clinicopathologic correlations

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraisakhri.com

Learning objectives

- Classify major STI pathogens by microbiologic group and clinicopathologic syndrome.
- Explain local infection, asymptomatic transmission, coinfection and vertical transmission.
- Link representative organisms to morphology, complications and diagnostic approaches.
- Distinguish genital ulcer syndromes, inflammatory tract disease and HPV-associated lesions.

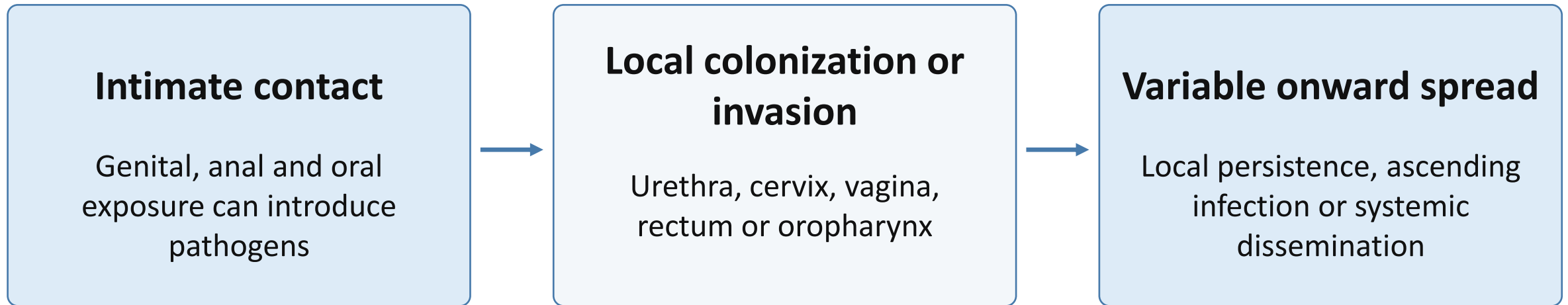
An etiologic framework

Pathogen class	Representative agents	Principal pathologic pattern
Viruses	HSV; HPV; HBV; HIV	Vesicles/ulcers; Papillomas or dysplasia; Systemic infection
Bacteria	N. Gonorrhoeae; T. Pallidum; H. Ducreyi	Suppurative inflammation; Chronic vasculitis; Ulcers
Obligate intracellular bacteria	C. Trachomatis	Urethritis/cervicitis; Ascending inflammation; Lymphadenitis
Protozoa	T. Vaginalis	Vaginitis or urethritis

Exposure and vulnerability

- Sexual contact can transmit pathogens with very different biology.
- Adolescents and young adults, men who have sex with men, and people injecting drugs as groups with increased STI burden.
- Sexual practices and inequitable access to care both contribute to risk.
- Epidemiologic categories guide prevention; They do not establish infection in an individual.

Transmission is not restricted to one route



Schematic

Predominantly sexual versus occasional sexual spread

Predominantly sexual

- *C. Trachomatis* and *N. Gonorrhoeae* are mainly spread by sexual contact.
- Direct mucosal exposure is central to acquisition.

Other organisms, shared transmission routes

- *Shigella* and *Entamoeba histolytica* usually spread fecal–orally.
- Oral–anal sexual contact can also transmit enteric pathogens.

Why asymptomatic infection matters

- A person may be infectious without recognizing symptoms.
- Silent infection permits continuing transmission to partners.
- Absence of genital pain or discharge does not exclude mucosal infection.
- Upper genital tract complications may develop after unrecognized lower tract infection.

STI coinfection: Two linked mechanisms

Shared exposures

- Risk factors and exposure networks overlap across STIs.
- Several pathogens may be transmitted to the same person.
- Coinfection cannot be excluded by finding one pathogen.

Biologic facilitation

- Gonococcal and chlamydial epithelial injury alters mucosal barriers.
- With HIV exposure, mucosal injury can increase acquisition risk.
- Risk factors and local tissue injury are distinct mechanisms.

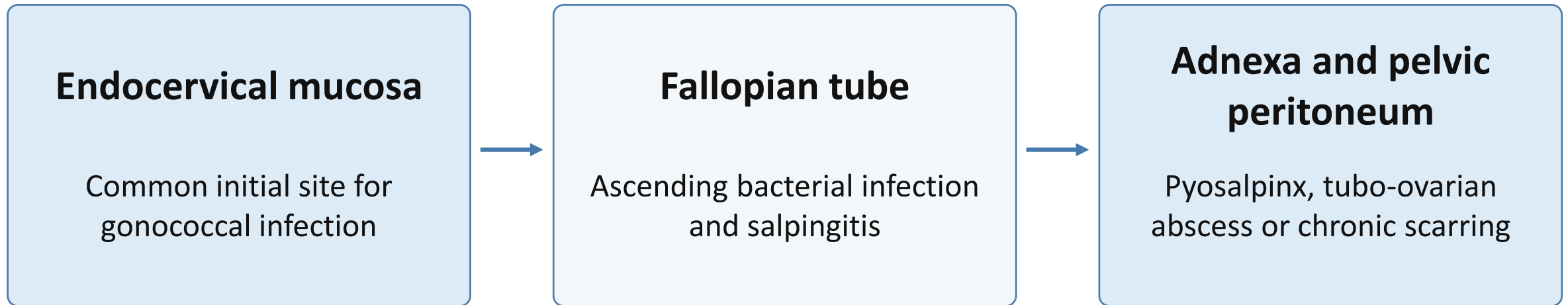
Syndromes help localize disease

Presentation	High-yield organisms	Dominant pathologic process
Urethritis/cervicitis	N. Gonorrhoeae; C. Trachomatis	Mucosal inflammation, often suppurative
Painful genital ulcers	HSV; H. Ducreyi	Viral cytolysis or ulcerative bacterial inflammation
Painless chancre	T. Pallidum	Treponemal infection with endarteritis
Papillary anogenital lesions	Low-risk HPV	Exophytic squamous proliferation
Vaginitis	T. Vaginalis	Mucosal inflammation

Anatomic entry sites predict sequelae

- Urethral inflammation manifests as urethritis and may coexist with upper urinary/genital tract disease.
- Cervical infection can ascend through the female reproductive tract.
- Rectal and oropharyngeal exposure can produce proctitis or pharyngitis.
- Blood or lymphatic spread produces disseminated or nodal disease in selected STIs.

Ascending infection in the female genital tract



Schematic

A pathogen may produce multiple tissue responses

- Gonococcal and chlamydial infections can cause acute mucosal inflammation.
- HSV causes epithelial ballooning, vesicles, ulceration and viral cytopathic change.
- Syphilis produces plasma cell–rich inflammation and small-vessel endarteritis.
- HPV drives productive papillomatous lesions or oncogenic squamous alterations.

Robbins Table 8.4: Virus-associated disease

Agent	Key STI manifestations	Important tissue consequence
HSV	Primary or recurrent genital herpes	Painful ulceration; Neonatal visceral/CNS disease
HBV	Sexual transmission can cause hepatitis	Hepatic inflammation
HPV	Condyloma, cervical dysplasia; Anogenital cancers	Benign warts or high-risk oncogenesis
HIV	Systemic HIV infection and AIDS	Immunodeficiency

Robbins Table 8.4: Nonviral agents

Agent	Typical syndrome	Complication / distinction
N. Gonorrhoeae	Urethritis; Cervicitis; Proctitis	PID; Septic arthritis; Neonatal conjunctivitis
C. Trachomatis	Urethritis; Cervicitis; LGV	PID; Lymphadenitis; Scarring
T. Pallidum	Syphilis	Multistage systemic infection
H. Ducreyi / K. Granulomatis	Ulcerative genital disease	Painful bubo / chronic granulomatous ulcer
T. Vaginalis	Vaginitis; Urethritis	Inflammatory vaginal symptoms

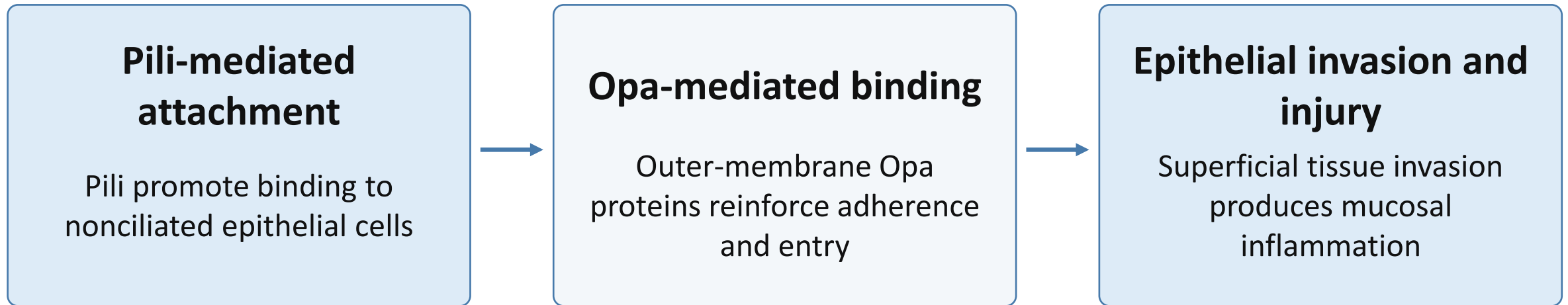
Partner and public-health implications

- Many STIs are reportable conditions; Requirements vary by jurisdiction.
- Partner testing and treatment interrupt transmission chains.
- Care pathways must account for people without symptoms.
- Reported surveillance rates should not be treated as fixed biological properties.

Gonorrhea: Mucosal infection

- *Neisseria gonorrhoeae* is a pathogenic gram-negative diplococcus.
- Infection frequently begins in urethral, cervical, pharyngeal or anorectal mucosa.
- Urethritis is a common presentation in males; Cervical infection in females may be silent.
- Untreated infection may ascend or disseminate.

Gonococcal attachment and invasion



Schematic

Why gonococci can reinfect

- Neisseria varies surface antigens targeted by host immune responses.
- Pilin gene recombination changes the expressed pilus proteins.
- Variation in Opa expression further changes bacterial surface features.
- These mechanisms aid immune evasion; Immunity after exposure is incomplete.

Gonorrhea: Lower tract manifestations

Male genital tract

- Urethritis is a classic manifestation.
- Epididymitis and prostatitis are recognized complications.
- Mucopurulent inflammation may cause dysuria and discharge.

Female genital tract

- Cervicitis frequently has few or no symptoms.
- Endometritis/salpingitis may follow upward spread.
- Long-term sequelae include infertility and ectopic pregnancy.

Gonococcal suppurative morphology

- Acute mucosal inflammation contains abundant neutrophils.
- Exudate may show intracellular gram-negative diplococci within neutrophils.
- A smear can support an impression, but identification requires appropriate microbiologic testing.
- Test selection depends on clinical site and local laboratory pathways.

Gonorrhea: Localized versus disseminated

Pattern	Features	Pathologic significance
Localized mucosal	Urethritis, cervicitis, proctitis, pharyngitis	Surface epithelial invasion and inflammation
Ascending genital	Salpingitis; PID	Scarring and reproductive injury
Disseminated	Septic arthritis; Hemorrhagic papules/pustules	Hematogenous spread
Neonatal	Conjunctivitis; Occasional sepsis	Potentially sight-threatening infection

Disseminated gonococcal infection

- Bloodstream spread is less common than local mucosal infection.
- Adults may develop septic arthritis with hemorrhagic papules and pustules.
- Terminal complement pathway deficiency predisposes to invasive disease.
- A genital symptom history may be absent despite dissemination.

Gonorrhea: Microbiologic diagnosis

- Nucleic-acid amplification tests detect gonococcal nucleic acids.
- Culture remains valuable, including when antimicrobial resistance is relevant.
- Tissue morphology alone is insufficient for organism confirmation.
- Evolving cephalosporin resistance; Specific regimens require current guidance.

Case: Cervicitis followed by pelvic pain

TEACHING SCENARIO

A sexually active patient has subtle lower genital tract symptoms, followed by pelvic pain and adnexal tenderness.

Reasoning prompts

- Identify the initial mucosal site.
- Trace the likely route of extension.
- Name a potentially permanent consequence.

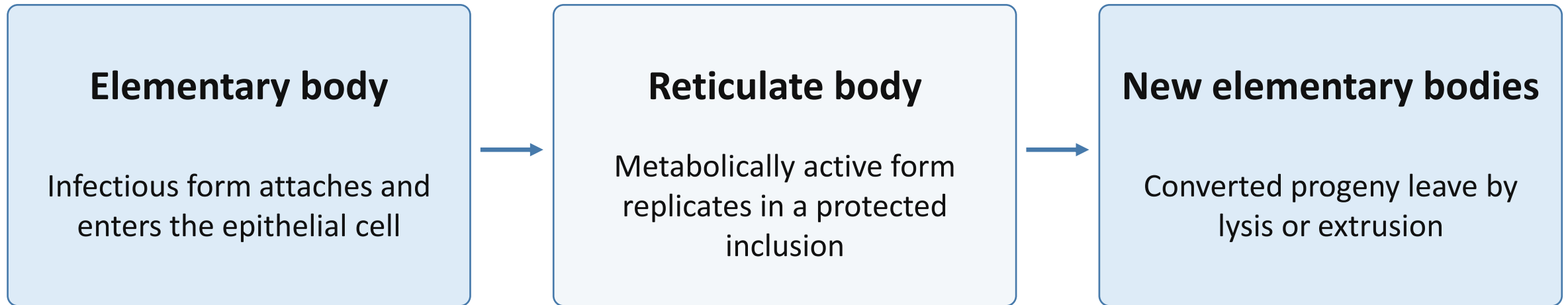
Clinicopathologic resolution

Endocervical infection may ascend to the fallopian tubes. Suppurative salpingitis can heal with tubal fibrosis, causing infertility or ectopic pregnancy.

Chlamydia: Obligate intracellular biology

- Chlamydia trachomatis is a small obligate intracellular bacterium.
- Its life cycle separates an infectious elementary body from a replicating reticulate body.
- Intracellular replication occurs within an altered host-derived membrane inclusion.
- This biology differs fundamentally from extracellular gonococcal growth.

The chlamydial developmental cycle



Schematic

C. Trachomatis serovars and syndrome

Serovars	Predominant disease	Anatomic implication
D–K	Urogenital infection; Inclusion conjunctivitis	Mucosal epithelial infection
L1–L3	Lymphogranuloma venereum	Lymphatic and anogenital disease
A–C	Trachoma	Ocular infection; Not the genital STI serovars

Urogenital chlamydia is often silent

- Urethritis in males may be asymptomatic more often than gonococcal urethritis.
- Cervical infection frequently produces no recognized symptoms.
- Chlamydial and gonococcal syndromes substantially overlap.
- Absence of symptoms does not prevent subsequent PID or transmission.

Chlamydial urethritis: Microscopic pattern

- The mucopurulent discharge is neutrophil-rich.
- Urethral histopathology can closely resemble gonorrhea.
- Chlamydial organisms are not visible in routine Gram-stained exudate.
- NAATs on swabs or urine are described for genital diagnosis.

Gonococcal versus chlamydial urethritis

Gonococcal

- A gram-negative diplococcus.
- May show intracellular diplococci in purulent exudate.
- Pili/Opa proteins promote epithelial entry.

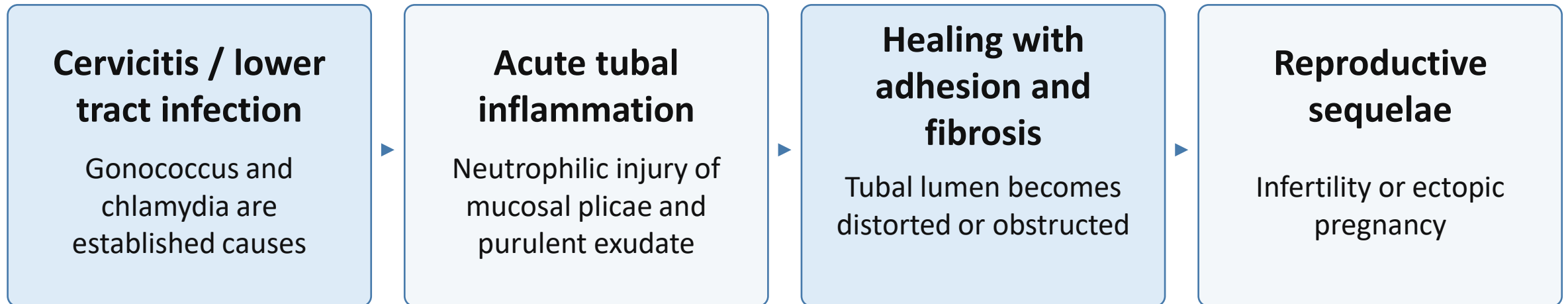
Chlamydial

- Obligate intracellular developmental cycle.
- Routine Gram stain does not demonstrate the organism.
- Can produce indistinguishable inflammatory morphology.

Extragenital chlamydial disease

- Recognized manifestations include proctitis, pharyngitis and conjunctivitis.
- Epididymitis and prostatitis can occur in male genital infection.
- Perihepatic inflammation and PID may complicate female genital infection.
- The site of exposure and spread determines the disease phenotype.

Pelvic inflammatory disease: Pathology pathway



Schematic

Acute salpingitis: What happens in the tube?

- Congestion and neutrophilic infiltration damage the tubal epithelium.
- Mucosal folds are denuded and may slough.
- Purulent exudate fills the tubal lumen and can escape via the fimbriae.
- Extension can produce salpingo-oophoritis and tubo-ovarian abscess.

Pyosalpinx and tubo-ovarian abscess

- Pyosalpinx is accumulation of pus within a fallopian tube.
- Suppurative inflammation can extend to ovarian tissue.
- Combined tubal and ovarian infection can form a tubo-ovarian abscess.
- These lesions represent anatomically progressive, destructive infection.

Chronic salpingitis: Scarring after infection

- Even after organisms disappear, epithelial loss initiates repair.
- Denuded tubal plicae adhere, forming distorted blind pockets.
- Fibrosis narrows the lumen and can compromise fimbrial function.
- Resulting tubal dysfunction provides the basis for infertility or ectopic gestation.

Acute versus chronic salpingitis

Acute

- Edematous congested mucosa.
- Neutrophils and luminal pus.
- Tubal epithelial injury; Possible abscess.

Chronic / healed

- Adhesion and fusion of mucosal plicae.
- Fibrotic distortion and luminal obstruction.
- Hydrosalpinx, infertility or ectopic pregnancy.

Case: Infertility following a remote STI

TEACHING SCENARIO

A patient with a history of prior symptomatic cervicitis now has difficulty conceiving; Imaging suggests damaged fallopian tubes.

Reasoning prompts

- Identify the microscopic injury that started the process.
- Explain why infection may be absent now.
- State the structural basis of infertility.

Clinicopathologic resolution

Previous suppurative salpingitis causes epithelial destruction; Chronic adhesion/fibrosis persists after microbial clearance and impairs gamete transport.

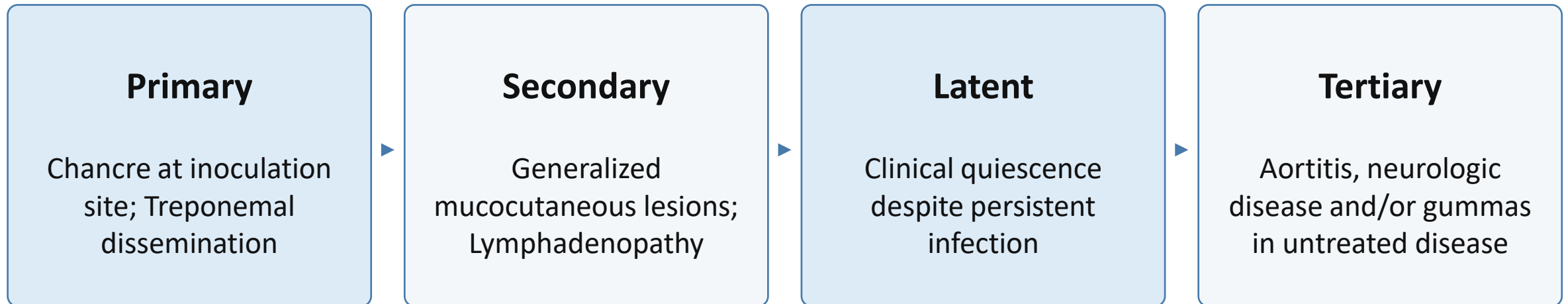
Genital ulcer patterns: First distinction

Agent	Lesion pattern	Reason this is useful
T. Pallidum	Classically firm, relatively painless chancre	Vascular / plasma cell-rich inflammation
H. Ducreyi	Soft painful ulcer, often tender buboes	Necrotizing suppurative ulceration
HSV	Painful clustered vesicles evolving to ulcers	Virus-mediated epithelial cytolysis
K. Granulomatis	Chronic soft ulcer / exuberant granulation	Granulation tissue and intracellular bacteria

Syphilis: A systemic spirochetal infection

- *Treponema pallidum* subsp. *Pallidum* produces chronic multistage infection.
- Organisms are too slender to appreciate reliably by routine Gram stain.
- Silver stains or immunofluorescence may demonstrate spirochetes in tissues.
- Transplacental spread can cause congenital syphilis.

Syphilis: Stages and pathology



Schematic

The vascular hallmark of syphilis

- Small-vessel proliferative endarteritis is characteristic across stages.
- A conspicuous plasma cell–rich perivascular infiltrate accompanies it.
- Vascular narrowing contributes to downstream ischemic tissue damage.
- Host responses suppress but may not eradicate treponemes.

Primary syphilis: The chancre

- A firm, elevated lesion arises at the site of inoculation.
- The surface may erode to a shallow, usually painless ulcer.
- Treponemes are abundant and can disseminate hematogenously.
- Spontaneous healing does not imply elimination of systemic infection.

Secondary syphilis: Dissemination

- Superficial mucocutaneous lesions may involve palms and soles.
- Condylomata lata are broad-based plaques in moist anogenital areas.
- Lymphadenopathy and systemic symptoms may accompany the rash.
- Subsequent clinical latency may conceal persistent infection.

Condyloma lata versus condyloma acuminatum

Condyloma lata

- Secondary syphilis manifestation.
- Broad-based moist anogenital plaques.
- Caused by T. Pallidum; Systemic infection.

Condyloma acuminatum

- Benign low-risk HPV wart.
- Exophytic papillary squamous proliferation.
- Koilocytic atypia may be present.

Tertiary syphilis: Organ targets

Syndrome	Anatomic target	Pathologic outcome
Cardiovascular	Ascending aorta and aortic root	Aortitis, root dilation, insufficiency / aneurysm
Neurosyphilis	CNS	Meningovascular and/or parenchymal manifestations
Gummatous	Skin, bone, oral and upper airway tissues	Nodular granulomatous-destructive lesions

Syphilitic aortitis: Mechanism and effects

- Tertiary inflammatory vascular injury affects the proximal aorta.
- Chronic aortitis predisposes to aortic root and arch dilatation.
- Aortic regurgitation and proximal aneurysm may follow.
- Pathologic manifestations can arise long after initial genital disease.

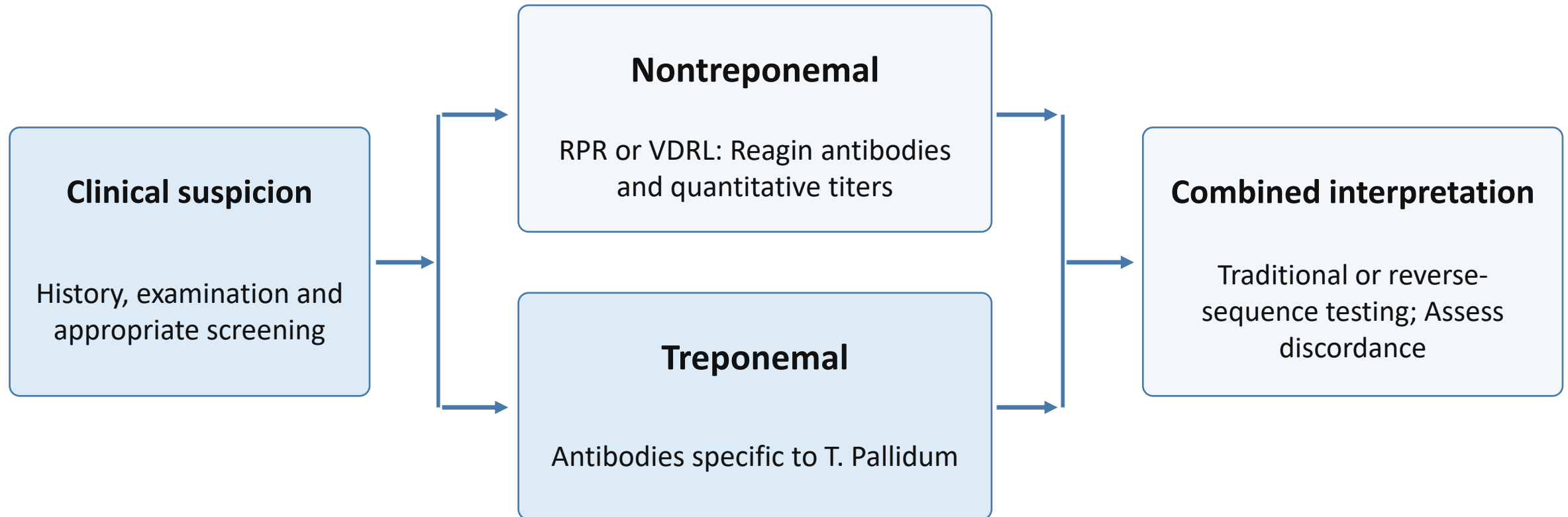
Neurosyphilis: Clinical–pathologic range

- Treponemes can involve the CNS relatively early in infection.
- Neurosyphilis may be clinically silent despite CSF abnormalities.
- Symptomatic disease can include meningovascular and other neurologic syndromes.
- Nervous-system involvement changes clinical evaluation and treatment decisions.

Gummas: Delayed tissue destruction

- Gummas are nodular, often destructive tertiary syphilitic lesions.
- They can involve bone, skin and upper aerodigestive mucosa.
- Delayed immune responses are believed to contribute to the lesions.
- Gummas are uncommon where effective antimicrobial treatment is accessible.

Syphilis testing: Two complementary serologies



Schematic — parallel mechanisms

Treponemal versus nontreponemal tests

Nontreponemal (RPR / VDRL)

- Not specific for *T. Pallidum*.
- Quantitative titers can help monitor treatment response.
- A positive result needs appropriate confirmatory evaluation.

Treponemal

- Detects organism-specific antibody.
- Often remains reactive after successful treatment.
- Can be used for screening or confirmation.

Case: Painless ulcer and later generalized rash

TEACHING SCENARIO

An initially painless indurated genital ulcer resolves; Weeks later a generalized rash including palms develops.

Reasoning prompts

- Connect the two clinical episodes.
- State the common histopathologic vascular lesion.
- Name appropriate assay classes.

Clinicopathologic resolution

Primary and secondary syphilis form a sequence of systemic *T. Pallidum* infection. Plasma cell–rich endarteritis is characteristic. Use treponemal and nontreponemal testing together.

Chancroid: Ulcerative infection

- *Haemophilus ducreyi* causes an acute ulcerative STI.
- The initial papule becomes an irregular, painful, nonindurated ulcer.
- An inflammatory exudate often covers the ulcer base.
- Tender regional nodes may suppurate and drain as buboes.

Chancroid: Layered microscopic response

- The ulcer surface shows neutrophilic debris and fibrin.
- Underlying granulation tissue contains necrosis and thrombosed vessels.
- A dense lymphoplasmacytic infiltrate is deeper in the lesion.
- Organisms may be difficult to identify among colonizing bacteria.

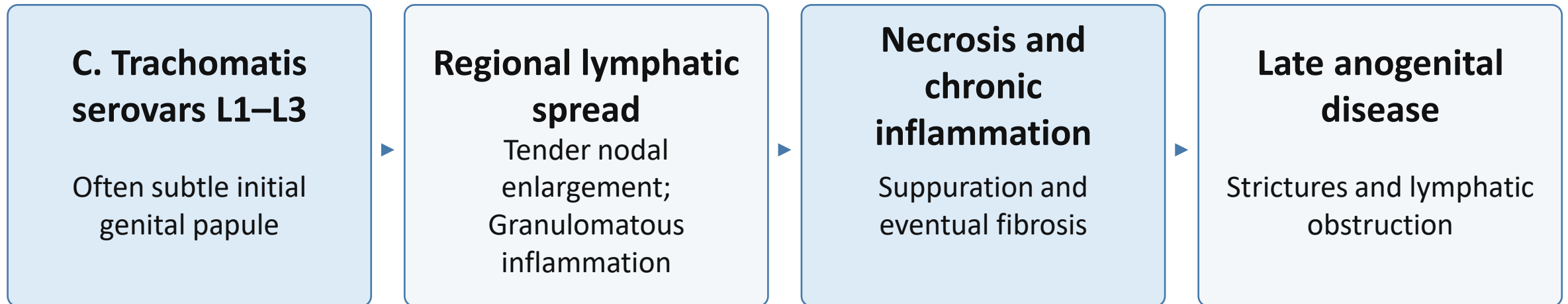
Donovanosis: Exuberant granulation and scarring

- *Klebsiella granulomatis* causes granuloma inguinale (donovanosis).
- Chronic ulcers develop prominent soft granulation tissue.
- Pseudoepitheliomatous hyperplasia can mimic malignancy.
- Advanced untreated disease may produce scarring, strictures and lymphedema.

Donovan bodies: A diagnostic clue

- Exudate smears can show minute encapsulated coccobacilli inside macrophages.
- These organisms are termed Donovan bodies.
- Giemsa and some silver stains can reveal the organisms.
- Regional lymph nodes are typically spared or show nonspecific reactions.

Lymphogranuloma venereum: Tissue progression



Schematic

LGV: Characteristic nodal lesion

- Lymph nodes show a mixed granulomatous and neutrophilic inflammatory response.
- Irregular foci of neutrophilic necrosis can form stellate abscesses.
- Healing fibrosis may obstruct local lymphatic channels.
- Chronic anogenital strictures are a late complication.

Three bacterial ulcer syndromes

Chancroid versus donovanosis

- Chancroid: Painful soft ulcer; Suppurative tender nodes.
- Donovanosis: Chronic ulcer with abundant granulation; Donovan bodies.
- Both can scar when untreated.

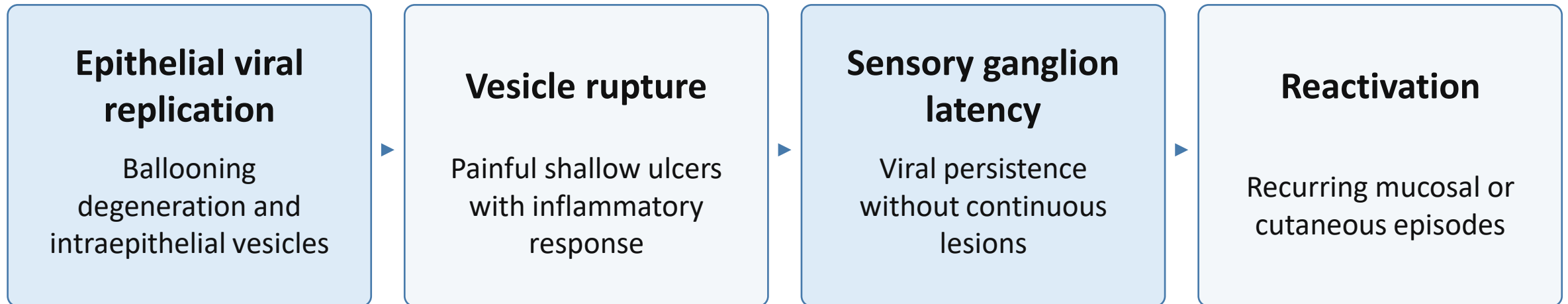
Syphilis versus LGV

- Primary syphilis: Indurated usually painless chancre.
- LGV: Often minor initial papule, then pronounced nodal disease.
- Syphilis produces endarteritis; LGV produces granulomatous/necrotizing lymphadenitis.

HSV genital infection and latency

- Both HSV-1 and HSV-2 can cause genital infection; HSV-2 predominates in classic genital herpes.
- Primary infection causes epithelial vesicles and painful ulcers.
- Virus reaches lumbosacral sensory ganglia and establishes latency.
- Reactivation explains recurrent mucocutaneous lesions.

Herpetic lesion: From infection to recurrence



Schematic

HSV morphology: Cytopathic signature

- HSV infection may produce multinucleated epithelial cells.
- Intranuclear inclusions show ground-glass alteration and chromatin margination.
- Biopsied lesions often show ulceration and acute inflammation.
- Cytopathic changes support the diagnosis but specific viral tests provide identification.

Genital HSV: Active lesions versus latency

Active mucocutaneous phase

- Vesicles or ulcers contain infectious viral particles.
- Symptoms may include pain, dysuria and tender nodes.
- Detection from active lesions can confirm infection.

Latent / recurrent phase

- Viral genome persists in sensory ganglia.
- Subclinical shedding permits some transmission without lesions.
- Reactivation is more frequent with impaired immune function.

Neonatal HSV: Disproportionate injury

- Maternal genital HSV can transmit during passage through the birth canal.
- Risk is especially concerning with active primary infection at delivery.
- Neonatal HSV can disseminate to viscera and the CNS.
- This contrasts with the often localized disease of older immunocompetent individuals.

Case: Clustered painful genital ulcers

TEACHING SCENARIO

Painful vesicles progress to superficial ulcers. A cervical smear contains multinucleated epithelial cells with ground-glass nuclear change.

Reasoning prompts

- Identify the likely pathogen family.
- Explain recurrent episodes.
- Name a particularly vulnerable exposed population.

Clinicopathologic resolution

Genital HSV causes epithelial cytopathic change. Sensory-ganglion latency supports recurrence. Perinatally exposed newborns risk serious systemic and CNS disease.

HPV has two distinct genital pathologies

- Low-risk HPV types, predominantly 6 and 11, produce genital warts.
- High-risk HPV types are associated with cervical and other anogenital squamous cancers.
- Genital HPV infection is often asymptomatic and may clear without lesions.
- Persistence of oncogenic infection increases the risk of intraepithelial neoplasia.

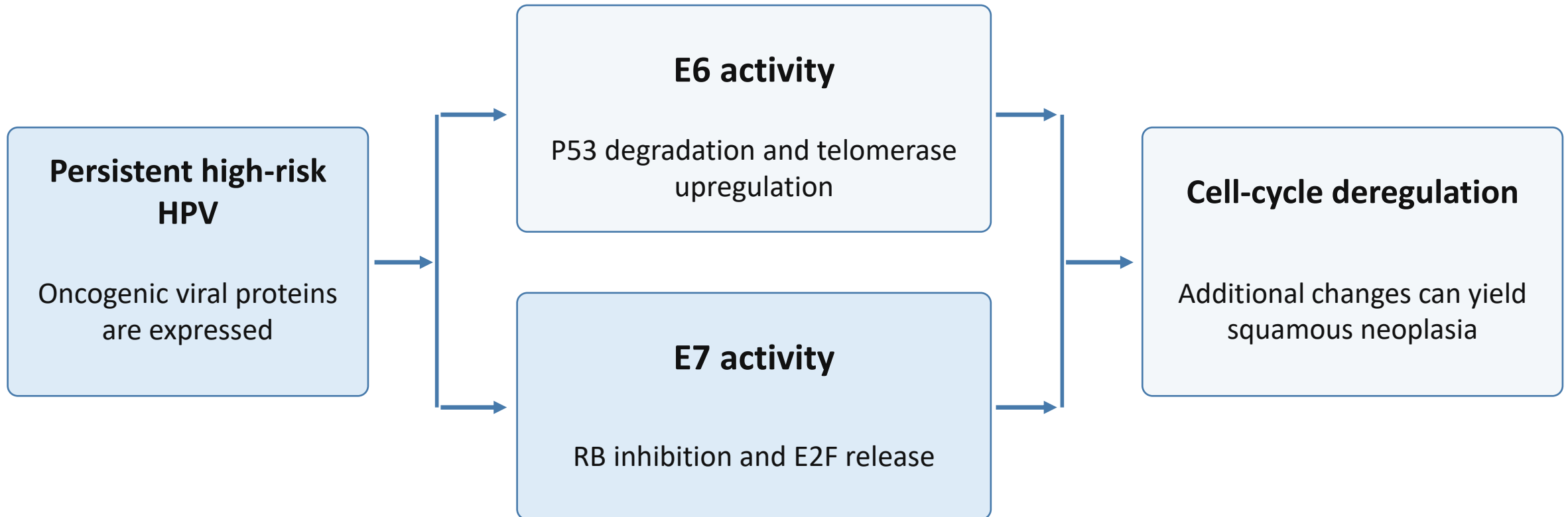
Low-risk versus high-risk HPV

Feature	Low-risk HPV	High-risk HPV
Common types	6, 11	16, 18 and others
Typical pathology	Condyloma acuminatum	Squamous intraepithelial lesions / carcinomas
Cell behavior	Productive papillomatous proliferation	Dysregulated cell-cycle control
Clinical framing	Warts are not precancerous lesions	Persistent infection contributes to carcinogenesis

Condyloma acuminatum: Gross and microscopic

- External genital or perineal lesions may be sessile or pedunculated.
- Exophytic branching fibrovascular papillae are lined by acanthotic squamous epithelium.
- Orderly squamous maturation is generally retained in benign warts.
- Koilocytes display perinuclear halos with altered nuclei.

High-risk HPV: Oncogenic mechanism



Schematic — parallel mechanisms

The transformation zone and HPV

- HPV infects immature basal squamous cells after access to susceptible epithelium.
- The cervical transformation zone is particularly susceptible to high-risk HPV infection.
- Persistent infection can give rise to precursor squamous lesions.
- HPV-related cancer development generally requires additional genetic/epigenetic alterations.

HPV-associated versus HPV-independent vulvar cancer

HPV-associated

- Linked to high-risk HPV, especially HPV-16.
- Develops from HPV-associated squamous intraepithelial lesions.
- May coexist with HPV-related lesions at other anogenital sites.

HPV-independent

- Usually associated with chronic vulvar disorders.
- Can arise through differentiated vulvar intraepithelial neoplasia.
- Frequently involves somatic TP53 alterations.

HPV prevention is a pathology intervention

- Vaccination against HPV prevents infections caused by vaccine-targeted types.
- Prevention reduces development of low-risk genital warts and high-risk HPV precursor lesions.
- Cervical screening detects intraepithelial lesions before invasive cancer.
- Vaccination and screening address different steps in carcinogenesis.

Case: Exophytic papillary anogenital lesion

TEACHING SCENARIO

A papillary genital lesion has thickened squamous epithelium and scattered koilocytes but preserved maturation.

Reasoning prompts

- Name the lesion.
- Identify the usual viral-risk category.
- Distinguish it from secondary syphilis.

Clinicopathologic resolution

Condyloma acuminatum is a benign low-risk HPV lesion (usually HPV 6/11). Condyloma lata is a manifestation of secondary syphilis, not a papillary HPV wart.

Trichomoniasis: Protozoal vaginitis

- *Trichomonas vaginalis* is a flagellated protozoan transmitted commonly through sexual contact.
- Vaginal infection can cause frothy yellow discharge and vulvovaginal discomfort.
- Dysuria and dyspareunia may be present; Infection may also be asymptomatic.
- Cervical vascular dilatation can produce a “strawberry cervix.”

Not all vaginitis is an STI

Trichomoniasis

- Sexually transmitted flagellated protozoan.
- Inflammatory vaginitis; Frothy discharge may occur.
- Characteristic erythematous cervix in some patients.

Candidiasis and bacterial vaginosis

- Candidiasis usually follows disturbance of vaginal ecology and is not classified as an STI.
- Bacterial vaginosis is a polymicrobial dysbiosis with malodorous discharge.
- Similar symptoms do not imply identical transmission pathways.

Cervicitis: Infection versus reactive atypia

- Gonococci, chlamydiae, mycoplasmas and HSV can cause clinically important cervicitis.
- Cervical inflammation can produce reparative epithelial change.
- Reactive atypia may complicate cytologic interpretation.
- Identify the infectious process and assess for upper genital tract complications.

Nongonococcal urethritis is heterogeneous

- Chlamydia trachomatis is one major infectious cause.
- Ureaplasma and other organisms can produce urethral symptoms.
- Some cases have no organism identified and some inflammation is noninfectious.
- Urethritis can warn of disease elsewhere in the genitourinary tract.

Morphologic clues and their limitations

Morphologic finding	Favors	Important limitation
Intracellular diplococci in exudate	Gonorrhea	Confirm with appropriate pathogen tests
Multinucleation and nuclear inclusions	HSV	Cytopathic appearance is not site-specific
Koilocytic atypia	HPV	Does not itself grade a lesion
Plasma cell–rich endarteritis	Syphilis	Needs serologic / organism correlation
Donovan bodies in macrophages	Donovanosis	Requires correct staining and specimen context

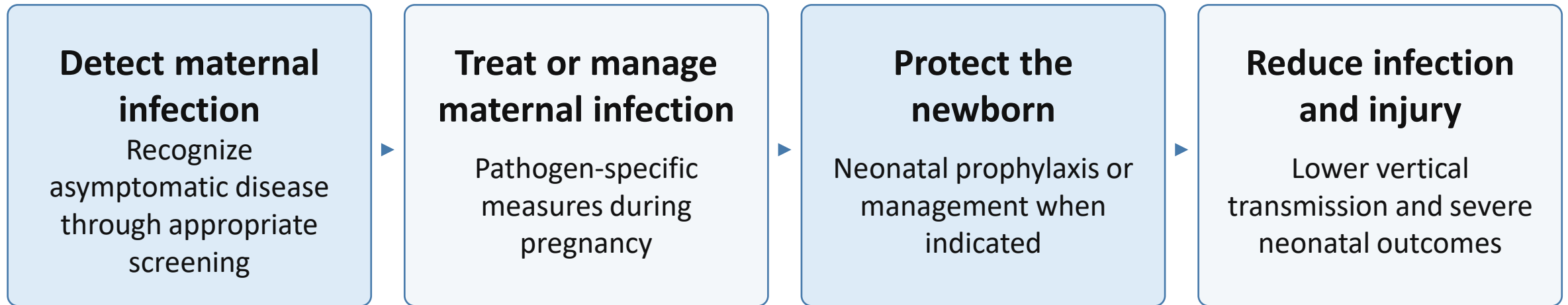
Vertical transmission: Pathogen and damage

Maternal infection	Transmission / neonatal presentation	Core implication
C. Trachomatis	Perinatal neonatal conjunctivitis	Maternal diagnosis has neonatal consequences
N. Gonorrhoeae	Neonatal conjunctivitis, potentially blindness	Prevention and prompt care are essential
HSV	Peripartum CNS or disseminated disease	Primary active genital HSV is particularly concerning
T. Pallidum	Transplacental congenital syphilis	Fetal loss and multisystem childhood disease
HIV	Prenatal or perinatal HIV infection	Antiretroviral interventions markedly reduce transmission

Congenital syphilis: Early and late disease

- Transplacental *T. Pallidum* can cause fetal loss or severe neonatal disease.
- Early manifestations include snuffles, skin rash, hepatomegaly and skeletal abnormalities.
- Delayed disease can include interstitial keratitis, hearing loss and characteristic dental abnormalities.
- Pregnancy screening and appropriate treatment interrupt mother-to-child transmission.

Perinatal prevention: Interrupting the pathway



Schematic

Diagnostic strategy: Syndrome is a starting point

- Use the distribution of symptoms and lesions to localize disease.
- Combine clinical examination with pathogen-directed assays.
- Do not use histology alone to exclude simultaneous infections.
- Interpret tests in the context of exposure site and disease stage.

Test selection: What each detects

Method	Common use in this lecture	What it contributes
Nucleic-acid amplification	Gonorrhea; Chlamydia	Direct organism nucleic-acid detection
Culture	Selected gonococcal specimens	Organism recovery; Resistance workup
Syphilis serology	RPR/VDRL plus treponemal assay	Stage-sensitive, complementary antibody information
Lesion-based HSV assay	Genital herpes	Virus detection from symptomatic lesion
Cytology / histology	HPV lesions; HSV changes; Ulcers	Tissue effect and differential diagnosis

Integrated case: Pelvic pain with negative smear

TEACHING SCENARIO

A patient has cervicitis, pelvic pain and tubal tenderness. Routine Gram stain does not reveal a definitive organism.

Reasoning prompts

- Does a negative direct smear exclude chlamydial disease?
- Which organ injury threatens future fertility?
- What test class is relevant to the common agents?

Clinicopathologic resolution

No. Chlamydia is not visible on routine Gram stain. Ascending infection may cause suppurative salpingitis and later fibrosis. NAATs are appropriate for gonorrhea/chlamydia detection.

Integrated case: Painful versus painless ulcer

TEACHING SCENARIO

Two patients present with genital ulcers: One has a painful soft ulcer and tender nodes; The other has a firm painless chancre.

Reasoning prompts

- Give a leading pathogen for each pattern.
- Describe one discriminating microscopic feature.
- Explain why a clinical pattern alone is insufficient.

Clinicopathologic resolution

Consider *H. Ducreyi* for the soft painful ulcer and *T. Pallidum* for a firm painless chancre. Chancroid shows layered neutrophilic ulcer inflammation; Syphilis favors plasma cell–rich endarteritis. Confirm with appropriate tests.

Final pathology synthesis

Dominant process	Representative infection	High-value consequence
Suppurative mucosal injury	Gonorrhea; Chlamydia	Ascending tubal scarring
Endarteritis and chronic inflammation	Syphilis	Vascular, neurologic and congenital disease
Viral epithelial cytolysis	Genital HSV	Latency, recurrence; Neonatal spread
HPV-driven squamous proliferation	Condyloma / persistent high-risk HPV	Benign wart versus premalignant lesion
Granulation and chronic ulceration	Donovanosis / chancroid	Scarring, tissue destruction

Clinical reasoning: Five discriminators

- Which site and route of exposure are plausible?
- Is inflammation purulent, ulcerative, papillary or systemic?
- Could asymptomatic or multiple infections coexist?
- What permanent organ injury or neonatal risk must be prevented?
- Which pathogen-directed assay can establish etiology?

Further reading in Robbins

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th edition.
- Infectious Diseases: sexually transmitted infections and individual microbial diseases.
- Neoplasia: the molecular pathogenesis of human papillomavirus-associated tumors.
- The Lower Urinary Tract and Male Genital System; The Female Genital Tract: anatomic pathology and clinical sequelae.