

HERPES SIMPLEX VIRUS

Genital infection of the female reproductive tract

Pathogenesis • morphology • clinical interpretation

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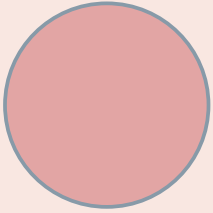
Learning objectives

- Describe HSV-1/HSV-2 infection in vulvar, vaginal and cervical tissues.
- Explain epithelial replication, neuronal latency and recurrent shedding.
- Recognize viral cytopathic changes and compare diagnostic approaches.
- Connect maternal genital HSV to neonatal transmission and prevention.

Why HSV matters in lower genital tract pathology

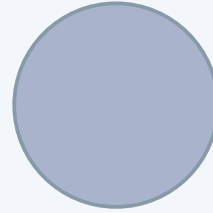
- HSV causes painful genital ulceration and may also present as cervicitis.
- Clinical findings must be linked to epithelial cytopathic injury and viral detection.
- Latency creates recurrent disease despite resolution of visible lesions.

Anatomic distribution of genital HSV



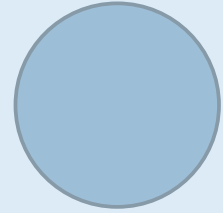
Vulva

Visible skin and mucosal lesions



Vagina

Internal lesions may produce
discharge



Cervix

Internal lesions may produce
pelvic pain

Conceptual site overview — not to anatomical scale

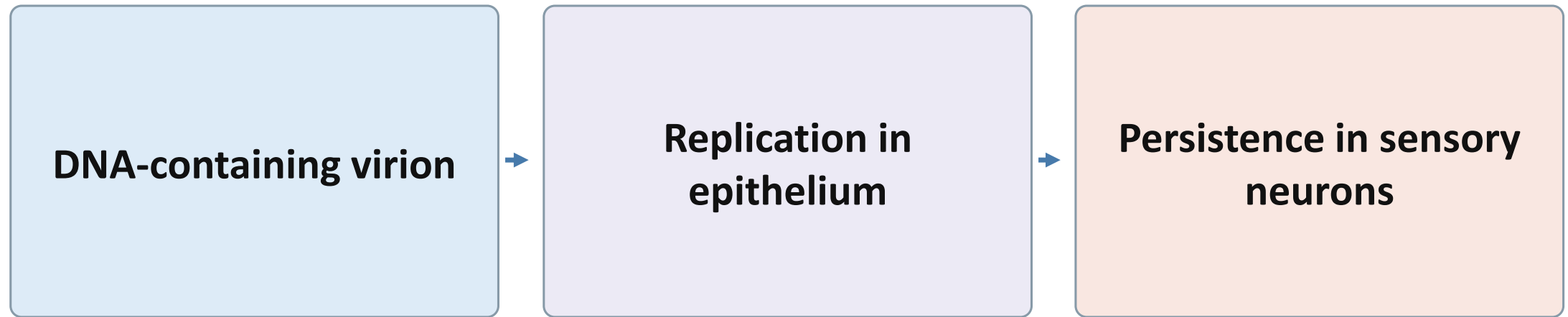
Two closely related herpes simplex viruses

Feature	HSV-1	HSV-2
Usual association	Perioral infection	Genital infection
Possible genital disease	Yes	Yes
Possible oral disease	Yes	Yes

HSV type does not rigidly predict anatomic site

- HSV-1 can be recovered from genital lesions.
- HSV-2 can also infect the oral region.
- Type-specific identification is distinct from recognizing HSV cytopathic effect.

HSV is a latent double-stranded DNA virus



Primary infection and lifelong persistence are separate biologic states.

Productive infection versus neuronal latency

Property	Productive infection	Latency
Main location	Epithelial entry sites	Sensory neuron
Viral output	Infectious progeny	No infectious virions
Clinical consequence	Lesions and shedding	Potential future reactivation

Textbook epidemiology: Seropositivity is not the same as symptoms

- Roughly 30% HSV-2 seropositivity among females by age 40.
- Seropositivity reflects immune recognition, not necessarily visible genital lesions.
- The quoted figure is a textbook population estimate, not a universal prevalence rate.

Most newly infected people do not have recognized symptoms

At acquisition	Approximate source description
Symptomatic	About one-third of newly infected individuals
Without recognized symptoms	Remaining newly infected individuals

Acquisition begins at a mucosal or cutaneous entry site

Exposure to HSV



Replication at entry site



Mucocutaneous injury

Initial lesions generally appear within days

3–7 days

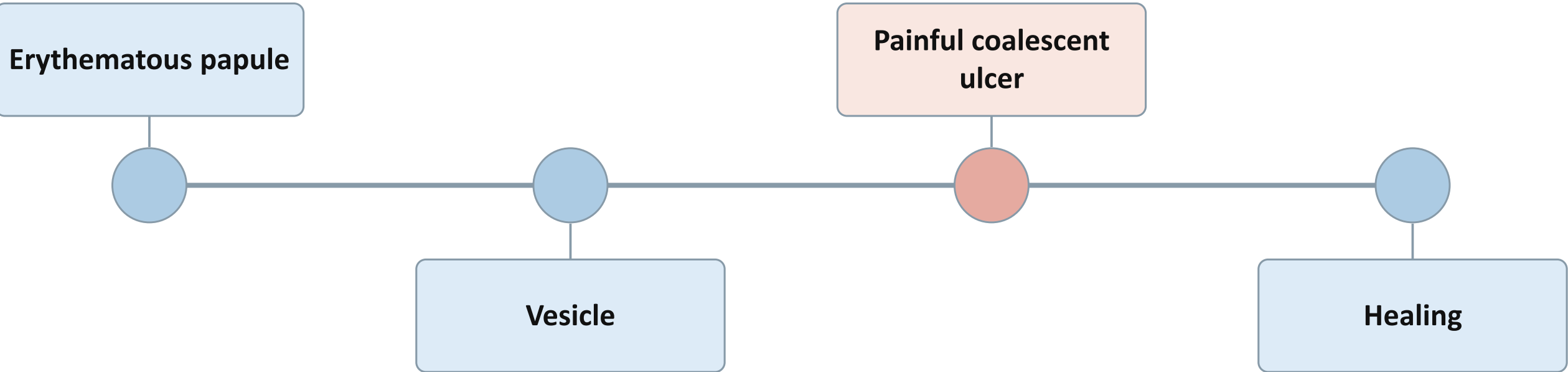
Typical source interval between
transmission and lesion appearance

The clinical interval cannot establish viral type by
itself.

Primary symptomatic infection has systemic correlates

- Fever and malaise may accompany a first symptomatic episode.
- Tender inguinal lymph nodes support a regional inflammatory response.
- Systemic symptoms should be interpreted with the local genital findings.

Genital HSV lesions follow a characteristic sequence



Vulvar HSV: Visible mucocutaneous ulceration

- Vesicles and ulcers are often readily appreciated on vulvar skin or mucosa.
- Painful clustered lesions support the clinical suspicion of HSV.
- Clinical recognition is helpful, but laboratory detection can establish infection.

Cervical and vaginal HSV may not look like external ulcers

- Internal lesions may manifest as purulent discharge and pelvic pain.
- The absence of an obvious vulvar eruption does not exclude genital HSV.
- The location of lesions determines whether clinical visualization is straightforward.

Periurethral lesions can impair micturition

**Urethral-adjacent
ulceration**



Pain during urination



**Possible urinary
retention**

Clinical pain reflects an ulcerative mucosal process

Epithelial injury



**Ulceration and acute
inflammation**



**Pain and local
tenderness**

Active vesicles and ulcers contain infectious virus

- Vesicles and ulcer exudates can contain numerous viral particles.
- Active mucosal lesions are associated with efficient transmission.
- Reducing symptomatic lesions is not identical to abolishing viral shedding.

Visible lesions heal, but infection is not eliminated

1–3 weeks

Typical source duration for spontaneous healing of cutaneous and mucosal lesions

The virus can already have established latency during the acute episode.

HSV gains access to sensory neuronal pathways

**Mucosal / skin
replication**

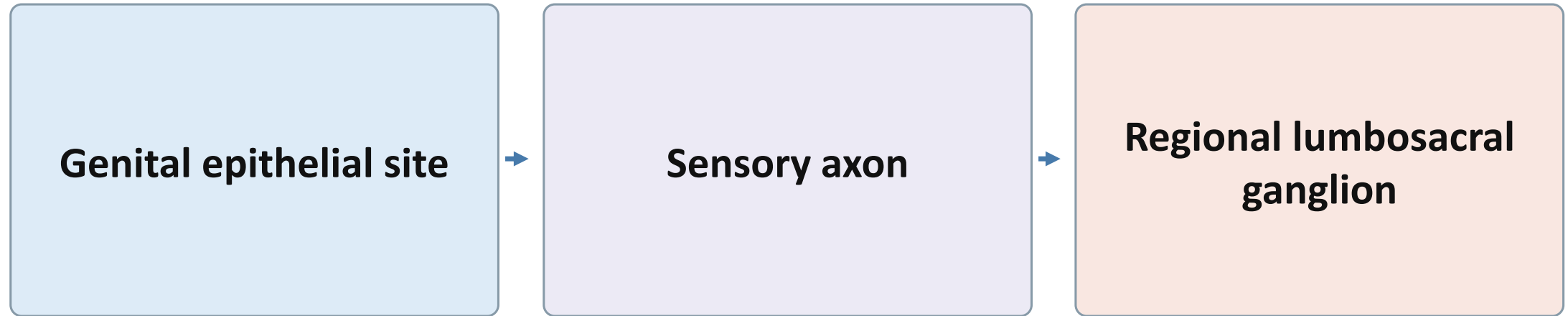


Sensory axonal entry



**Transport to ganglion cell
body**

Genital HSV establishes latency in lumbosacral ganglia

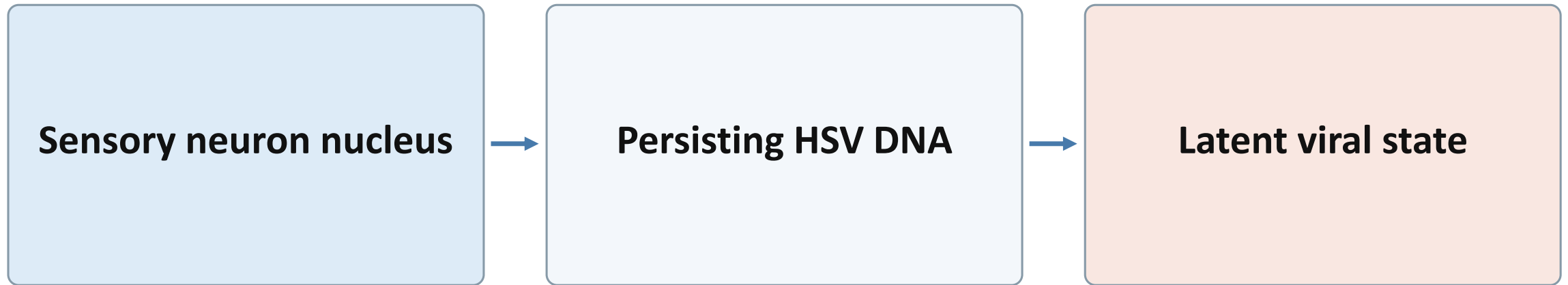


The neuronal reservoir persists after surface healing.

Latency means persistence without productive virion release

- Viral genomes persist in neuronal nuclei.
- No infectious virions are produced during true latency.
- Reactivation restarts productive replication and can restore mucosal shedding.

The HSV genome remains in the neuronal nucleus



Latency-associated transcripts distinguish the latent state

- Latency-associated transcripts (LATs) are expressed in neurons.
- No detectable viral protein production during latency.
- LATs are implicated in maintaining a nonproductive infection state.

LATs may support survival and silence lytic viral genes

Anti-apoptotic effects

Resistance to neuron
apoptosis

Chromatin-based silencing

Reduced lytic gene
expression

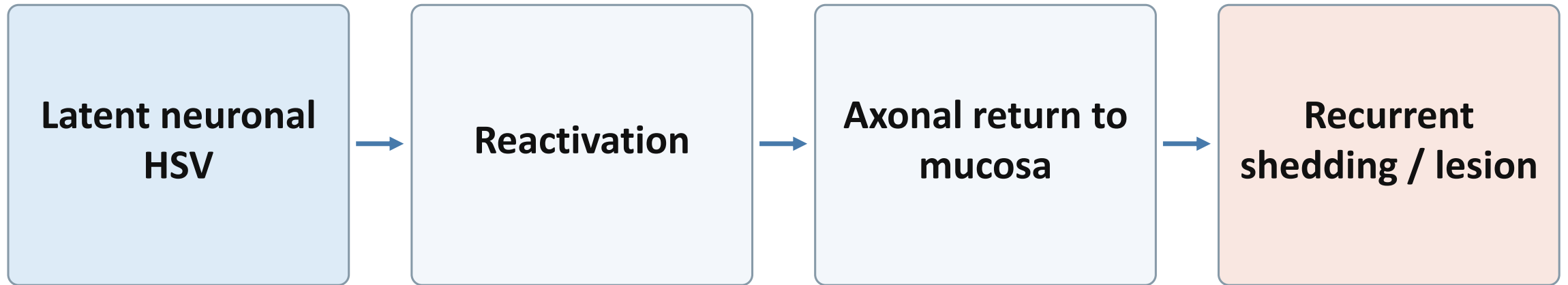
MicroRNA precursors

Downregulation of selected
lytic genes

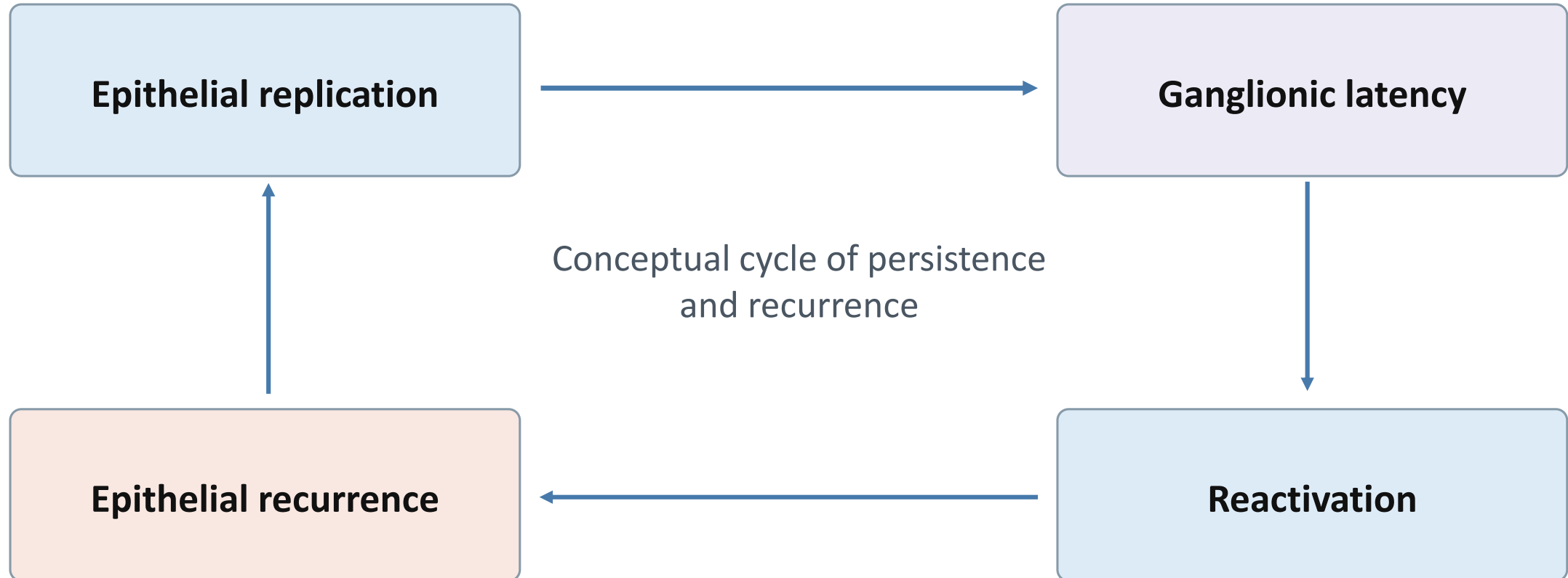
Reactivation can follow reduced immune control

- Stress, trauma, concurrent infection and hormonal change as triggers.
- Trigger-associated reactivation resumes productive viral replication.
- Not all reactivation episodes produce recognizable symptoms.

Reactivation reverses the direction of viral travel



Recurrent episodes arise from a persistent neural reservoir



Subclinical shedding separates infectivity from visible disease

State	Visible lesions	Potential shedding
Symptomatic active infection	Often present	Yes
Subclinical reactivation	Absent	Possible
Latency itself	Absent	No virion production

Immunosuppression makes recurrence more consequential

- Reactivation and recurrent lesions are particularly common with impaired immunity.
- Control of cell-mediated responses is important in HSV infection.
- Disseminated infection is a recognized risk in severely immunocompromised hosts.

HSV can evade cytotoxic T-cell recognition



HSV glycoprotein gE disrupts antibody functions

Viral gE binds IgG Fc

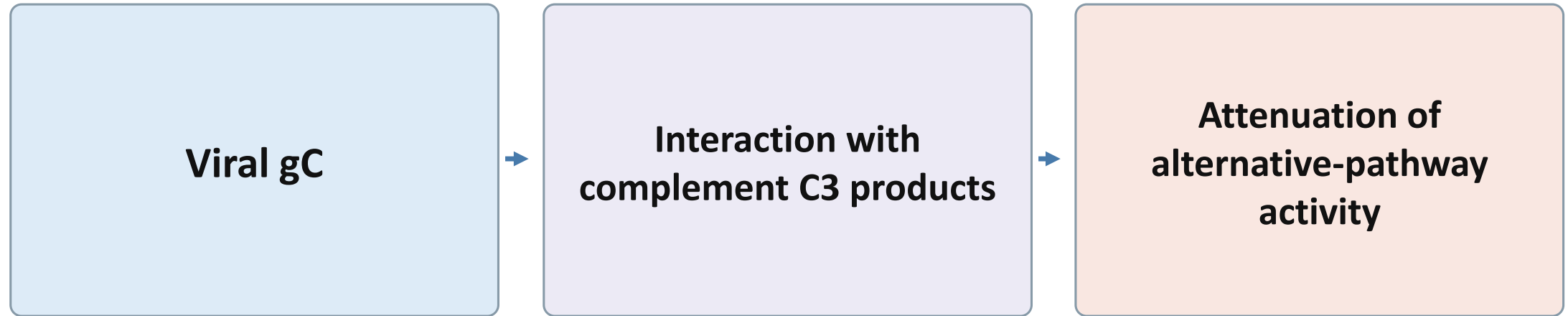


**Interference with selected
antibody effector actions**



**Reduced complement /
cellular targeting**

HSV glycoprotein gC interferes with complement



Why immunity does not guarantee viral eradication

Neuronal persistence

Viral DNA remains latent

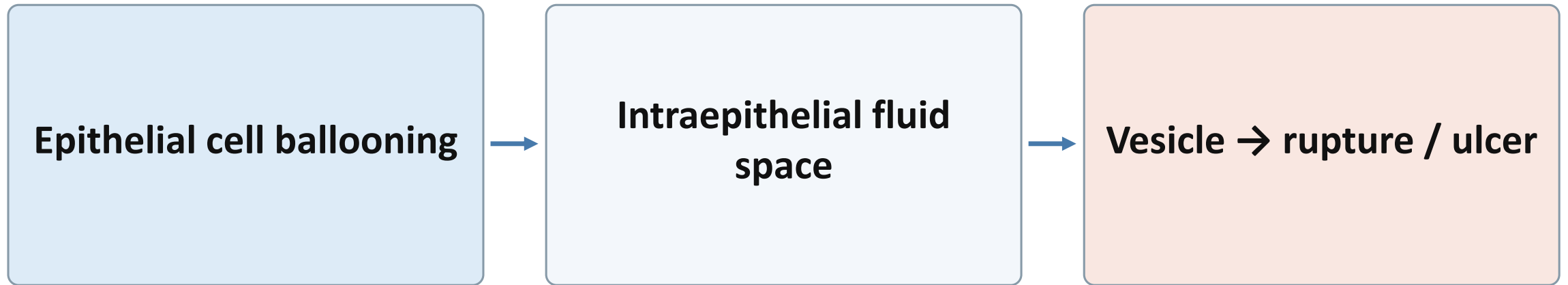
Immune evasion

MHC-I and
antibody/complement
interference

Periodic reactivation

Local shedding may recur

Early HSV epithelial injury produces intraepithelial vesicles



Schematic mechanism; Not a histologic image.

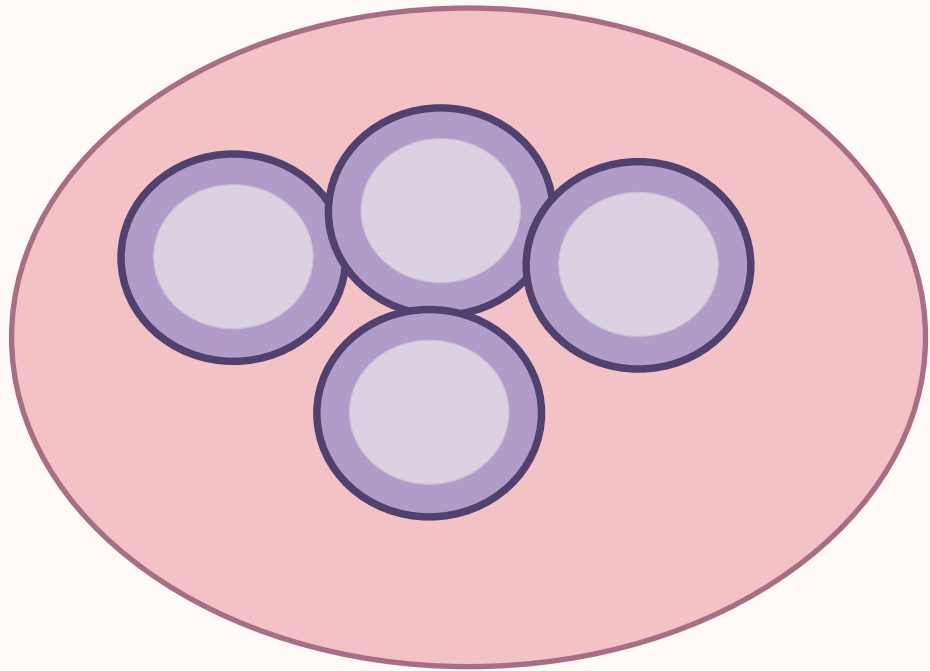
Late biopsy may primarily show ulceration

- Biopsied genital lesions have often progressed beyond the vesicular stage.
- Surface epithelium may be desquamated or absent.
- Marked acute inflammation is commonly present in the ulcer bed.

The ulcer bed is not the same as the diagnostic infected cell

Lesion compartment	Expected interpretive finding
Ulcer bed	Acute inflammatory exudate and epithelial loss
Residual infected squamous cells	HSV-specific cytopathic alteration
Practical limitation	Advanced ulceration may reduce intact diagnostic epithelium

HSV induces multinucleated squamous cells



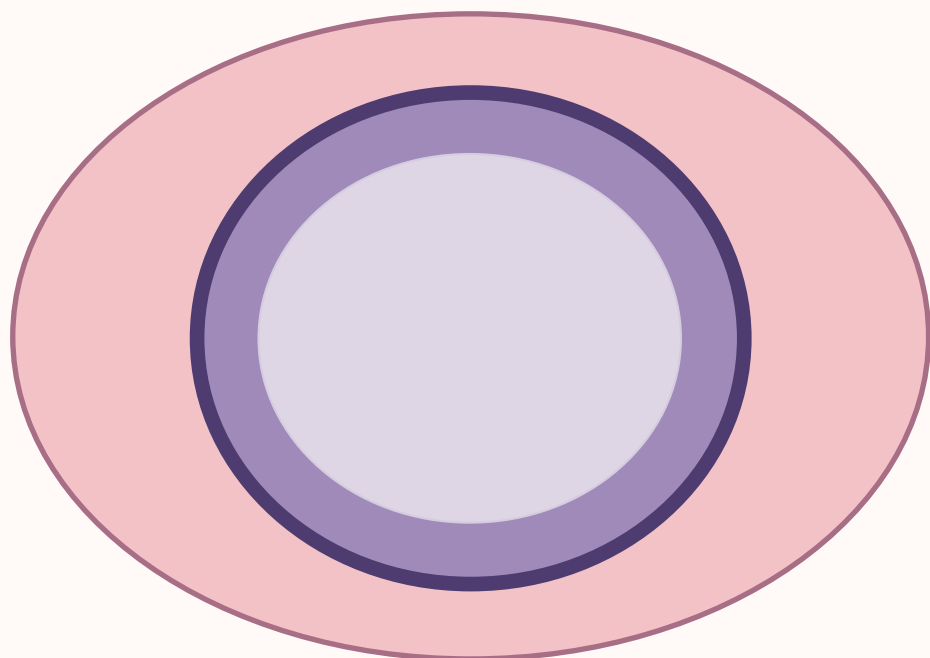
Schematic illustration — not a clinical or cytologic specimen

Multinucleation

Cells may fuse to form syncytia.

This is characteristic but must be interpreted in context.

Ground-glass nuclei are a key cytologic clue



Peripheral chromatin rim

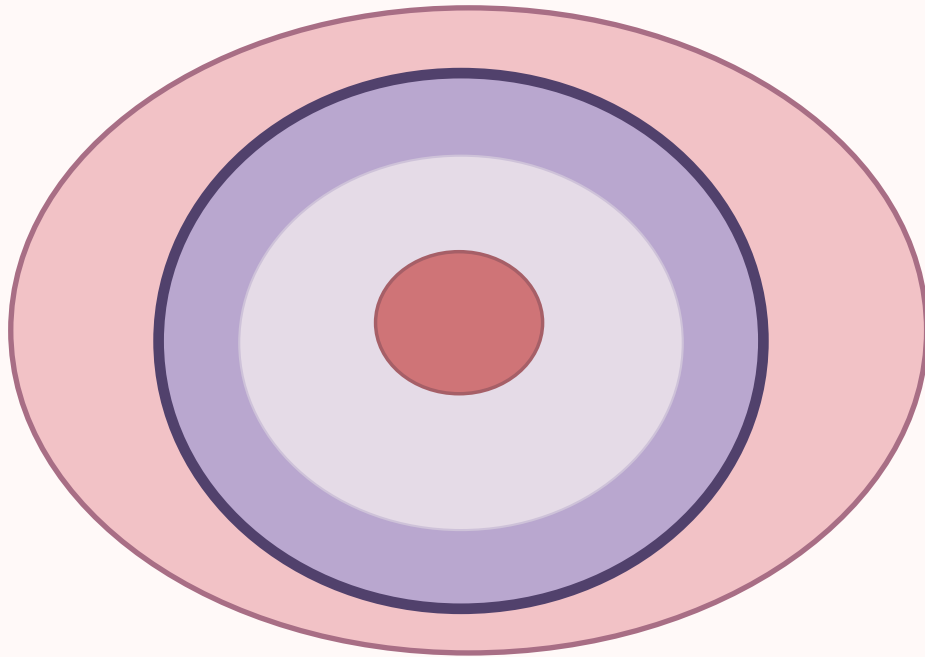
Schematic illustration — not a clinical or cytologic specimen

Ground-glass chromatin

HSV-infected nuclei may show homogenized pale nuclear interiors.

Observe the entire pattern, rather than one isolated feature.

HSV produces intranuclear inclusions



Intranuclear body with surrounding clearing

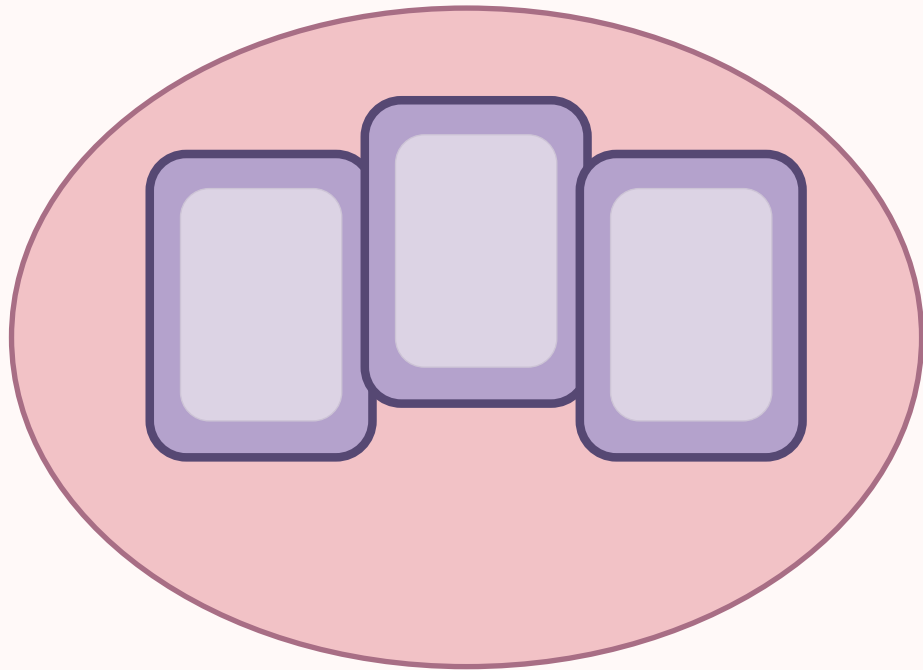
Schematic illustration — not a clinical or cytologic specimen

Cowdry type A inclusions

Pink to purple intranuclear material may displace normal chromatin.

Nuclear inclusions support herpesvirus cytopathic infection.

Nuclear molding reflects close apposition of fused nuclei



Abutting nuclei with locally flattened interfaces

Schematic illustration — not a clinical or cytologic specimen

Nuclear molding

In multinucleated epithelial cells, nuclear contours press against each other.

Chromatin can be marginated at the nuclear periphery.

Read the full pattern of HSV cytopathic effect

Cell architecture

Multinucleated squamous cells

Nuclear texture

Ground-glass change and chromatin margination

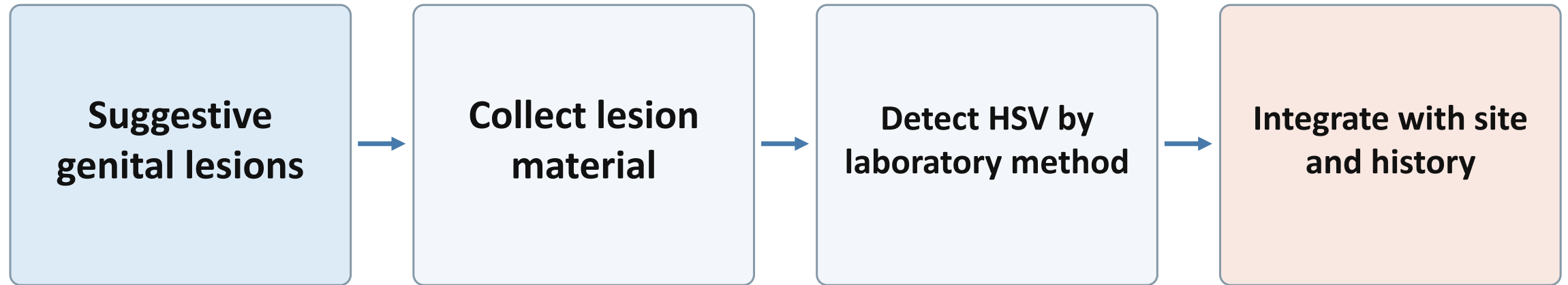
Inclusions

Cowdry A-type intranuclear material

A positive morphologic pattern does not establish HSV type

- HSV-1 and HSV-2 share similar cytopathic alterations.
- Virologic methods or type-specific assessment are needed for serotype attribution.
- A smear is a morphologic clue; It is not equivalent to viral genotyping.

Clinical recognition and direct detection are complementary



Traditional viral culture demonstrates replication

- Lesional exudate is inoculated into a permissive tissue culture.
- Growing virus produces an observable cytopathic effect.
- Viral isolates can subsequently be typed.

Culture-based cytopathic effects take time to develop

48–72 hours

Time interval given by Robbins for observing culture cytopathic effect

Culture-based detection is not the only laboratory option.

PCR detects HSV nucleic acid in lesion material

- PCR as a more sensitive option for lesional secretions.
- The result confirms HSV nucleic acid detection rather than proving a visible ulcer is present.
- Type-specific assays may further distinguish HSV-1 from HSV-2.

Immunologic assays may detect HSV in lesions

Test approach	Target / interpretive role
Direct immunofluorescence	Viral antigen in lesion-associated material
ELISA	Assay-dependent viral or antibody detection
Serologic type specificity	Antibodies against variant HSV glycoprotein G

Serum antibodies reflect immune history, not an active lesion

- Early primary infection may precede development of detectable anti-HSV antibodies.
- Once developed, anti-HSV antibodies support prior exposure and persistence.
- Seropositivity alone does not localize active infection or prove a particular lesion is herpetic.

A source-grounded diagnostic reasoning pathway

Typical genital lesion or cervicitis?



Sample appropriate lesion material



PCR / culture / antigen-based methods



Interpret results with clinical findings

Transmission is most efficient during active disease

- Active vesicles and ulcers contain abundant infectious virus.
- HSV can pass between sexual partners during symptomatic episodes.
- Viral activity at mucosal surfaces underlies transmission risk.

Subclinical shedding maintains risk between episodes

- Shedding may occur without an apparent genital lesion.
- An interval without symptoms does not guarantee absence of transmission.
- Latency and subclinical reactivation should not be conflated.

Barrier measures and antiviral therapy lower—but do not abolish—risk

Condom use

Reduces contact-associated transmission risk

Antiviral therapy

Reduces the symptomatic phase and transmission risk

Residual hazard

Incomplete protection, including silent shedding

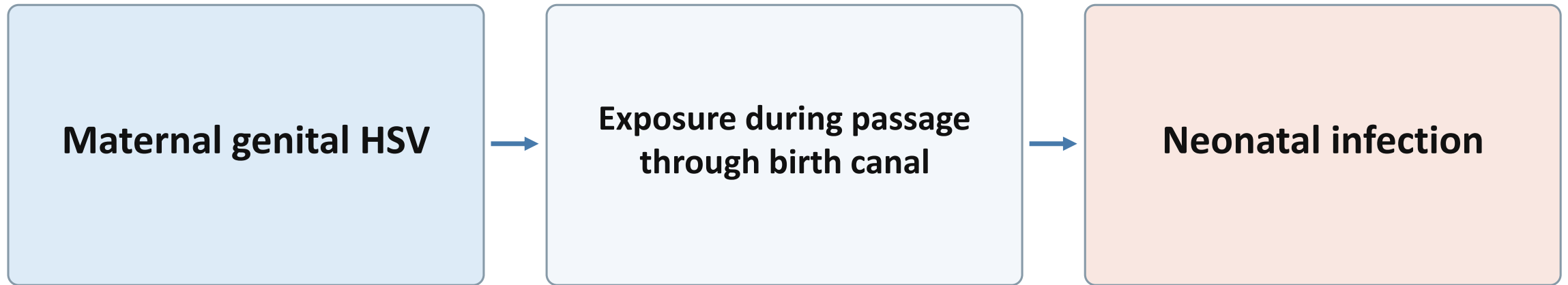
Prior HSV-1 infection may modify HSV-2 acquisition risk

- Reduced HSV-2 susceptibility after previous HSV-1 infection.
- This represents partial protection, not reliable immunity to HSV-2.
- Anatomic distribution and viral type should remain conceptually separate.

HSV transmission has sex-related asymmetry

- Genital HSV is more readily transmitted to females than males.
- This is a broad epidemiologic observation, not a patient-specific prediction.
- Risk counseling must still account for shedding without symptoms.

Maternal genital HSV can be transmitted at birth



Primary maternal infection near delivery has special importance

- Greatest neonatal risk when maternal infection is active at delivery.
- The risk is particularly concerning with maternal primary infection.
- Clinical classification of maternal infection therefore matters for perinatal risk.

Neonatal HSV may produce disseminated organ injury

Lymphoreticular involvement

Lymphadenopathy and
splenomegaly

Visceral necrosis

Lung, liver and adrenal
involvement

Central nervous system

CNS involvement in severe
disease

Delivery planning is an important preventive intervention

- Robbins recommends cesarean delivery when active genital infection is present at delivery, especially primary infection.
- The purpose is to reduce neonatal exposure during passage through the birth canal.
- Patient-specific intrapartum decisions require current obstetric protocols beyond this pathology source.

Genital HSV increases susceptibility to HIV transmission

Genital ulceration



**Compromised mucosal
barrier / inflammation**



**Increased HIV acquisition
/ transmission risk**

Antivirals reduce episodes but do not remove latent virus

Target	Antiviral effect described in Robbins
Initial symptomatic episode	Shortened duration
Recurrent symptomatic episode	Shortened duration
Neuronal latent infection	Not eradicated

A preventive HSV vaccine remains an unmet goal

- No effective vaccine at the time of publication.
- The enduring neuronal reservoir helps explain the need for preventive strategies.
- This statement reflects the supplied textbook rather than a real-time vaccine-development review.

Different lower tract infections produce distinct patterns

Condition	Characteristic presentation
Genital HSV	Painful vesicles / superficial ulcers
Candida vulvovaginitis	Pruritus; erythema; curdlike discharge
Trichomoniasis	Possible frothy discharge; vulvovaginal discomfort
Bacterial vaginosis	Thin, malodorous discharge

HSV and HPV have different pathologic consequences

Characteristic	HSV	HPV
Lower genital tract concern	Ulcerative infection	Neoplastic transformation
Typical emphasized pathology	Vesicular / ulcerative injury	Cervical, vaginal, vulvar neoplasia
Major virus property in this lesson	Neuronal latency	Oncogenic role of some HPV types

Clinical case: Painful vulvar lesions

A patient presents with painful clustered genital vesicles and tender inguinal nodes.

What evolution of skin findings would strengthen HSV suspicion?

Which specimen could establish viral detection?

Case interpretation: Characteristic progression and testing

Papules progressing to vesicles and coalescent painful ulcers support HSV.

Collect material from active lesions for HSV detection.

Symptoms alone cannot reliably distinguish HSV-1 from HSV-2.

Clinical case: Purulent cervicitis without obvious vulvar vesicles

A patient has purulent cervical discharge and pelvic pain but no visible vulvar ulcers.

Can genital HSV still be considered?

What additional evidence would improve diagnostic specificity?

Case interpretation: Internal genital HSV is possible

HSV may involve the vagina and cervix without externally obvious lesions.

Direct virologic testing can support suspected HSV infection.

Other causes of cervicitis remain in the differential diagnosis.

Clinical case: Active lesions at delivery

A pregnant patient has active genital vesicles at the onset of labor.

What is the major pathology-related neonatal hazard?

Why is maternal primary infection especially important?

Case interpretation: Prevent exposure to infectious genital HSV

Neonatal acquisition can occur during passage through the infected birth canal.

High risk with active primary maternal infection.

The textbook supports cesarean delivery in this setting to reduce exposure.

Clinicopathologic synthesis: Local infection versus persistence

Stage	Underlying pathology	Clinical consequence
Entry / replication	Epithelial cytopathic injury	Vesicles and ulcers
Neuronal latency	Persisting viral DNA	Asymptomatic reservoir
Reactivation	Return to epithelial sites	Recurrent lesions or silent shedding

Summary: What a pathologist should recognize

- Genital HSV can involve vulva, vagina and cervix.
- Multinucleated squamous cells with ground-glass inclusions suggest herpesvirus infection.
- Ulcer beds may lack intact diagnostic epithelium.
- Viral detection and clinical correlation complete the interpretation.

Summary: What a clinician should anticipate

- Symptomatic disease resolves while neuronal latency remains.
- Subclinical shedding limits purely symptom-based prevention.
- Maternal active genital infection at delivery creates neonatal risk.
- Antivirals shorten symptomatic episodes but do not eradicate latency.

Source references

Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. (2026). Chapter 22: The Female Genital Tract, pp. 896–898.

Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. (2026). Chapter 8: Infectious Diseases, pp. 320–322.

Clinical algorithms, drug regimens, and contemporary practice recommendations were not independently reviewed for this source-faithful pathology lecture.