

Varicella-Zoster Virus

Primary infection · varicella (chickenpox)

Latent infection · sensory ganglia

Reactivation · herpes zoster (shingles)

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning objectives

- Connect respiratory infection and hematogenous spread to the generalized varicella eruption.
- Explain sensory-ganglion latency and subsequent dermatomal reactivation.
- Recognize characteristic cutaneous and neural pathology and major complications.
- Distinguish clinical presentations, diagnostic approach, and preventive strategies.

One virus, two distinct clinical syndromes

Primary infection: Varicella

Disseminated vesicular exanthem

Rash develops in successive waves

Typically self-limited in immunocompetent children

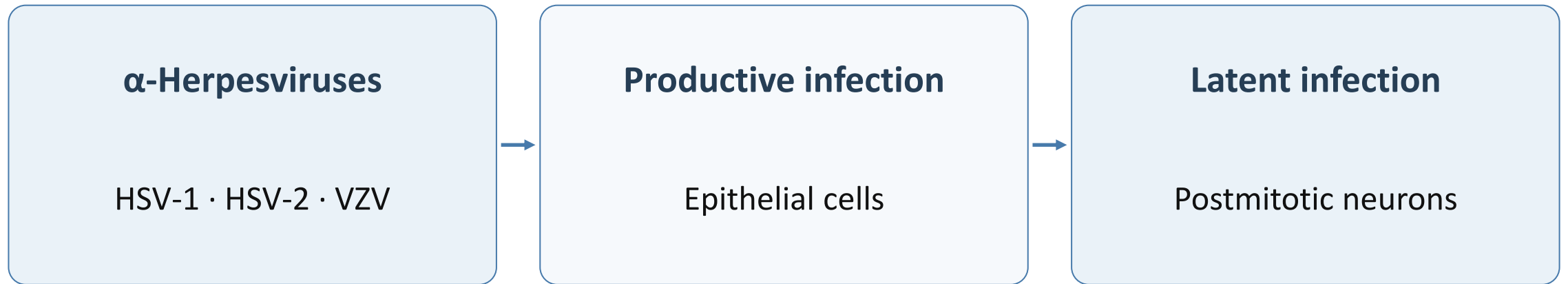
Reactivation: Herpes zoster

Painful, dermatomal vesicular eruption

Virus travels along sensory nerves

Morbidity increases with age or immunosuppression

VZV belongs to the α -herpesvirus group



Epithelial–neural tropism shapes the disease

Epithelial infection

- Skin and mucosal epithelium support productive infection and vesicle formation.
- The primary exanthem reflects widespread cutaneous involvement.

Neural infection

- Sensory ganglia provide a long-term latent reservoir.
- Reactivation follows sensory pathways back toward skin.

Latency is genome persistence without virion release

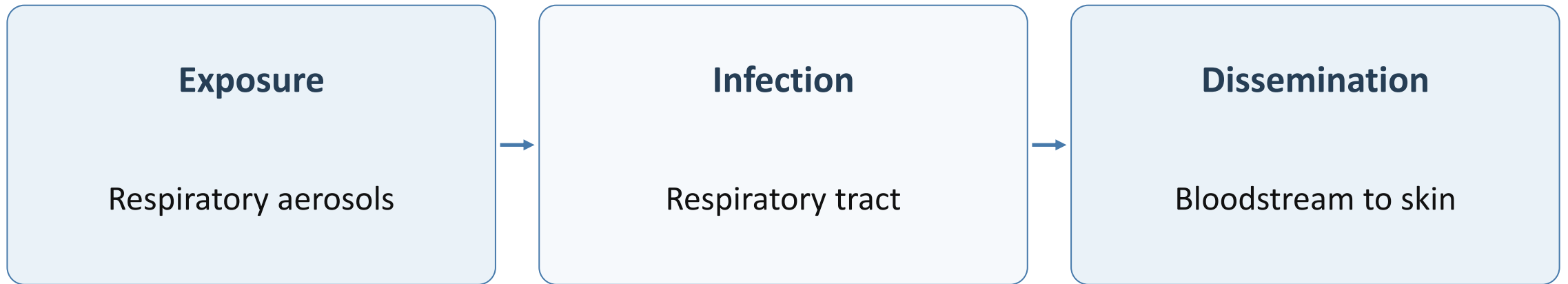
- Herpesvirus latency retains viral genomes within host cells.
- No infectious virus is produced during the latent state.
- Reactivation resumes viral replication and permits tissue injury and transmission.
- VZV's latent reservoir lies in sensory ganglia.

The natural history has three linked phases



- Infection is not eliminated when the chickenpox lesions heal.
- The interval before zoster may extend many years.

Respiratory aerosols enable acquisition



- Epidemic VZV transmission with the more localized primary spread of HSV.

Hematogenous dissemination produces a generalized rash

- Following respiratory acquisition, VZV disseminates hematogenously.
- Widespread skin infection creates vesicular lesions at anatomically separated sites.
- This systemic route helps explain the different distribution of primary varicella and localized recurrent zoster.

VZV and HSV have different patterns of spread

VZV

Spread via respiratory aerosols

Hematogenous dissemination in primary infection

Widespread primary cutaneous eruption

HSV (comparison)

Primary replication at mucosal or cutaneous entry site

Local epithelial lesions in characteristic distributions

Also becomes latent in sensory neurons

Host immune status modifies severity

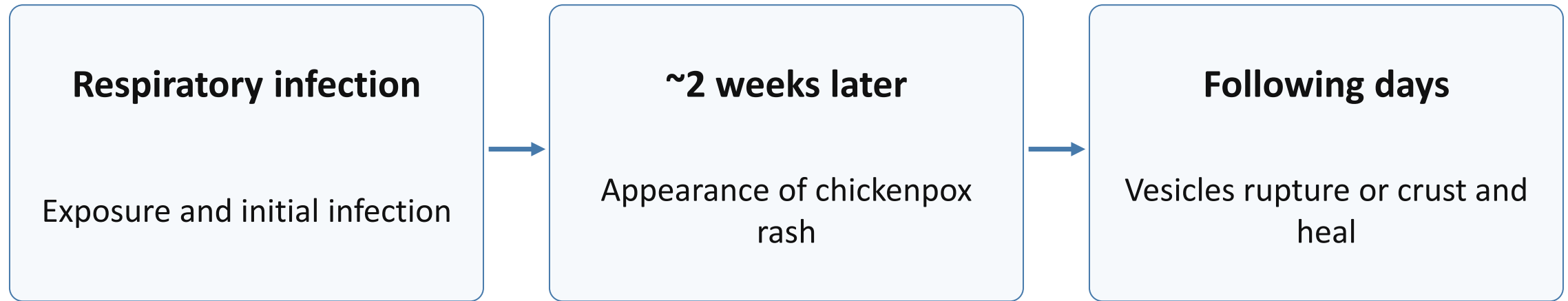
Immunocompetent child

- Primary chickenpox is generally mild.
- A primary infection usually resolves without permanent skin injury.

Adult or immunosuppressed host

- Primary chickenpox can be more severe.
- Severe or disseminated complications are more consequential.

The varicella rash follows a respiratory incubation



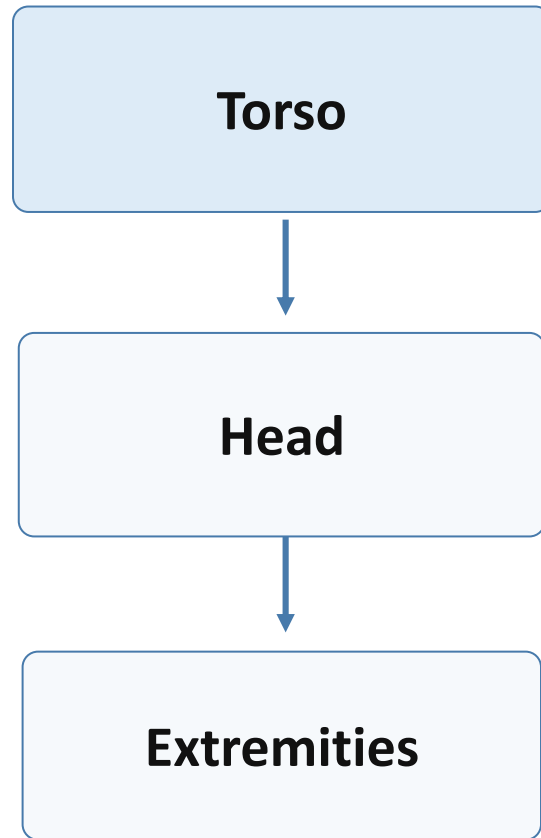
- “Approximately 2 weeks” is the interval specified in the Robbins morphology section.

Varicella lesions arise in successive waves

- New lesions appear in multiple crops rather than as one uniform eruption.
- At a given examination, lesions may be at different stages of evolution.
- This temporal heterogeneity is diagnostically informative when assessing a vesicular exanthem.

The exanthem spreads centrifugally from the torso

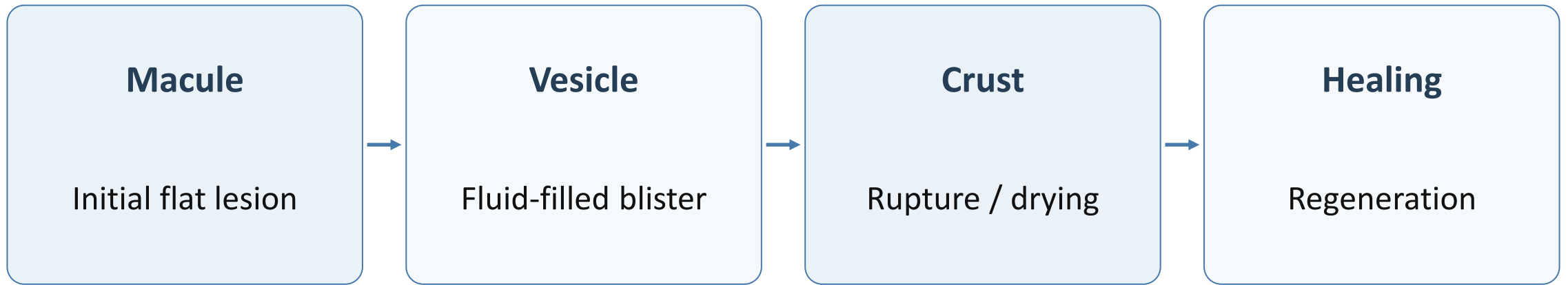
Source pattern: Torso → head and extremities.



The eruption is generalized rather than confined to a single dermatome.

Distribution and lesion timing should be interpreted together.

A varicella lesion progresses from macule to vesicle



- Most uncomplicated lesions heal without a scar.

“Dewdrop on a rose petal” describes the vesicle

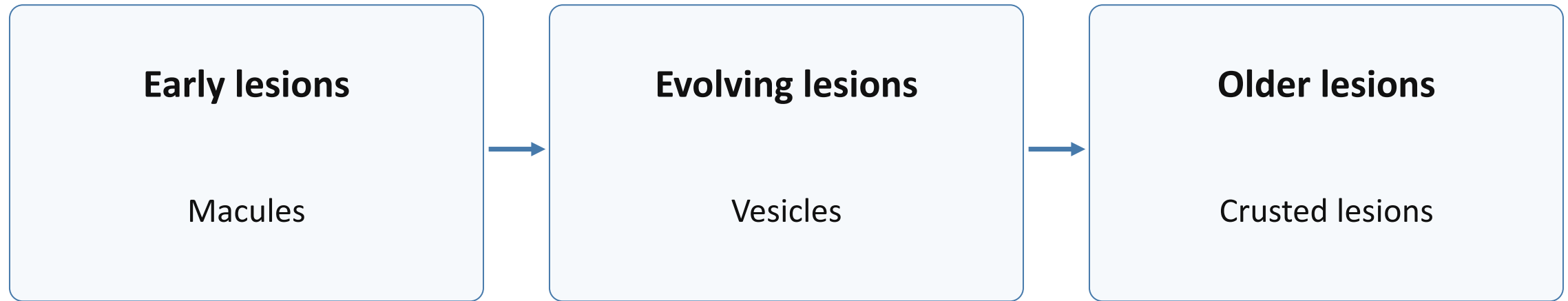
Visible lesion

- A delicate vesicle becomes the dominant feature.
- The phrase describes the clinical appearance, not a histologic diagnosis.

Histologic correlate

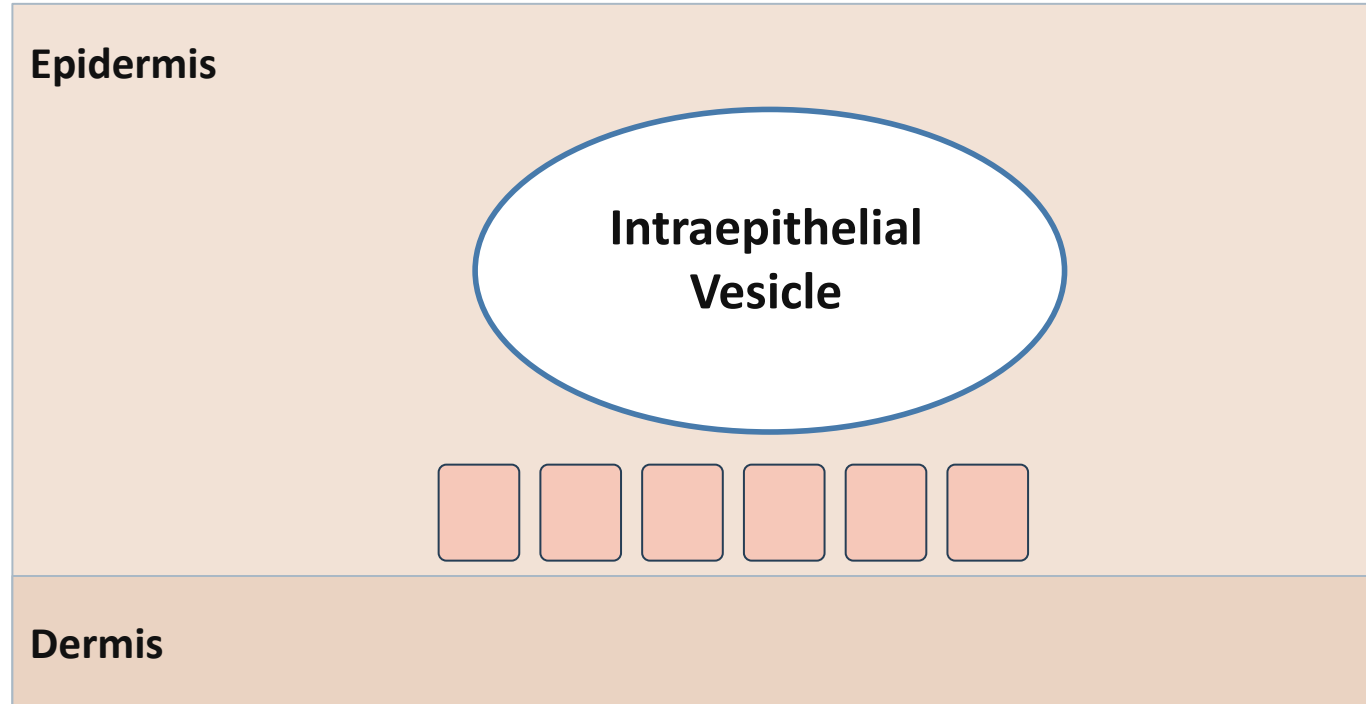
- An intraepithelial cavity forms within infected epidermis.
- Inclusion-bearing epithelial cells may line the vesicle base.

Different lesion stages can coexist



- Sequential crops account for coexistence of these morphologic stages.

VZV forms an intraepithelial vesicle

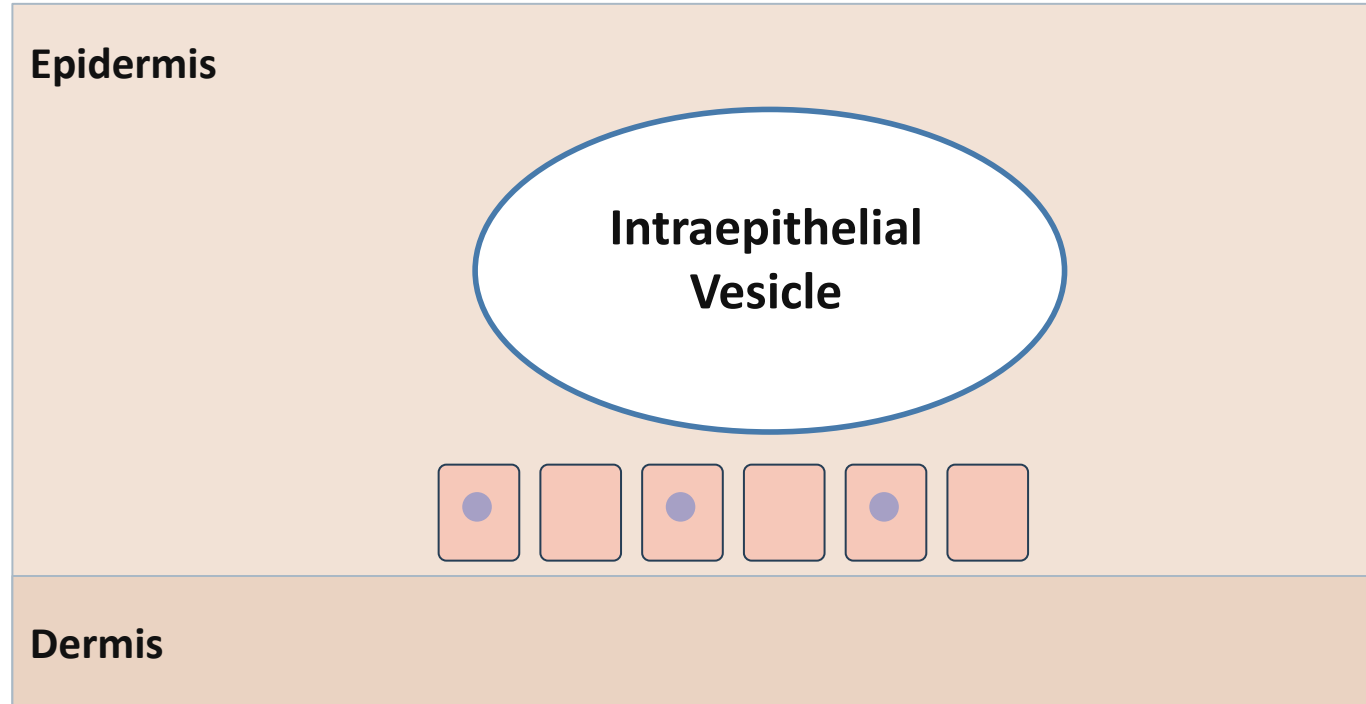


The vesicle cavity lies within epidermal epithelium.

Adjacent infected epithelial cells remain part of the blister architecture.

This is a simplified structural schematic—not a tissue photomicrograph.

Intranuclear inclusions identify infected epithelial cells



Viral inclusion bodies are found in epithelial cells at the base of the vesicle.

The inclusion is intranuclear, not an extracellular blister component.

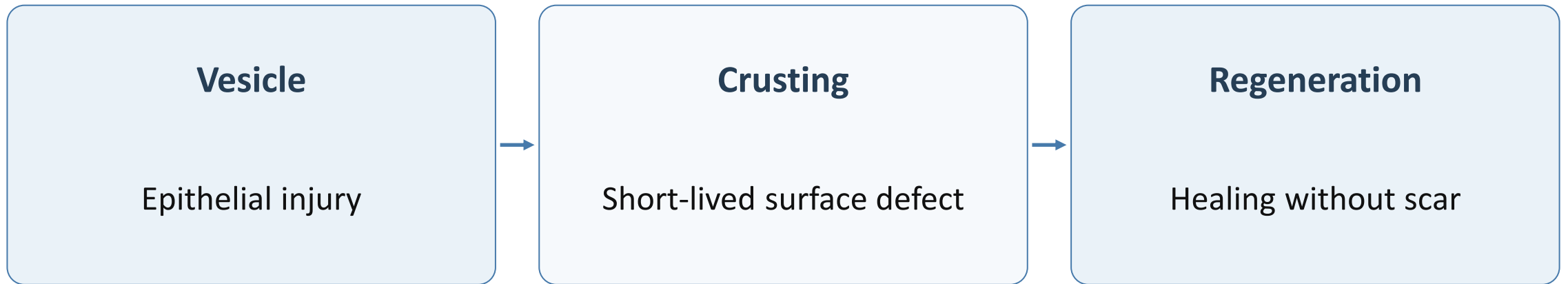
Other herpesviruses can produce similar cytopathic changes.

Intranuclear inclusions (schematic)

Herpesvirus nuclear inclusions require context

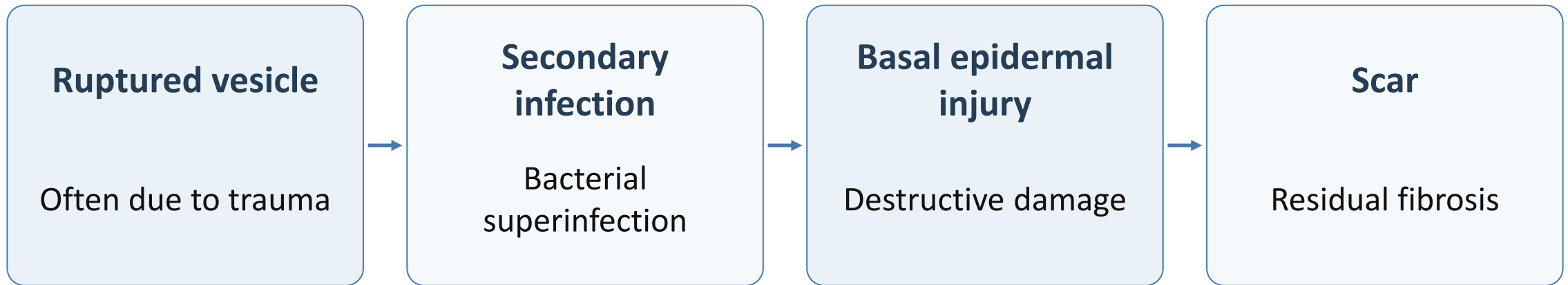
- Glassy intranuclear viral inclusions in a herpesvirus blister.
- Herpetic cytopathic morphology supports the virus family but does not independently distinguish VZV from HSV.
- Combine the distribution and clinical setting with pathogen-specific testing.

Most varicella lesions heal by regeneration



- Superficial lesions can resolve with preservation of regenerative epidermal structures.

Bacterial superinfection may result in scarring



- The extent of tissue destruction—not the mere presence of a vesicle—determines scarring.

Primary chickenpox and zoster have different origins

Chickenpox

Primary VZV infection

Respiratory exposure with bloodborne dissemination

Generalized eruption

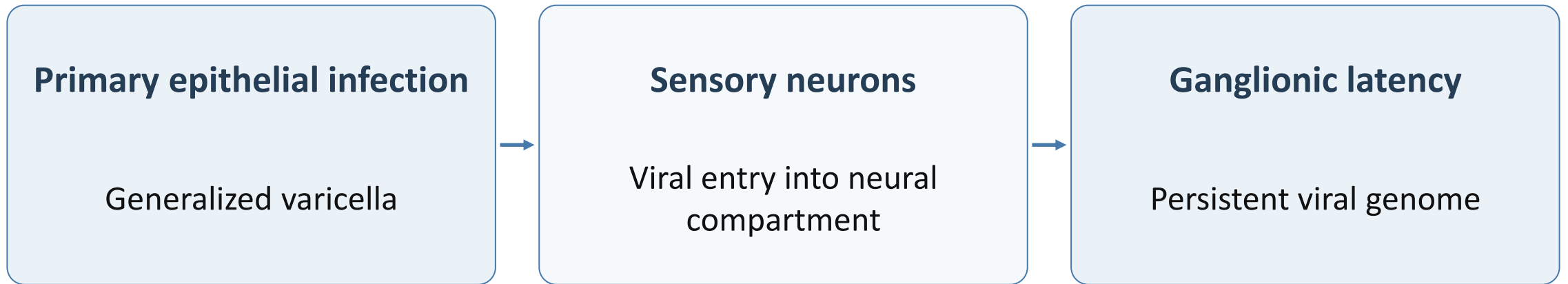
Shingles

Reactivation of previously latent VZV

Sensory-nerve spread to skin

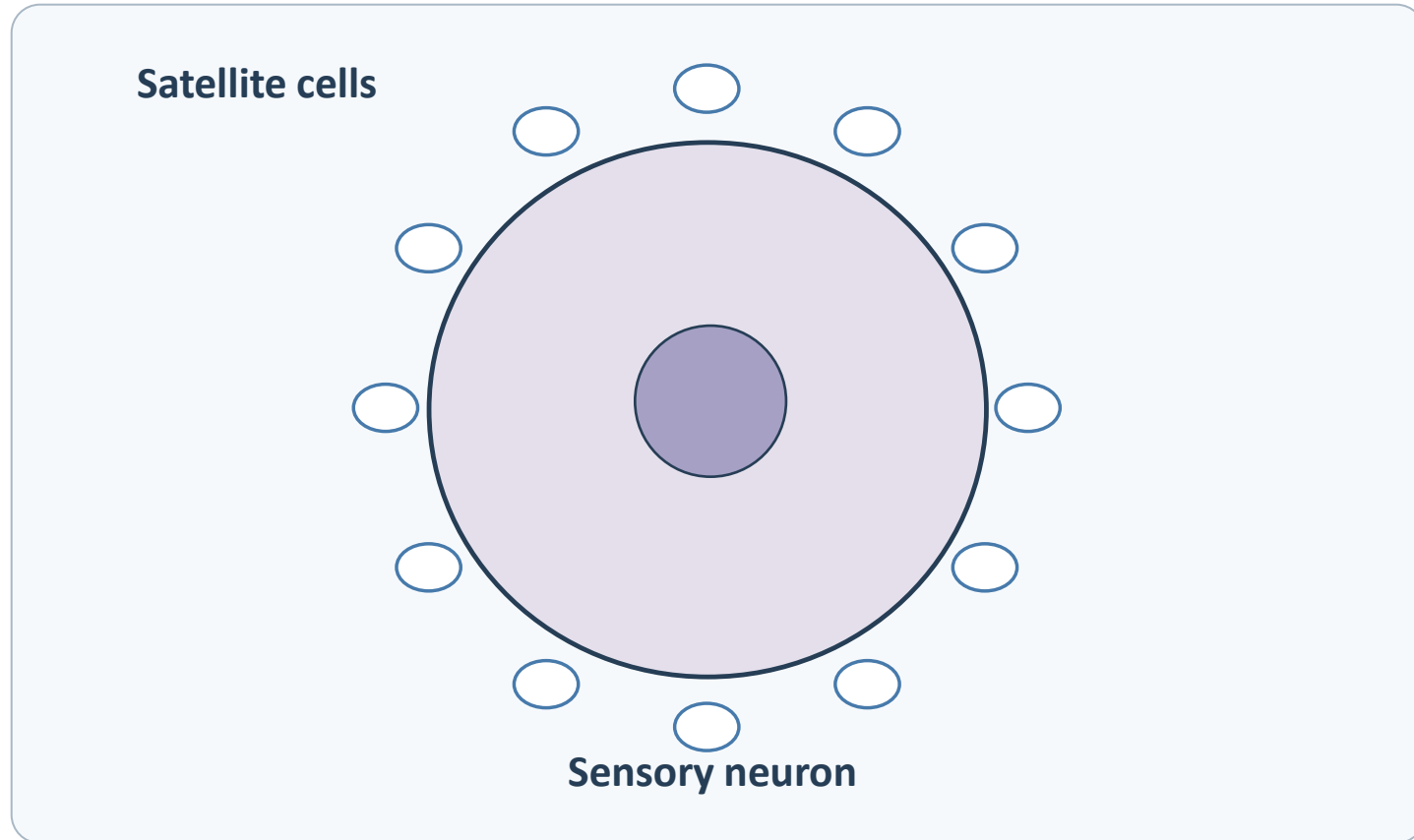
Localized dermatomal eruption

Latency develops after the primary eruption



- The skin's visible healing does not imply clearance of latent viral genomes.

Dorsal-root ganglia provide a latent reservoir



Schematic — no diagnostic micrograph

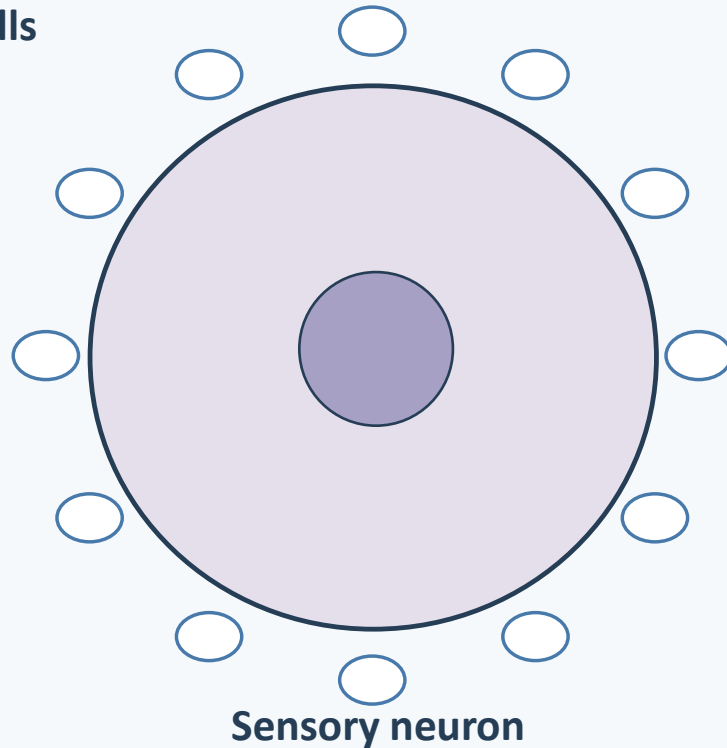
Latent VZV in sensory ganglia.

Neurons and/or their surrounding satellite cells may harbor the virus.

Latency explains long asymptomatic intervals between clinical syndromes.

Neurons and satellite cells are distinct ganglion compartments

Satellite cells



Sensory neuron

Large sensory neuronal cell bodies occupy the ganglion.

Satellite supporting cells surround neuronal somata.

The textbook recognizes latency in neurons and/or these neighboring cells.

Schematic — no diagnostic micrograph

A latent genome is not the same as infectious shedding

Latency

Viral genome persists in the host cell

No production of infectious virus

Clinically silent reservoir

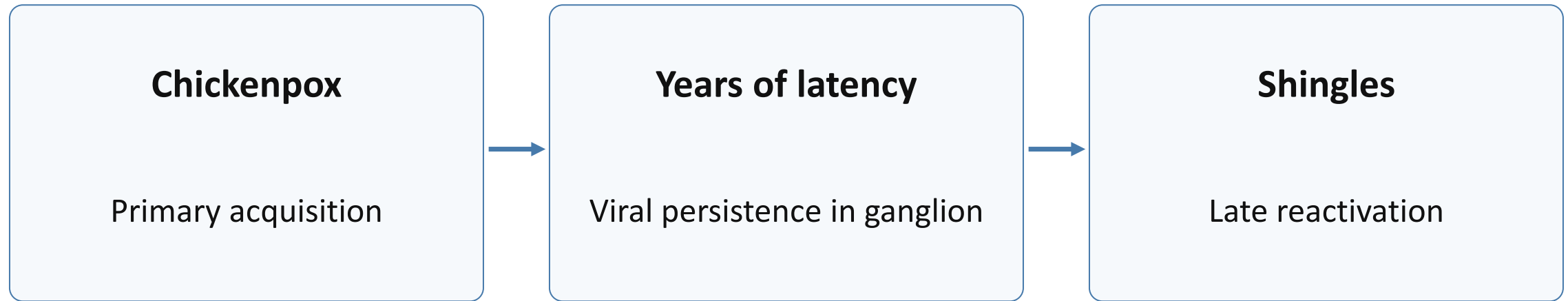
Reactivation

Productive viral replication resumes

Infectious virus may be released

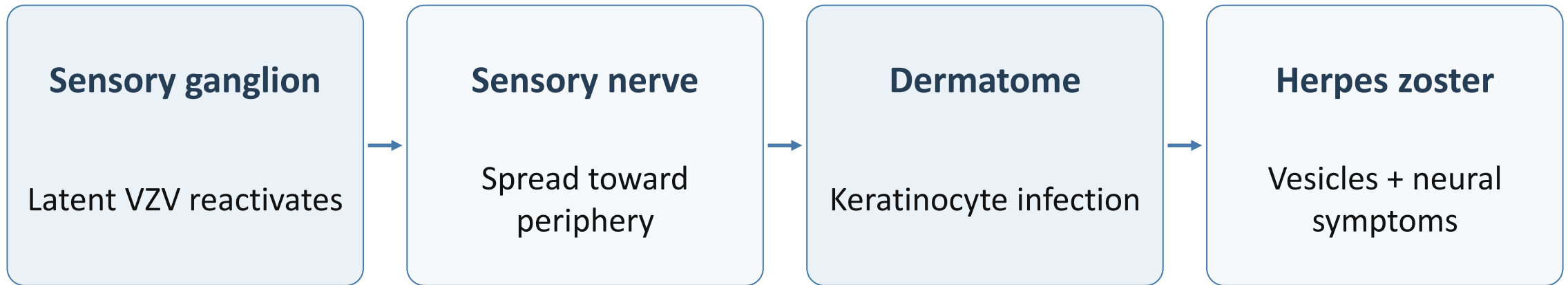
Skin and nerve injury can reappear

Reactivation may follow a long silent interval



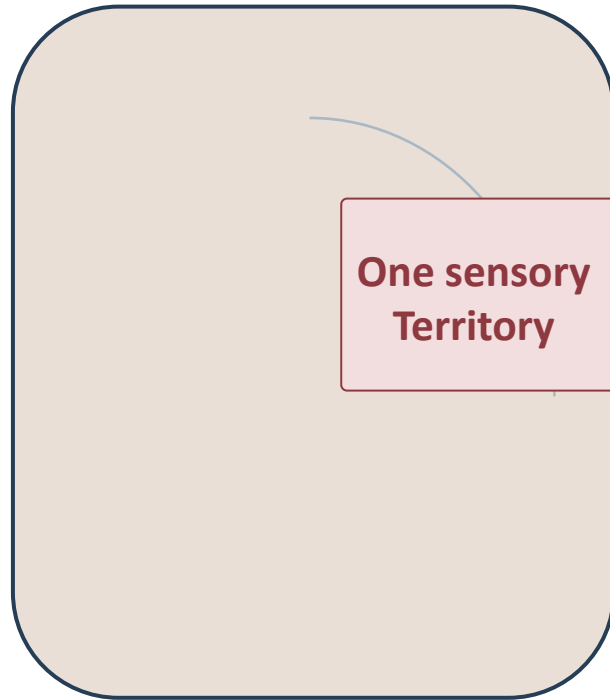
- That zoster can develop many years after chickenpox.

Reactivated virus reaches skin along sensory nerves



- The nerve pathway links the lesion distribution to the neural site of disease.

A dermatome maps cutaneous sensory innervation



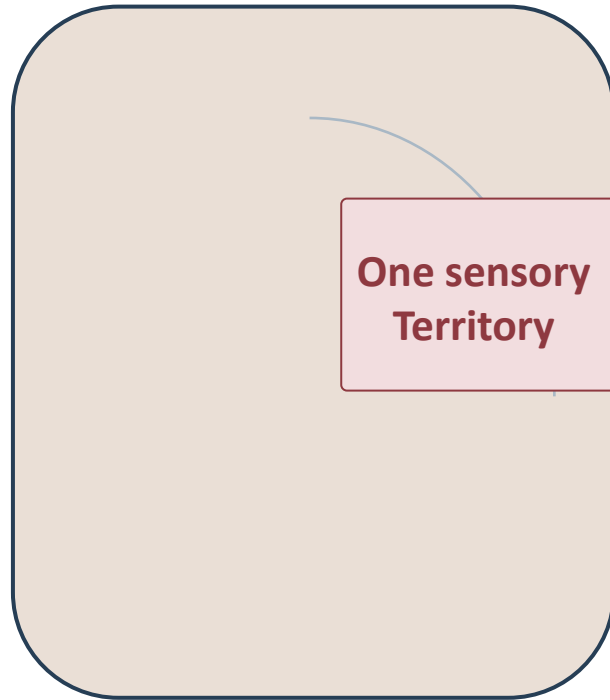
Schematic, not an anatomical dermatome map

Zoster is distributed in one or more dermatomes.

The involved territory reflects its sensory-nerve origin.

This is a localization schematic, not a precise dermatome atlas.

VZV reactivation produces localized cutaneous lesions



Schematic, not an anatomical dermatome map

The eruption is typically confined to one or several sensory territories.

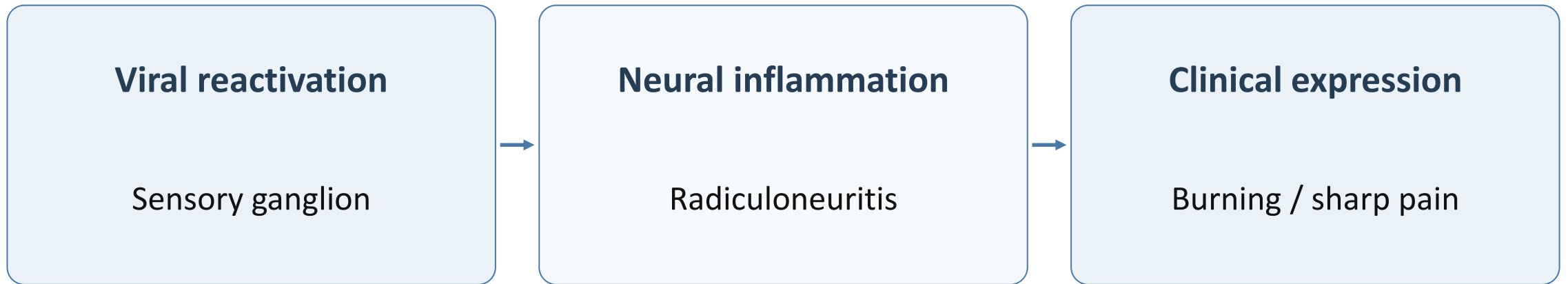
Infected keratinocytes generate vesicular lesions.

The cutaneous pattern differs from widespread hematogenous varicella.

Zoster produces neuropathic symptoms

- Intense itching, burning, or sharp pain may accompany the vesicles.
- Pain can be prominent because the sensory nerve roots are inflamed.
- The cutaneous disease and the neural pathology are parts of one process.

Radiculoneuritis explains the pain of shingles



- Pain is not explained solely by the visible epidermal vesicles.

Trigeminal involvement can be especially painful

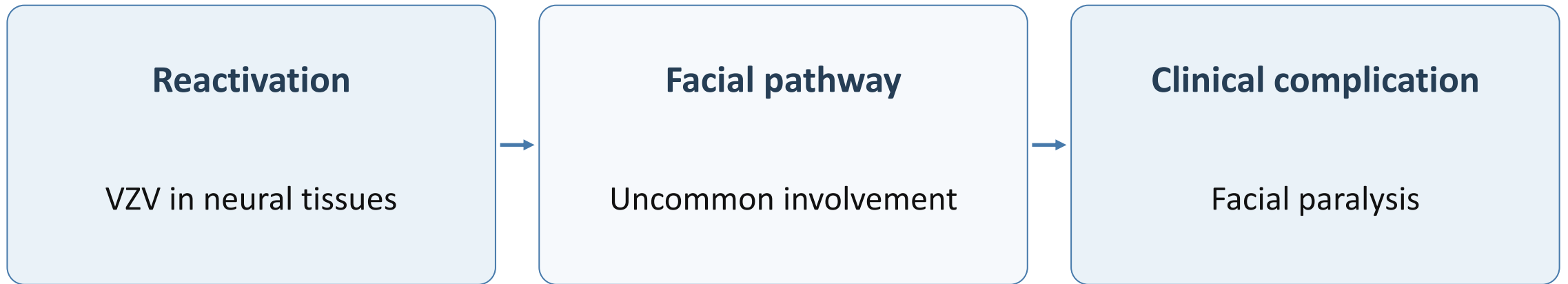
Ganglion location

- VZV latency may involve trigeminal sensory ganglia.
- Reactivation affects the sensory territory supplied by involved branches.

Clinical consequence

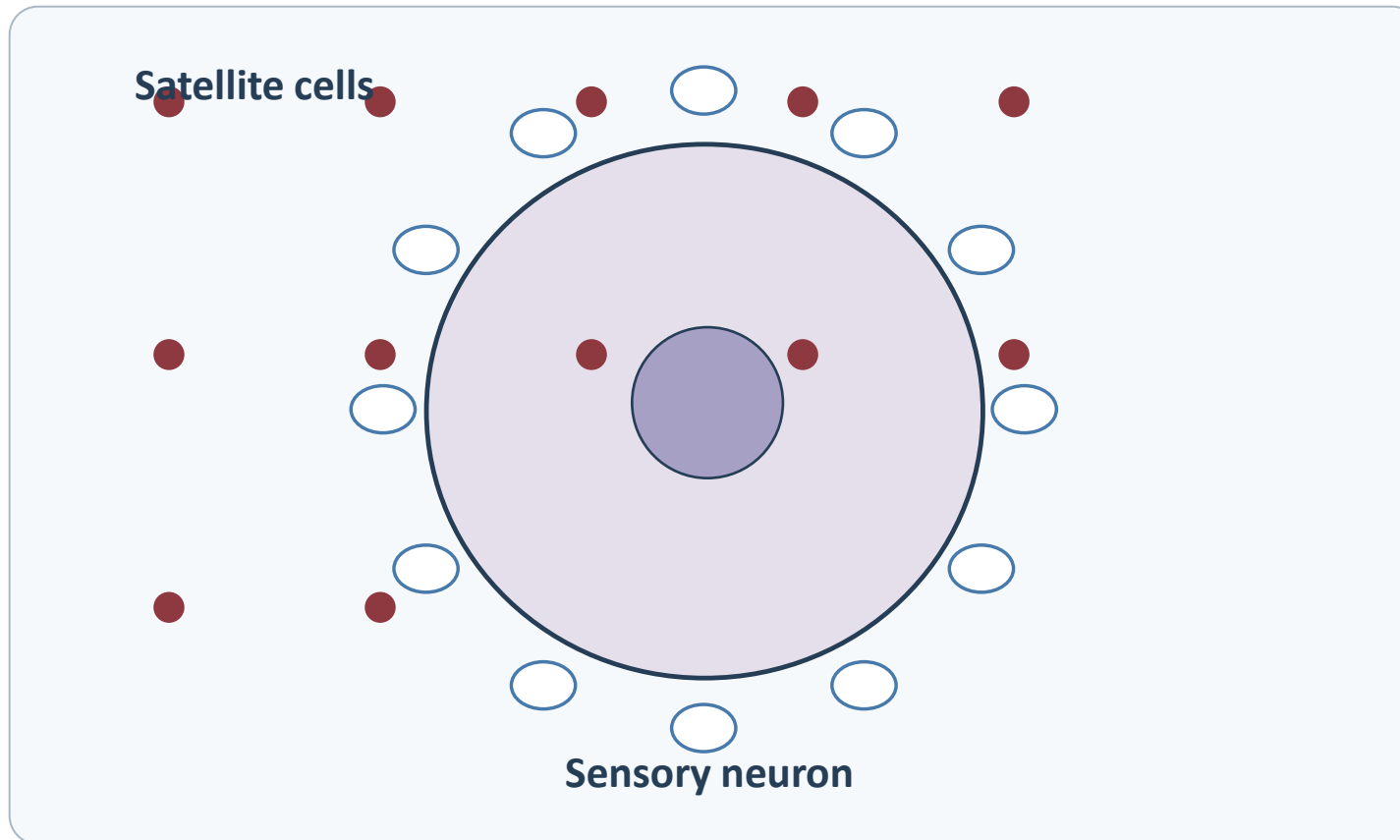
- Severe pain with trigeminal zoster.
- The site of neural involvement modifies morbidity.

Ramsay Hunt syndrome reflects facial-nerve involvement



- This as an uncommon complication.

Sensory ganglia develop inflammatory injury



Schematic — no diagnostic micrograph

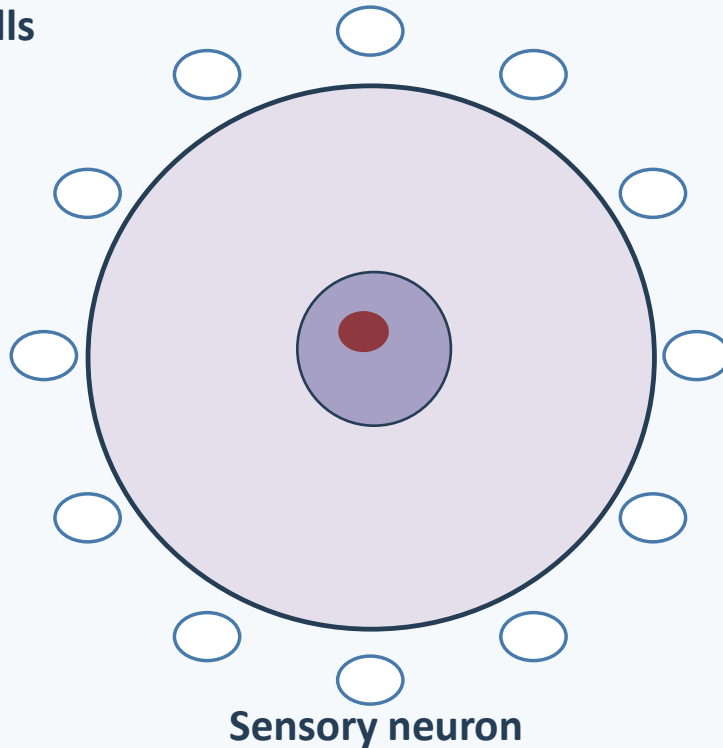
Zoster may produce a dense inflammatory infiltrate within sensory ganglia.

The cells are predominantly mononuclear.

Ganglionic pathology provides the anatomic basis for radicular pain.

Herpetic inclusions occur in ganglionic cells

Satellite cells



Sensory neuron

Intranuclear inclusions occur in neurons and supporting cells.

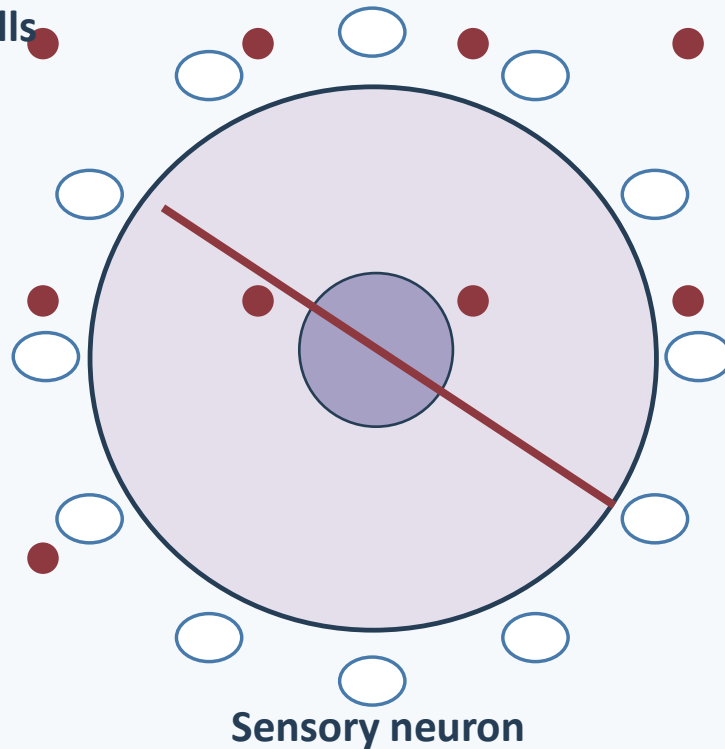
This indicates cytopathic infection beyond the skin.

Tissue observations complement the cutaneous distribution and symptoms.

Schematic — no diagnostic micrograph

Ganglion-cell necrosis is a recognized lesion

Satellite cells



Sensory neuron

Schematic — no diagnostic micrograph

Robbins Figure 8.14 identifies ganglion-cell necrosis with inflammation.

Neuronal injury links viral reactivation to nerve dysfunction.

The diagram shows relationships only; It is not the textbook micrograph.

Varicella and zoster differ in topography

Feature	Varicella	Herpes zoster
Timing	Primary infection	Reactivation after latency
Distribution	Generalized, multiple crops	One or several dermatomes
Symptoms	Vesicular exanthem	Neural pain + vesicles
Pathway	Bloodborne dissemination	Sensory-nerve spread

Their skin lesions share a herpetic pattern

Finding	Varicella	Herpes zoster
Vesicles	Intraepithelial	Keratinocyte infection causes vesicles
Nuclear inclusions	At base of vesicle	Herpetic changes in affected cells
Neural association	Latency follows primary episode	Radiculoneuritis accompanies lesions
Distribution	Generalized	Dermatomal

Recurrence is uncommon in immunocompetent hosts

- Repeat episodes of shingles in only approximately 1%–4% of infected immunocompetent individuals.
- Recurrence may occur more than once in older or immunosuppressed hosts.
- The quantitative statement is textbook-specific, not an updated contemporary population estimate.

Age and immunosuppression alter zoster morbidity

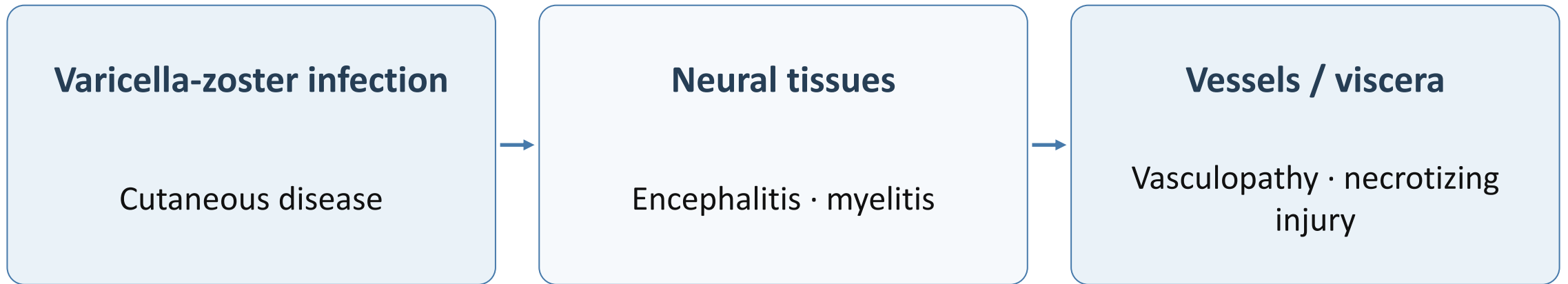
Older patients

- Herpes zoster can be a substantial source of morbidity.
- Postherpetic neuralgia is highlighted in the CNS chapter.

Immunosuppressed patients

- Multiple recurrences may occur.
- Severe organ complications and visceral injury are more concerning.

VZV complications extend beyond the skin



- The importance of these complications in immunosuppressed hosts.

Interstitial pneumonia is a visceral manifestation

- VZV can cause interstitial pneumonia.
- This establishes that disease may extend beyond the cutaneous and neural compartments.
- The possibility is particularly important in an immunosuppressed patient with VZV infection.

Encephalitis represents central nervous system involvement

- VZV is among the viral causes of encephalitis.
- Risk is influenced by host susceptibility, including TLR3 mutations.
- Severe neurological symptoms should not be interpreted as ordinary uncomplicated shingles.

Transverse myelitis is another neural complication

- The spinal cord can be affected during VZV infection.
- Transverse myelitis among possible complications.
- This differs anatomically from inflammation restricted to a peripheral sensory root.

VZV-associated vasculopathy affects blood vessels

Primary tissue target

- The vascular compartment can be involved in VZV disease.
- Vasculopathy among the recognized complications.

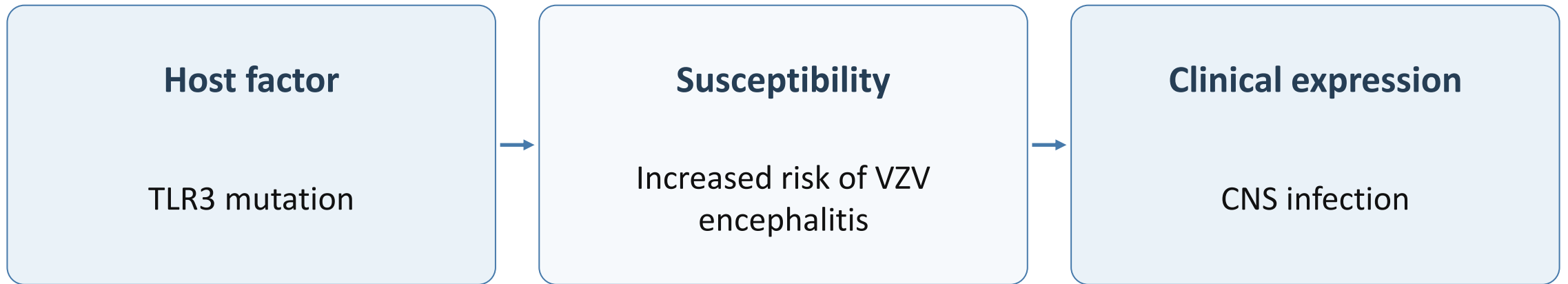
Clinicopathologic implication

- A neurologic syndrome may involve mechanisms beyond direct ganglion infection.
- Pathology must be interpreted in the full clinical context.

Visceral lesions may undergo necrosis

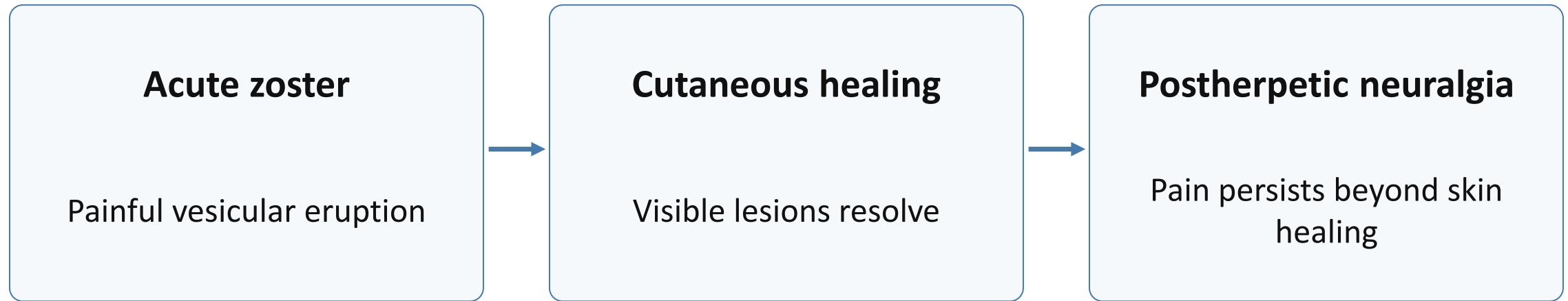
- VZV can produce necrotizing visceral lesions.
- Robbins especially associates severe visceral complications with immunosuppression.
- This is a major reason not to regard VZV exclusively as a cutaneous infection.

TLR3-associated susceptibility is relevant to encephalitis



- The source describes an association, not a deterministic outcome for carriers.

Postherpetic neuralgia persists after zoster



- Robbins Chapter 28 particularly emphasizes this complication in people older than 60 years.

Postherpetic neuralgia may include allodynia

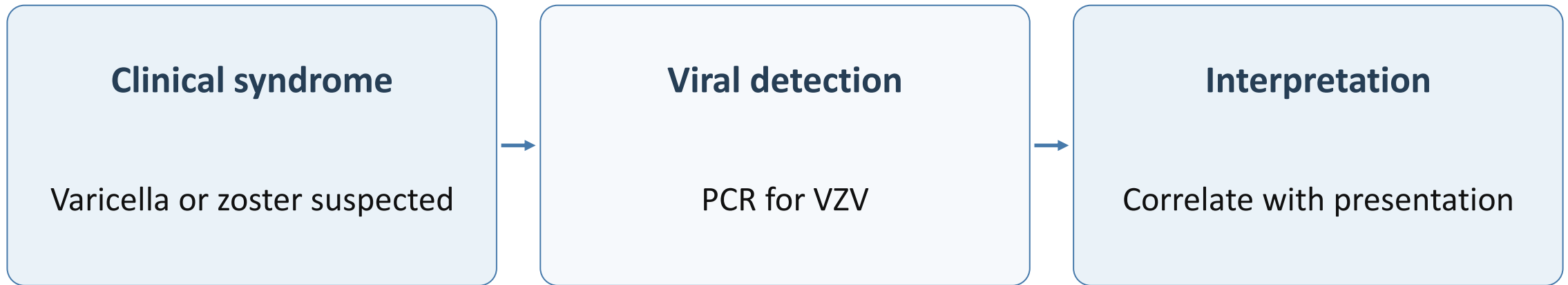
Persisting pain

- Pain can continue after the acute eruption resolves.
- It contributes to long-term morbidity after reactivation.

Stimulus sensitivity

- A normally nonpainful stimulus may provoke pain.
- This is a neuropathic clinical feature, not continued vesicular formation.

PCR is the principal diagnostic method described



- PCR as the primary diagnostic approach; Specimen-level protocols are not supplied in this excerpt.

Clinical context distinguishes VZV from HSV

Feature	VZV	HSV
Primary spread	Respiratory / hematogenous	Replicates at entry epithelium
Primary rash	Widespread crops	Often localized mucocutaneous
Reactivation	Often dermatomal zoster	Recurrent mucocutaneous disease
Latency	Sensory ganglia	Sensory neurons

Diagnosis integrates localization and viral detection

Pattern recognition

- Generalized lesions in multiple stages suggest primary varicella.
- Dermatomal painful vesicles suggest herpes zoster.

Etiologic confirmation

- VZV PCR is the principal method named.
- Herpetic inclusions alone are not uniquely VZV-specific.

Varicella vaccination prevents primary disease

- Robbins recommends a live attenuated VZV vaccine for children.
- The strategy addresses infection before later latency and reactivation.
- This presentation follows the textbook description, not a jurisdiction-specific vaccination schedule.

Recombinant vaccination targets shingles risk

- Robbins recommends recombinant zoster vaccination for adults older than 50 years.
- It also identifies younger adults at increased risk due to immunodeficiency or immunosuppression.
- Current local eligibility and schedules should be checked against local health-authority guidance.

Case 1 · generalized vesicular eruption

Hypothetical teaching case

- A previously well child develops successive crops of vesicles after a respiratory illness.
- Some lesions are early macules while others have crusted.
- The lesions occupy the torso, head, and extremities.

Clinical reasoning question

What mechanism explains the generalized, asynchronous eruption?

Case 2 · localized painful eruption

Hypothetical teaching case

- An older adult develops burning pain followed by vesicles in a localized sensory territory.
- The eruption is not generalized.
- The presentation occurs years after a childhood chickenpox episode.

Clinical reasoning question

Which tissue reservoir and route explain this pattern?

Case 3 · pain after visible lesions resolve

Hypothetical teaching case

- An individual older than 60 years had a painful dermatomal vesicular eruption.
- The skin has healed, but pain continues.
- Light touch can now provoke discomfort.

Clinical reasoning question

What persistent complication best explains the symptoms?

Case 4 · beyond cutaneous zoster

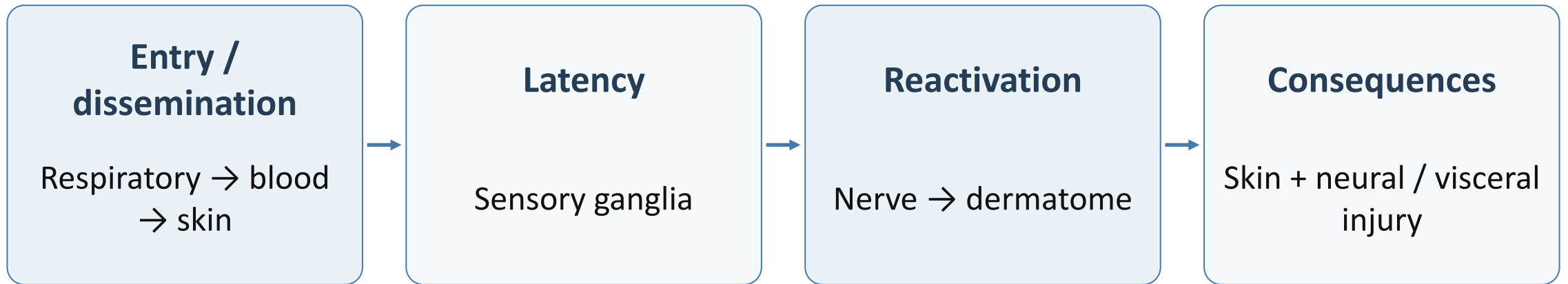
Hypothetical teaching case

- An immunosuppressed patient with VZV develops progressive systemic or neurologic findings.
- Localized skin morphology alone is insufficient to characterize the illness.
- Several noncutaneous VZV complications.

Clinical reasoning question

Which organ complications merit consideration?

Clinicopathologic synthesis



- Disease distribution is best explained by the changing anatomical route of viral spread.

What should the pathologist recognize?

- Cutaneous VZV creates intraepithelial vesicles with infected epithelial cells and intranuclear inclusions.
- Ganglionic VZV can show mononuclear inflammation, herpetic inclusions, and neuronal injury.
- Morphology is interpreted together with distribution, host status, neurologic findings, and PCR.

Principal source

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th edition (2026).

Infectious Diseases: herpesvirus latency and varicella-zoster virus.

The Central Nervous System: varicella-zoster virus and postherpetic neuralgia.