

Varicella-Zoster Virus

Latency, ganglion pathology, herpes zoster, and neurologic complications

Neuropathology and clinicopathologic correlations

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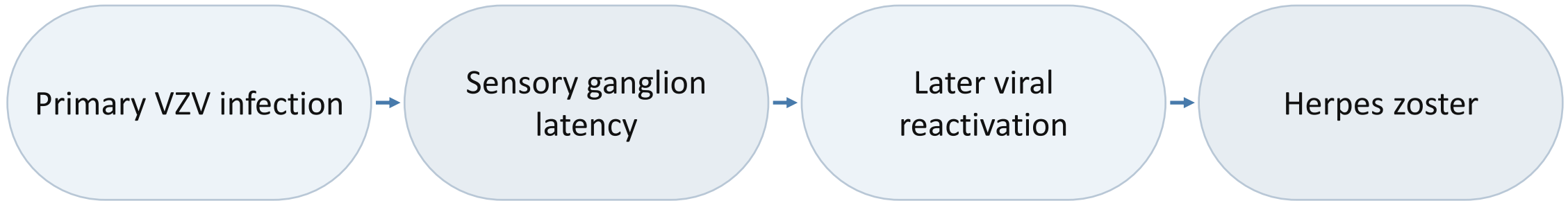
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Learning outcomes

- Explain how primary VZV infection establishes neuronal latency.
- Relate viral reactivation to dermatomal vesicles and radicular pain.
- Recognize ganglion, peripheral nerve, and CNS complications.
- Integrate morphology, clinical patterns, PCR diagnosis, and prevention.

One virus, two clinically distinct diseases



Primary infection causes chickenpox; Recurrent disease causes shingles.

Chickenpox versus herpes zoster

Chickenpox

Primary infection with VZV

Generalized vesicular eruption

Often milder in healthy children

May precede years of silent latency

Herpes zoster

Reactivation of latent VZV

One or several sensory dermatomes

Often pronounced neuropathic pain

Greater burden in older or immunosuppressed patients

Neural tropism explains long-term disease

- VZV involves mucosal epithelium, skin, and sensory neurons.
- Primary illness may resolve while viral latency persists in ganglia.
- Skin eruption and neural injury can therefore occur years apart.
- The recurrent rash identifies the peripheral sensory territory involved.

VZV and herpes simplex: Relevant distinctions

Varicella-zoster virus

Respiratory aerosol spread emphasized

Hematogenous dissemination during primary infection

Generalized chickenpox is characteristic

Infrequent symptomatic reactivation relative to HSV

Herpes simplex viruses

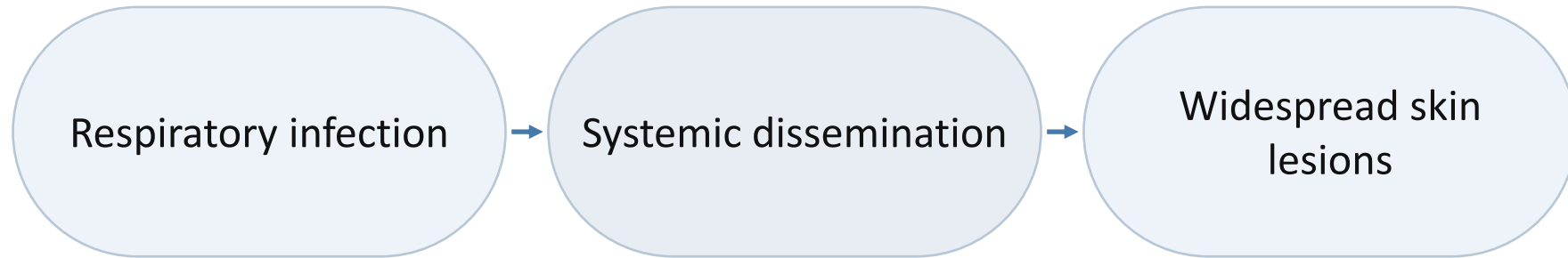
Related neurotropic herpesviruses

Classically localized mucocutaneous recurrence

Also establish latency in sensory neurons

Similar intranuclear cytopathic changes

From respiratory exposure to chickenpox



Respiratory aerosol transmission and hematogenous spread.

Primary infection is usually a systemic exanthem

- Chickenpox is the clinical expression of primary VZV infection.
- The skin eruption is widespread rather than segmental.
- In immunocompetent children, infection is often self-limited.
- Adults and immunocompromised people may experience more severe illness.

Distribution is a major diagnostic clue

Primary varicella

Lesions arise on the torso and spread to head and extremities

Multiple waves of new lesions

No single nerve territory explains the rash

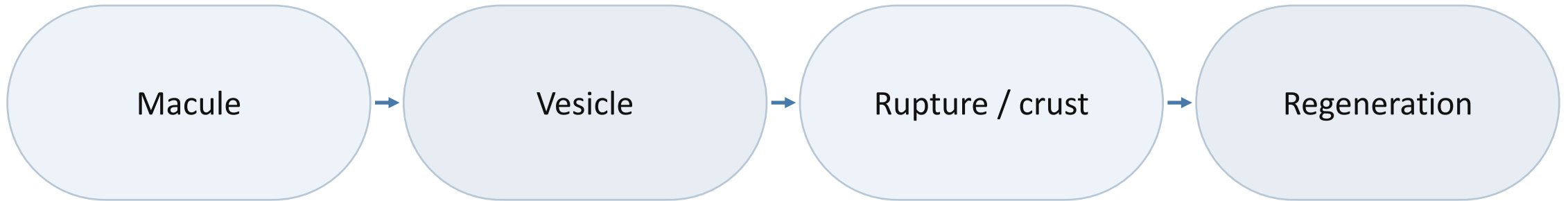
Reactivated zoster

Groups of vesicles in a sensory dermatome

One or several adjacent dermatomes

Pain can localize to the same nerve territory

Chickenpox rash: Lesion evolution

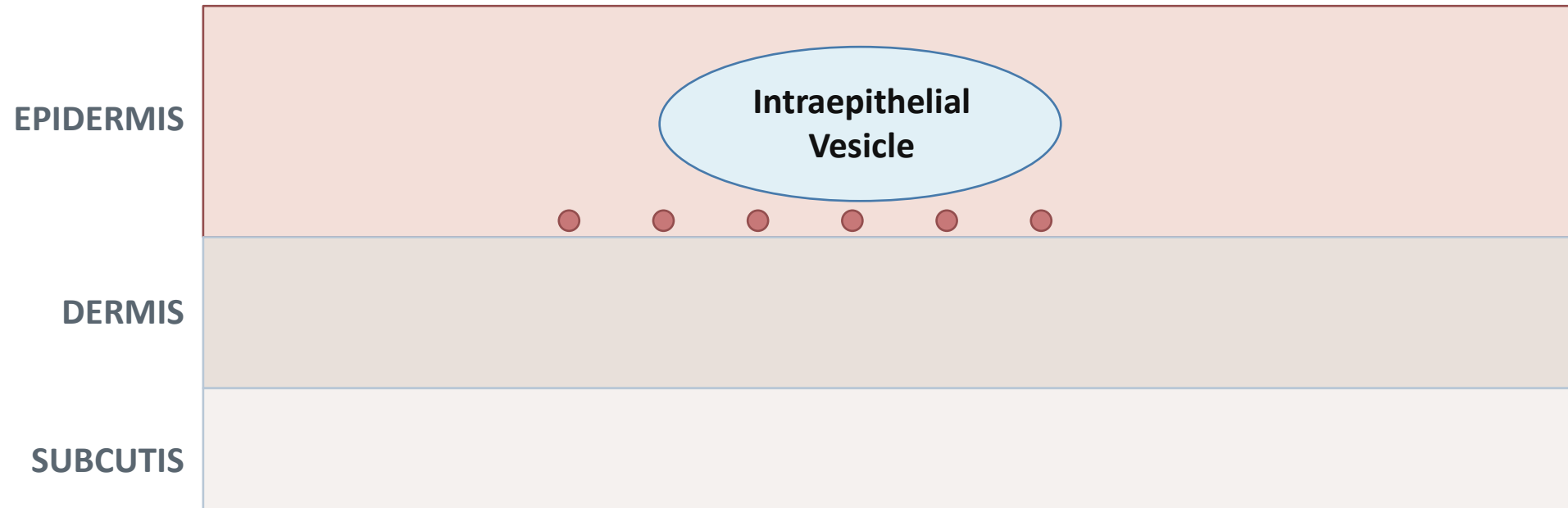


Individual lesions progress while additional crops may appear.

Chickenpox vesicles are intraepithelial

- Histologically, vesicular separation is located within the epithelium.
- Infected epithelial cells occur around the base of the vesicle.
- Viral cytopathic changes may include intranuclear inclusions.
- These are histologic features, not a substitute for viral identification.

Schematic: Intraepithelial skin vesicle

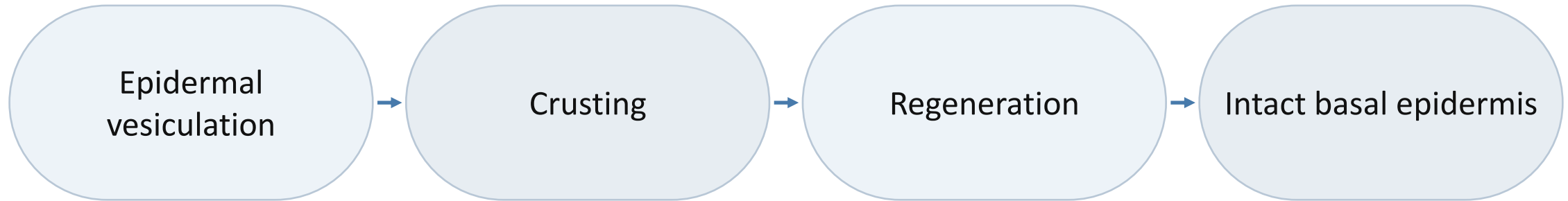


Original schematic — not an H&E micrograph

Viral inclusions: Anatomic context

- Herpesvirus-infected epithelial cells may show intranuclear inclusions.
- Glassy inclusions in a herpesvirus blister.
- Similar nuclear changes may occur with HSV; Morphology alone is not specific.
- Interpret viral cytopathic effects together with clinical findings and PCR.

Why uncomplicated lesions often heal without scars



Deep destruction is not a required feature of uncomplicated chickenpox.

Healing versus scar formation

Uncomplicated lesion

Vesicle ruptures and crusts

Epithelial repair follows

Typically no permanent scar

Trauma or superinfection

Additional tissue destruction can occur

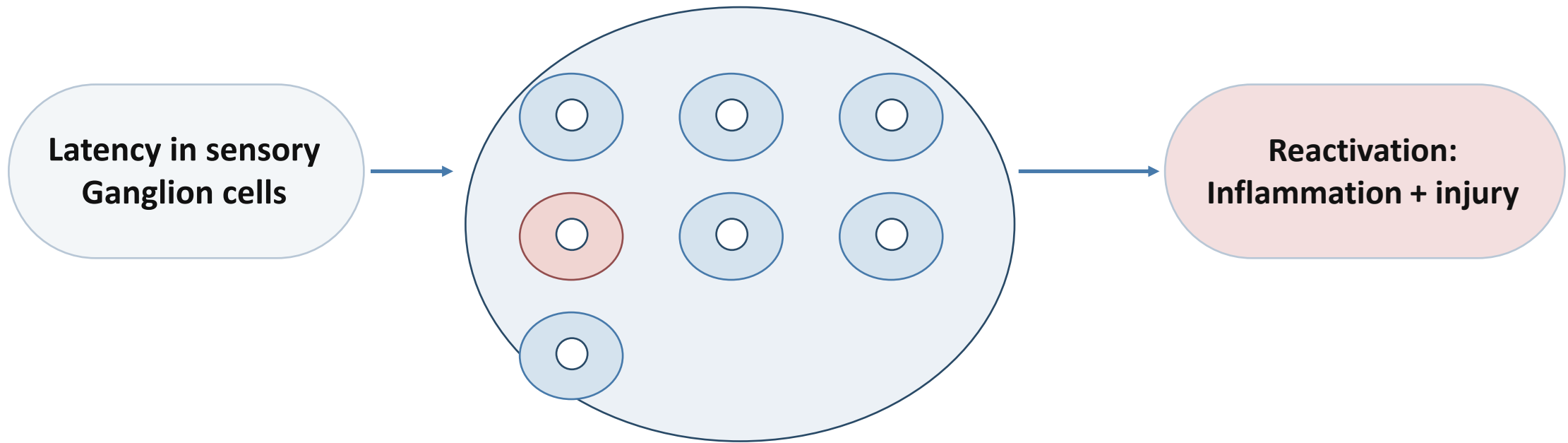
Basal epidermal layer may be damaged

Residual scarring can result

The end of chickenpox is not viral eradication

- Cutaneous lesions resolve while VZV enters a latent state.
- Latent virus is retained in peripheral sensory ganglia.
- The time between primary illness and reactivation may span decades.
- The subsequent disease is zoster, not a new generalized chickenpox episode.

Sensory ganglia as the reservoir of latency



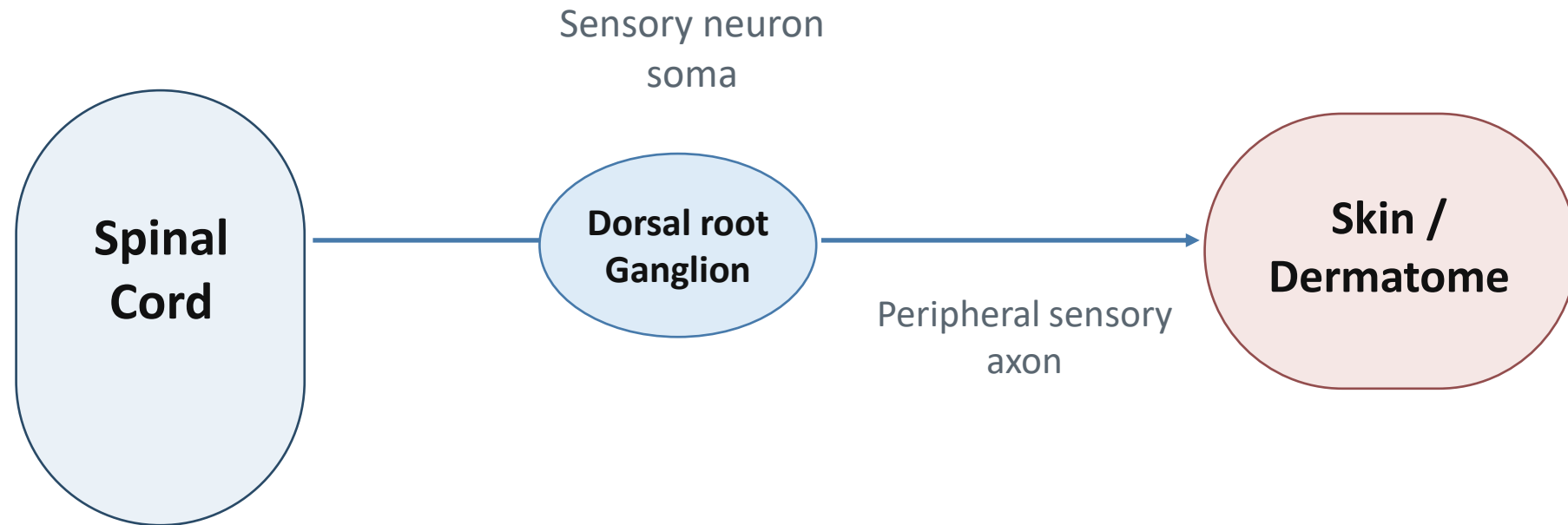
Ganglion cell bodies

Latent virus persists in neural tissue after skin disease resolves.

Dorsal root ganglia: Important neuronal reservoir

- Cell bodies of spinal sensory neurons lie in dorsal root ganglia.
- VZV latency has been described in neurons and associated satellite cells.
- A ganglion is anatomically linked to a defined cutaneous sensory territory.
- This link provides the anatomical basis of a dermatomal recurrence.

Sensory pathway: Ganglion to the skin

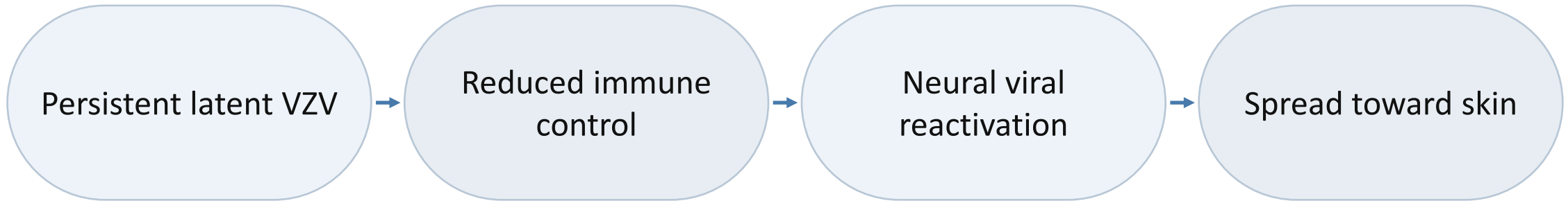


The affected ganglion connects the spinal sensory pathway to a dermatome.

Trigeminal ganglia: A second major reservoir

- The trigeminal system contains sensory neurons serving the face.
- Reactivation in this system can produce severe zoster pain.
- Trigeminal involvement is prominent among recurrent presentations.
- Clinical consequences depend on the neural distribution affected.

Reactivation begins inside a latent reservoir



Decreased cell-mediated immunity is suspected; Determinants are not fully understood.

Cell-mediated immunity is clinically relevant

- VZV persistence and clinical reactivation reflect host–virus interaction.
- Robbins implicates decreased cell-mediated immune control in reactivation.
- Risk rises with older age or immunosuppression.
- Not every latent infection leads to clinically apparent zoster.

Who is more vulnerable to zoster morbidity?

Older adults

Reactivation and pain complications are clinically important

Postherpetic neuralgia is emphasized particularly after age 60

Recurrent episodes may occur

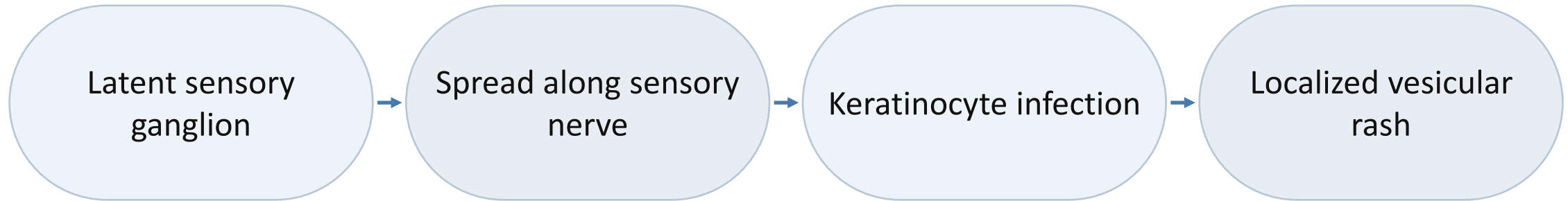
Immunocompromised people

Reactivation may be recurrent or extensive

Neural and visceral complications are important

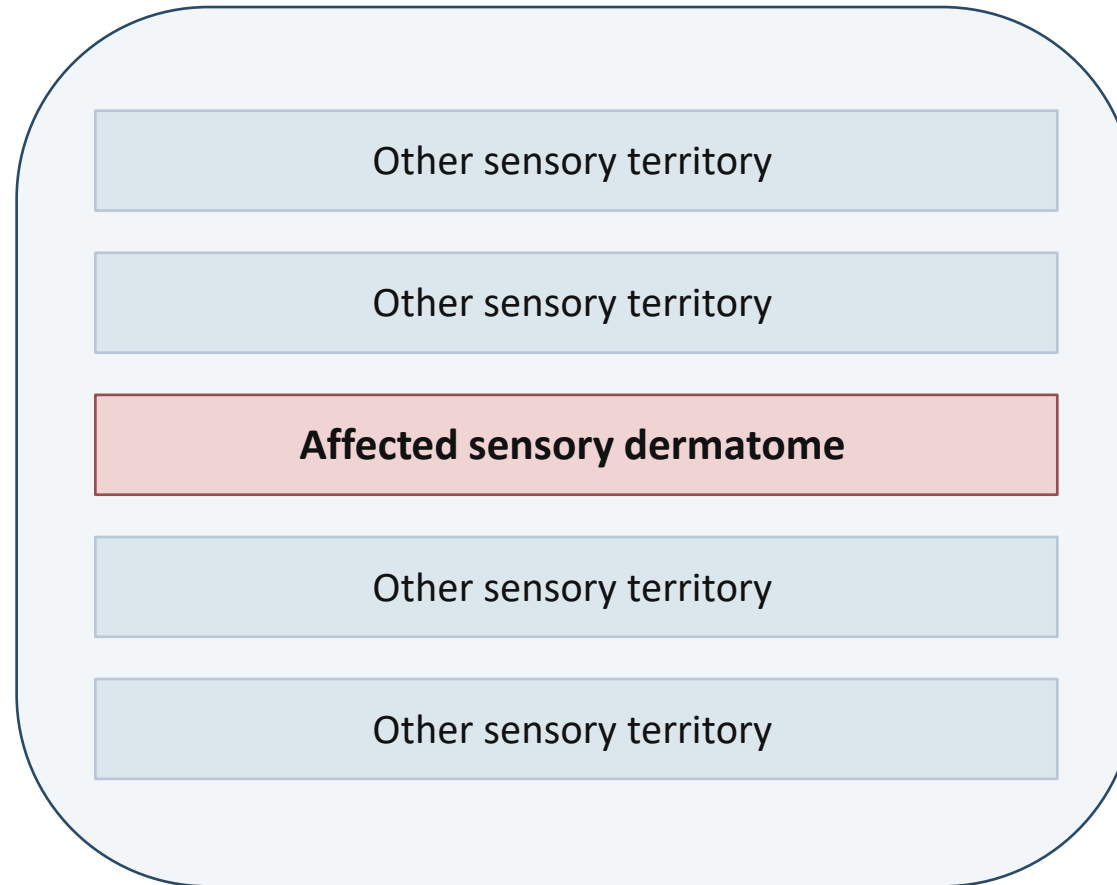
Disseminated infection requires particular attention

Axonal spread creates a dermatome-specific eruption



The neural projection determines the skin territory involved.

Dermatomal localization: Schematic



Schematic banded organization — not an anatomical atlas

Thoracic and trigeminal dermatomes are common

- Thoracic segments frequently produce a unilateral truncal eruption.
- Trigeminal sensory territories can produce facial zoster.
- Symptoms and vesicles usually share the same distribution.
- The dermatome pattern helps localize the infected sensory pathway.

A generalized rash is not the same as a dermatomal rash

Generalized distribution

More characteristic of primary varicella

Crops distributed across the body

Hematogenous dissemination is central

Segmental distribution

More characteristic of reactivated zoster

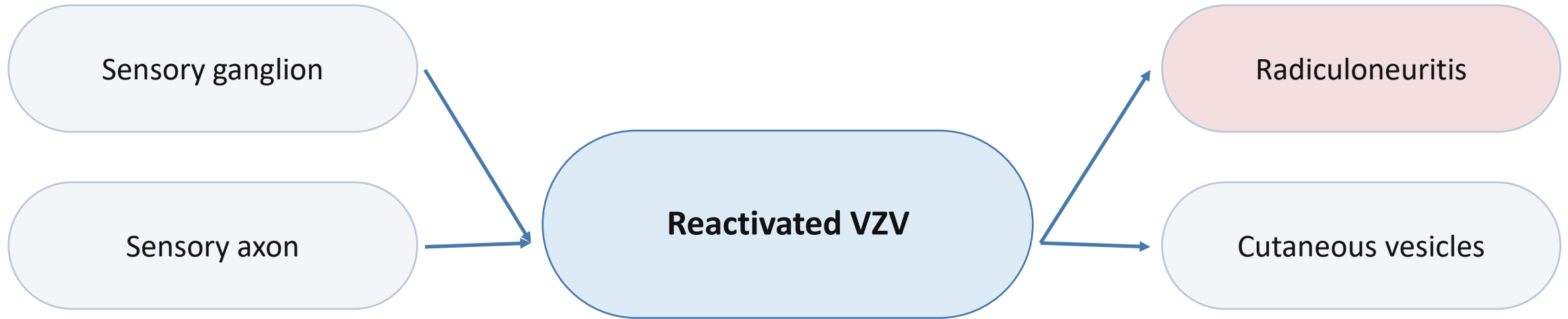
Grouped vesicles follow sensory innervation

Neural transport links ganglion to skin

Zoster skin lesions are more than cutaneous infection

- VZV infection of keratinocytes produces vesicular lesions.
- Concomitant radiculoneuritis can generate intense neuropathic pain.
- Burning, sharp pain, or itching may accompany the rash.
- Painful skin findings thus indicate possible sensory neural injury.

Three connected components of shingles



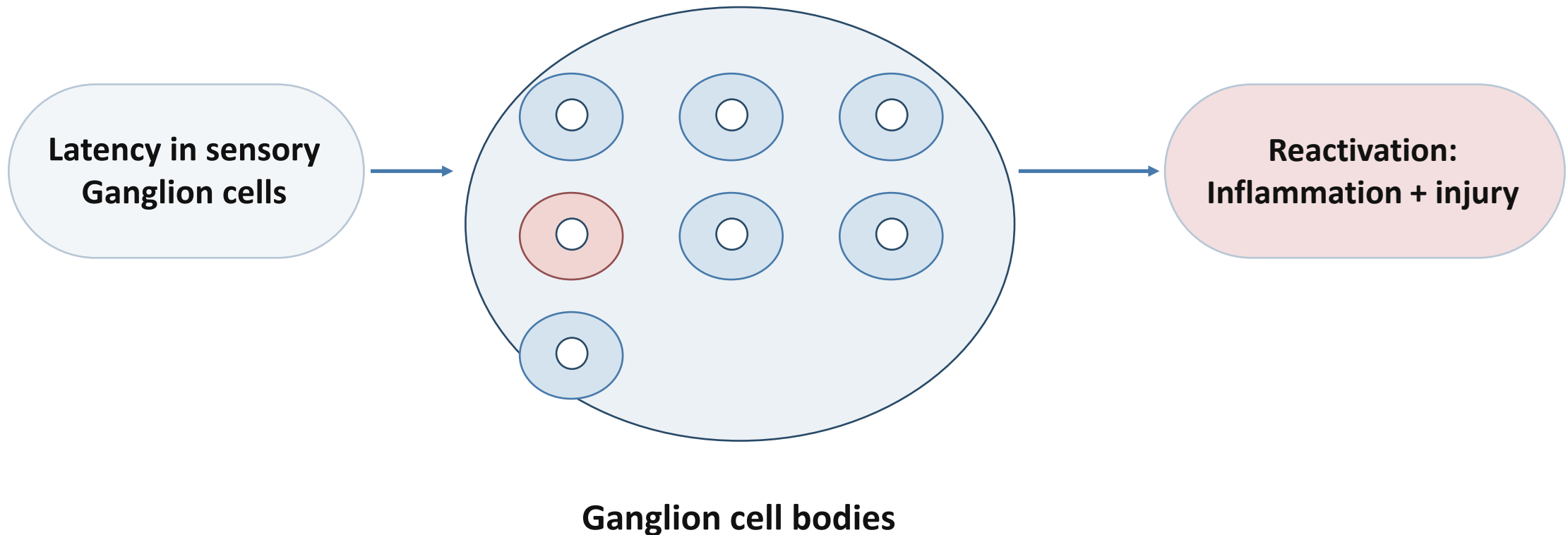
Localized zoster is usually self-limited

- The vesicular eruption commonly resolves as infection subsides.
- The course is not always free of lasting neural complications.
- Persistent pain can outlast the visible skin lesions.
- Older age is an important context when assessing this possibility.

Affected ganglia show inflammatory destruction

- Sensory ganglia may contain a dense mononuclear infiltrate.
- Infected ganglion neurons can undergo cell death.
- Focal necrosis and hemorrhage may accompany severe lesions.
- Inflammatory injury provides a structural basis for neural dysfunction.

Ganglion injury: Illustrated cellular pattern



Schematic of the sensory neuronal compartment; Not a micrograph.

Neuronal loss and inflammatory infiltration

Ganglion cell injury

Neuronal death can occur

Focal necrosis and hemorrhage may be present

Damaged neurons no longer maintain normal axons

Inflammatory response

Mononuclear inflammatory cells can be abundant

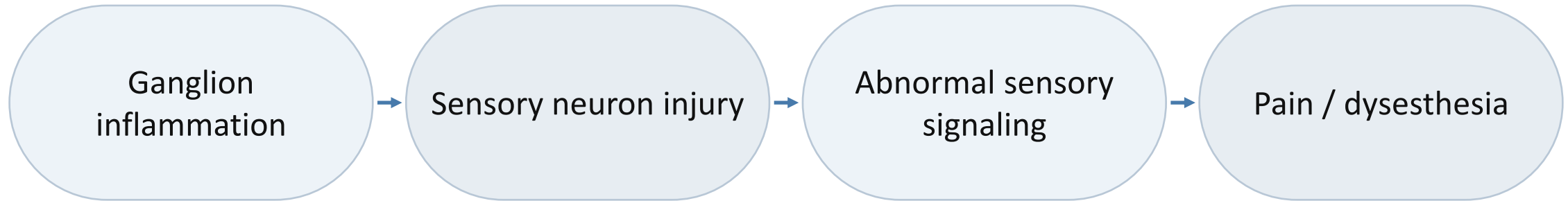
Inflammation involves the sensory ganglion

The process can extend into associated neural pathways

Peripheral axons degenerate after neuron loss

- Peripheral sensory fibers arise from ganglion neurons.
- Death of the neuronal cell body can produce axonal degeneration.
- Degenerating axons belonging to injured sensory neurons.
- This creates a link from viral ganglionitis to persistent sensory symptoms.

Neuropathic pain: A pathologic sequence



The sequence illustrates clinicopathologic interpretation, not a measured pathway.

Radiculoneuritis explains severe zoster pain

- Pain can arise from the inflamed sensory root and associated nerve.
- It may be described as burning, sharp, or intense.
- Pain distribution often corresponds to the rash distribution.
- Trigeminal zoster may be especially painful.

Postherpetic neuralgia: Persistence after eruption

- Pain can persist after the acute zoster eruption resolves.
- The syndrome is especially important in people older than 60 years.
- The involved sensory territory remains the clinical focus.
- Persistent pain demonstrates that neural damage can outlast skin infection.

Pain from active zoster versus postherpetic neuralgia

Acute zoster pain

Associated with vesicular skin disease

Radiculoneuritis accompanies active neural infection

Burning or sharp pain and itching may occur

Postherpetic neuralgia

Pain persists beyond cutaneous healing

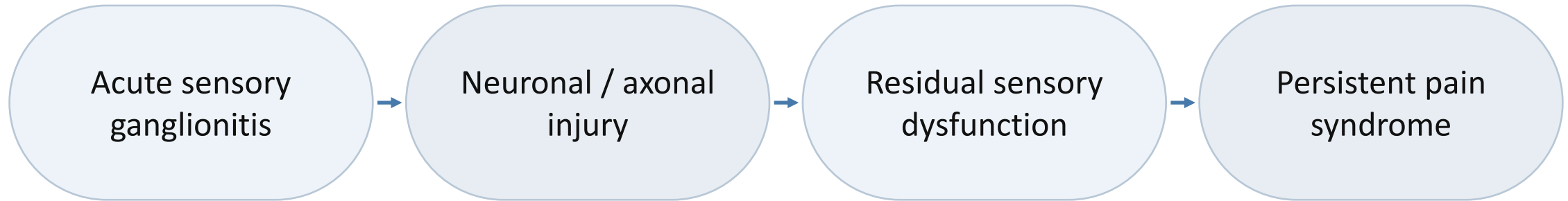
Often more important in older adults

Stimuli ordinarily not painful may evoke pain

Allodynia is a relevant clinical descriptor

- Allodynia is pain evoked by a stimulus that is normally not painful.
- Robbins explicitly identifies this phenomenon in postherpetic neuralgia.
- It indicates abnormal sensory processing in an injured pathway.
- A healed rash does not exclude ongoing neuropathic pain.

Why a healed rash may leave ongoing disability

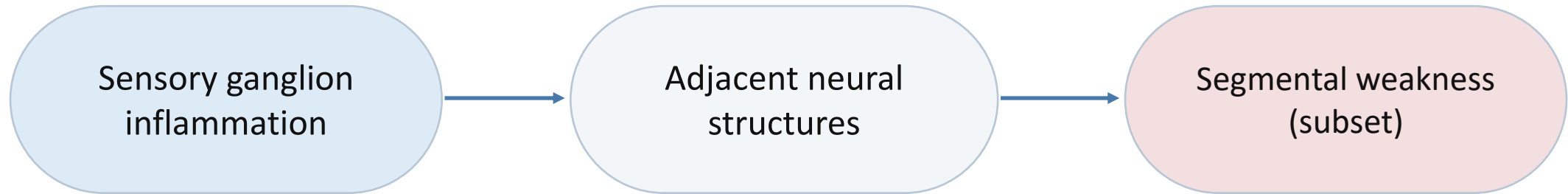


Postherpetic neuralgia is a neural complication rather than a persistent vesicular eruption.

Motor weakness is possible but less common

- Although VZV predominantly involves sensory ganglia, motor symptoms can occur.
- Weakness may follow a distribution related to the involved segment.
- Corresponding anterior horn motor neurons can be damaged.
- Cranial motor nuclei may also be affected at related levels.

From sensory ganglionitis to segmental weakness



Motor involvement occurs in a subset; Do not assume it in every patient.

Ramsay Hunt syndrome: Cranial nerve correlation

- VZV can involve the geniculate ganglion region.
- Associated facial nerve dysfunction may produce facial paralysis.
- This is a distinctive cranial neuropathic complication of zoster.
- A concurrent vesicular eruption and facial weakness should prompt consideration.

Neurologic disease extends beyond sensory ganglia

- VZV can cause encephalitis involving brain tissue.
- Transverse myelitis can involve spinal cord tissue.
- VZV vasculopathy is also a recognized complication.
- These are complications, not the usual course of primary chickenpox.

Neurologic complications: Site of injury



Encephalitis is a documented VZV complication

- Encephalitis among potential VZV manifestations.
- Central nervous system involvement is especially important in susceptible hosts.
- Such disease is conceptually distinct from uncomplicated dermatomal shingles.
- The source does not give a VZV-specific encephalitis morphology or frequency.

Transverse myelitis: Spinal cord involvement

- VZV can cause inflammatory disease of the spinal cord.
- Cord injury differs from peripheral sensory ganglionitis.
- Clinical localization helps separate cord syndromes from radiculopathy.
- Specific diagnostic criteria are not supplied in the selected Robbins excerpt.

VZV vasculopathy: Vascular nervous-system disease

- VZV vasculopathy is listed as a possible complication.
- Vascular involvement should not be conflated with ordinary radicular pain.
- The source establishes the association but gives no subtype classification.
- Avoid assuming every neurologic deficit reflects ganglionitis alone.

Two neurologic compartments to distinguish

Peripheral sensory system

Sensory ganglion inflammation

Axonal degeneration / radiculoneuritis

Dermatomal pain, sometimes weakness

Central nervous system

Encephalitis

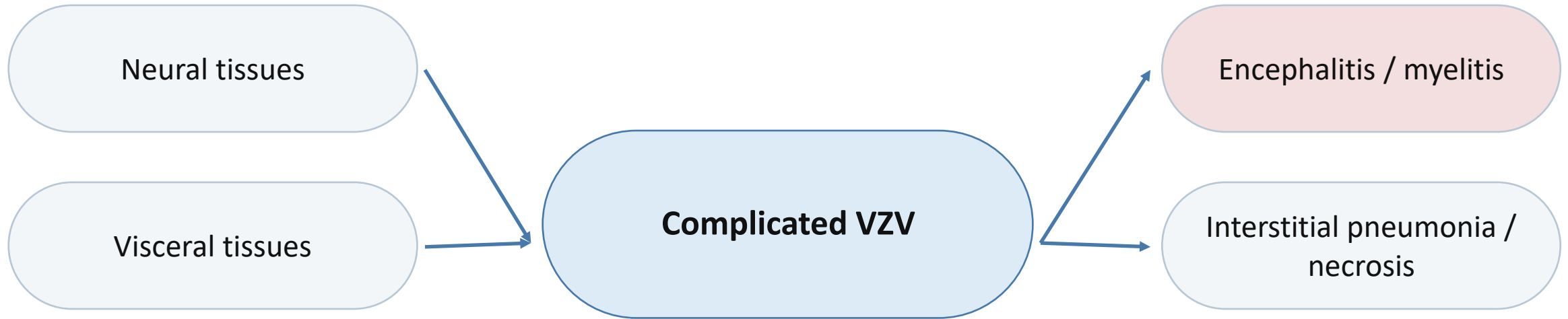
Transverse myelitis

Vasculopathy affecting neurologic function

Immunosuppression changes the severity spectrum

- Severe primary infection and zoster may occur in immunocompromised people.
- Complications can extend beyond skin and peripheral nerves.
- Interstitial pneumonia and necrotizing visceral lesions.
- Encephalitis, myelitis, and vasculopathy are also recognized.

Beyond skin: Distribution of complicated infection



Host susceptibility: TLR3 is an example

- Certain TLR3 mutations with greater susceptibility to VZV encephalitis.
- This is a genetic susceptibility observation, not a universal mechanism.
- VZV risk still depends on broader host immune competence.
- The excerpt does not define a clinical genetic-testing algorithm.

PCR is the primary method cited for VZV diagnosis

- Polymerase chain reaction as the primary diagnostic method.
- PCR detects viral nucleic acid rather than inferring the organism from morphology.
- Interpret results in the context of the clinical syndrome and sampled site.
- The excerpt does not specify specimen protocols, test thresholds, or sensitivities.

Morphologic clues and their limitations

Finding	What it supports	What it cannot prove
Intraepithelial vesicle	Viral vesicular cytopathic injury	VZV species on its own
Intranuclear inclusions	Herpesvirus-type cell injury	VZV versus HSV identification
Ganglion neuron loss	Neural damage in zoster context	A unique cause without testing
Mononuclear ganglionitis	Inflammatory response in ganglion	Viral identity without corroboration

Distinguishing VZV from HSV clinically

Evidence favoring VZV

Primary generalized chickenpox history

Later painful dermatomal shingles

Latency in sensory ganglia

VZV PCR for confirmation

Potential overlap with HSV

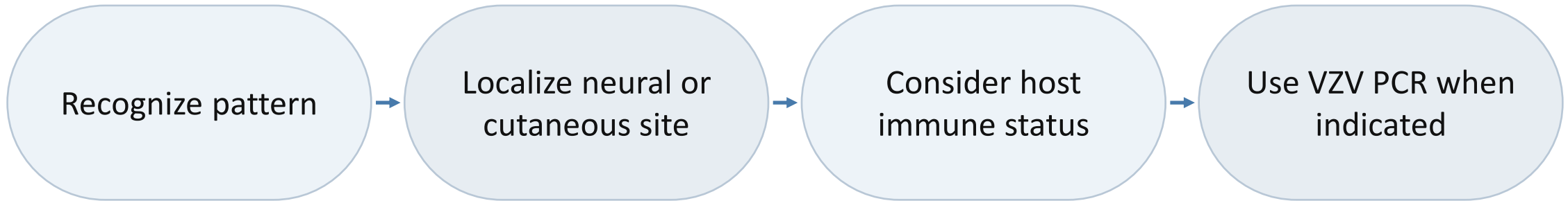
Both are neurotropic herpesviruses

Both may produce vesicular skin lesions

Both may cause intranuclear inclusions

Morphology alone may not distinguish the agents

A practical diagnosis framework



Clinical interpretation remains essential; No sensitivity or algorithmic cutoff is claimed.

Prevention targets two phases of VZV disease

Primary infection prevention

Live attenuated varicella vaccination in childhood

Aims to prevent chickenpox and its sequelae

Exact local schedules vary

Reactivation complication prevention

Recombinant zoster vaccination in adults over 50

Also for younger adults at increased risk

Targets zoster and related complications

Vaccination relevance to neuropathology

- Latent infection makes the burden of VZV extend beyond childhood.
- Preventing reactivation reduces potential neural morbidity.
- Postherpetic neuralgia is a particularly relevant outcome.
- The selected text does not supply country-specific vaccine schedules.

Clinical application: Generalized vesicles

A previously healthy child develops crops of widespread vesicular lesions after a respiratory illness. Lesions at different stages are present across the torso and extremities.

What is the most likely infection phase?

Primary varicella (chickenpox), with systemic cutaneous dissemination.

Clinical application: Dermatomal pain

An older adult develops a painful band of grouped vesicles along one side of the trunk. Burning pain localizes to the same region.

What makes this a neural disorder as well as a skin disease?

Reactivated VZV travels along a sensory pathway and may cause radiculoneuritis.

Clinical application: Pain after healing

After a shingles rash resolves, a person reports persistent pain when light clothing contacts the previously affected skin.

Name the key complication and sensory phenomenon.

Postherpetic neuralgia with allodynia.

Clinical application: Facial paralysis

A patient with shingles develops facial weakness associated with cranial nerve-region vesicular disease.

Which named zoster-related neurologic syndrome is relevant?

Ramsay Hunt syndrome: VZV-associated facial nerve involvement.

Clinical application: Immune compromise

An immunosuppressed adult with vesicular VZV disease develops systemic and neurologic symptoms rather than a limited cutaneous eruption.

What complications must be kept conceptually separate from simple zoster?

Visceral disease, encephalitis, myelitis, and vasculopathy.

Integrated pathology: Skin and nervous system

Cutaneous pathology

Macules evolve into intraepithelial vesicles

Viral nuclear inclusions may be present

Uncomplicated lesions crust and regenerate

Neural pathology

Latency persists in sensory ganglia

Reactivation causes inflammatory neuronal injury

Radiculoneuritis, axonal injury, and PHN can follow

Five clinicopathologic conclusions

- Primary varicella and herpes zoster are two phases of one infection.
- Sensory ganglion latency is the bridge between those phases.
- The neural distribution determines the recurrent skin eruption.
- Ganglion injury explains acute pain and possible persistent neuralgia.
- PCR and preventive vaccination complement morphologic understanding.

Selected textbook reading

Core reference

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

Relevant sections

Varicella-Zoster Virus — infections and neuropathology.

Peripheral nerve infections and viral diseases of the central nervous system.