Interventional Treatments for Postherpetic Neuralgia

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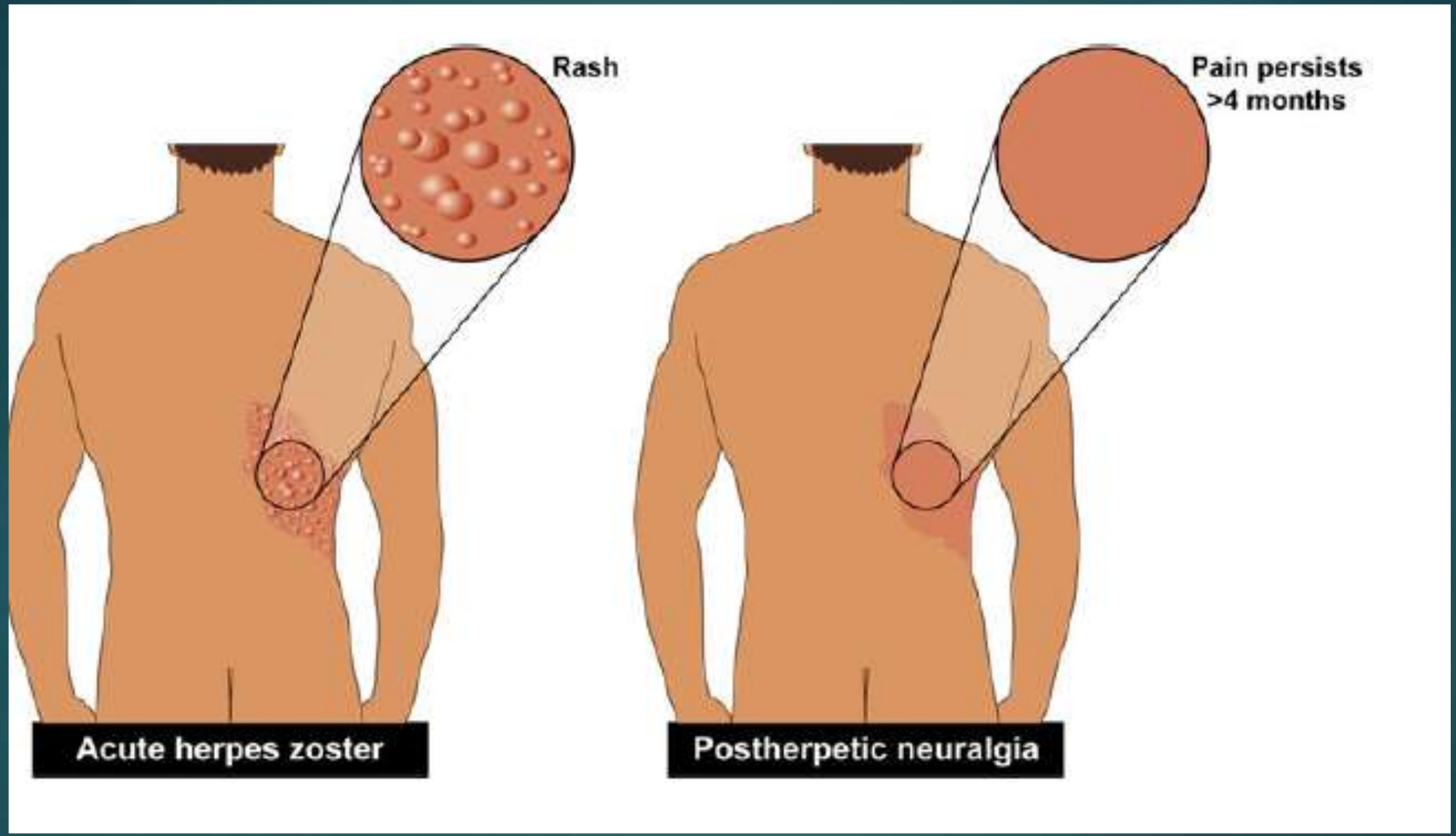
PAIN FELLOWSHIP

Post herpetic neuralgia

- One of the most resistant chronic pain problems, commonly affecting elderly patients.
- It presents as a pain that persists after the resolution of the rash caused by herpes zoster (HZ).

Pain associated with herpes zoster has three phases:

- An acute herpetic neuralgia: where the pain that accompanies the rash lasts up to 30 days after the onset of rash.
- Subacute herpetic neuralgia :that lasts for 30 – 120 days after the onset of rash
- Post-herpetic neuralgia, where the pain persists beyond 120 days after the onset of rash.


Rash
Pain persists
>4 months
Acute herpes zoster
Postherpetic neuralgia

Duration

- The duration of PHN is highly variable and about 50% of the patients recover within a year of onset of pain.

The pain of PHN usually follows the typical dermatomal distribution of the rash caused by herpes zoster

- *Unilateral Thoracic dermatomes*
- *Trigeminal nerve, especially the ophthalmic branch, are most frequently affected*

PAIN:

- Pain :Lancinating or electric shock–like sensation.
- Apart from this, patchy allodynia, hyperesthesia, and hypoesthesia can present to varying degrees in the affected region.
- These spontaneous pains, particularly the allodynia, can be disabling and debilitating leading to depression, social isolation, and increased health care utilization.

Pathophysiology

- Varicella zoster virus is a highly contagious double stranded DNA virus of the herpes family.
- Primary varicella manifests commonly as chickenpox in a nonimmune or incompletely immune person. During the primary infection, the virus gains entry into the sensory dorsal root ganglia.
- Reactivation of the virus occurs following depression of cell-mediated immunity and in advance-aged patients.
- The reactivated virus replicates and migrates down the sensory nerve leading to the dermatomal distribution of pain.
- The associated inflammation in the peripheral nerves leads to demyelination, wallerian degeneration, and fibrosis.
- Thus, as a result, uninhibited and amplified activity in unmyelinated primary afferents leads to pain associated with post-herpetic neuralgia

Risk Factors

- Delay in treating acute herpes infection
- Older age
- Pain severity
- Greater rash severity

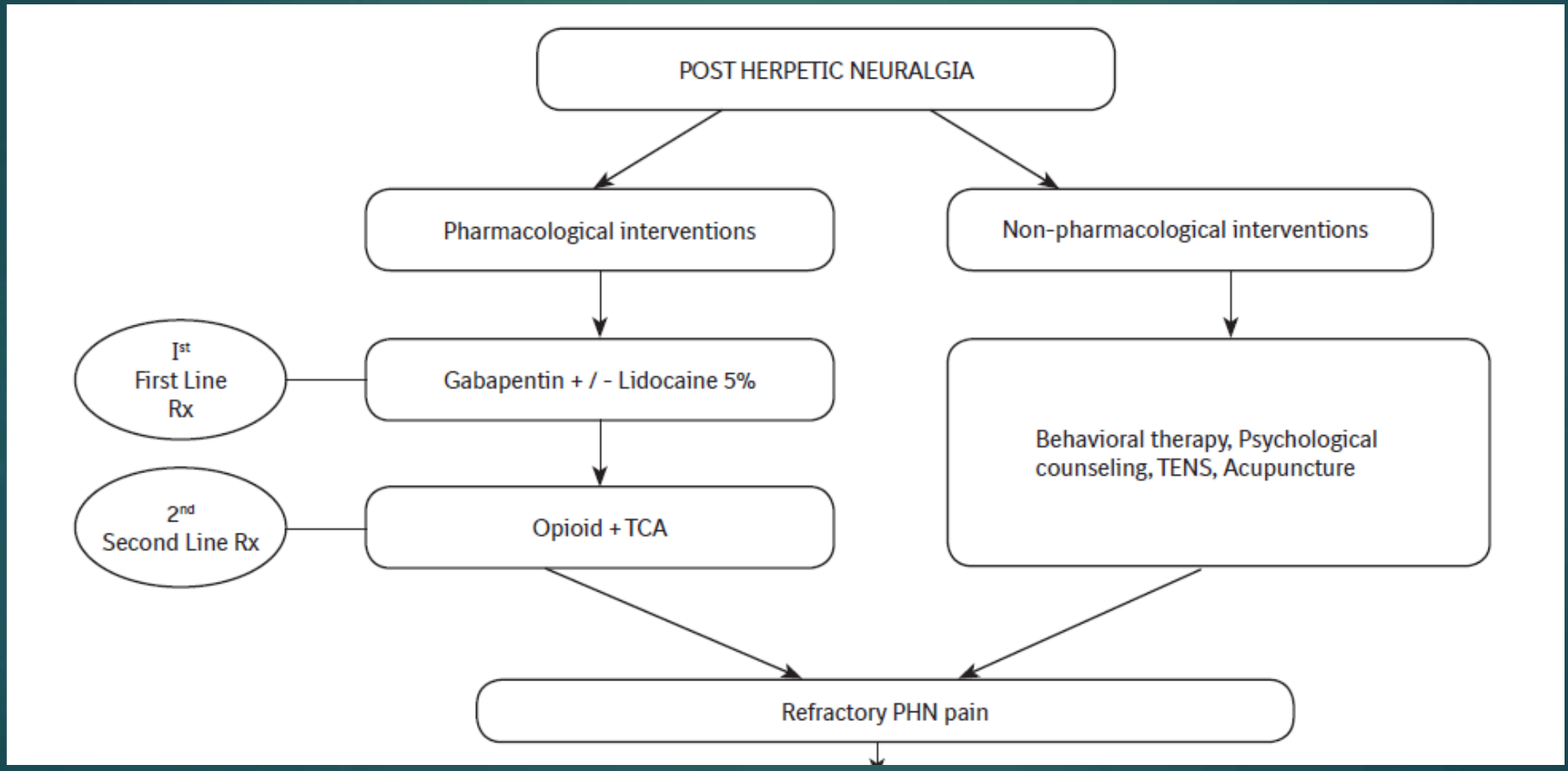
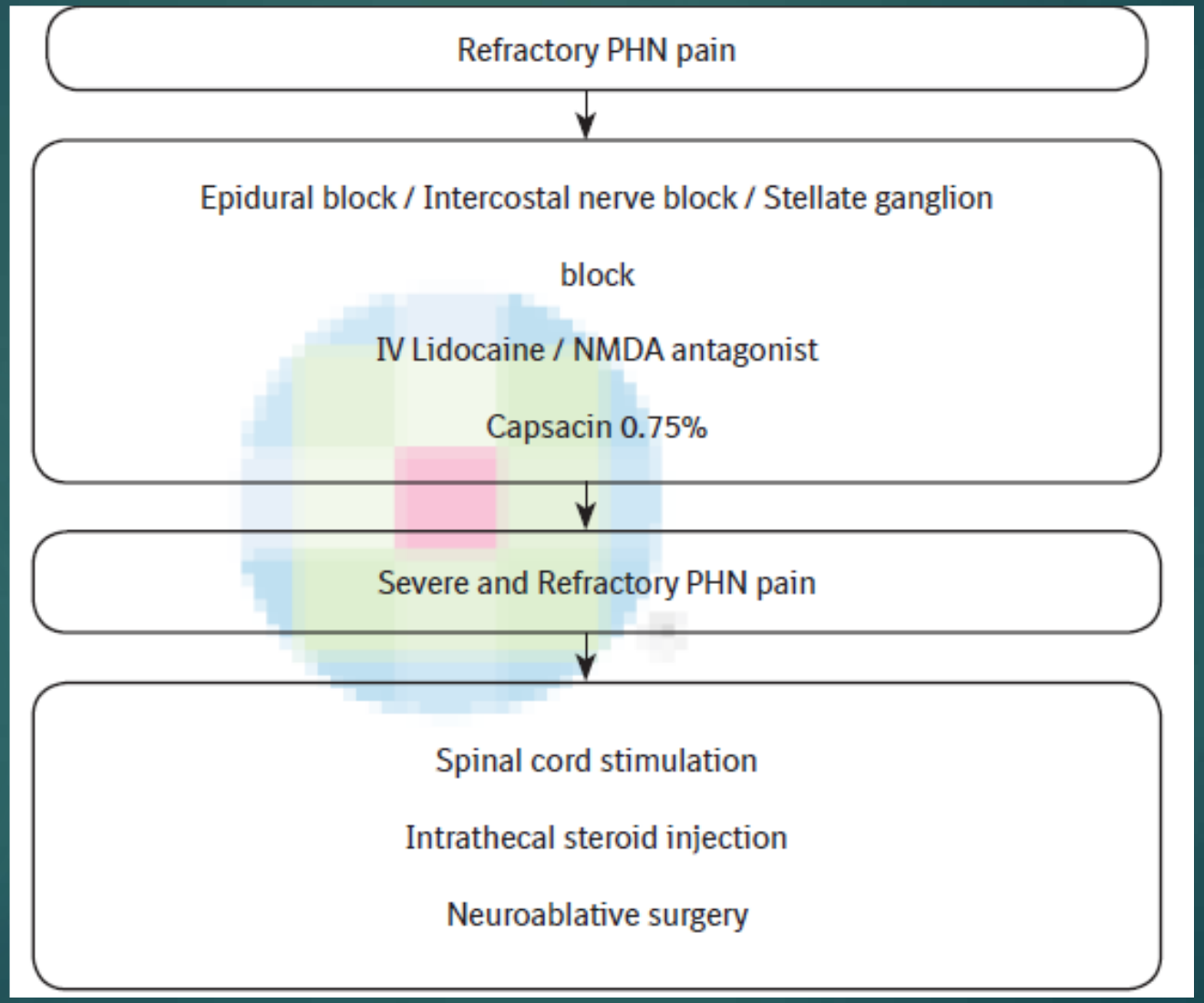

POST HERPETIC NEURALGIA
Pharmacological interventions
Non-pharmacological interventions
Ist
First Line
Rx
Gabapentin + / - Lidocaine 5%
Behavioral therapy, Psychological counseling, TENS, Acupuncture
2nd
Second Line Rx
Opioid + TCA
Refractory PHN pain

Table 1: Prevention of Post-herpetic neuralgia

Therapy	Drugs	Evidence
Antiviral Agents (within 72 hours of symptom onset)	Acyclovir Famciclovir Valacyclovir	A
TCA	Amitriptyline	B
Corticosteroids only in high-risk groups	Prednisolone	I
Nerve Blocks	Repetitive paravertebral nerve blocks with local anesthetics + / - steroids Sympathetic blocks (e.g, lumbar sympathetic, stellate ganglion block)	I

Table 2: Treatment options for Post-herpetic neuralgia

Medication	Dosage	Adverse effects
Antiepileptics		
Gabapentin	100 to 300 mg orally at bedtime; increase dosage by 100 to 300 mg every three days until dosage is 300 to 900 mg three times daily or response is adequate	Mild peripheral edema, cognitive impairment, somnolence, fatigue, dizziness, ataxia
Pregabalin	75 mg twice daily, increase to 150 mg bd daily within one week	Sleep disturbance, dizziness
Tricyclic antidepressants		
Amitriptyline Nortriptyline Imipramine Desipramine	10 to 25 mg orally at bedtime; increase dosage by 25 mg every two to four weeks until response is adequate, or to a maximum dosage of 150 mg per day.	Sedation, dry mouth, constipation, sweating, xerostomia, confusion, dysrhythmias, weight gain, dizziness
Opioids		
Oxycodone ER	10 – 40 mg every 12 hours, as titrated	Nausea, constipation, sedation, cognitive dysfunction, hormonal changes, skin irritation, vertigo
Morphine SR	5 – 50 mg every 12 hours, titrate as required	
Methadone	2.5 mg – 10 mg tds	
Transdermal buprenorphine	5 – 20 mcg / hour, changed every three days	
Transdermal fentanyl	25 mcg / hour – 100 mcg / hour.	
Tramadol	50 mg / day, increased to a maximum 400 mg / day	
Topical agents		
Capsaicin cream 0.025%	Applied to affected area three to five times daily	Localized erythema and uncomfortable burning, stinging or itching.
Capsaicin cream 0.075%		
Capsaicin cream 8%	Single-application placed on the skin for 60 minutes after pretreatment with lidocaine cream; Up to four patches may be applied at one time, and repeated as often as every three months	
5% Lidocaine gel	Apply to affected area every four to twelve hours, as needed.	Localized skin irritation
Transdermal 5% lidocaine	One-to-three patches worn for 12-hour intervals	
Eutectic mixture of local anesthetics (2.5% lignocaine, 2.5% prilocaine)	Apply to affected area every six to twelve hours, as needed.	


Refractory PHN pain
Epidural block / Intercostal nerve block / Stellate ganglion block
IV Lidocaine / NMDA antagonist
Capsacin 0.75%
Severe and Refractory PHN pain
Spinal cord stimulation
Intrathecal steroid injection
Neuroablative surgery

Systemic Therapy

N-methyl-D-aspartate Antagonist

Ketamine

Dextromethorphan

Mementine

Intravenous lidocaine

Interventional Therapies

Postherpetic neuralgia

- Chronic, persistent, debilitating pain
- Dermatomal distribution in patients who have recovered from shingles.
- Aching, itchy, lancinating, or sharp.
- Allodynia, hyperalgesia, areas of anesthesia, and deficits in thermal, tactile, pinprick, or vibration sensations
- Extending beyond the margins of the affected dermatomes.

At 3months after the onset of shingles:

- patients aged < 60 years have a 1.8% risk

- Patients aged > 60 years have risks of 3.3% after 12 months

Subcutaneous Botulinum Toxin A Injection

- Botulinum toxin is a neurotoxic protein purified from the bacterium Clostridium botulinum .
- The L -chain, which exhibits Zn2+-dependent protease activity inhibit the release of neurotransmitters(acetylcholine and substance P) from motor and sensory neurons, respectively .
- Additionally , botulinum toxin reduces peripheral nociceptive input by inhibiting the release of glutamate (peripheral neurotransmitter involved in neurogenic inflammation).

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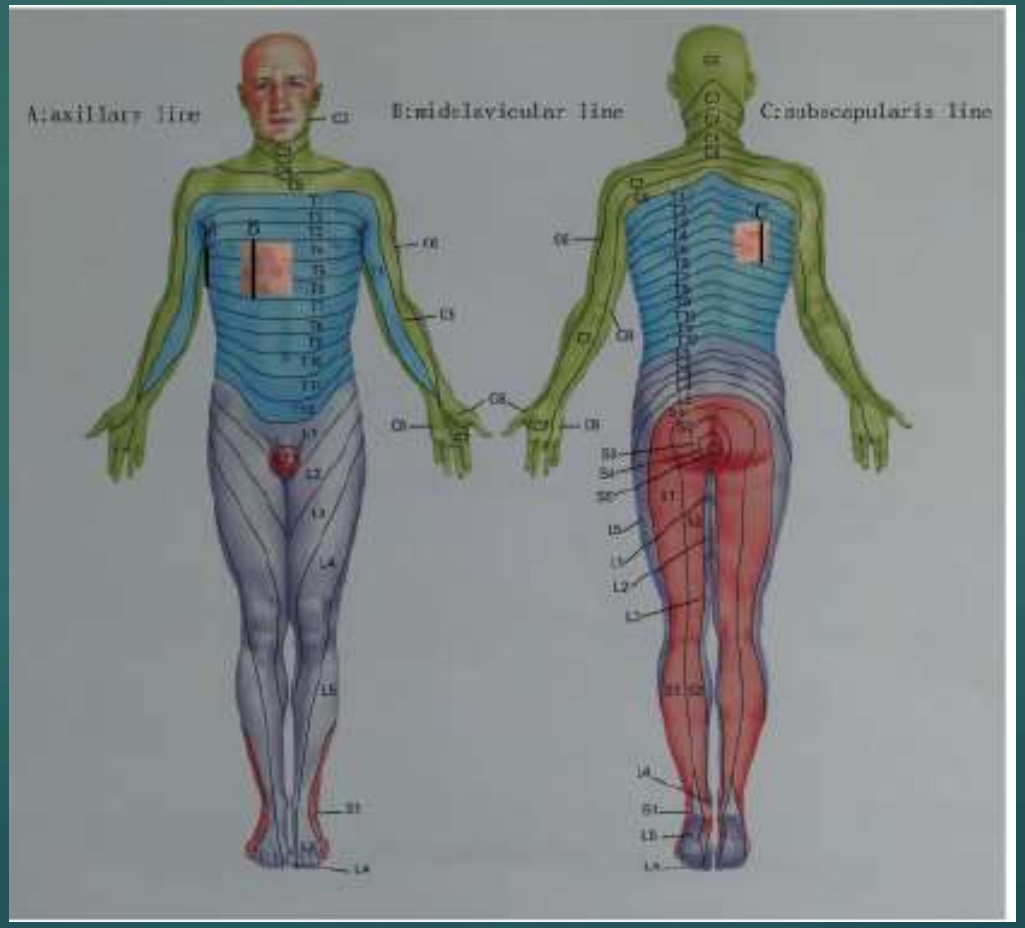
- Two randomized, double-blind, placebo-controlled trials have evaluated the effectiveness of subcutaneous botulinum toxin A injection for persistent moderate-to severe post-herpetic neuralgia .
- Botulinum toxin was injected subcutaneously within a 1- to 2-cm radius over the painful region.
- Per site 5-10 IU
- The maximum doses did not exceed 200 and 100 IU.
- Benefits in both studies : improved VAS scores and sleep durations and reduced numbers of patients using opioids.
- These effects emerged at 7 days after injection and persisted for 3 months.

Local Triamcinolone Injection

- Peripheral sensitization , which involves neural damage and inflammation with subsequent edema.
- The injured tissue releases inflammatory mediators that reduce the nociception threshold, and thus activate peripheral nociceptors.
- Corticosteroids may ameliorate post_herpetic neuralgia by modulating this inflammatory process.
- Local (i.e., intralesional) injection of triamcinolone plus lidocaine.
- 3 injections at 2-week intervals and reported pain relief at weeks 6 and 12.

Figure 1 The intracutaneous injections were placed along the axillary line (**A**), midclavicular line (**B**), and subscapularis line (**C**) between T4 and T6.



Transcutaneous Electrical Nerve Stimulation

- Noninvasive and safe application of electrical stimulation to the skin for pain control.
- Segmental inhibition in the dorsal horn as well as descending inhibition and stimulates the release of endogenous opioids to relieve pain at both low and high frequencies.
- Oral Pregabalin

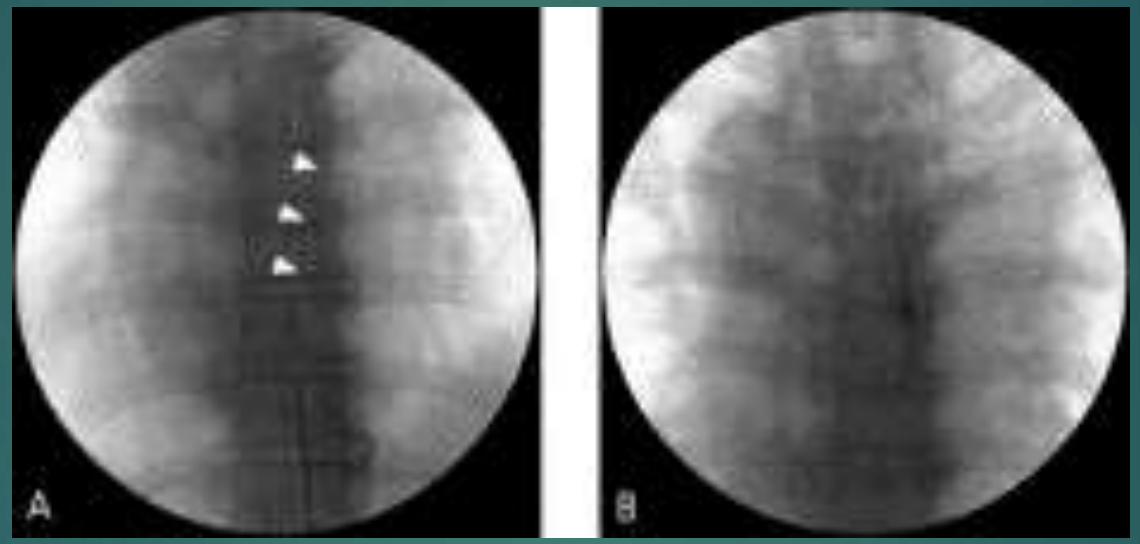
Neuraxial and sympathetic blocks

- Epidural(Paravertebral)
- Sympathetic block
- Intrathecal***

Epidural block.

- 18-gauge Tuohy needle was introduced into the interlaminar space at the second or third level below the target level under fluoroscopic guidance.

- The period of catheterization was limited to within 2 weeks, due to concerns regarding infection.


A
B

Paravertebral Block

- Paravertebral block, a common alternative to epidural injection, might provide short-term relief of intractable post-herpetic neuralgia.
- Repetitive paravertebral block comprising bupivacaine and clonidine.
- T3-level catheter for 3 weeks.

Figure 1 Ultrasound-guided thoracic paravertebral block in a sagittal image. Ultrasound image (**A**) and schematic image (**B**) are shown.

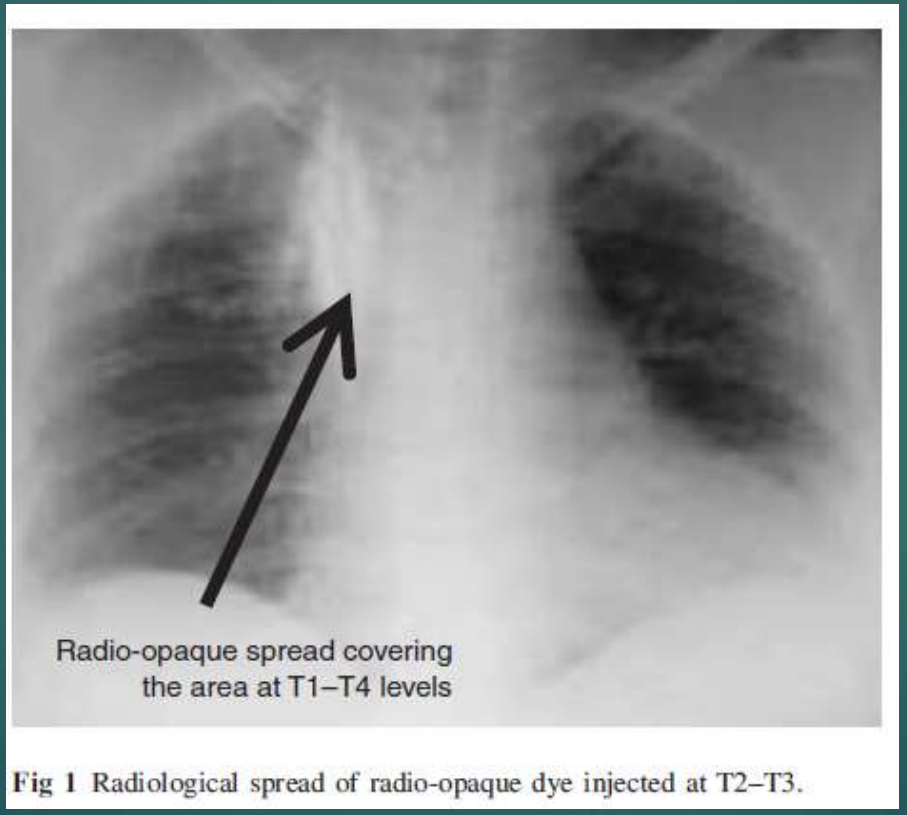
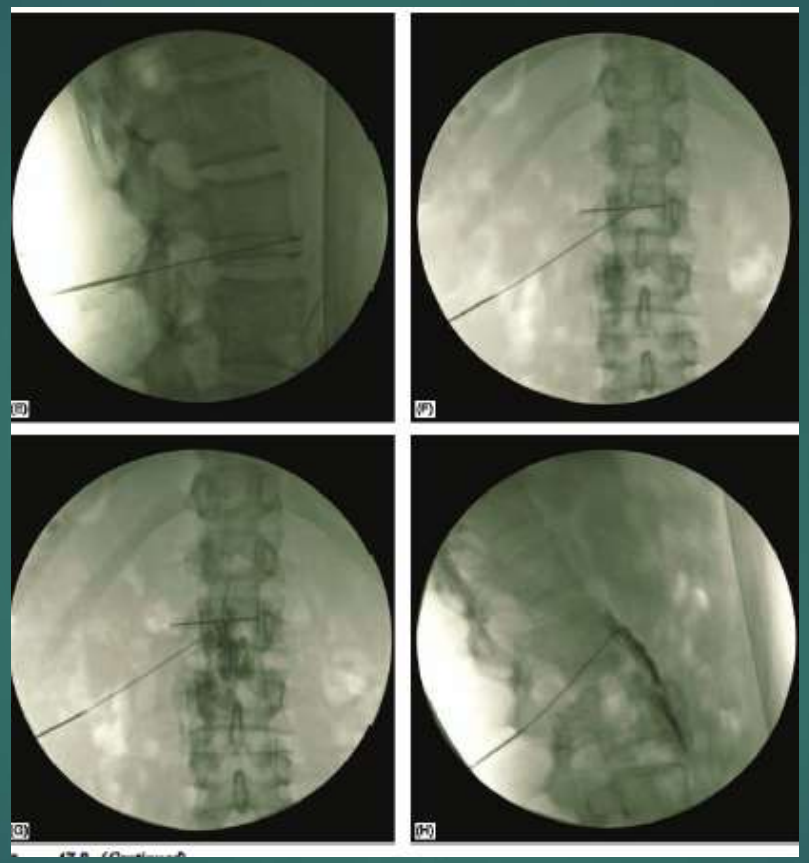


Fig 1 Radiological spread of radio-opaque dye injected at T2–T3.

Sympathetic Nerves Block

- The sympathetic nervous system is believed to be an important mediator of pain.
- After nerve injury or tissue inflammation, collateral sprouting in the peripheral and dorsal root ganglia and the upregulation of functional adrenoceptors may lead to the formation of anatomic and chemical couplings between sympathetic postganglionic and afferent neurons.
- Sympathetic terminals also contribute to the sensitization of nociceptive afferents.
- However, the mechanisms by which the sympathetic nervous system affects postherpetic neuralgia remain uncertain.



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- The patients selected for a trial of stellate ganglion block had not yet developed postherpetic neuralgia.
- 150-mg pregabalin twice daily.

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DRG PRF.

Dorsal Root Ganglion Destruction

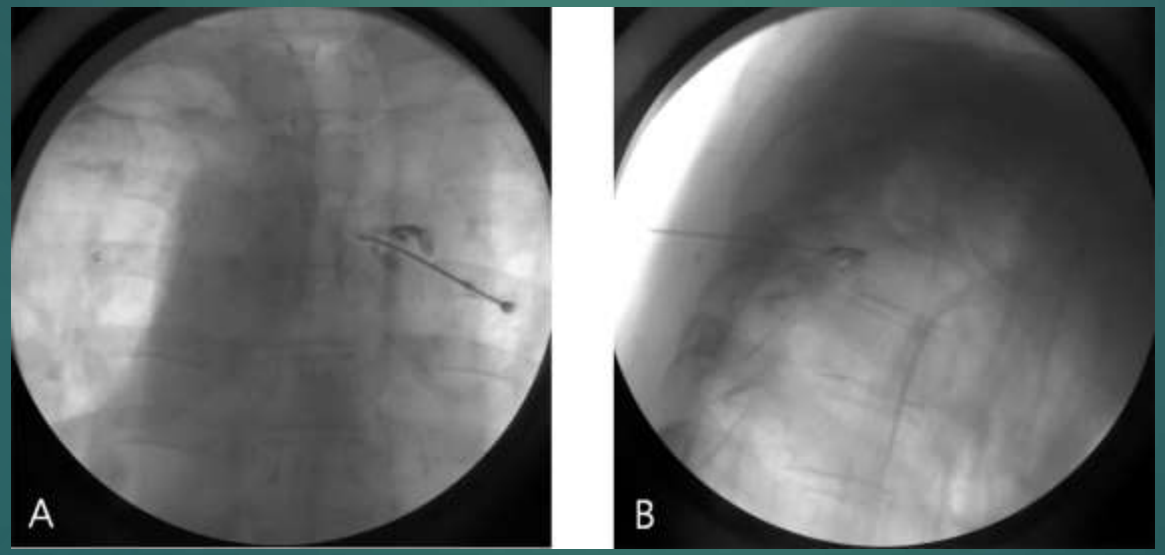
- Histopathologic studies have identified the loss of cells, axons, and myelin and concomitant fibrosis in the sensory ganglia of patients with severe post-herpetic neuralgia.

- Accordingly, the pain sensation may be caused by an ectopic discharge in the nociceptors and low-threshold afferents at the dorsal root ganglion.

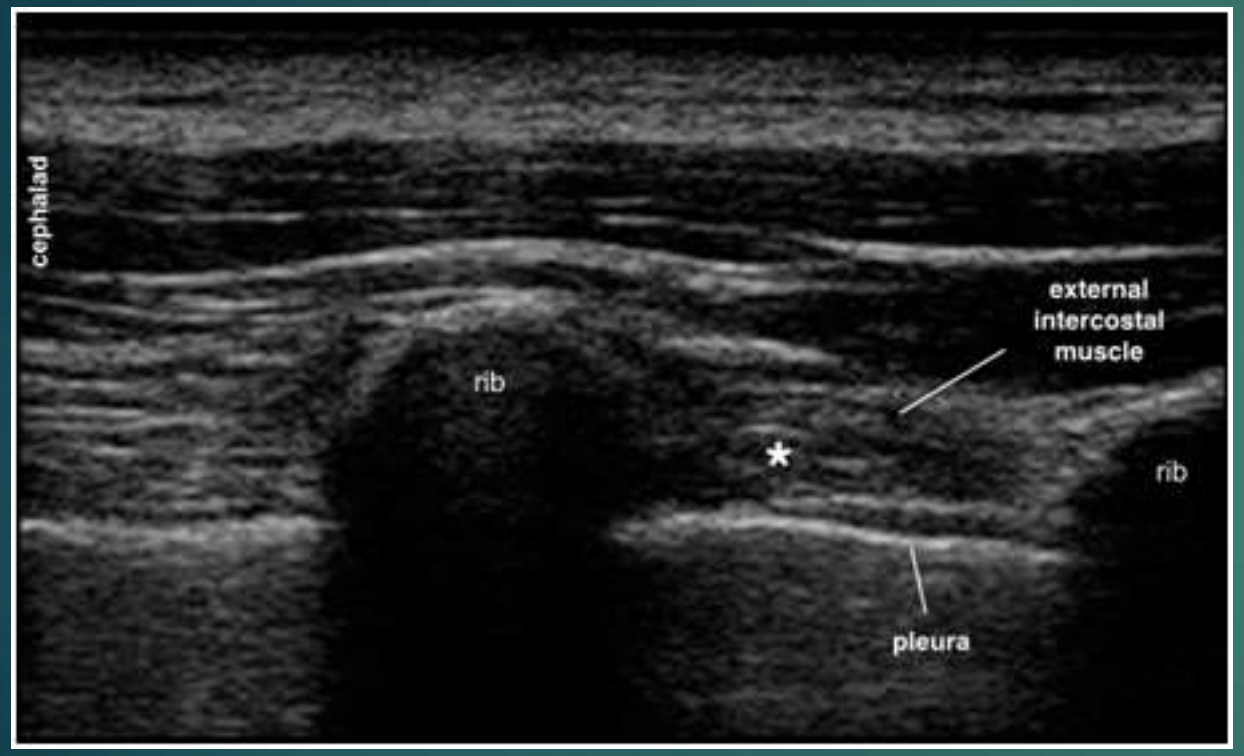
Pulsed Radiofrequency

- The underlying mechanism is attributed to the effects of a rapidly changing electrical field on neuronal membranes.
- Make electrolyte conduction and subsequent depolarization.
- Satisfactory pain relief that persisted for 6 months.
- Targeted the intercostal nerves .

- The needle tip was placed under the pedicle in the anteroposterior view and in the posterocranial portion of the intervertebral foramen in the lateral view for fluoroscopic imaging .
- Sensory stimulation was performed using a 50-Hz current. If a tingling sensation was observed in the affected dermatome below 0.5 V, the position of the needle was considered appropriate.
- After confirming the needle position, PRF of 42°C (20 milliseconds, 2 Hz, 45 V) was applied for 360 seconds. Impedance was maintained at less than 500 Ω throughout the procedure.


A
B

Intercostal Nerve Block

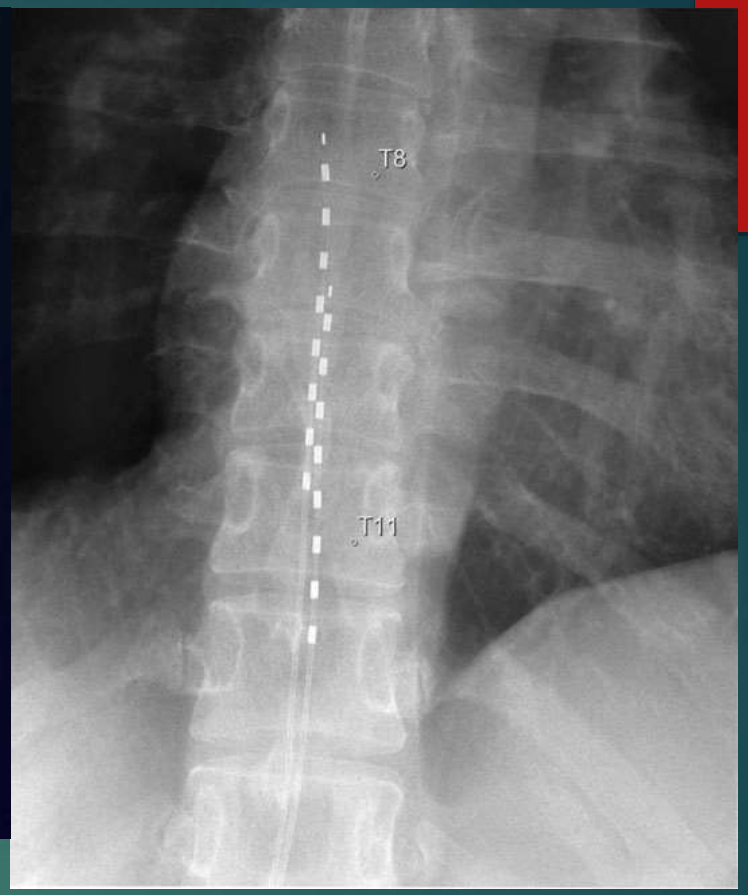


Intrathecal Injection of Methylprednisolone with Local Anesthetics or Midazolam

- Histopathologic studies : subacute or chronic inflammatory processes involving the infiltration and accumulation of lymphocytes around the spinal cord and interleukin-8.
- Intrathecal > epidural
- Preservatives are of considerable concern(potential risks of adhesive arachnoiditis).
- Midazolam : improvements in pain, allodynia, sleep quality, and changes in the area of allodynia.

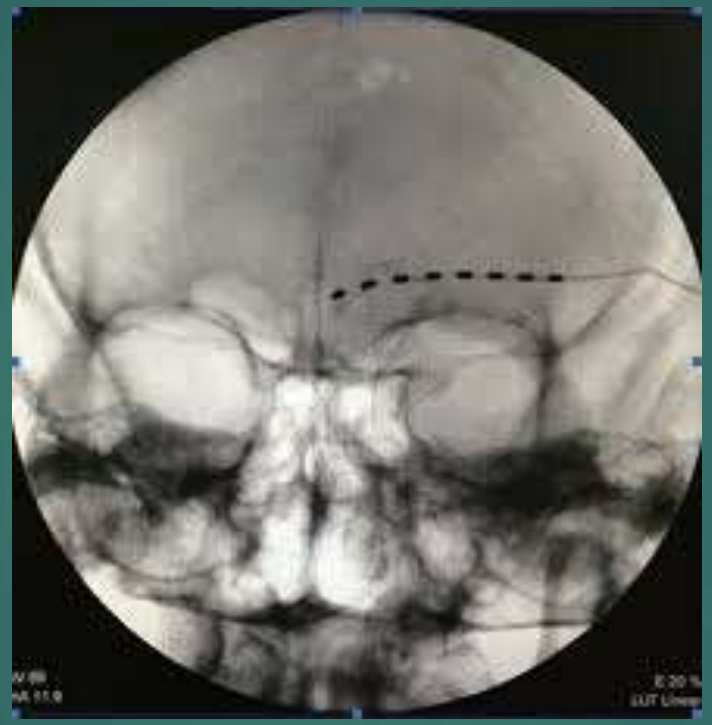
Spinal Cord Stimulation

- The "gate control theory of pain" suggests that neural signal transmission is regulated by the dorsal horn of the spinal cord.
- A-beta fibers inhibit the transmission of pain signals carried by C-fibers.
- Affect the levels of γ-aminobutyric acid and adenosine in the dorsal horn and consequently reduce neuropathic pain.


T8
T11

Peripheral Nerve Stimulation

- Initially, the patients received a diagnostic block to identify the segment in which temporary electrodes would be placed, and a permanent pacemaker was implanted subcutaneousl after successful trials.



Conclusion

- *The current evidence is insufficient for determining the single best interventional treatment.*

Considering

- Invasiveness
- Price
- Safety

THE END