

# NEUROPATHIC PAIN

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## Conditions with NP

- Diabetic peripheral neuropathy
- Post herpetic neuralgia
- HIV neuropathy
- Spinal cord injury
- Neuropathic cancer pain
- Phantom limb pain
- post-mastectomy pain
- Guillian-Barre ´ syndrome
- Chemotherapy-induced neuropathy
- Complex regional pain syndrome, types I & II
- Vitamin B12 Deficiency
- Spinal stenosis
- Lupus
- Multiple sclerosis
- Fibromyalgia
- Lead ingestion
- Traumatic injury: motor vehicle accident or gunshot
- Failed back surgery syndrome

Etcetera, etcetera, etcetera.....

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## Numbers/Demographics

**Estimated US Population 304,500,000**  
Medscape estimates 3% of our population have NP!

- ◆ Those with diabetes, 25% develop NP
- ◆ Of the 1 million annual cases of Shingles, 20% develop post-herpetic neuralgia
- ◆ Most common reason patients seek medical care is for pain
  - 20% for persistent chronic pain
- ◆ **Specialists theorize that most chronic pain is NP**

(Finnerup, 2007; CDC, 2008)

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## Neuropathic Pain (NP) Definition

“Initiated or caused by  
a primary lesion or dysfunction  
in the nervous system”

- The International Association for the Study of Pain (IASP)

### Further clarifications:

- ◆ Make a distinction between nociceptive and NP
- ◆ Differentiate from peripherally-generated and centrally-generated NP
- ◆ Note structure and process differences - neuroplasticity

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## Symptoms

- ◆ **Allodynia** – pain caused by something that is generally non-painful (light touch)
- ◆ **Hyperalgesia** - heightened response to normally painful stimulus
- ◆ **Hyperesthesias** – an exaggerated response to touch, such as to bed sheets
- ◆ **Hyperpathy** – persistent pain even after the cause of pain has been removed
- ◆ **Paresthesias and dyesthesias** – abnormal and unpleasant sensations that are described as tingling, pins and needles
- ◆ **Abherent algia** the pt feels requires continual movement, touch
- ◆ **Worse at night**
- ◆ **Worse after weight bearing**

(Svendsen, 2006; Parry/MacCarberg, 2007)

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## Pathophysiology

Basic nociceptive pain includes:

- ◆ **Transduction at the nociceptors**
  - Thermal, Chemical, or Mechanical stimuli
- ◆ **Transmission via C and A fibers**
- ◆ **Modulation**
  - Dorsal horn
  - Chemical receptors on the axon membrane
    - ◆ Opiate, GABA, Bradykinin, Histamine, Serotonin, Capsaicin
- ◆ **Perception**

(Abrams, 2007)

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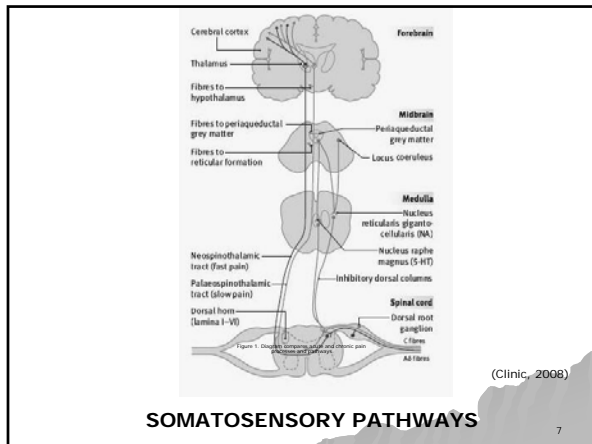
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### Abherent Neuroprocessing

- Sodium channels of unusual density produce persistent spontaneous discharge
- Calcium channels increase Substance P, glutamate, and norepinephrine
- Aberrant processing continues in PNS/CNS
- Receptor field size increases

(Tremont-Lucats, 2006, Hornick, 2007)

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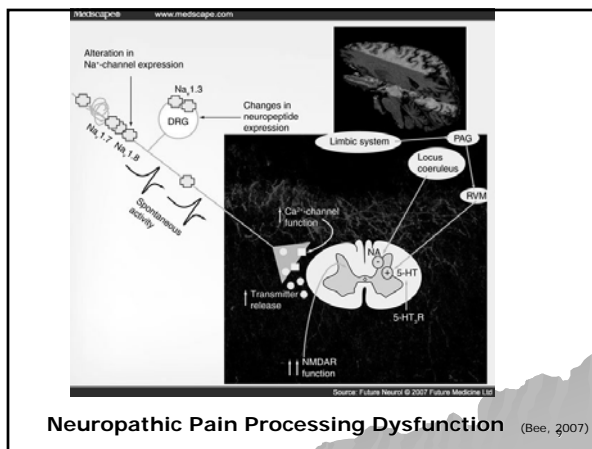
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## AND THAT MEANS???

The nerves are excited!!!!!!!!!!!!

### ◆ GOALS FOR NP TREATMENT

- Restore inhibitory neurotransmission – Sodium channels
- Modulate Calcium channels
- Block peripheral sensitization
- Block central sensitization
- "Retrain the nervous system"

(Hornick, 2007)

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## Assessment Tools

- ◆ Pain Quality Assessment Scale (PQAS) (2008)
- ◆ Self-Administered Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) (2005)
- ◆ Douleur Neuropathique 4 questions questionnaire (DN4) (2004)
- ◆ 12 item Neuropathic Pain Questionnaire (NPQ) (2003)
- ◆ The Neuropathic Pain Scale (1996)
- ◆ Quantitative sensory testing (QST) (1994)

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## Physical Assessment

- ◆ Pain location
- ◆ Distribution
- ◆ Intensity
- ◆ Quality
- ◆ Time course
- ◆ Underlying disease
- ◆ Area of possible nervous system lesion

(Jensen, 2003)

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## Lab Tests

- ◆ CBC with Diff
- ◆ Sed rate
- ◆ Chem profile
- ◆ Thyroid
- ◆ B12
- ◆ Folate
- ◆ Fasting blood sugar
- ◆ Gyclo Hgb
- ◆ Protein electrophoresis
- ◆ Lyme titers
- ◆ Hep B/C
- ◆ HIV
- ◆ Anti-nuclear
- ◆ Sjogren's titers
- ◆ Anitneutrophil cytoplasmic antibody
- ◆ Rheumatoid factor
- ◆ Cryoglobulins
- ◆ Anti-sulfide antibody titers
- ◆ Anti-HU titers
- ◆ Heavy metal – serum/urine screens
- ◆ CSF for demylinating diseases & meningeal carcinomatosis
- ◆ Biopsies Dx for vasculitis, amyloidosis, sarcoidosis, etc.

(Beth Israel Medical Center, 2008)

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McHUMOR.com by T. McCracken



"I'd say the nerve pain you're having in your jaw is due to an arrow through it, but perhaps you'd like to get a 2nd opinion from a dentist."

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## CONSIDERATIONS FOR TX

- ◆ Co-morbidities and complexities
- ◆ Potential adverse outcomes
- ◆ Potential drug interactions
- ◆ Costs associated with therapy
- ◆ Potential risks of medication abuse
- ◆ Individual variation
- ◆ Multimodalities
  - Polypharmacy
  - Can include pharmacological-nonpharmacological combinations

(Dworkin, 2007)

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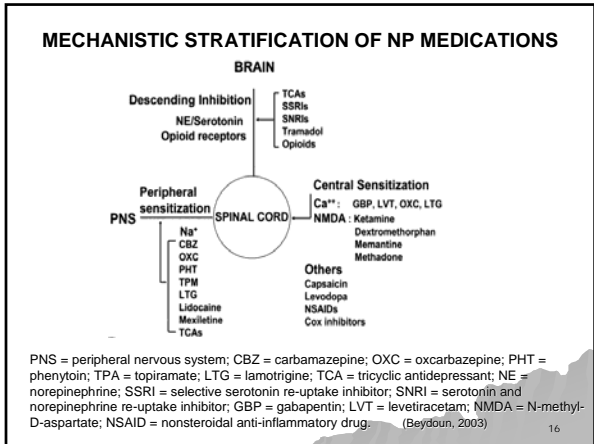
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## TREATMENT NOTE:

# Success is a pain reduction of 40-60%.

(Parry, 2006)

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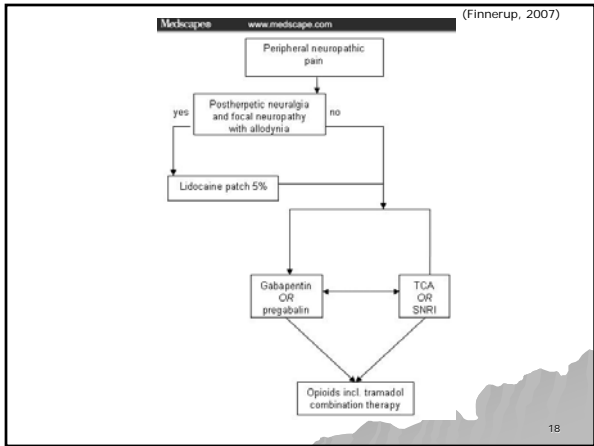
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## FIRST LINE MEDICATIONS

### - Calcium Channel Blockers/Modulators

- ◆ **Gabapentin (Neurontin®)**
  - + worsens cognitive or gait issues for elderly
- ◆ **Pregabalin (Lyrica®)**
  - + concern with renal impairment
  - + weight gain

(Dworkin, 2007)  
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## FIRST LINE Continued

### - Tricyclic Antidepressant (TCA)

- ◆ **Nortriptyline/Pamelor®**
- ◆ **Desipramine/Norpramin®**

- Monitor EKG
- Strong drug interactions with SSRIs
- Not recommended:  
amitriptyline (Elavil®) & imipramine (Tofranil®)

(Dworkin, 2007)  
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## FIRST LINE Continued

### - SSNRI - Selective serotonin & norepinephrine reuptake inhibitor

- ◆ **Duloxetine (Cymbalta®)** antidepressant
  - Contraindicated: uncontrolled glaucoma, end-stage renal
  - Monitor BP, suicide ideations
- ◆ **Venlafaxine (Effexor®)** antidepressant
  - Monitor EKG

(Finnerup, 2007)  
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## SECOND AND THIRD LINE

### ◆ Opioid analgesics

- Proven less sensitive, but assists with intense pain

### ◆ Tramadol (Ultram®)

- Don't use with SSRI, possible serotonin syndrome

### ◆ IV morphine

### ◆ IV lidocaine

- dissociative anesthetic

(Dworkin, 2007)  
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## Other Medications Used

### ◆ Methadone

- Looooooooooooooooong half life
- Contraindicated with liver dysfunction
- When changing from another opioid to methadone, reduce dose 75-95% of expected equianalgesic

### ◆ Buprenorphine

(Buprenex®, Subutex®)

- systemic potency 20-40 times > morphine
- long acting, low CNS effects, less constipation
- Used transdermally for up to 96hr
- Suboxone® is a combo of buprenorphine and naloxone

(Likar, 2006; Kress, 2008)  
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## Other Medications Used Continued

### - Calcium Channel Blockers/Modulators

#### ◆ Topiramate (Topamax®)

- Studies show noneffective, however...

#### ◆ Lamotrigine (Lamictal®)

- Black box warning re: Stevens-Johnson

#### ◆ Benzodiazepines

- Clonazepam (Klonopin®)
- Valium®

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**Other Medications Used Continued**

◆ **NMDA** (*N*-methyl-D-aspartic acid) antagonists

- Dextromethorphan
- Ketamine
- Nemantine (Namenda®)
- Riluzole (Rilutek®)
- Amantadine

◆ **Alpha-2-adrenergic agonists**

- Clonidine
  - ◆ PO, topical, intrathecal

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**Other Medications Used Continued**

◆ **Mexiletine po** (Mexitil®)

- Oral lidocaine
- Limited use r/t cardiac effects, nausea

◆ **Cholecystokinin-B antagonist** (Proglumide)

◆ **Calcitonin** Osteoporosis

◆ **Flecainide** (Tambocor ®)

◆ **Baclofen** Antispasmodic

◆ **Vitamin D supplementation**

◆ **Levetiracetam** (Keppra®) Anticonvulsant

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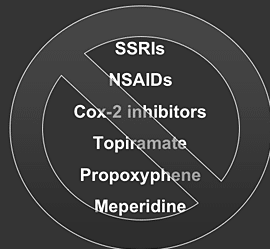
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**What NOT to use for Neuropathic Pain**



(Parry, 2007- Copyright © 2006 Dannemiller Memorial Educational Foundation - via Medscape)

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## TOPICALS AND PATCHES

### ◆ Patches

- Lidocaine – Lidoderm®
  - ◆ Patch and Gel
- Clonidine
- Diclofenac – Flector®, Voltaren®
- Buprenorphine - BuTrans patch®
- Sufentanil – Transdur®
- Bupivacaine - Eladur®

(Lyda, 2008)

### ◆ Alternatives

- Camphor (*Cinnamomum camphora*)
- Capsicum (*Capsicum* species)
- ◆ Counter irritants, likely safe

(Natural Medicine, 2008)  
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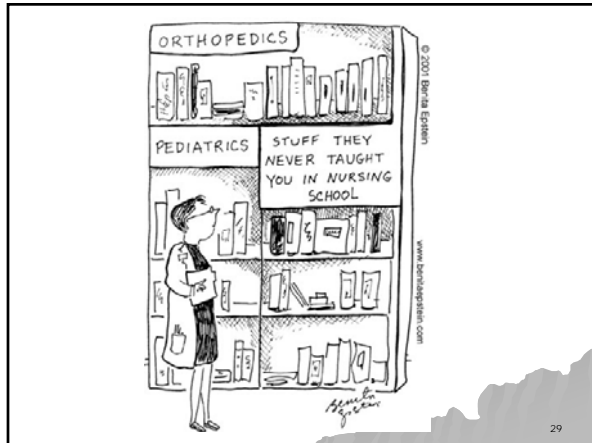
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## Interventional

### ◆ Spinal Cord Stimulators – Implanted

- Consider when polypharmacy failed
- The pathway is intact
- Successful external stimulator trial over 5-7 days

(Varrassi, 2005)  
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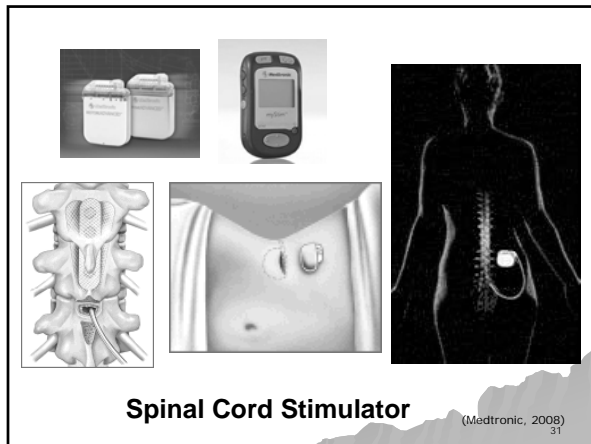
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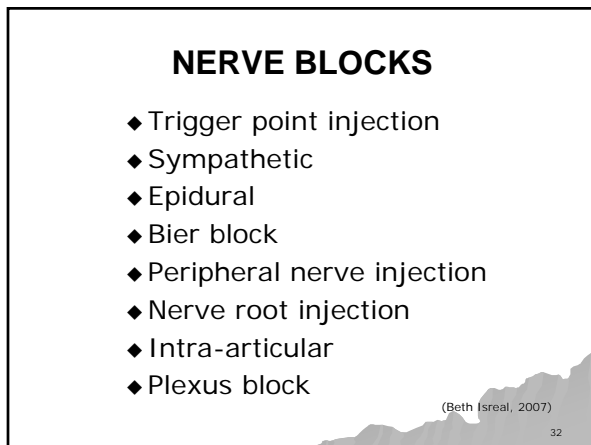
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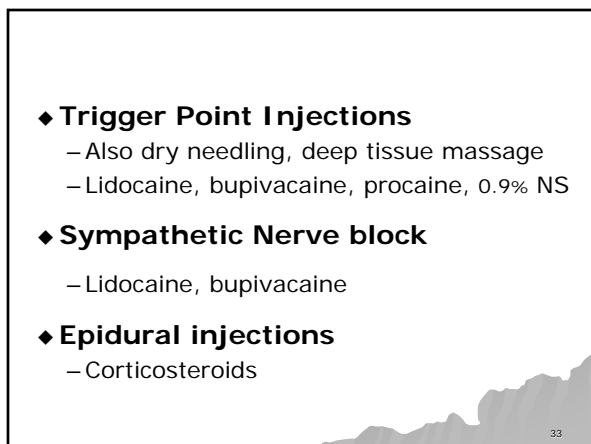
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◆ **Tunneled Epidural Catheter**

◆ **Motor Cortex Stimulator** –  
neurosurgical craniotomy

◆ **Peripheral stimulation Unit** –  
implanted

◆ **Phenol sympathectomy**  
– No positive effects

(Varrassi, 2005)

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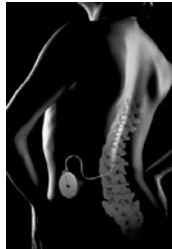
◆ **Implanted Intrathecal Catheter**

When to use is similar to  
stimulators:

- Polypharmacy failed
- Side Effects too intense

- **Clonidine**  
• usually in combination with  
other anesthetics or opioids

- **Ziconotide (Prialt®)**  
calcium channel blocker



Madaris, 2008

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**Complementary & Alternative**

◆ **Acupuncture**  
– Various types of acupuncture

◆ **Aromatherapy**  
Massage, Baths, Inhalations

– **Essential Oils**  
Juniper, V-6, peppermint, NeuroGen®,  
chamomile, sandalwood

– **Patchouli incense**

◆ **Acetyl-L-carnitine**

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## CAM Continued

- ◆ **Alpha-lipoic acid**

- ◆ **St. John's Wort** (*Hypericum perforatum*)
  - Check for drug-herb interactions

- ◆ **Cannabinoids**

- Dronabinol (Marinol®) provides significant pain relief (Finnerup, 2007)

- ◆ **CONSIDERED UNSAFE**

- L-tryptophan
- 5-HTP (Natural Medicine, 2008)

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## TREATMENT SUPPORT

- ◆ Stress reduction
- ◆ Good sleep hygiene
- ◆ Diet with protein/amino acids
- ◆ Physical activity
  - Walking, swimming
  - Physical Therapy
    - ◆ Assess for balance
    - ◆ Gentle Desensitization
    - ◆ Progress to flexibility and isometric strengthening exercises (AMA, 2007)

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## Is Neuropathic Pain Preventable?

- ◆ **Peri-operative with gabapentin or pregabalin**
  - ◆ IASP states 1200mg night before plus 5 days post-op
- ◆ **Tight Diabetic Glycemic Control**

(Campbell, 2006; AMA, 2007)

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## Continue the Prevention

### ◆ Treat Pain Consistently

- Repetitive noxious stimulation present
- "Wind up" - Progressive increase in # of action potentials
- Treat pain when it happens, don't let it become chronic and/or neuropathic

### ◆ Herpes Zoster Vaccine

- Of those receiving the vaccine yet still acquiring shingles, 67% decrease in incidence of PHN

(CDC, 2008; Perry, 2006)

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## EVALUATION

### ANY TREATMENT WILL TAKE TIME

- Achieve a steady state
- Titrate to 'effect and side effect'
- Reevaluate to increase/decrease
- Keep documentation about the trials - successes and failures
  - ◆ "What worked" "For how long" "What didn't work"
- Encourage the patient to keep their own records
  - ◆ **THEIR involvement is a MUST!**

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## General Rule for Treatment

- ◆ If effective, continue.
- ◆ If partially effective, consider multimodalities.
- ◆ If not effective, change your intervention. Try something else.

(Dworkin, 2007)

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*Thank you!*

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