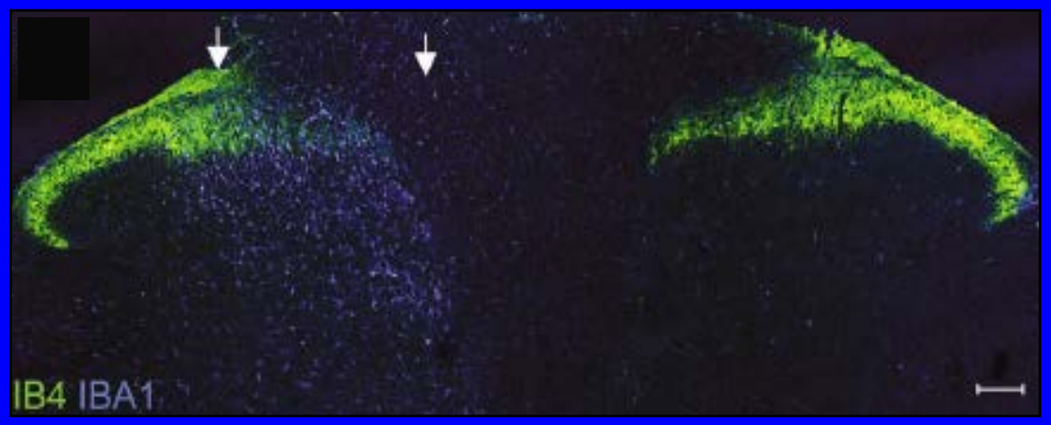
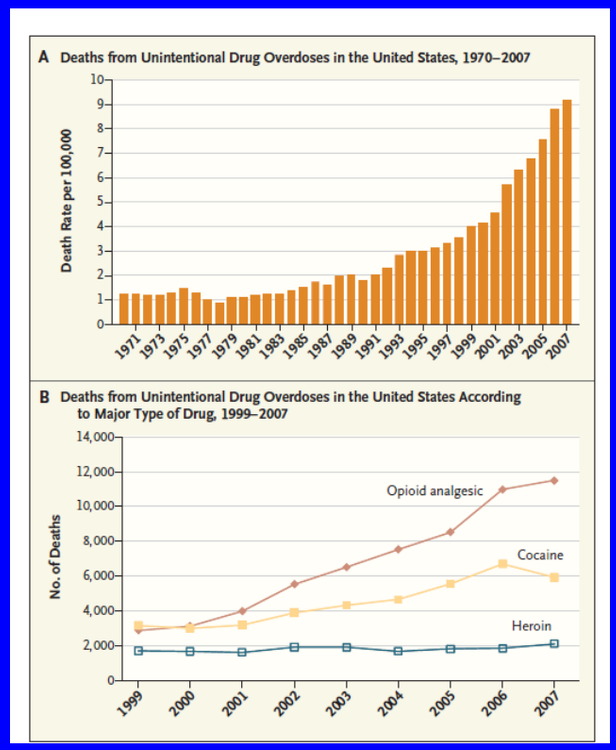
Pain Medicine
Clinical Update 2015





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Dept. of Anesthesia, Critical Care & Pain Medicine
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Conflicts of Interest

None

Goals

Review basic physiology of the pain system & describe a taxonomy that distinguishes physiological and pathological pain states

Present a stepwise assessment and treatment strategy for neuropathic pain

Discuss use of opioid analgesics including risk mitigation strategies

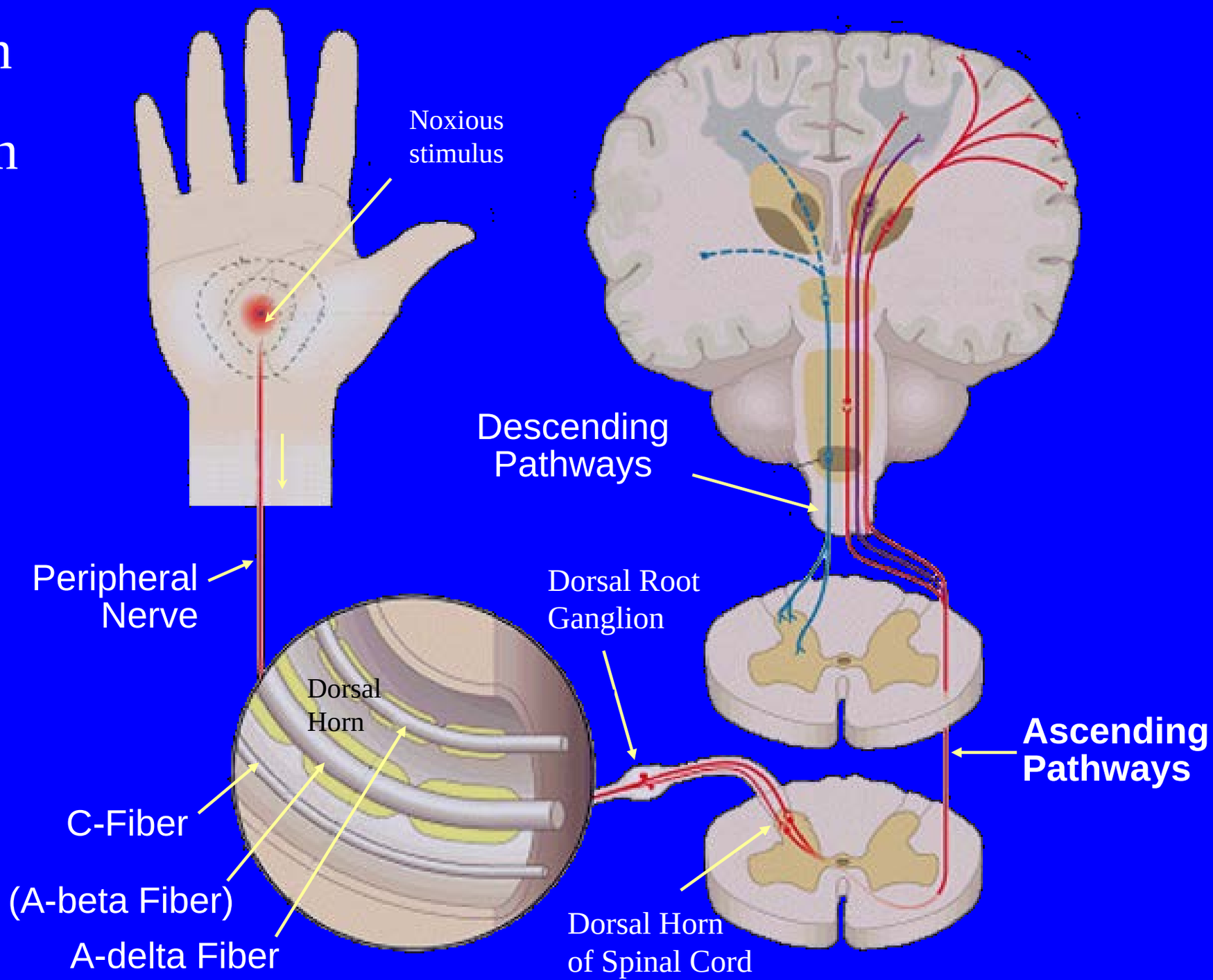
I. Physiology and Taxonomy of Pain

Perception of pain occurs in the brain

René Descartes
(1596 - 1650)

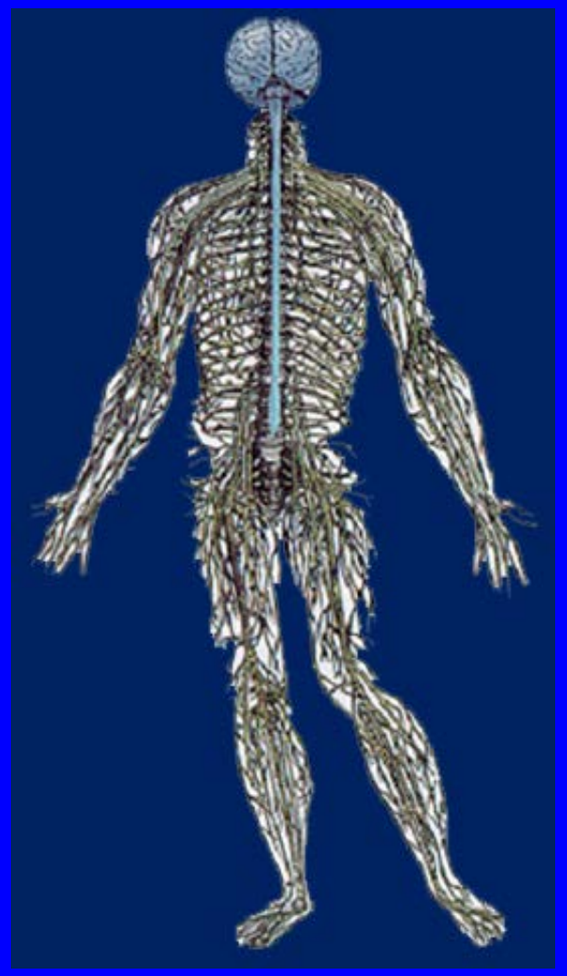
Physiology of nociception and pain

- Transduction
- Transmission
- Modulation
- Perception
- Behavior



Taxonomy of Pain

- Nociceptive
- Inflammatory
- Neuropathic



Nociceptive Pain

No pathology

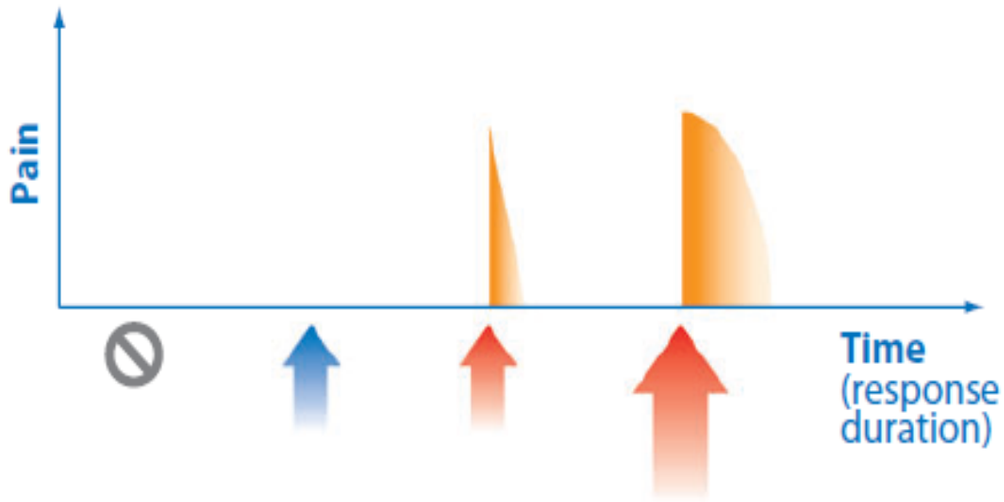
Requires an ongoing noxious stimulus

A high threshold (Aδ, C) protective alarm system

Nociceptive pain

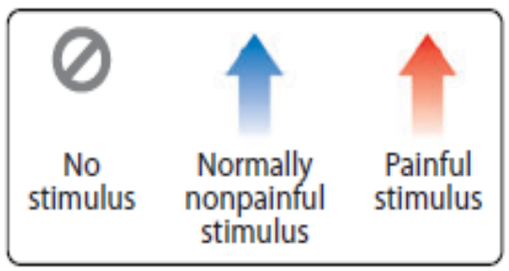
No nervous system lesion or inflammation

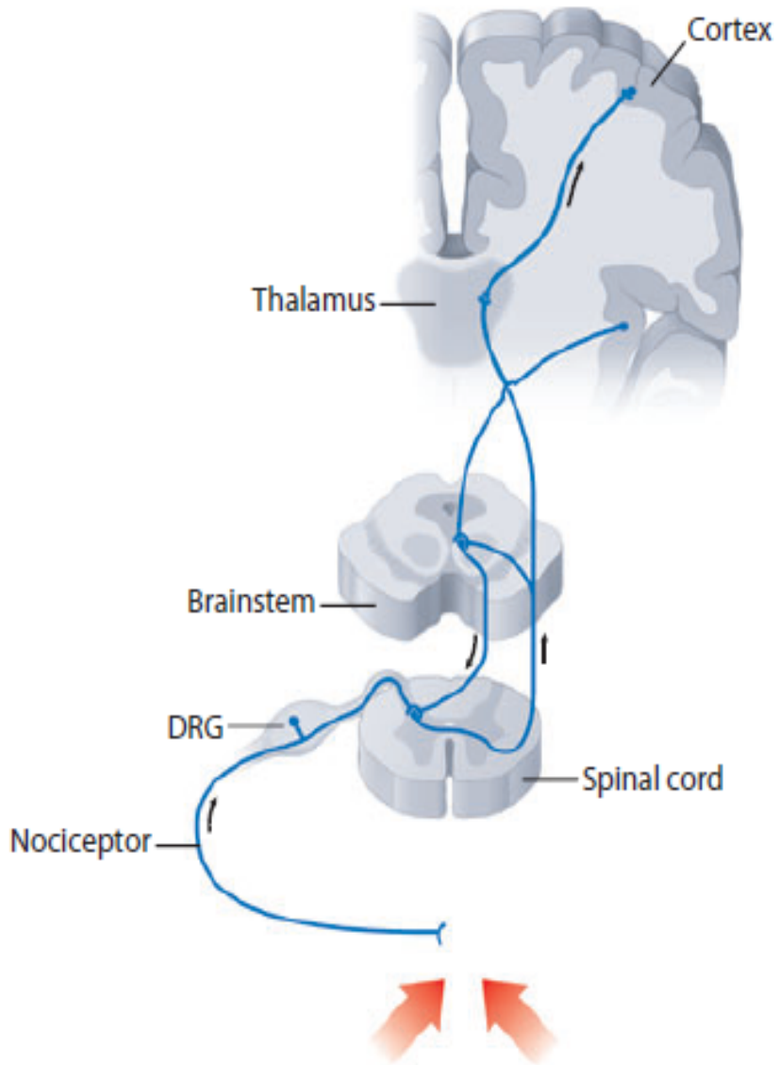
Stimulus-dependent pain
Evoked by high-intensity (noxious) stimuli



Adaptive

Protects by signaling potential tissue damage

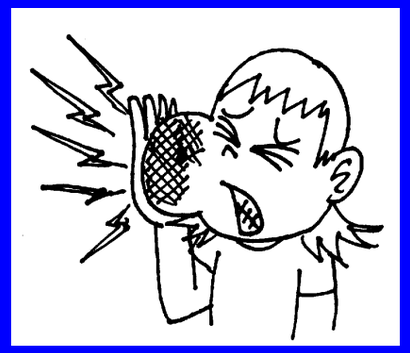


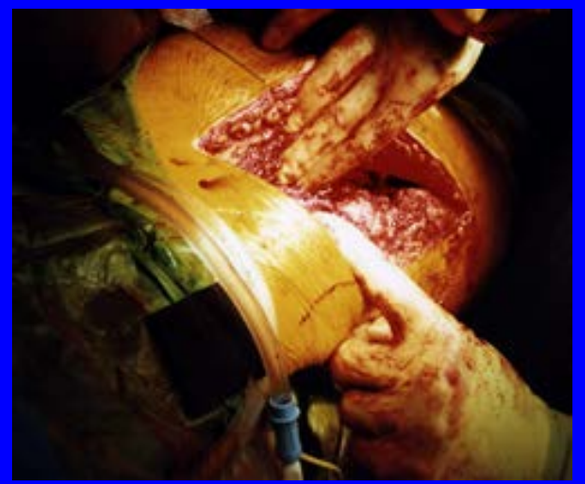


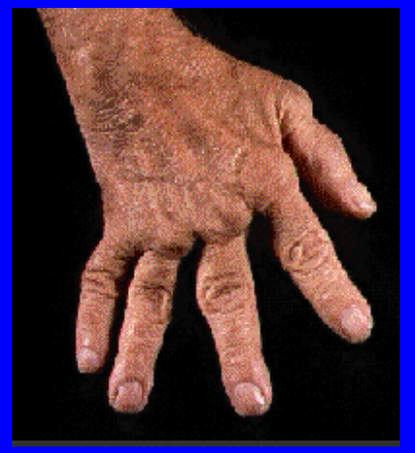
Physiological stimuli:
mechanical (pinprick), thermal (noxious heat or cold), chemical injury

Clinically relevant stimuli:
abnormal mechanical forces (osteoarthritis), organ injury (angina, ischemic claudication)

Inflammatory Pain







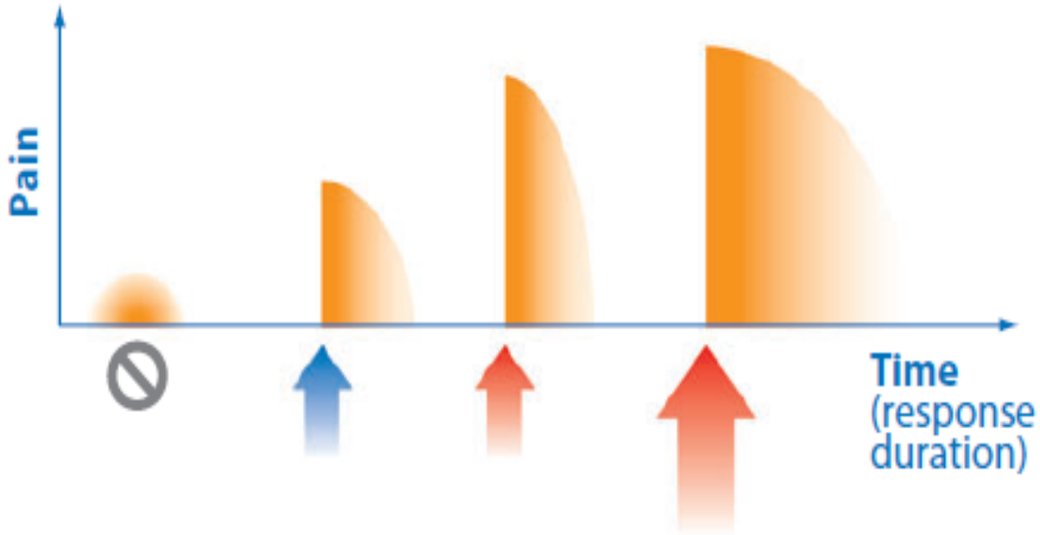
Tissue injury with inflammation

Allodynia, hyperalgesia, spontaneous pain

A low threshold protective system that promotes healing/repair

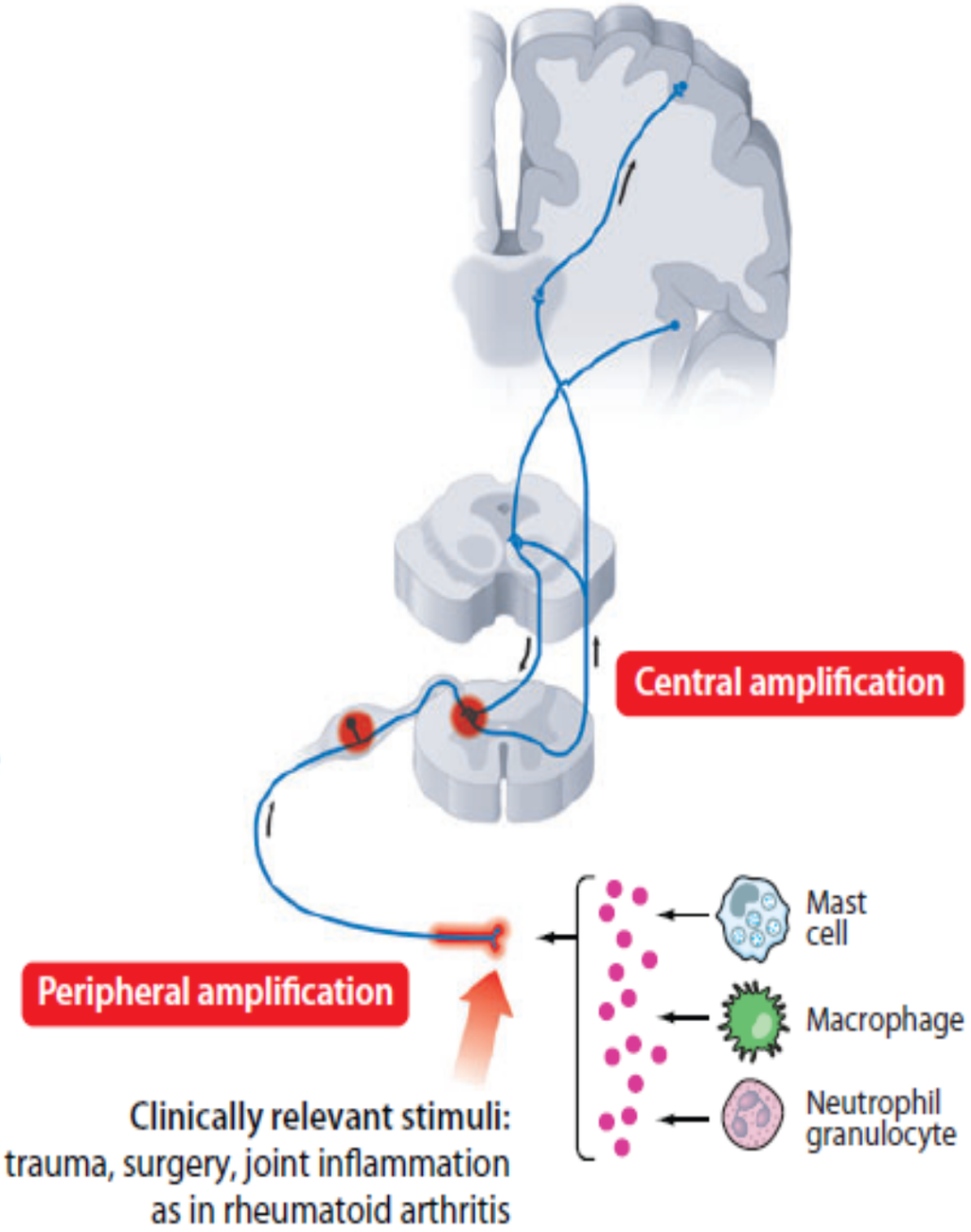
Inflammatory Pain

Spontaneous and stimulus-dependent pain
Sensory amplification
Evoked by low- and high-intensity stimuli



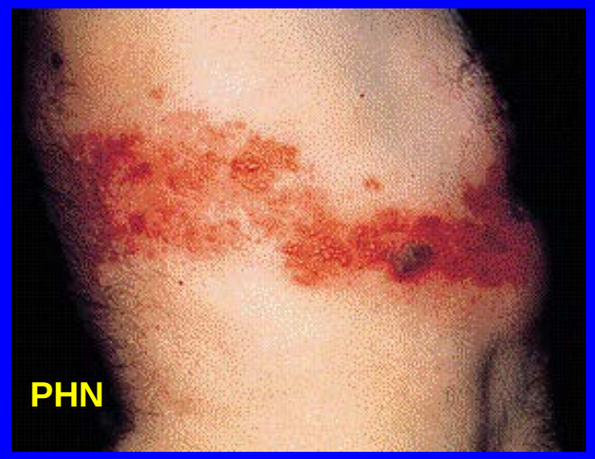
Adaptive and reversible

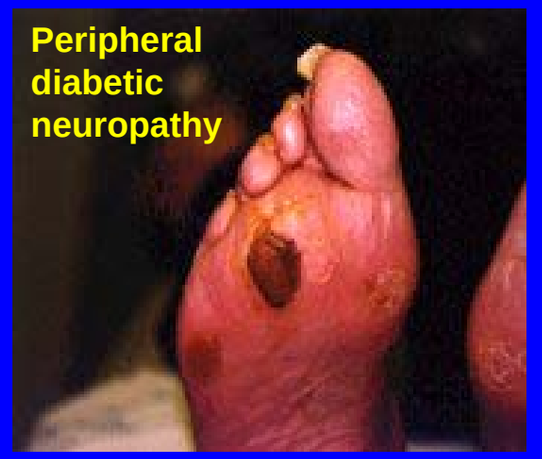
Protects by producing pain hypersensitivity during healing

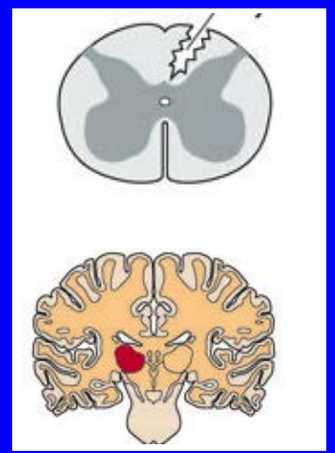


Clinically relevant stimuli:
tissue trauma, surgery, joint inflammation
as in rheumatoid arthritis

Neuropathic Pain





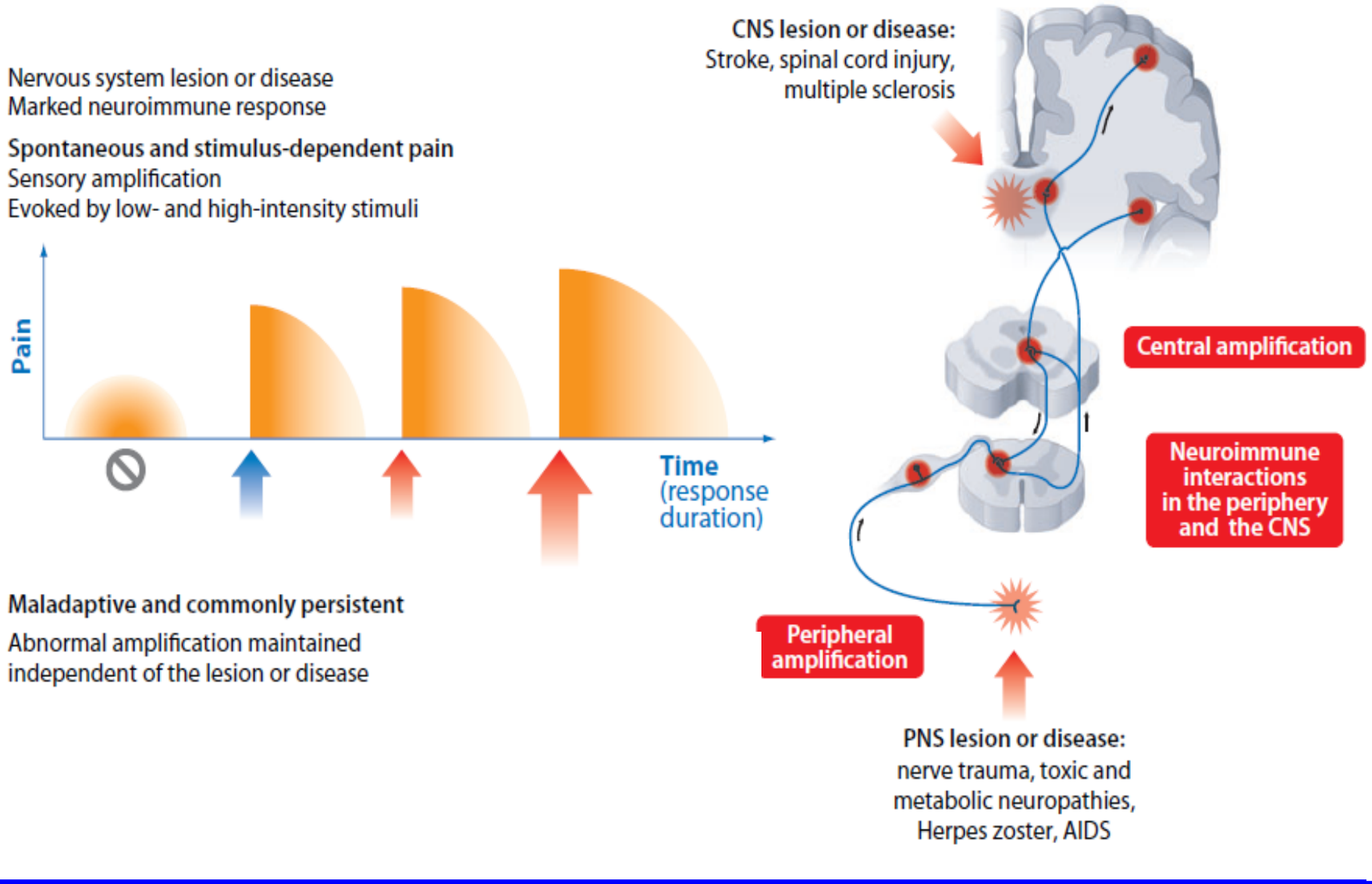


PNS or CNS lesions

Allodynia, hyperalgesia, spontaneous pain, negative symptoms

Low threshold – pathological/maladaptive

Neuropathic Pain



II. Assessment and Treatment of Neuropathic Pain

Learning objective: present an evidenced-based approach to treating neuropathic pain

Neuropathic Pain - Definition

Pain caused by a lesion or disease of the somatosensory nervous system (IASP).

Common Etiologies of Neuropathic Pain (PNS and/or CNS injury/dysfuncion)

- Stroke
- Spinal Cord Injury
- Metabolic abnormalities
  diabetes
- Chemotherapy/irradiation
- Neurotoxins
- Inherited neurodegeneration
- Nerve root compression
- Tumor infiltration
- Inflammation & infection
- Herpes Zoster
- Trigeminal neuralgia
- Mechanical irritation
- Nutritional deficiencies
- Trauma/surgery
- Multiple sclerosis
- Amputation
- HIV

Estimated Prevalence of Neuropathic Pain in the United States

Condition	Number of Cases
Painful diabetic neuropathy	600,000
Postherpetic neuralgia	500,000
Cancer-associated	200,000
Spinal cord injury	120,000
CRPS types I and II	100,000
HIV-associated	100,000[1]
Multiple sclerosis	50,000
Phantom pain	50,000
Post-stroke	30,000
Trigeminal neuralgia	15,000
Low back pain	2,100,000
Total (excluding back pain)	1,765,000
Total (including back pain)	**3,865,000**

Adapted from Bennett GJ. *Hosp Pract*. 1998;33:95-114.
Schifitto G et al. *Neurology*. 2002;58:1764-1768.

Symptoms of Neuropathic Pain

Evoked pain (stimulus-dependent)

- Allodynia
- Hyperalgesia

Spontaneous pain (stimulus-independent)

Loss of function (sensory, motor, autonomic)

A Stepwise Approach to Treating Neuropathic Pain

PAIN

Pain 132 (2007) 237–251

www.elsevier.com/locate/pain

Review and recommendations

Pharmacologic management of neuropathic pain: Evidence-based recommendations

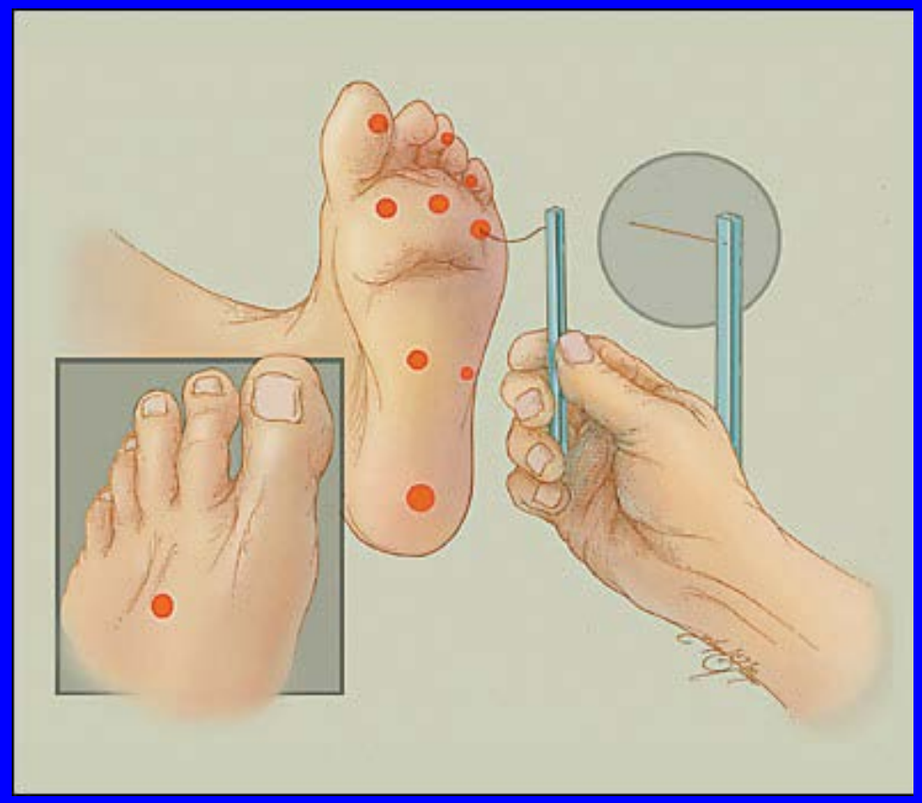
Robert H. Dworkin [a,*], Alec B. O'Connor [a], Miroslav Backonja [b], John T. Farrar [c], Nanna B. Finnerup [d], Troels S. Jensen [d], Eija A. Kalso [e], John D. Loeser [f], Christine Miaskowski [g], Turo J. Nurmikko [h], Russell K. Portenoy [i], Andrew S.C. Rice [j], Brett R. Stacey [k], Rolf-Detlef Treede [l], Dennis C. Turk [f], Mark S. Wallace [m]

Pharmacologic management of neuropathic pain

Step 1: Initial evaluation

- Assess – is NP present?
- If possible, treat the underlying cause of NP; refer specialist(s) as appropriate.
- Identify relevant co-morbidities (e.g., cardiac, renal, or hepatic disease, depression, gait instability) that might require dosage adjustment, additional monitoring of therapy, etc.
- Explain the diagnosis and treatment plan to the patient, and establish realistic expectations.

Establish the diagnosis, search for underlying etiology, and discuss…



Manage Expectations – Patient’s and Your Own

Pharmacologic management of neuropathic pain

Step 2: Symptom management

Initiate pain treatment with one or more of the following first-line agents:

1. A secondary amine TCA (e.g., nortriptyline) or an SNRI (duloxetine, milnacipran, venlafaxine)

2. A calcium channel α2-δ ligand: gabapentin or pregabalin

Pharmacologic management of neuropathic pain

(Step 2: Symptom mgt cont.)

- For patients with localized peripheral NP: topical lidocaine used alone or in combination with one of the first-line therapies.
- For patients with acute NP or episodic exacerbations of severe NP, and when prompt pain relief is required during titration of a first-line medication, opioid analgesics or tramadol/tapentadol may be used alone or in combination with one of the first-line therapies.
- Consider non-pharmacologic treatments, and initiate as appropriate.

Pharmacologic management of neuropathic pain

Step 3: Reassessment

- Reassess pain, functional status and quality of life regularly.
- If substantial pain relief and tolerable side effects, continue treatment.
- If partial pain relief after an adequate trial, add another first-line NP medication.
- If no or inadequate pain relief (e.g., < 30% reduction) at target dosage, switch to an alternative first-line medication or add a second agent.

Polypharmacy is often beneficial and necessary

Nortriptyline and gabapentin, alone and in combination for neuropathic pain: a double-blind, randomised controlled crossover trial

Ian Gilron, Joan M Bailey, Dongsheng Tu, Ronald R Holden, Alan C Jackson, Robyn L Houlden

Lancet 2009; 374: 1252–61

Published Online September 30, 2009 DOI:10.1016/S0140-6736(09)61081-3

See Comment page 1218

Department of Anesthesiology (Prof I Gilron MD

Summary

Background Drugs for neuropathic pain have incomplete efficacy and dose-limiting side-effects when given as monotherapy. We assessed the efficacy and tolerability of combined nortriptyline and gabapentin compared with each drug given alone.

Methods In this double-blind, double-dummy, crossover trial, patients with diabetic polyneuropathy or postherpetic neuralgia, and who had a daily pain score of at least 4 (scale 0–10), were enrolled and treated at one study site in Canada between Nov 5, 2004, and Dec 13, 2007. 56 patients were randomised in a 1:1:1 ratio with a balanced Latin

Pharmacologic management of neuropathic pain

Step 4: Referral as appropriate

If trials of first-line medications alone and in combination fail, consider second- and third-line medications or referral to a pain specialist, ideally at a multidisciplinary pain center, and/or other appropriate specialists.

FDA Approved Medications for Neuropathic & Chronic Pain

1. Carbamazepine (Tegretol) - trigeminal neuralgia
2. Triptans (5HT1 agonists) - migraine headache
3. Gabapentin (Neurontin) - postherpetic neuralgia
4. Duloxetine (Cymbalta) - diabetic peripheral neuralgia, fibromyalgia, chronic musculoskeletal pain
5. Pregabalin (Lyrica) - postherpetic neuralgia, diabetic peripheral neuralgia, fibromyalgia
6. Transdermal lidocaine 5% (Lidoderm) - postherpetic neuralgia
7. Transdermal capsaicin 8% (Qutenza) - postherptetic neuralgia
8. Milnacipran (Savella) - fibromyalgia
9. Prialt (ziconotide) - severe chronic pain in patients who are refractory to other therapies. Intrathecal delivery only.

First line Rx: TCAs/SNRIs

Treatment selection considerations for first-line medications and for opioid agonists

Medication class	Therapeutic index	Major side effects	Precautions	Other benefits	Cost
Secondary amine TCAs					
Nortriptyline, desipramine (use a tertiary amine TCA only if a secondary amine TCA is not available)	+	Sedation, dry mouth, blurred vision, weight gain, urinary retention	Cardiac disease, glaucoma, suicide risk, seizure disorder, concomitant use of tramadol	Improvement of depression, improvement of insomnia	$
SSNRIs					
Duloxetine[c]	++	Nausea	Hepatic dysfunction, renal insufficiency, alcohol abuse, concomitant use of tramadol	Improvement of depression	$$
Venlafaxine	+	Nausea	Concomitant use of tramadol, cardiac disease, withdrawal syndrome with abrupt discontinuation	Improvement of depression	$/$$

First line Rx: calcium channel α2-δ ligands

Treatment selection considerations for first-line medications and for opioid agonists

Medication class	Therapeutic index	Major side effects	Precautions	Other benefits	Cost
Calcium channel α2-δ ligands					
Gabapentin	++	Sedation, dizziness, peripheral edema	Renal insufficiency	Improvement of sleep disturbance, no clinically significant drug interactions	$/$$
Pregabalin[c]	++	Sedation, dizziness, peripheral edema	Renal insufficiency	Improvement of sleep disturbance, improvement of anxiety, no clinically significant drug interactions	$$

Opioids as a second line Rx (?)

Treatment selection considerations for first-line medications and for opioid agonists

Medication class	Therapeutic index	Major side effects	Precautions	Other benefits	Cost
Opioid agonists					
Morphine, oxycodone, methadone, levorphanol	+	Nausea/vomiting, constipation, drowsiness, dizziness	History of substance abuse, suicide risk, driving impairment during treatment initiation	Rapid onset of analgesic benefit	$/$$
Tramadol	+	Nausea/vomiting, constipation, drowsiness, dizziness seizures	History of substance abuse, suicide risk, driving impairment during treatment initiation, seizure disorder, concomitant use of SSRI, SSNRI, TCA	Rapid onset of analgesic benefit	$/$$

Third-line NP Agents

- Other antiepileptic and antidepressant medications – e.g., topiramate, lamotrigine, etc.
- Na-channel blockers – e.g., mexiletine
- Topical capsaicin 8% (PHN)
- NMDA receptor antagonists

Special Populations with Neuropathic Pain

Central neuropathic pain

- Post-stroke pain → TCAs
- Spinal-cord injury pain → α2-δ ligands
- Multiple sclerosis → cannabinoids? (limited data, risk of psychosis)

Chronic radicular pain

- Little long-term outcome outcome data, but 1st line NP agents are likely effective

Summary

- A substantial body of evidence guides the pharmacologic treatment of patients with neuropathic pain (LEVEL I).
- Polypharmacy often required.
- The utility of chronic opioid management for NP is controversial.

IV. Opioid Therapy for Chronic, non-Terminal Pain: Utility and Risk Mitigation

Opioid Therapy: Fear

"There is a Reason They Call it Dope"

by James E. Brick MD, *EB Flink Professor and Chair of Medicine, West Virginia University, Morgantown* and
John F. Brick MD, *Professor and Chair, Neurology, West Virginia University, Morgantown*

Among the lists ranking various states and their attributes our beloved West Virginia is usually at the extremes of the rankings, either very good (e.g. murders) (e.g. obesity and its concor For several years we have on the "bad end" of the sc prescription narcotic drug and overdoses. These pub problems have now reach proportions all over West perhaps particularly south Route 60 where US 119 is referred to with gallows h the "Hillbilly Heroin High frequently have an outrea down there and hardly a v by without us hearing of a seeking home invasion or violence in a small town t dreamed of such 20 years

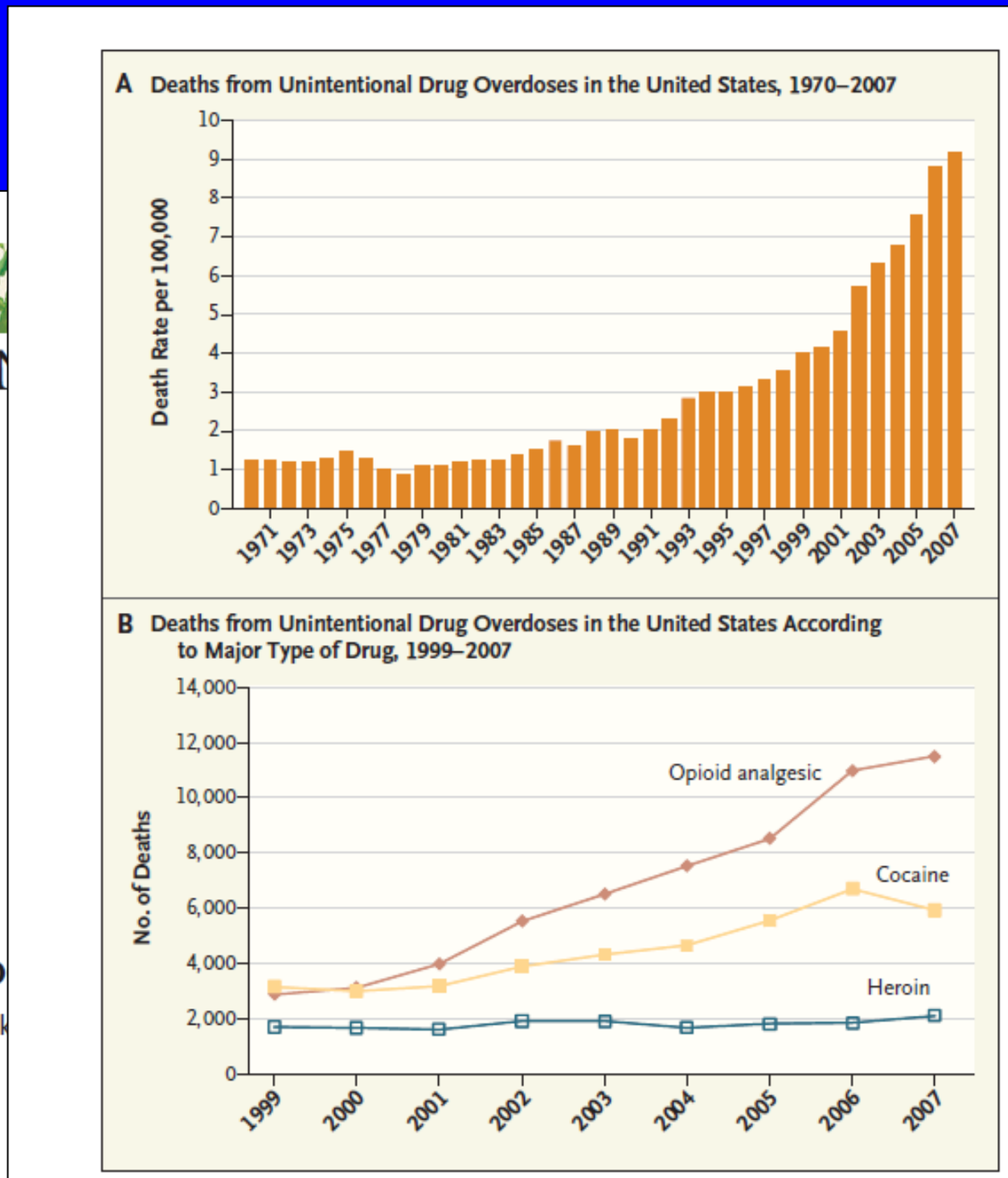
as patients in pain but many did, and though lots of these drugs come into WV from out of state, prescriptions are certainly a major

themselves who are caught up in this. We now know many babies are born every year in West Virginia with abused drugs in their cord blood. ut something, seek to become doctors don't dependent/ wish family t these drugs to Efforts to stem multiple forms. that narcotic w often begins ven for acute has taken cotic exposure ip to the ER. t Virginia have the prescription thoughtfulness

professional parents' knees. These drugs have serious implications. Patients taking them on a chronic basis are in danger of "losing their soul" to them. Don't get your patients started on chronic narcotics for nonmalignant pain. It's as simple as that. Don't go there to begin with. Just say no. Barring that, think long and hard about it and other options and make sure your patient knows what they may be getting in for.

W V Med J. 2013 Nov-Dec;109(6):6. "There is a reason they call it dope". Brick JE, Brick JF.

Opioid Misuse & Abuse: A National Scourge



U.S. Rates of Death from Unintentional Drug Overdoses and Numbers of Deaths, According to Major Type of Drug.

Shown are nationwide rates of death from unintentional drug overdoses from 1970 through 2007 (Panel A) and the numbers of such deaths from opioid analgesics, cocaine, and heroin from 1999 through 2007 (Panel B). Data are from the National Vital Statistics System, Centers for Disease Control and Prevention.

NEJM 18 Nov 2010

Chronic Opioid Therapy: Paucity of Outcome Data

Open-label study to evaluate the efficacy and safety of extended-release hydromorphone in patients with chronic neuropathic pain. Nalamachu S, Ruck D, Nalamasu R, Fasbinder S, Bansal R.

OBJECTIVE:
To assess the efficacy and safety of once-daily hydromorphone extended-release tablets (OROS [Alza Corporation, Mountain View, CA] hydromorphone ER) in patients with chronic neuropathic pain.

DESIGN:
Single-center, open-label, 12-week study.

PATIENTS:
Opioid-tolerant patients with chronic neuropathic pain for $6 months (N = 30). Interventions: Patients were converted from previous opioid therapy to OROS hydromorphone ER using a 5:1 morphine:hydromorphone equianalgesic dosing ratio, with an initial 50 percent reduction of the calculated equianalgesic dose, titrated every 3-4 days to adequate analgesia over 2 weeks.

OUTCOME MEASURES:
The primary efficacy measure was change from baseline to week 12 (end of study) on question #5 ("average pain") of the Brief Pain Inventory (BPI). Secondary measures included least pain, worst pain, current pain, and sleep interference on the BPI, as well as the Pain Quality Assessment Scale (PQAS) and patient global assessment of treatment satisfaction. Results: Thirty patients were enrolled and received $1 dose of OROS hydromorphone ER, titrated to a final mean dose of 26.4 mg/d. Mean (SE) BPI change from baseline to end of study was -1.3 (0.59) for current pain ($p < 0.05$) and -1.8 (0.61) for worst pain ($p < 0.01$). Mean (SE) change from baseline was also significant for BPI scores for sleep interference (-1.7 [0.61]; $p < 0.01$) and PQAS scores (-24.8 [7.9], $p < 0.01$). The majority (81 percent) of patients were satisfied or very satisfied with treatment. The most common treatment-related adverse events were dizziness, headache, and nausea (two patients each).

CONCLUSIONS:
Patients with chronic neuropathic pain were safely and effectively converted to and maintained on OROS hydromorphone ER.

J Opioid Mgt 2013

Opioid Therapy: Federal and State Efforts

COMMONWEALTH OF MASSACHUSETTS
BOARD OF REGISTRATION IN MEDICINE

Commonwealth of Massachusetts, Department of Public Health
Drug Control Program
Prescription Monitoring Program
99 Chauncy Street, Boston, MA 02111
Telephone 617 983-6700

Prescriber Guide to Interpreting Prescription Monitoring Program Data

This guide is designed to assist prescribers in understanding the scope and limitations of the patient prescription history reports and electronic alerts of the Massachusetts Online Prescription Monitoring Program (MA Online PMP). Developed in consultation with pain and addiction specialists, it provides guidance in treating all patients including those for whom prescribers may have concern. It is important to note that, whether in the context of an electronic alert or a routine patient prescription history lookup, this guide does not mandate any particular action on the part of the prescriber.

About the MA Online PMP

The MA Online PMP is a secure website that can be utilized by authorized providers to retrieve the most recent twelve months' of Schedule II - V dispensed prescription histories on their

Chronic Opioid Therapy is Almost Never a Monotherapy

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Disclosures:

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0894-9115/13/9201-0077/0

Pain

ORIGINAL RESEARCH ARTICLE

The Effects of Interdisciplinary Team Assessment and a Rehabilitation Program for Patients with Chronic Pain

ABSTRACT

Pietilä Holmner E, Fahlström M, Nordström A: The effects of interdisciplinary team assessment and a rehabilitation program for patients with chronic pain. Am J Phys Med Rehabil 2013;92:77–83.

Objective: The aim of this study was to evaluate the effects of interdisciplinary team assessment and a 4-wk rehabilitation program in chronic pain patients.

Design: This was a longitudinal cohort study evaluating interdisciplinary pain rehabilitation measures in a specialist care setting. A total of 93 women (42.2 ± 9.5 yrs) with chronic musculoskeletal pain (median pain duration, 8 yrs) were

- Don’t rush to initiate opioid therapy, particularly if you have not cared for the patient longitudinally. Employ a step-wise approach to pain treatment.
- Prior to initiating opioids:
  - Goals of therapy with indicators of success and ‘failure’
  - Opioid agreement (communication tool)
  - Toxicology at time of initial request
  - Psychological assessment/opioid risk stratification
- Start low, go slow, and don’t titrate to heroic doses
- Regular, meaningful reassessment
- Trust but verify
  - Call other providers (**communication** is key)
  - Call pharmacies
  - Check prescription monitoring program, if available
  - Random toxicology (urine/saliva) – provide a little rope when appropriate
  - Utilize a multidisciplinary approach

Opioid Therapy – other thoughts…

- Remain open minded. There is much more that we don't know than we do know.

- Don't be an extremist.
  - ➢ I never prescribe (OIH), or
  - ➢ I don't believe in a dose ceiling.

- Chronic pain in the elderly is very common and there are frequently few meaningful treatment options. Low dose opioid therapy may be the best analgesic choice.

Case Study:

82 y/o formerly high-functioning male presents with low back and lower extremity pain secondary to severe non-operable spinal stenosis and painful peripheral neuropathy.

Thank You