
KNOW
PAIN IN
GENERAL

Development Committee

Mario H. Cardiel, MD, MSc
Rheumatologist
Morelia, Mexico

Andrei Danilov, MD, DSc
Neurologist
Moscow, Russia

Smail Daoudi, MD
Neurologist
Tizi Ouzou, Algeria

João Batista S. Garcia, MD, PhD
Anesthesiologist
São Luis, Brazil

Yuzhou Guan, MD
Neurologist
Beijing, China

Jianhao Lin, MD
Orthopedist
Beijing, China

Supranee Niruthisard, MD
Anesthesiologist, Pain Specialist
Bangkok, Thailand

Germán Ochoa, MD
Orthopedist, Spine Surgeon and Pain Specialist
Bogotá, Colombia

Milton Raff, MD, BSc
Consultant Anesthetist
Cape Town, South Africa

Raymond L. Rosales, MD, PhD
Neurologist
Manila, Philippines

Ammar Salti, MD
Consultant Anesthetist
Abu Dhabi, United Arab Emirates

Jose Antonio San Juan, MD
Orthopedic Surgeon
Cebu City, Philippines

Xinping Tian, MD
Rheumatologist
Beijing, China

Işin Ünal-Çevik, MD, PhD
Neurologist, Neuroscientist and Pain Specialist
Ankara, Turkey

This program was sponsored by Pfizer Inc.

Learning Objectives

- After completing this module, participants will be able to:
  - Describe the classification of pain according to pain mechanisms, duration, severity and type of tissue involved
  - Discuss overall prevalence of pain
  - Assess patients presenting with pain
  - Select appropriate pharmacological and non-pharmacological strategies based on type of pain
  - Know when to refer patients to specialists

Table of Contents

- What is pain?
- How common is pain?
- What are the underlying types of pain?
- How should pain be assessed in clinical practice?
- How should pain be treated based on its pathophysiology?

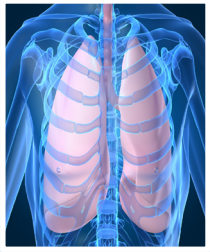
What is pain?

An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

International Association for the Study of Pain (IASP) 2011

International Association for the Study of Pain. *IASP Taxonomy.* Available at: http://www.iasp-pain.org/AM/Template.cfm?Section=Pain_Definitions. Accessed: July 15, 2013.

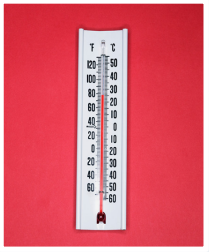
Pain Is the 5th Vital Sign



Respiration

Pulse

Blood pressure



Temperature

Pain

Phillips DM. *JAMA* 2000; 284(4):428-9.

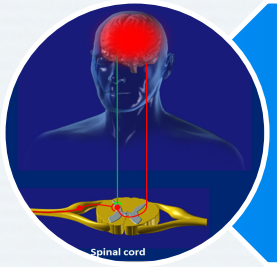
Overview of Pain

Protective role: vital early warning system

- Senses noxious stimuli
- Triggers withdrawal reflex and heightens sensitivity after tissue damage to reduce risk of further damage

Unpleasant experience:

- Suffering – physical, emotional and cognitive dimensions
- Continuous unrelieved pain can affect physical (e.g., cardiovascular, renal, gastrointestinal systems, etc.) and psychological states



Maladaptive response:

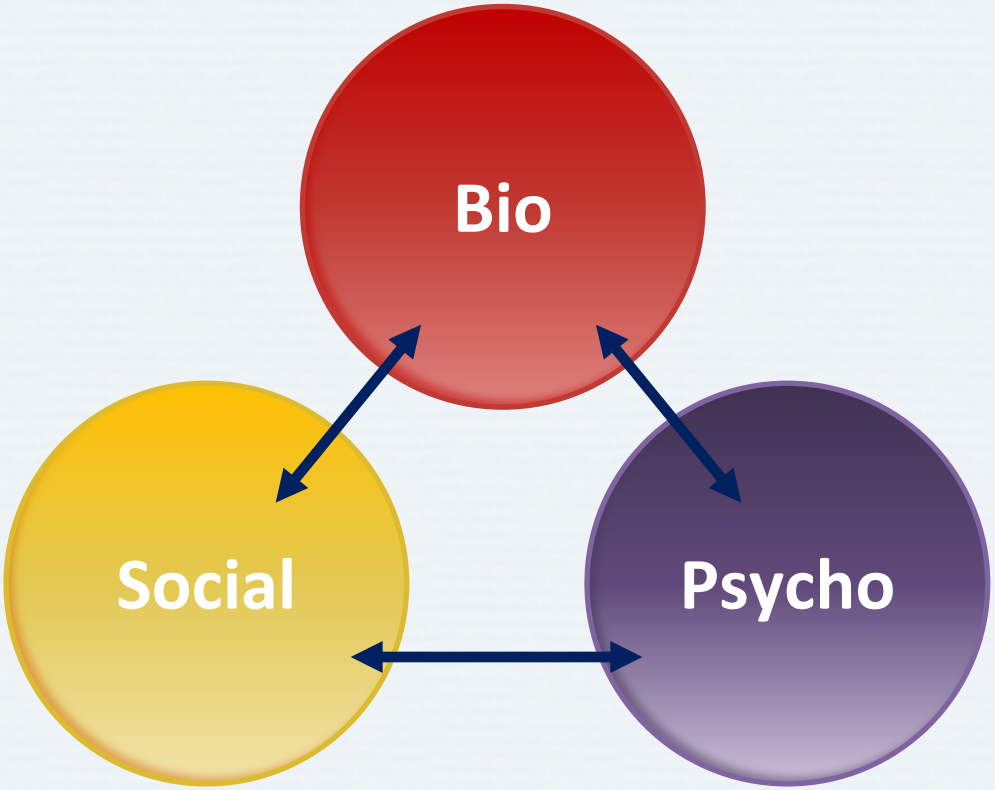
- Neuropathic and central sensitization/dysfunctional pain
- Not protective
- Lessens quality of life

Costigan M *et al*. *Annu Rev Neurosci* 2009; 32:1-32; Wells N *et al.* In: Hughes RG (ed). *Patient Safety and Quality: An Evidence-Based Handbook for Nurses.* Agency for Healthcare Research and Quality; Rockville, MD: 2008; Woolf CJ *et al. Ann Intern Med* 2004; 140(6):441-51.

Discussion Question

DOES EVERYONE FEEL PAIN THE SAME WAY?

Biopsychosocial Model of Pain

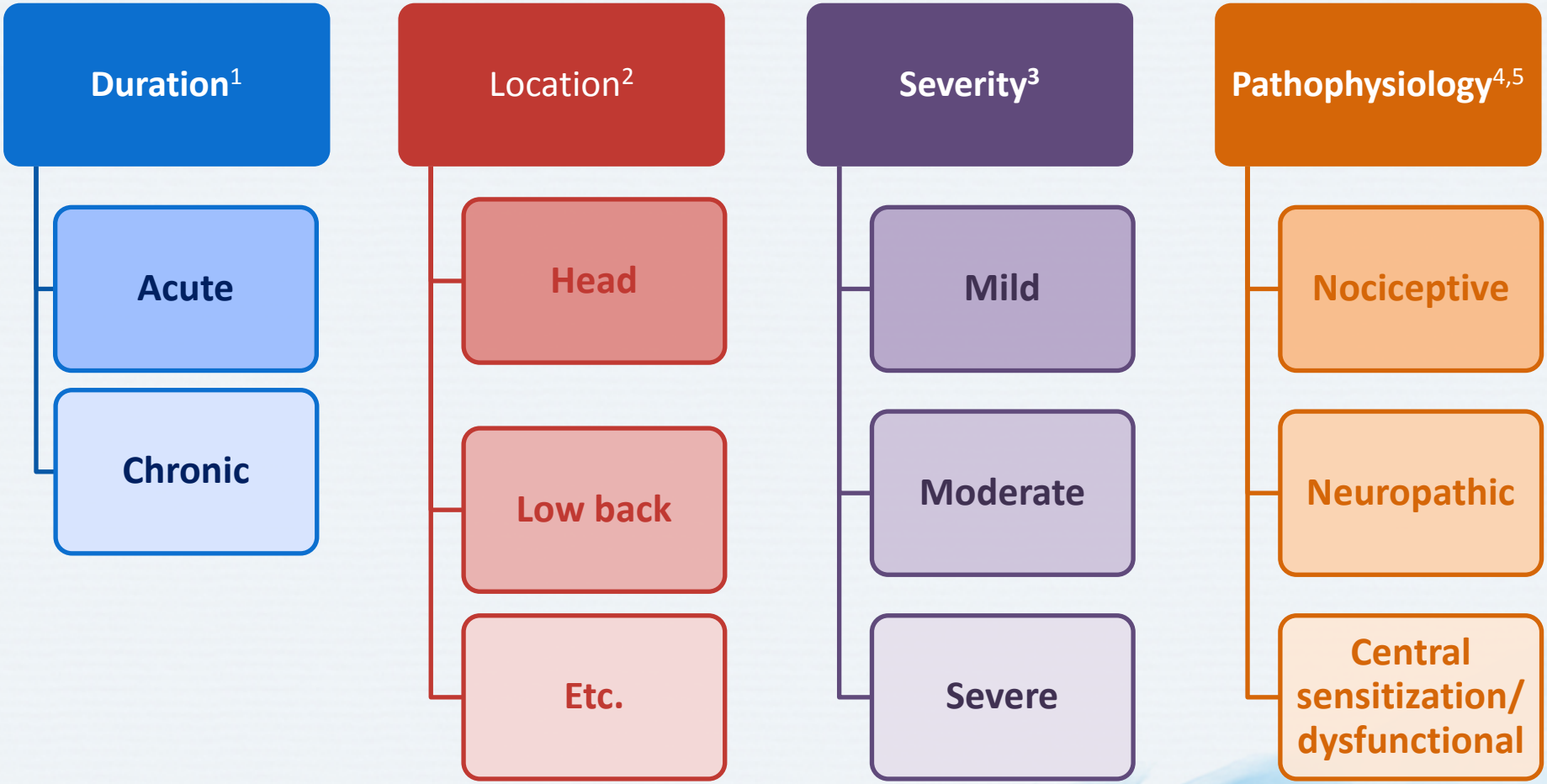


Gatchel RJ *et al. Psychol Bull* 2007; 133(4):581-624.

Discussion Question

FROM A PRACTICAL POINT OF VIEW, HOW DO YOU CLASSIFY PAIN?

Pain Classification



1. McMahon SB, Koltzenburg M. In: McMahon SB, Koltzenburg M (eds). *Wall and Melzack's Textbook of Pain*. 5th ed. Elsevier; London, UK: 2006;
2. Loeser D *et al* (eds). *Bonica's Management of Pain*. 3rd ed. Lippincott Williams & Wilkins; Hagerstown, MD: 2001;
3. Hanley MA *et al. J Pain* 2006; 7(2):129-33; 4. Jensen TS *et al. Pain* 2011; 152(10):2204-5; 5. Woolf CJ. *Pain* 2011; 152(3 Suppl):S2-15.

The Pain Continuum

Insult

Time to resolution

Acute pain → **Chronic pain**

Normal, time-limited response to 'noxious' experience (less than 3 months)

- Usually obvious tissue damage
- Serves a protective function
- Pain resolves upon healing

Pain that has persisted beyond normal tissue healing time (usually more than 3 months)

- Usually has no protective function
- Degrades health and function

Acute pain may become chronic

Chapman CR, Stillman M. In: Kruger L (ed). *Pain and Touch*. Academic Press; New York, NY: 1996; Cole BE. *Hosp Physician* 2002; 38(6):23-30;
International Association for the Study of Pain. *Unrelieved Pain Is a Major Global Healthcare Problem.*
Available at: http://www.iasp-pain.org/AM/Template.cfm?Section=Press_Release&Template=/CM/ContentDisplay.cfm&ContentID=2908. Accessed: July 24: 2013;
National Pain Summit Initiative. *National Pain Strategy: Pain Management for All Australians.*
Available at: http://www.iasp-pain.org/PainSummit/Australia_2010PainStrategy.pdf. Accessed: July 24, 2013;
Turk DC, Okifuji A. In: Loeser D *et al* (eds.). *Bonica's Management of Pain*. 3rd ed. Lippincott Williams & Wilkins; Hagerstown, MD: 2001.

Discussion Question

HOW MANY PATIENTS IN ACUTE PAIN DO YOU SEE DURING A TYPICAL WEEK?

Prevalence of Acute Pain

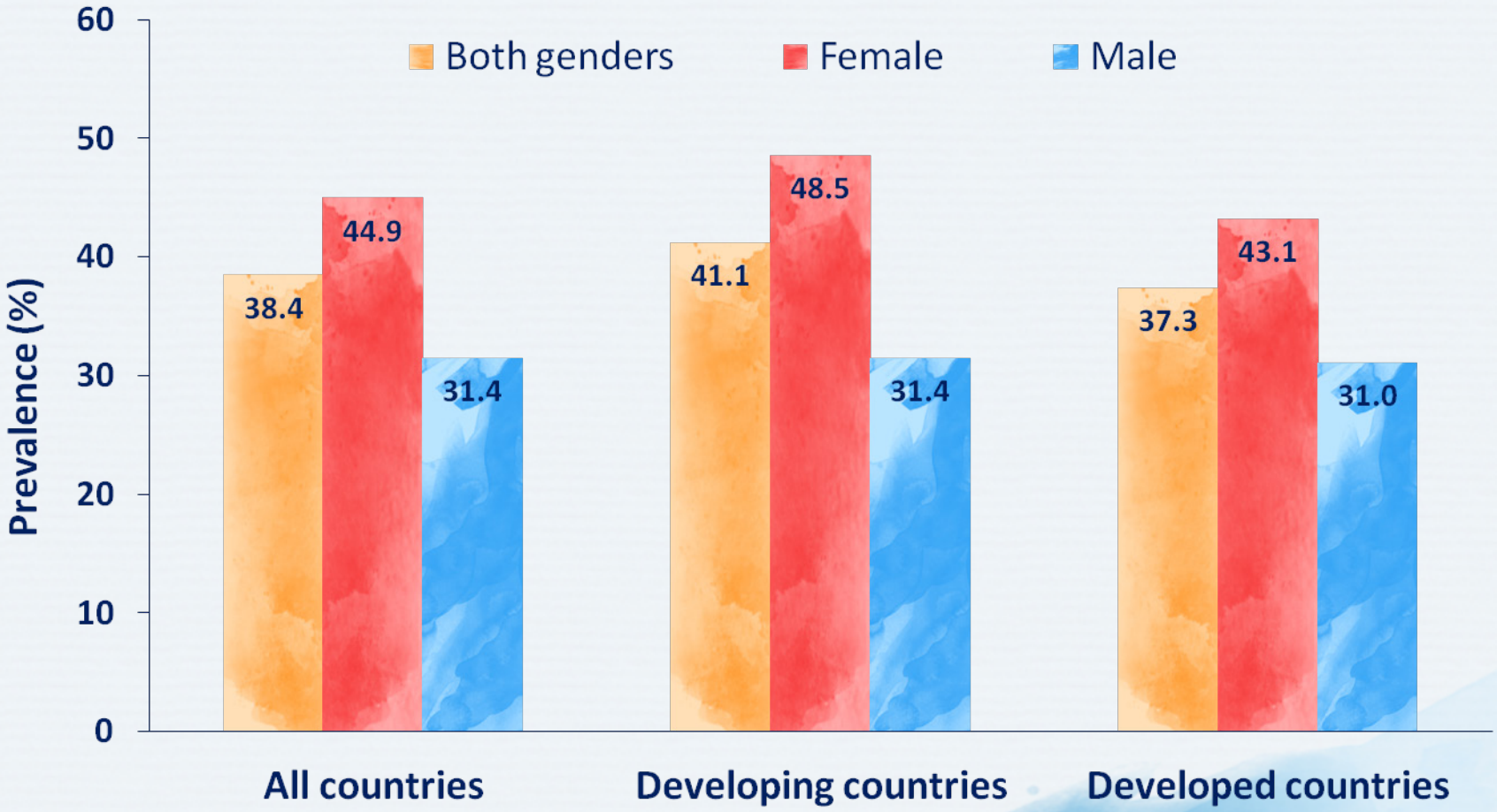
- **Lifetime** prevalence in general population:
  - Approaches **100%** for acute pain leading to use of analgesics[1]
- **Emergency room** patients:
  - Pain accounts for **>2/3** of emergency room visits[2]
- **Hospitalized** patients:
  - **>50%** report pain[3]

1. Diener HC *et al. J Headache Pain* 2008; 9(4):225-31; 2. Todd KH, Miner JR. In: Fishman SM *et al* (eds). *Bonica's Management of Pain.* 4th ed. Lippincott, Williams and Wilkins; Philadelphia, PA: 2010; 3. Dix P *et al. Br J Anaesth* 2004; 92(2):235-7.

Discussion Question

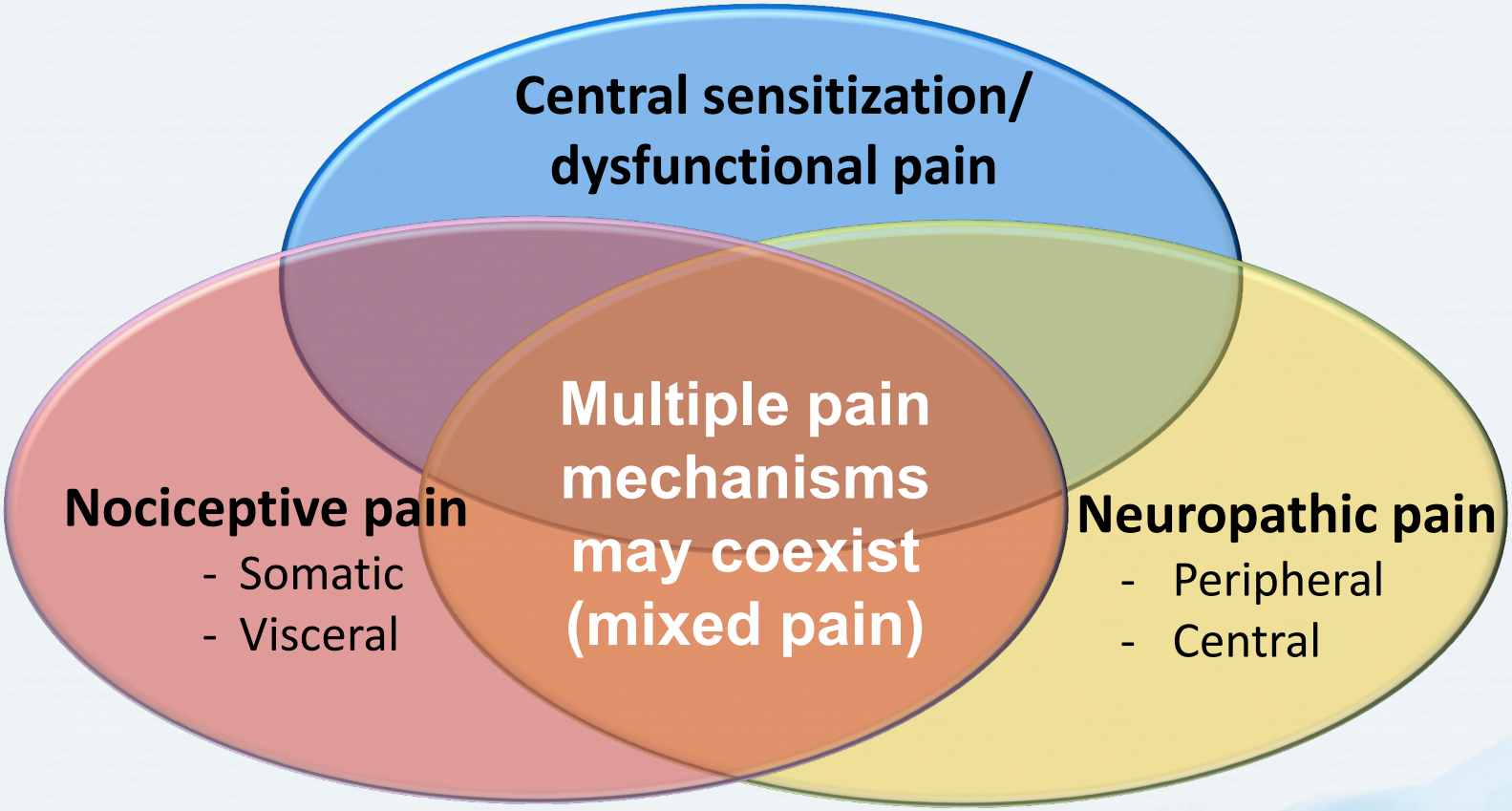
WHAT PROPORTION OF PATIENTS IN YOUR PRACTICE SUFFERS FROM CHRONIC PAIN?

Prevalence of Chronic Pain



Tsang A *et al. J Pain* 2006; 9(10):883-91.

Pathophysiological Classification of Pain



Freynhagen R, Baron R. *Curr Pain Headache Rep* 2009; 13(3):185-90; Jensen TS *et al. Pain* 2011; 152(10):2204-5;
Julius D *et al.* In: McMahon SB, Koltzenburg M (eds). *Wall and Melzack's Textbook of Pain.* 5th ed. Elsevier; London, UK: 2006;
Ross E. *Expert Opin Pharmacother* 2001; 2(1):1529-30; Webster LR. *Am J Manag Care* 2008; 14(5 Suppl 1):S116-22; Woolf CJ. *Pain* 2011; 152(3 Suppl):S2-15.

What is nociceptive pain?

Definition

- Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors
- Can be somatic or visceral

Pain Quality

- Usually aching or throbbing
- Usually time-limited (resolves when damaged tissue heals)
- Usually well localized if somatic
- May be referred if visceral
- Can become chronic

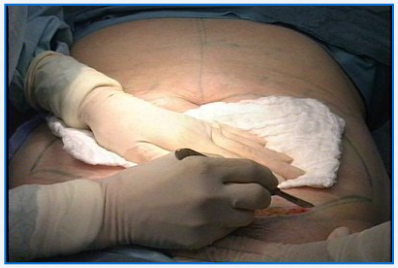
Felson DT. *Arthritis Res Ther* 2009; 11(1):203; International Association for the Study of Pain. *IASP Taxonomy.* Available at: http://www.iasp-pain.org/AM/Template.cfm?Section=Pain_Definitions. Accessed: July 15, 2013; McMahon SB, Koltzenburg M (eds). *Wall and Melzack's Textbook of Pain.* 5th ed. Elsevier; London, UK: 2006; Woolf CJ. *Pain* 2011;152(3 Suppl):S2-15.

Nociceptive Pain

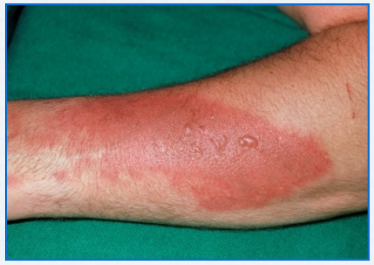
Somatic

Musculoskeletal injury

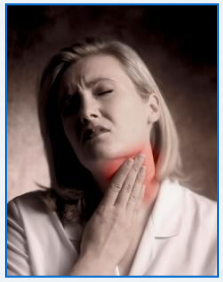
Trauma



Post-operative pain

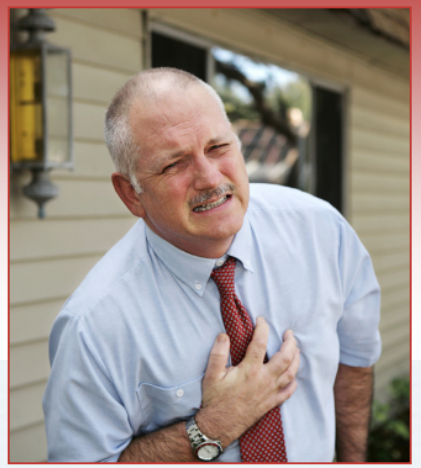


Burn pain



Infection, e.g., pharyngitis

Visceral



Ischemic, e.g., myocardial infarction

Abdominal colic

Dysmenorrhea

Fishman SM *et al* (eds). *Bonica's Management of Pain.* 4th ed. Lippincott, Williams and Wilkins; Philadelphia, PA: 2010.

Somatic vs. Visceral Pain

Somatic

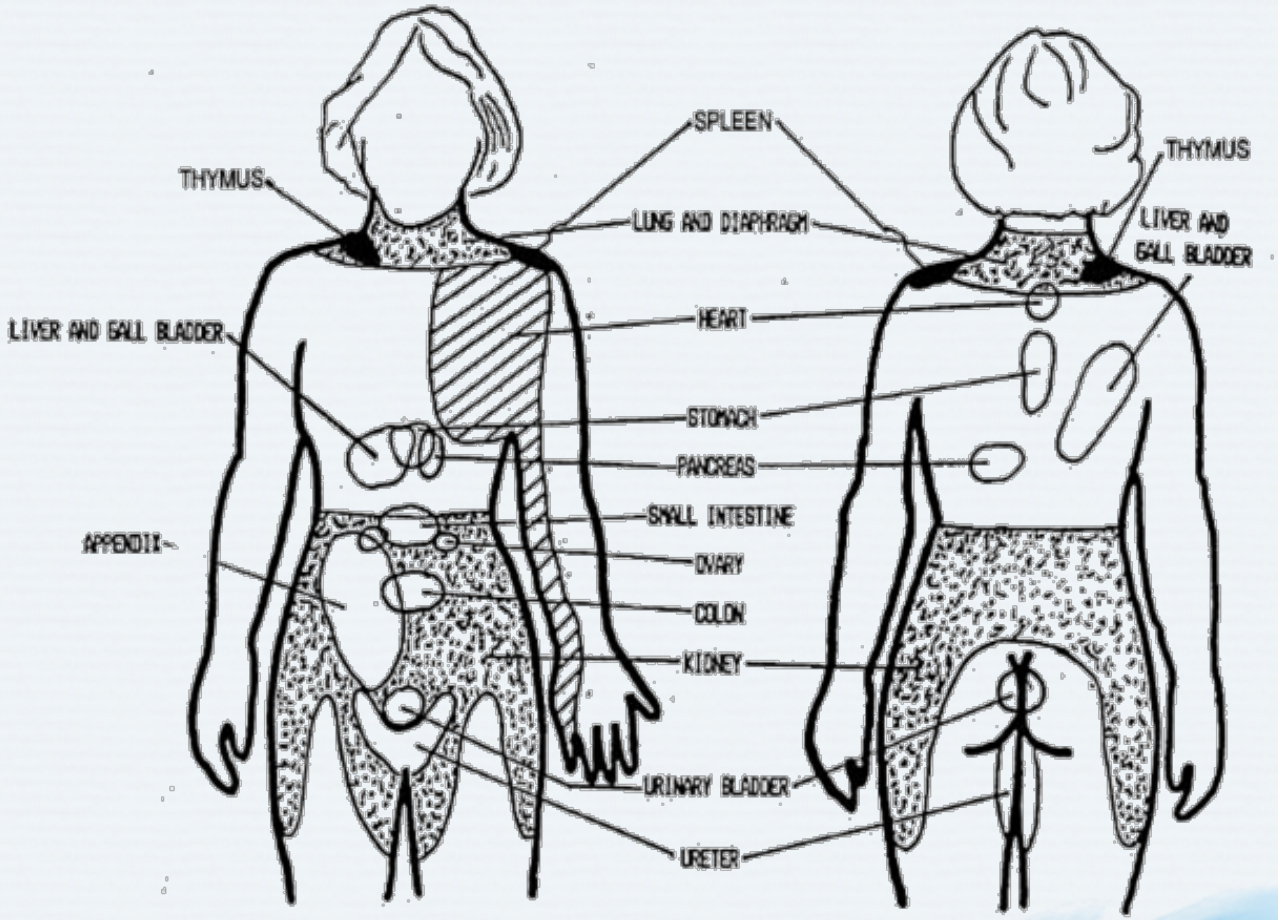
- Nociceptors are involved
- Often well localized
- Usually described as throbbing or aching
- Can be superficial (skin, muscle) or deep (joints, tendons, bones)

Visceral

- Involves hollow organ and smooth muscle nociceptors that are sensitive to stretching, hypoxia and inflammation
- Pain is usually referred, poorly localized, vague and diffuse
- May be associated with autonomic symptoms (e.g., pallor, sweating, nausea, blood pressure and heart rate changes)

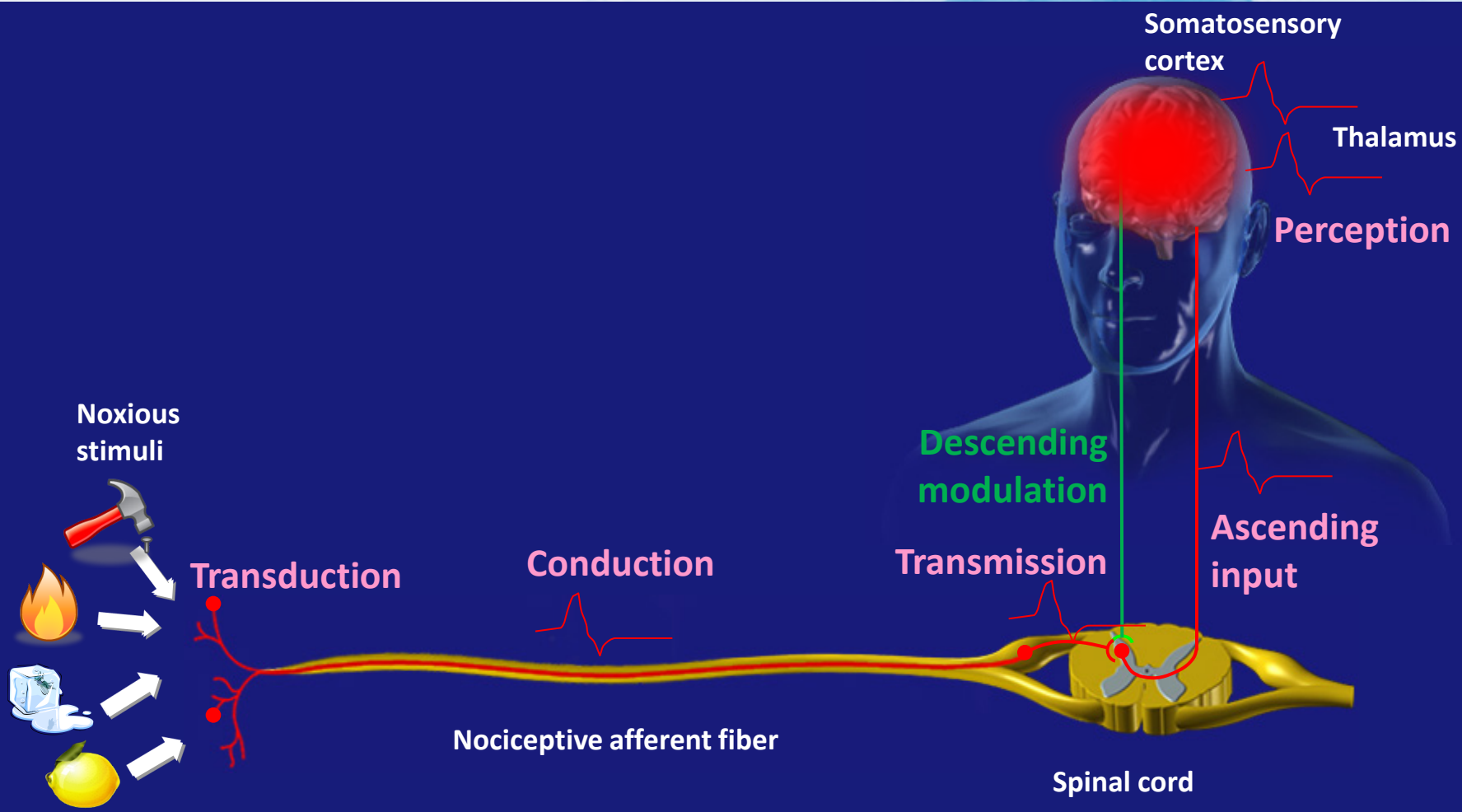
McMahon SB, Koltzenburg M (eds). *Wall and Melzack's Textbook of Pain.* 5th ed. Elsevier; London, UK: 2006;
Sikandar S, Dickenson AH. *Curr Opin Support Palliat Care* 2012; 6(1):17-26.

Referred Pain



Hudspith MJ *et al.* In: Hemmings HC, Hopkins PM (eds). *Foundations of Anesthesia*. 2nd ed. Elsevier; Philadelphia, PA: 2006;
Schmitt WH Jr. *Uplink* 1998; 10:1-3.

Nociception: Neural Process of Encoding Noxious Stimuli



Consequences of encoding may be autonomic (e.g., elevated blood pressure) or behavioral (motor withdrawal reflex or more complex nocifensive behavior). Pain perception is not necessarily implied.

Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7.

Transduction via Endogenous Mediators

Noxious stimuli

- Mechanical
- Thermal
- Chemical

Mediators

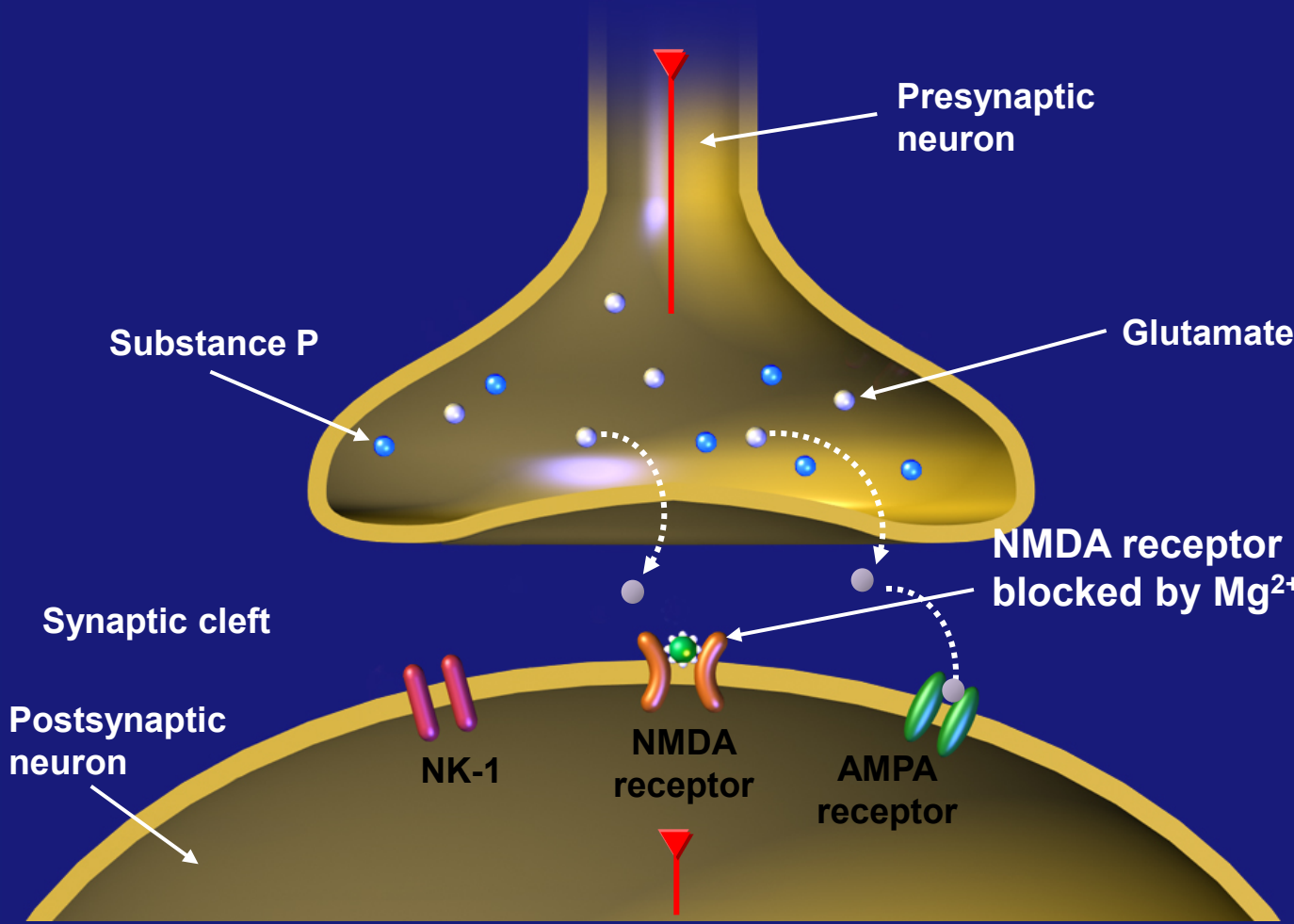
- Prostaglandins
- Leukotrienes
- Substance P
- Histamine
- Bradykinin
- Serotonin
- Hydroxyacids
- Reactive oxygen species
- Inflammatory cytokines and chemokines

Receptors/channels on nociceptors

Julius D, Basbaum AI. *Nature* 2001; 413(6852):203-10; Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7; Woolf CJ, Salter MW. *Science* 2000; 288(5472):1765-68.

Transmission via Neurotransmitters

1. Impulses reach terminals of presynaptic neuron
2. Glutamate is released into synaptic cleft
3. Glutamate binds to AMPA receptor
4. Impulse is transmitted to postsynaptic neuron



AMPA = 2-amino-3-(3-hydroxy-5-methyl-isoxazol-4-yl) propanoic acid; NK = neurokinin; NMDA = N-methyl-D-aspartate

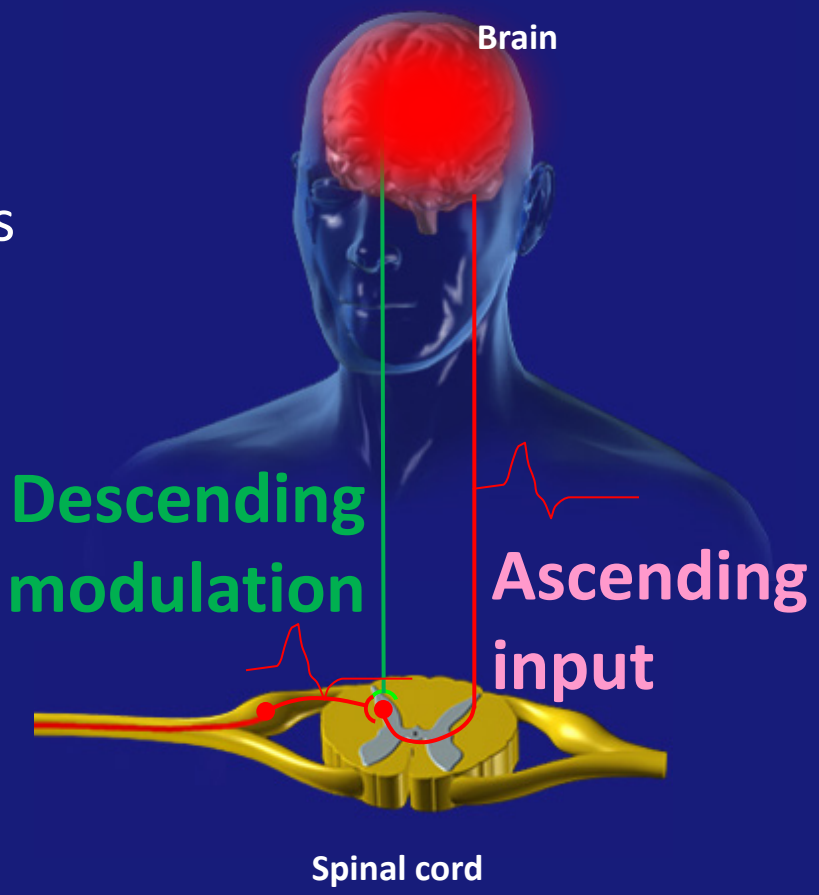
Fields HL *et al.* In: McMahon SB, Koltzenburg M (eds). *Wall and Melzack's Textbook of Pain.* 5th ed. Elsevier; London, UK: 2006; Julius D, Basbaum AI. *Nature* 2001; 413(6852):203-10; Woolf CJ, Salter MW. *Science* 2000; 288(5472):1765-68.

Pain Modulation

- Pain is modulated via **ascending nociceptive** and **descending inhibitory/facilitatory** spinal tracts

Ascending Nociceptive
C fibers Aδ fibers

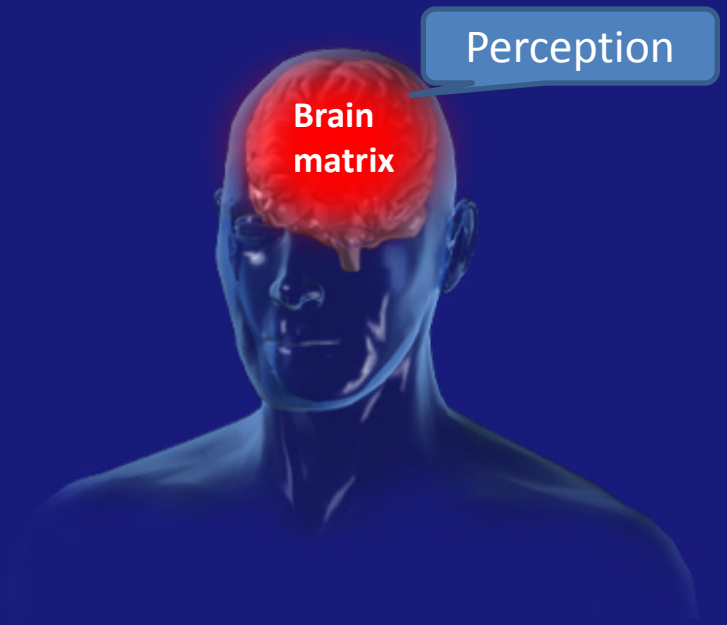
Descending Inhibitory/facilitatory
Serotonin Norepinephrine Dopamine



Benarroch EE. *Neurology* 2008 ; 71(3):217-21; Fields HL *et al.* In: McMahon SB, Koltzenburg M (Eds). *Wall and Melzack's Textbook of Pain.* 5th ed. Elsevier; London, UK: 2006; Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7.

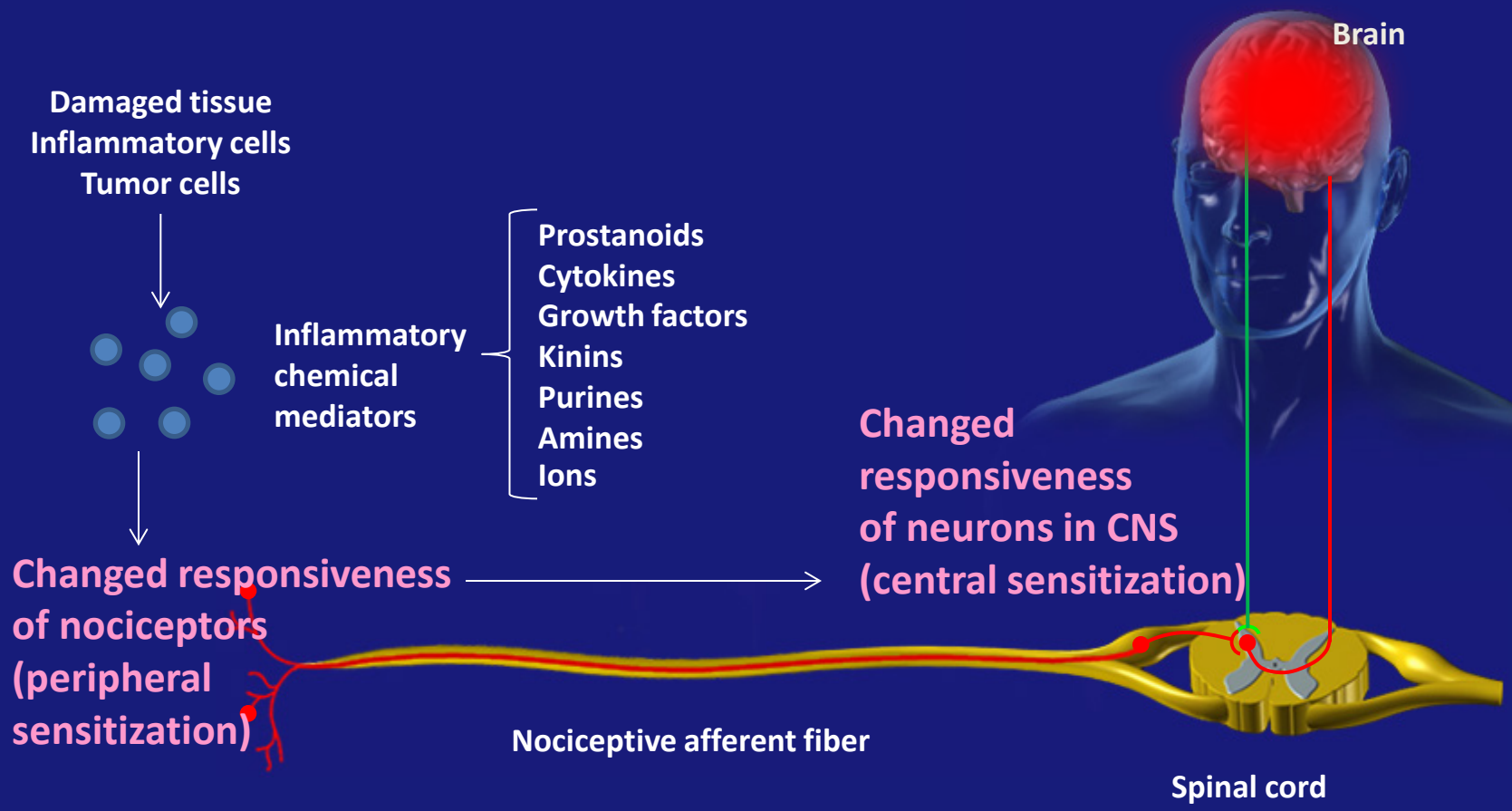
Pain Perception

- Spinal cord transmits pain signals to specific nuclei in the thalamus, and from there to wide variety of regions in the brain – collectively known as the "pain matrix"
- Pain perception can also be altered without any external stimuli (i.e., through emotion, distraction, placebo, etc.)



Tracey A, Dickenson A. *Cell* 2012; 148(6):1308-e2.

Inflammation



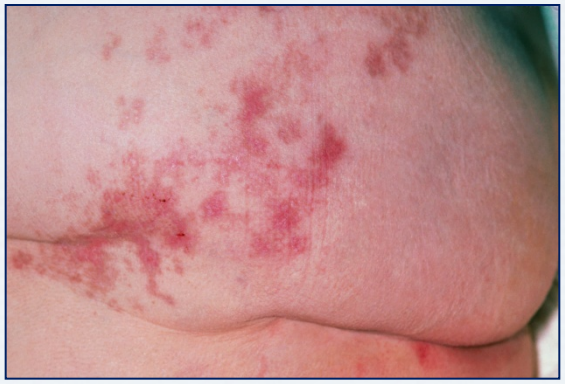
CNS = central nervous system

Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7.

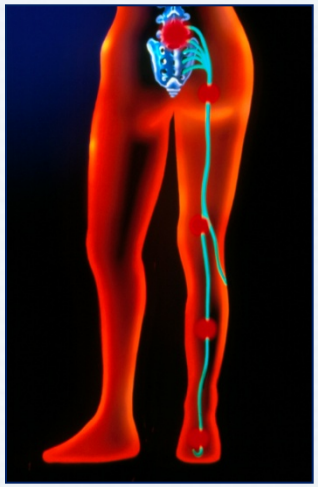
Recognizing Neuropathic Pain

Post-stroke pain

Diabetic peripheral neuropathy



Postherpetic neuralgia



Lumbar radicular pain

Common descriptors

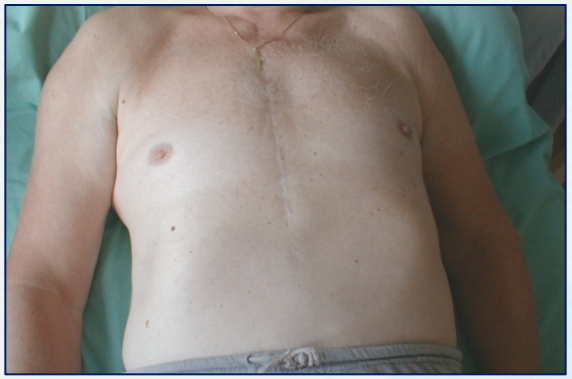
Shooting

Electric shock-like

Burning

Tingling

Numbness



Chronic post-surgical pain

1. Baron R *et al. Lancet Neurol* 2010; 9(8):807-19.

What is neuropathic pain?

Definition

- Pain caused by a lesion or disease of the somatosensory nervous system
- Can be peripheral or central

Pain Quality

- Burning
- Lancinating
- Electric shock-like
- Often diffuse
- Frequently with allodynia and/or hyperalgesia

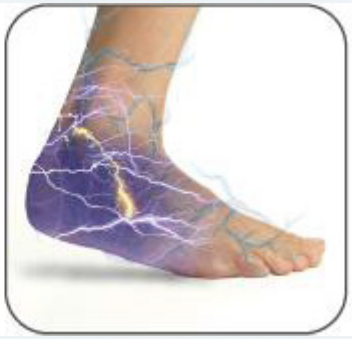
Chong MS, Bajwa ZH. *J Pain Symptom Manage* 2003; 25(5 Suppl):S4-11; Cruccu G *et al. Eur J Neurol* 2004; 11(3):153-62; Dray A. *Br J Anaesth* 2008; 101(1):48-58; International Association for the Study of Pain. *IASP Taxonomy.* Available at: http://www.iasp-pain.org/AM/Template.cfm?Section=Pain_Definitions. Accessed: July 15, 2013; McMahon SB, Koltzenburg M (eds). *Wall and Melzack's Textbook of Pain.* 5th ed. Elsevier; London, UK: 2006; Woolf CJ. *Pain* 2011;152(3 Suppl):S2-15.

Common Descriptors of Neuropathic Pain

Burning

Tingling

Pins and needles

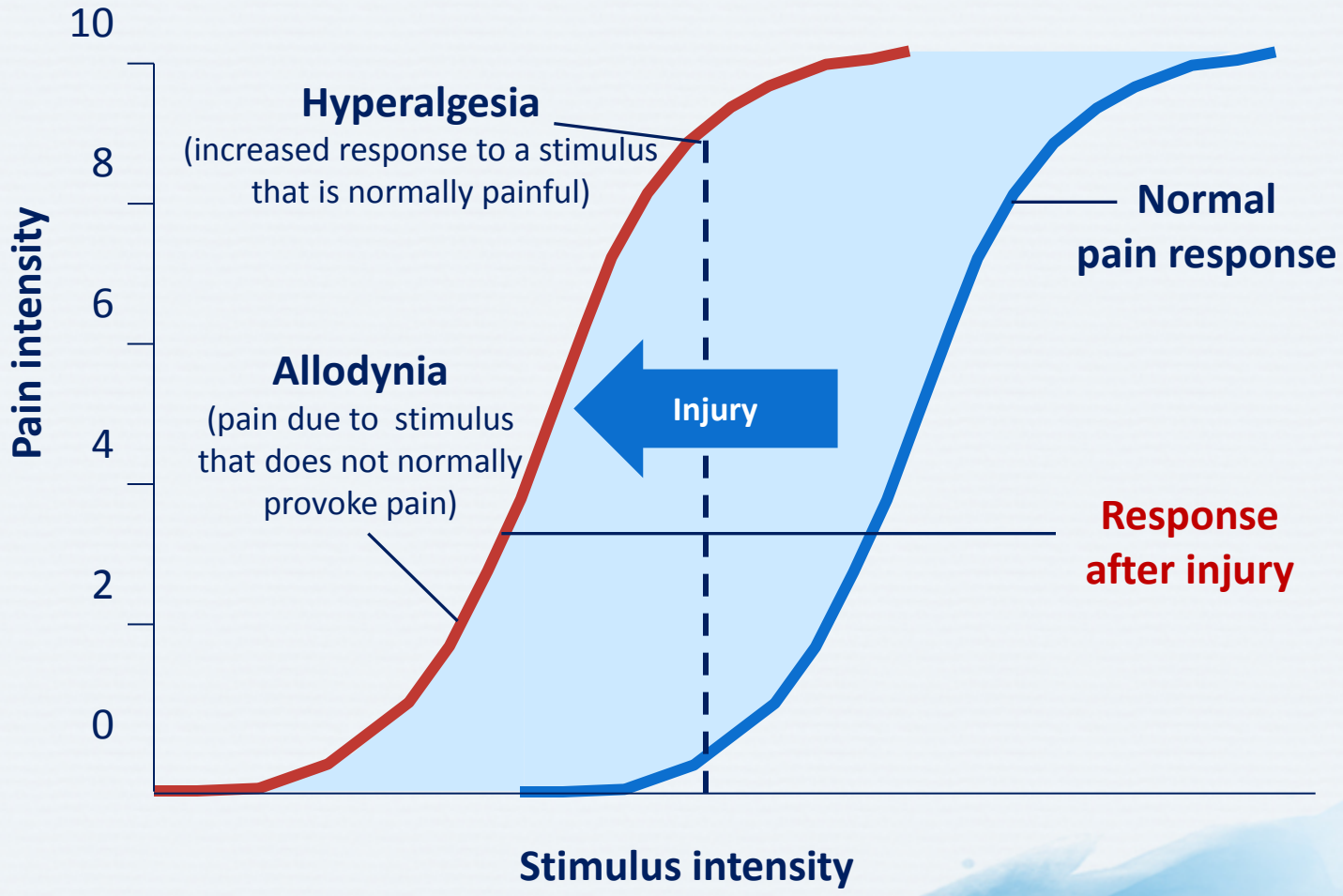


Electric shock-like

Numbness

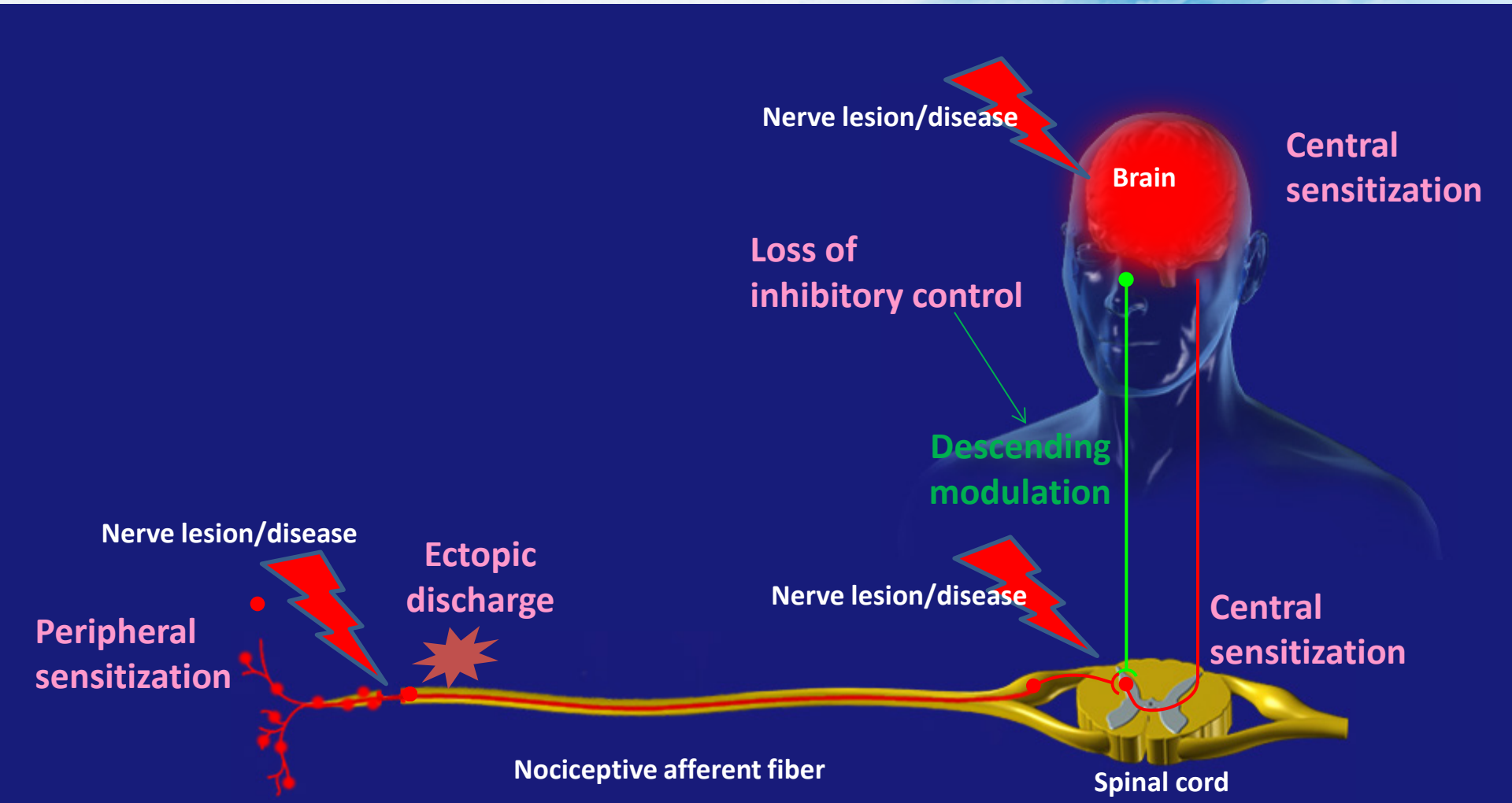
Baron R *et al. Lancet Neurol* 2010; 9(8):807-19; Gilron I *et al. CMAJ* 2006; 175(3):265-75.

Neuropathic Pain Is Characterized by Changes in Pain Response to Painful Stimuli



Adapted from: Gottschalk A *et al. Am Fam Physician* 2001; 63(10):1979-84.

Mechanisms of Neuropathic Pain



Gilron I *et al. CMAJ* 2006; 175(3):265-75; Jarvis MF, Boyce-Rustay JM. *Curr Pharm Des* 2009; 15(15):1711-6; Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7.

What is central sensitization/ dysfunctional pain?

Definition

- Amplification of neural signaling within the CNS that elicits pain hypersensitivity

Examples

- Fibromyalgia
- Irritable bowel syndrome
- Interstitial cystitis
- Temporomandibular joint pain
- May be present in many patients with chronic low back pain, osteoarthritis and rheumatoid arthritis

Pain Quality

- Burning
- Lancinating
- Electric shock-like
- Often diffuse
- Frequently with allodynia and/or hyperalgesia

CNS = central nervous system

Woolf CJ. *Pain* 2011; 152(3 Suppl):S2-15.

Importance of Pain Assessment

Pain is a significant predictor of morbidity and mortality.

- Screen for red flags requiring immediate investigation and/or referral
- Identify underlying cause
  - Pain is better managed if the underlying causes are determined and addressed
- Recognize type of pain to help guide selection of appropriate therapies for treatment of pain
- Determine baseline pain intensity to future enable assessment of efficacy of treatment

Forde G, Stanos S. *J Fam Pract* 2007; 56(8 Suppl Hot Topics):S21-30; Sokka T, Pincus T. Poster presentation at ACR 2005.

Discussion Question

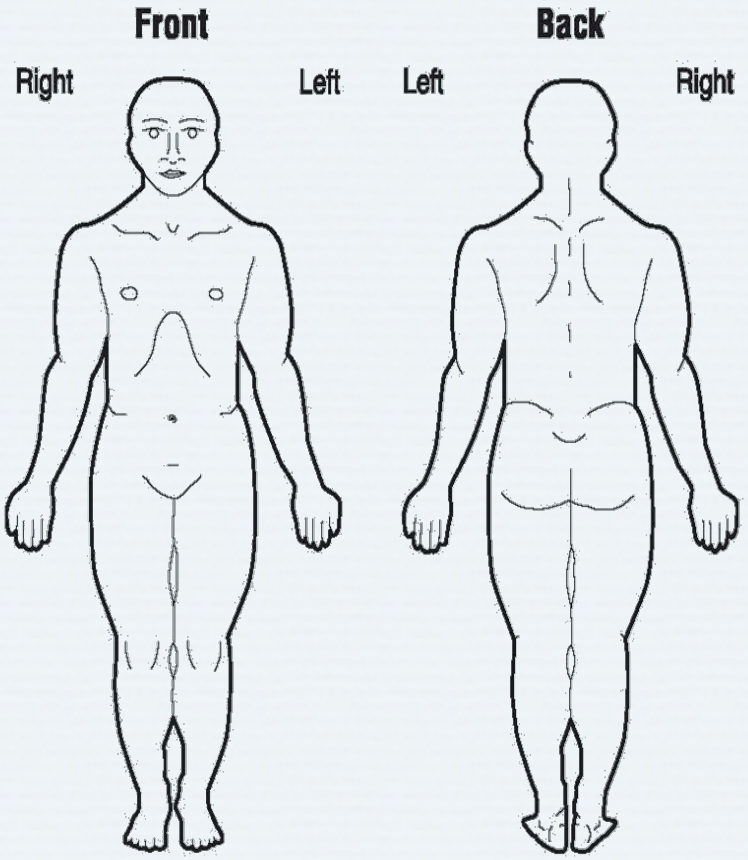
HOW DO YOU ASSESS PAIN IN YOUR PRACTICE?

Pain History Worksheet

- Site of pain
- What causes or worsens the pain?
- Intensity and character of pain
- Associated symptoms?
- Pain-related impairment in functioning?
- Relevant medical history

Ayad AE *et al. J Int Med Res* 2011; 39(4):1123-41.

Locate the Pain

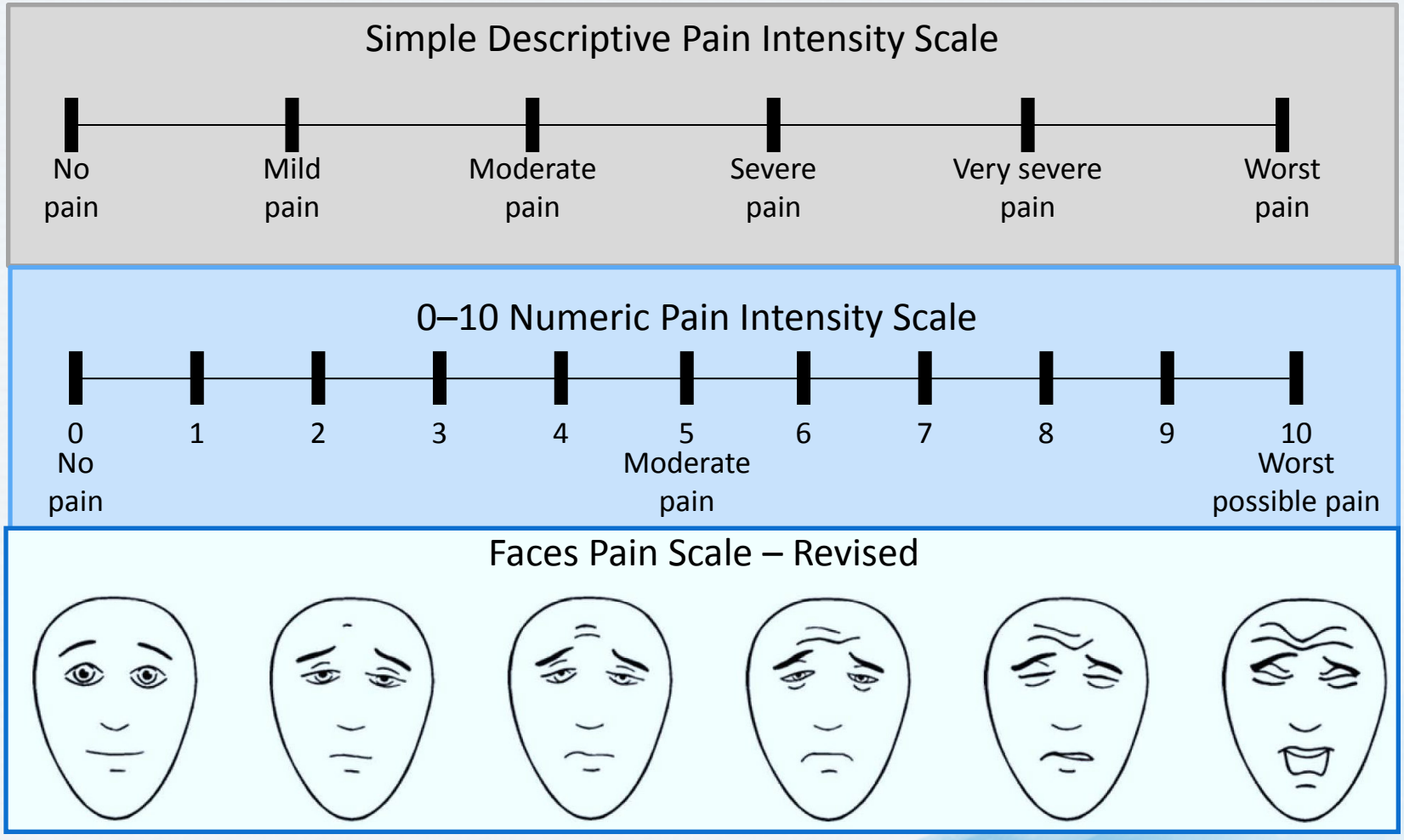


Body maps are useful for the precise location of pain symptoms and sensory signs.*

***In cases of referred pain, the location of the pain and of the injury or nerve lesion/dysfunction may not be correlated**

Gilron I *et al. CMAJ* 2006; 175(3):265-75; Walk D *et al. Clin J Pain* 2009; 25(7):632-40.

Determine Pain Intensity



International Association for the Study of Pain. *Faces Pain Scale – Revised.* Available at: http://www.iasp-pain.org/Content/NavigationMenu/GeneralResourceLinks/FacesPainScaleRevised/default.htm. Accessed: July 15, 2013;
Iverson RE *et al. Plast Reconstr Surg* 2006; 118(4):1060-9.

Discussion Question

DO YOU USE A SCREENING TOOL FOR NEUROPATHIC PAIN IN YOUR PRACTICE?

IF SO, WHICH TOOL AND WHY?

Neuropathic Pain Screening Tools

	LANSS	DN4	NPQ	painDETECT	ID Pain
Symptoms					
Pricking, tingling, pins and needles	x	x	x	x	x
Electric shocks of shooting	X				
Hot or burning	X				
Numbness		x	x	x	x
Pain [illegible]	X				x
Painf[illegible]					
Clinical examination					
Brush allodynia	X	x			
Raised soft touch threshold					
Altered pin prick threshold	X				

Neuropathic pain screening tools rely largely on common verbal descriptors of pain

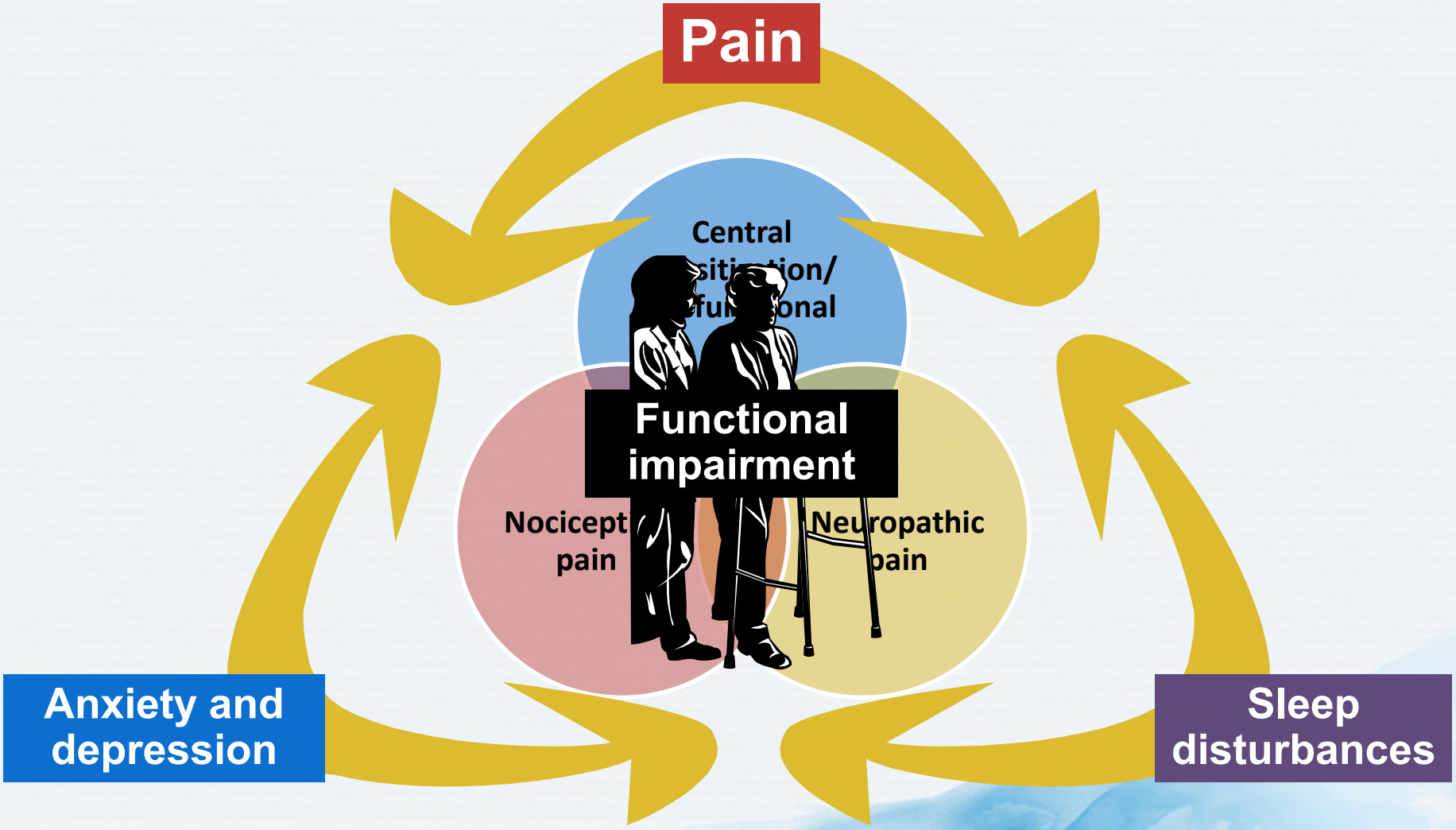
Select tool(s) based on ***ease of use*** and ***validation in the local language***

Some screening tools also include bedside neurological examination

DN4 = Douleur Neuropathique en 4 Questions (DN4) questionnaire;
LANSS = Leeds Assessment of Neuropathic Symptoms and Signs; NPQ = Neuropathic Pain Questionnaire

Bennett MI *et al. Pain* 2007; 127(3):199-203; Haanpää M *et al. Pain* 2011; 152(1):14-27.

Evaluate Impact of Pain on Functioning



Nicholson B, Verma S. *Pain Med* 2004; 5(Suppl 1):S9-27.

Identify and Treat Underlying Cause

Whenever possible, it is important to identify and treat the underlying cause of pain!

Forde G, Stanos S. *J Fam Pract* 2007; 56(8 Suppl Hot Topics):S21-30.

Be Alert for Red Flags

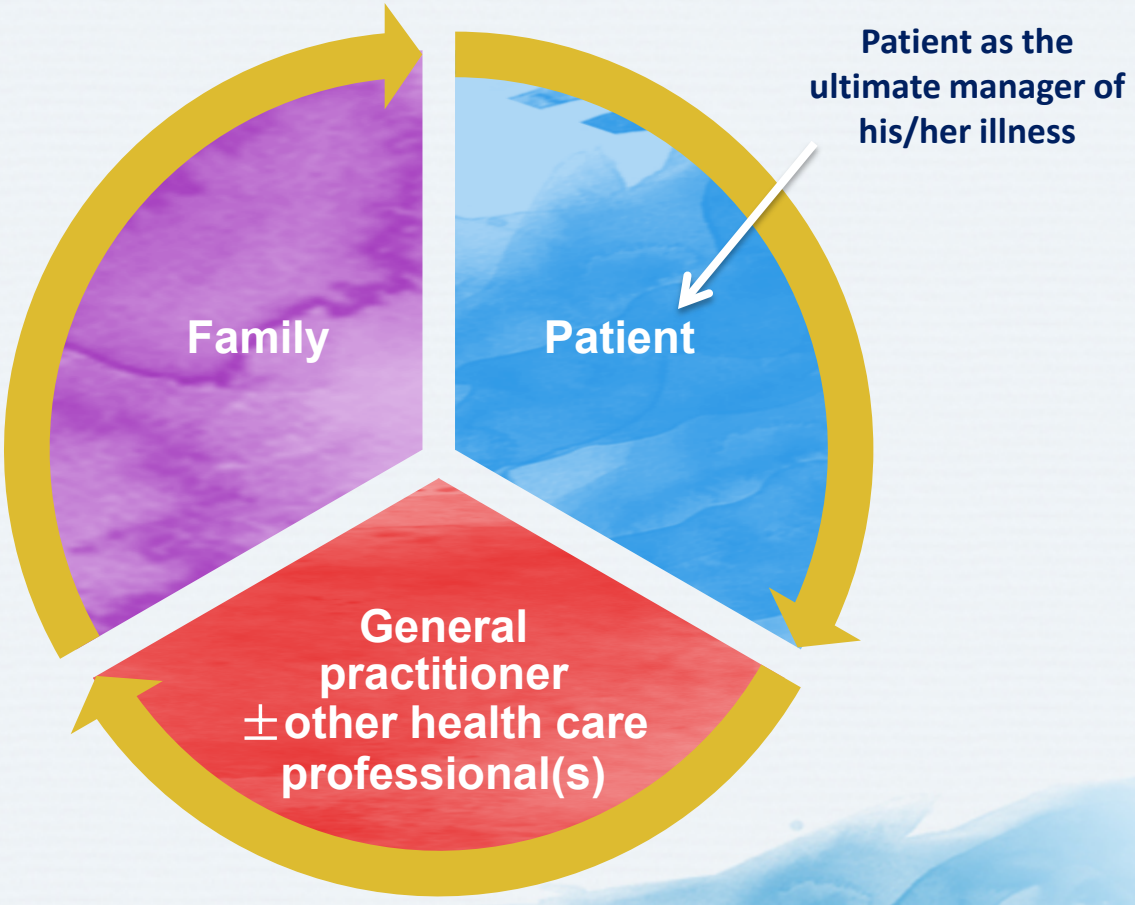
Evaluate for patients presenting with pain the presence of **red flags**!

Initiate appropriate investigations/ management or refer to specialist

Littlejohn GO. *J R Coll Physicians Edinb* 2005; 35(4):340-4.

Deciding on the Best Course of Treatment for the Patient

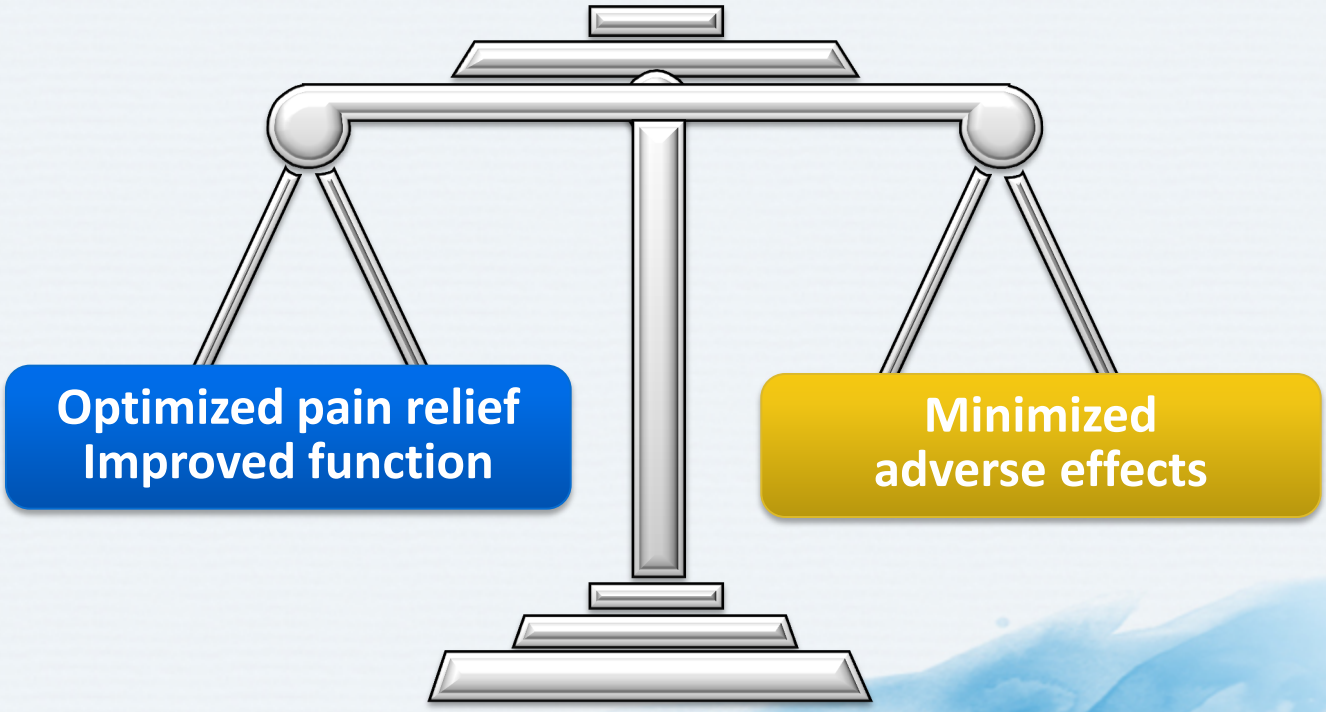
Collaborative Care



Ayad AE *et al. J Int Med Res* 2011; 39(4):1123-41; Saltman D *et al. Med J Aust* 2001; 175(Suppl):S92-6.

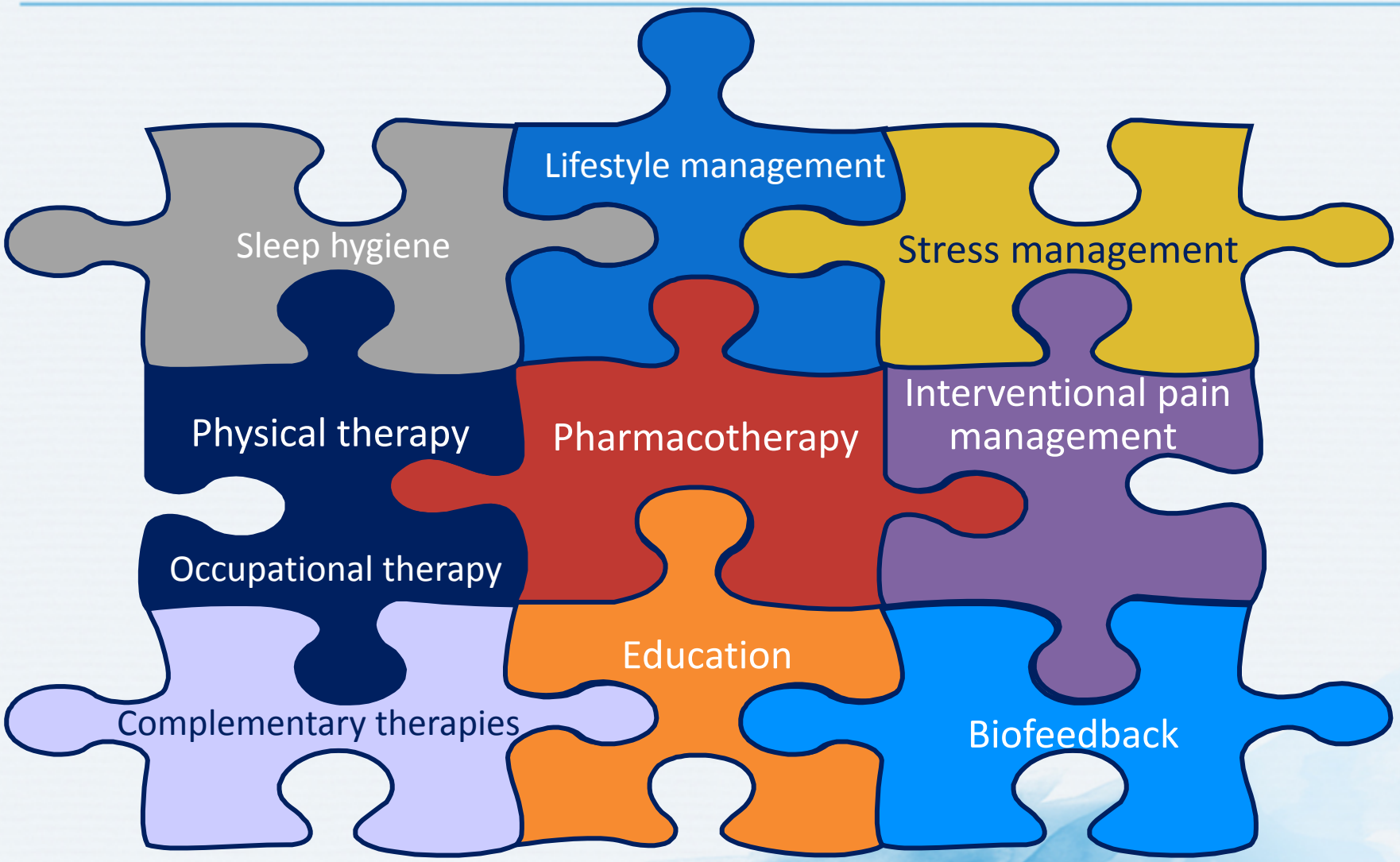
Goals in Pain Management

- Involve the patient in the decision-making process
- Agree on realistic treatment goals **before** starting a treatment plan



Farrar JT *et al. Pain* 2001; 94(2):149-58; Gilron I *et al. CMAJ* 2006; 175(3):265-75.

Multimodal Treatment of Pain Based on Biopsychosocial Approach



Gatchel RJ *et al. Psychol Bull* 2007; 133(4):581-624; Institute of Medicine. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research.*; National Academies Press; Washington, DC: 2011; Mayo Foundation for Medical Education and Research. *Comprehensive Pain Rehabilitation Center Program Guide.* Mayo Clinic; Rochester, MN: 2006.

Discussion Question

What non-pharmacological approaches to managing pain do you incorporate into your practice? Are there non-pharmacological modalities your patients regularly ask about?

Non-pharmacological Interventions

- Non-pharmacological interventions are commonly used in clinical practice
- Establishing reliable evidence of efficacy and effectiveness can be challenging in terms of design and interpretation of studies

Type of therapy	Examples
Psychological	• Hypnosis • Relaxation • Cognitive behavioral therapy
Physical	• Acupuncture • Transcutaneous electrical nerve stimulation • Healing touch and massage • Occupational therapy
Clinical process	• Pain assessment • Physician advice and communication • Education

Bennett MI, Closs SJ. *Pain Clinical Updates* 2010; 18(2):1-6.

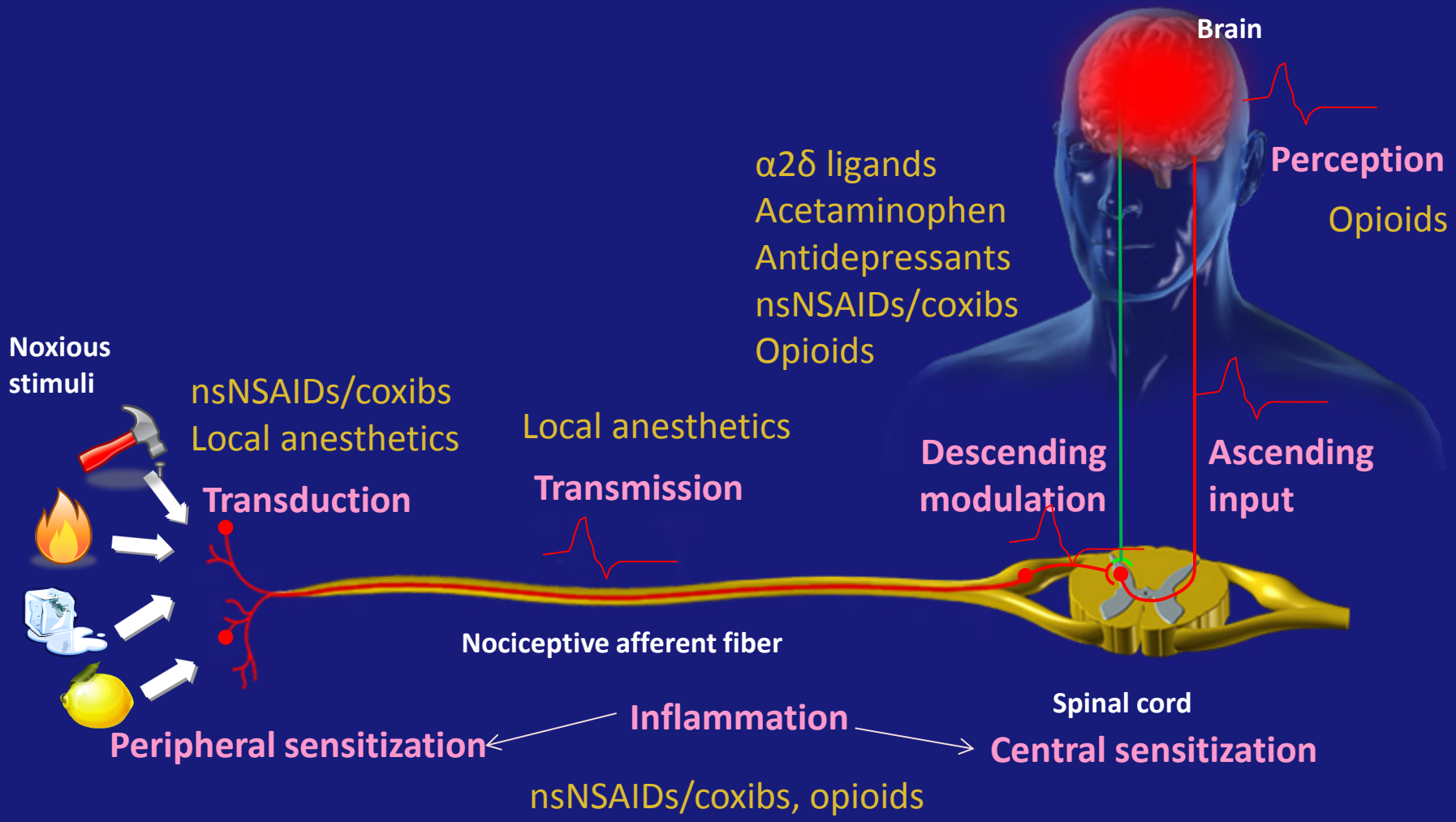
Evidence of Potential Benefits of Complementary and Alternative Medicine

	Arthritis	Headache	Low back pain	Neck pain
Acupuncture	√	√	√	X
Balneotherapy (mineral baths)	X			
Feverfew		X		
Gamma linoleic acid	X			
Glucosamine/chondroitin	X			
Herbal remedies	X		X	
Massage			√	
Spinal manipulation		√	√	X
Progressive relaxation			√	
Prolotherapy			X	
Tai chi	X			
Yoga			√	

√ = promising evidence of potential benefit; X = limited, mixed or no evidence to support use

National institutes of Health. *Chronic Pain and CAM: At a Glance. A*vailable at: http://nccam.nih.gov/health/pain/chronic.htm. Accessed: July 29, 2013.

Mechanism-Based Pharmacological Treatment of Nociceptive/Inflammatory Pain



Coxib = COX-2 inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7.

Acetaminophen

- Action at molecular level is unclear
- Potential mechanisms include:
  - Inhibition of COX enzymes (COX-2 and/or COX-3)
  - Interaction with opioid pathway
  - Activation of serotoninergic bulbospinal pathway
  - Involvement of nitric oxide pathway
  - Increase in cannabinoid-vanilloid tone

Mattia A, Coluzzi F. *Minerva Anestesiol* 2009; 75(11):644-53.

What are NSAIDs (nsNSAIDs/coxibs)?

NSAID = Non-Steroidal Anti-Inflammatory Drug

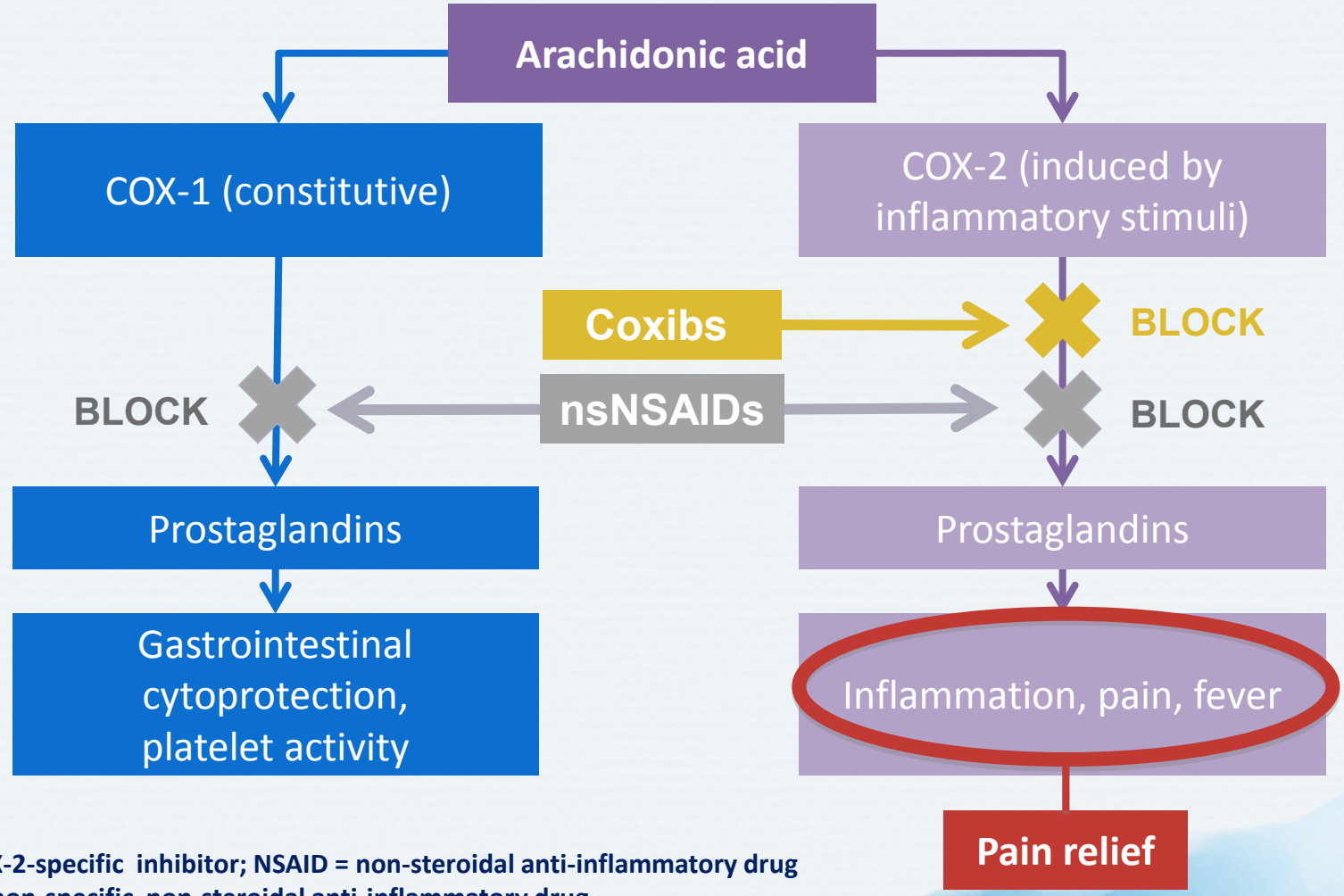
- Analgesic effect via inhibition of prostaglandin production
- Broad class incorporating many different medications:

Examples of nsNSAIDs:	*Examples of Coxibs:*
– Diclofenac	– Celecoxib
– Ibuprofen	– Etoricoxib
– Naproxen	– Parecoxib

ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Brune K. In: Kopf A *et al* (eds). *Guide to Pain Management in Low-Resource Settings.* International Association for the Study of Pain; Seattle, WA: 2010.

How do nsNSAIDs/coxibs work?



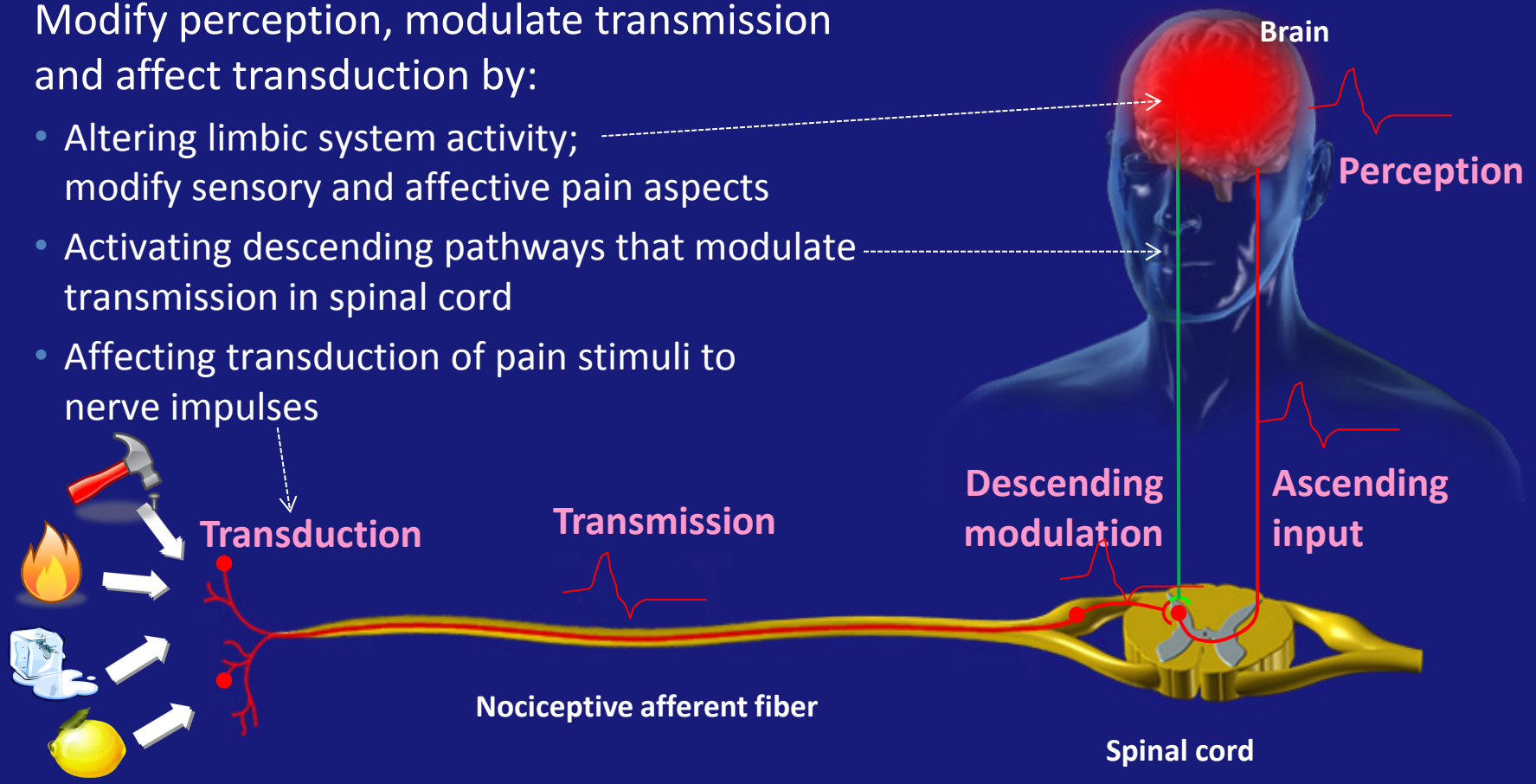
Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug
nsNSAID = non-specific non-steroidal anti-inflammatory drug

Gastrosource. *Non-steroidal Anti-inflammatory Drug (NSAID)-Associated Upper Gastrointestinal Side-Effects*. Available at: http://www.gastrosource.com/11674565?itemId=11674565. Accessed: December 4, 2010; Vane JR, Botting RM. *Inflamm Res* 1995;44(1):1-10.

How Opioids Affect Pain

Modify perception, modulate transmission and affect transduction by:

- Altering limbic system activity; modify sensory and affective pain aspects
- Activating descending pathways that modulate transmission in spinal cord
- Affecting transduction of pain stimuli to nerve impulses



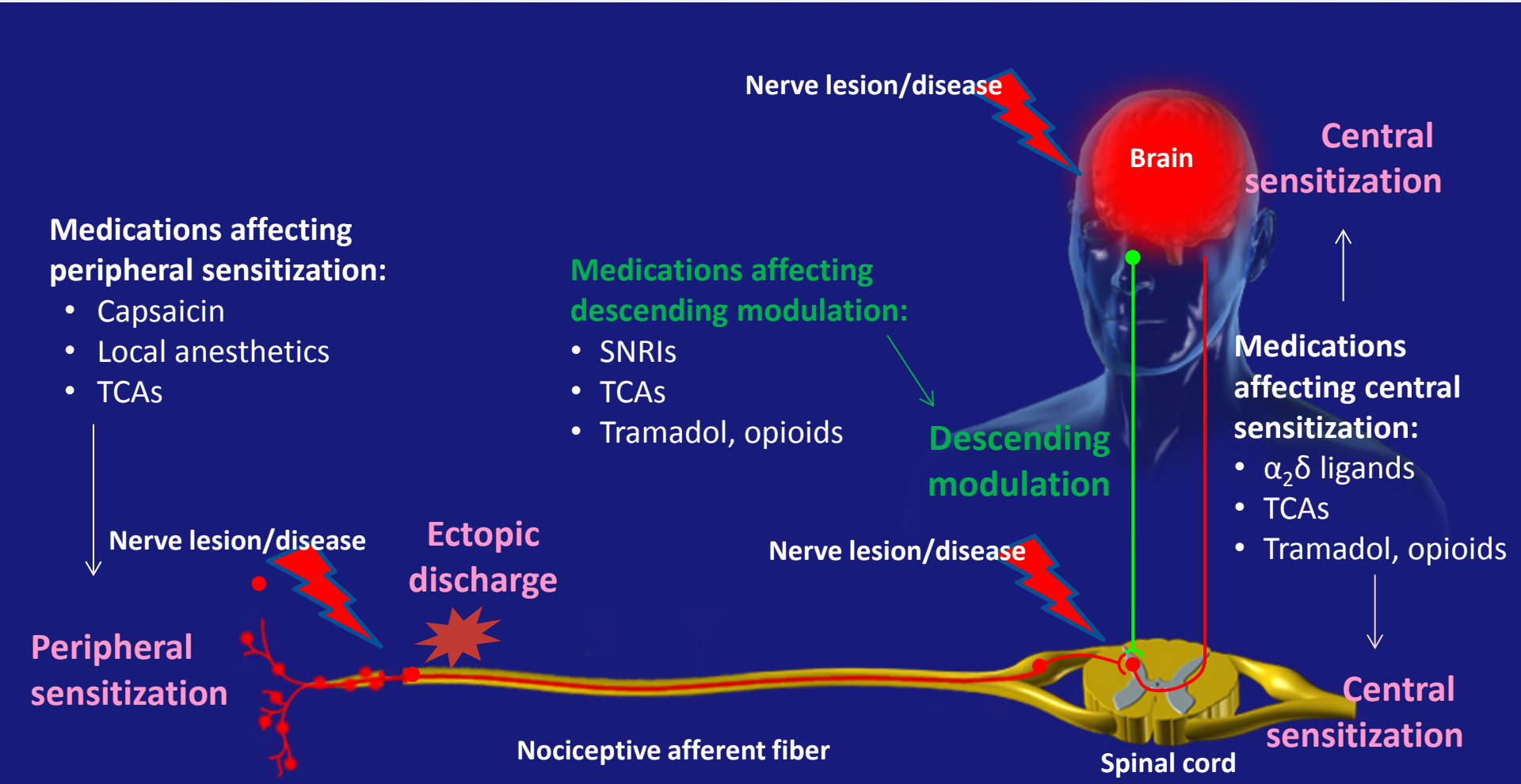
Reisine T, Pasternak G. In: Hardman JG *et al* (eds). *Goodman and Gilman's: The Pharmacological Basics of Therapeutics.* 9th ed. McGraw-Hill; New York, NY: 1996; Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7; Trescot AM *et al. Pain Physician* 2008; 11(2 Suppl):S133-53.

Discussion Question

BESIDES NOCICEPTION, WHAT ARE SOME OTHER PATHOPHYSIOLOGICAL MECHANISMS OF PAIN?

WHAT PHARMACOLOGICAL AGENTS MIGHT YOU USE TO TREAT PATIENTS SUFFERING FROM THESE TYPES OF PAIN?

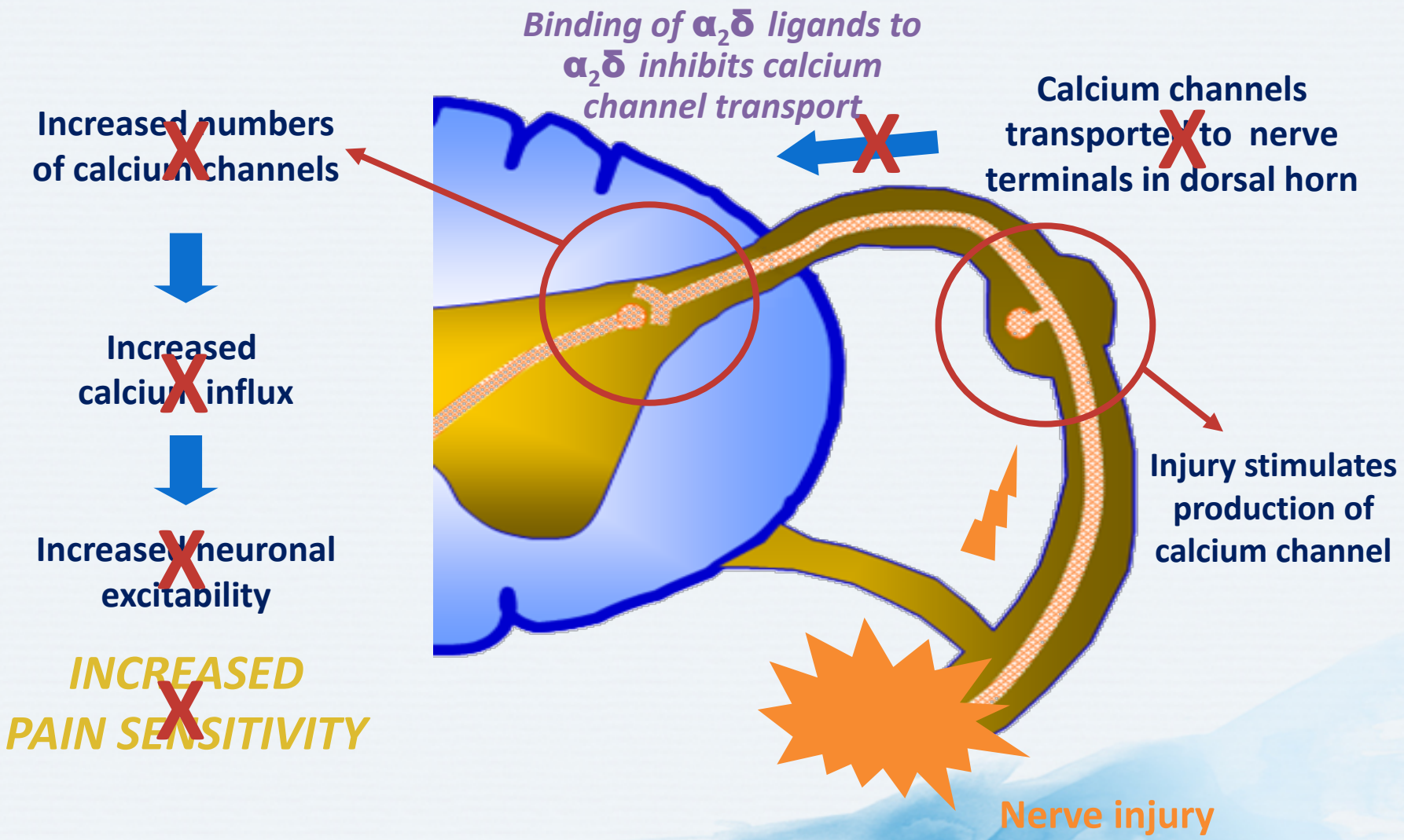
Mechanism-Based Pharmacological Treatment of Neuropathic Pain



SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Adapted from: Attal N *et al. Eur J Neurol* 2010; 17(9):1113-e88; Beydoun A, Backonja MM. *J Pain Symptom Manage* 2003; 25(5 Suppl):S18-30; Jarvis MF, Boyce-Rustay JM. *Curr Pharm Des* 2009; 15(15):1711-6; Gilron I *et al. CMAJ* 2006; 175(3):265-75; Moisset X, Bouhassira D. NeuroImage 2007; 37(Suppl 1):S80-8; Morlion B. Curr Med Res Opin 2011; 27(1):11-33; Scholz J, Woolf CJ. Nat Neurosci 2002; 5(Suppl):1062-7.

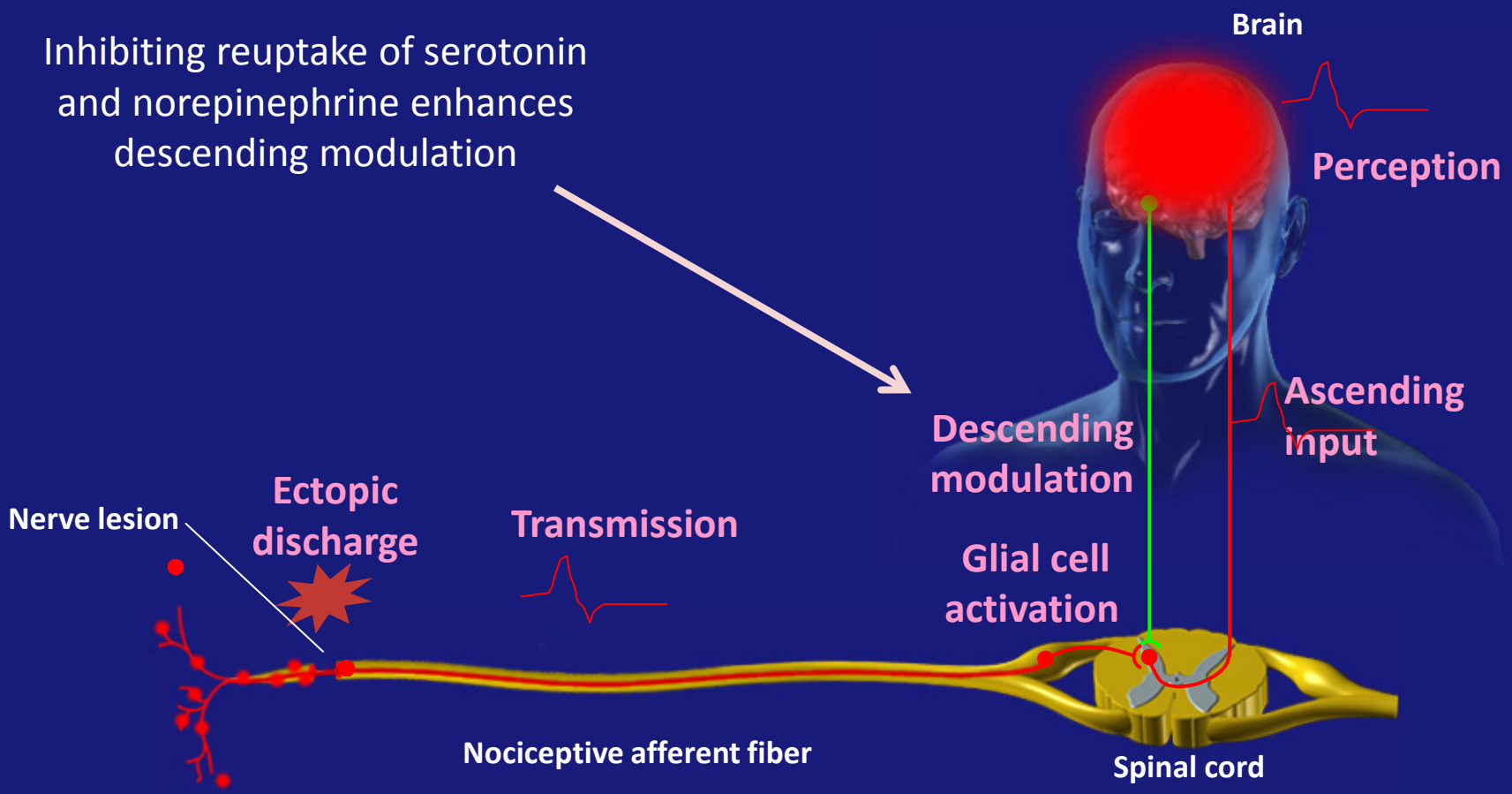
Role of $\alpha_2\delta$-Linked Calcium Channels in Neuropathic Pain



Note: gabapentin and pregabalin are $\alpha_2\delta$ ligands

Bauer CS *et al. J Neurosci* 2009; 29(13):4076-88.

How Antidepressants Modulate Pain

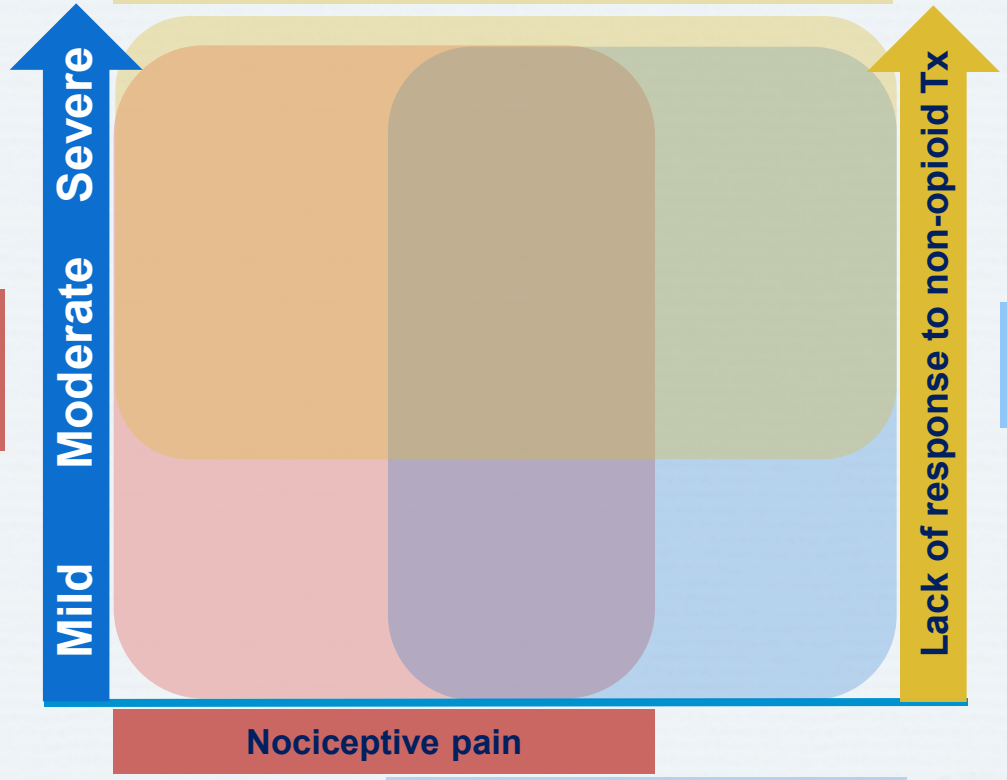


Verdu B *et al. Drugs* 2008; 68(18):2611-2632.

Assessment of Pain Pathophysiology Can Help Guide Appropriate Medication Therapy

Opioids
For management of **moderate** to **severe** pain in appropriate patients

Most opioid treatment guidelines for chronic pain recommend use for patients after inadequate response to non-opioid therapy*



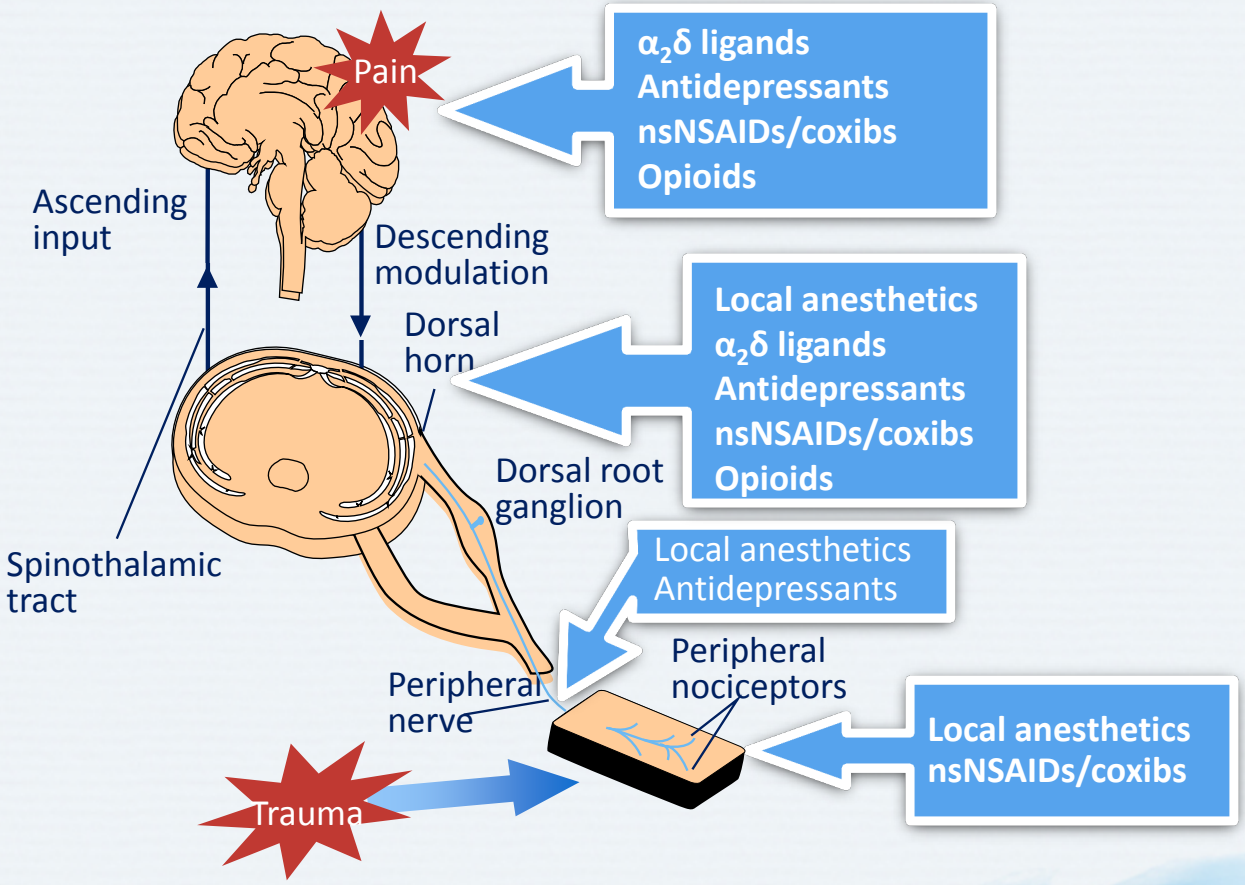
Acetaminophen
nsNSAIDs/coxibs

$\alpha_2\delta$ ligands
Antidepressants

***Selected on the basis of the pathophysiology of patient's pain, provided there are no contraindications for its use**
Coxib = COX-2-specific inhibitor;
nsNSAID = non-specific non-steroidal anti-inflammatory drug

Chou R *et al. J Pain* 2009; 10(2):113-30;
Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7.

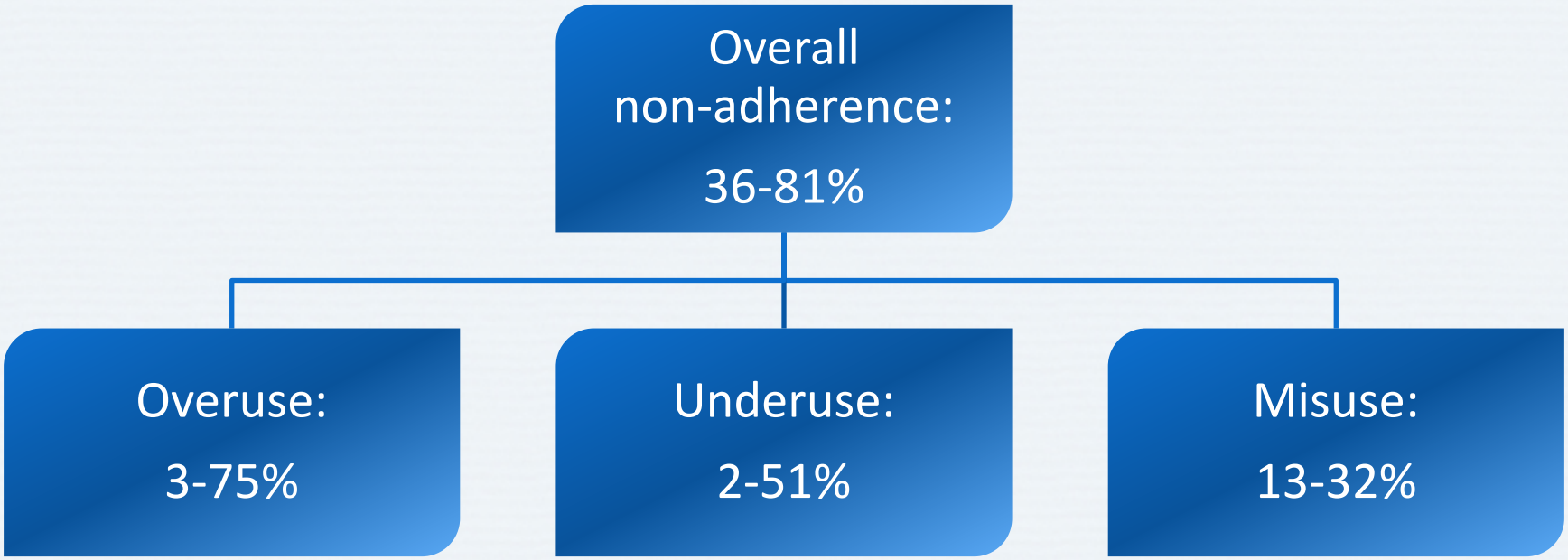
Analgesics Affect Different Parts of the Pain Pathway



Coxib = COX-2 inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Adapted from: Gottschalk A *et al. Am Fam Physician* 2001; 63(10):1979-84; Verdu B *et al. Drugs* 2008; 68(18):2611-32.

Non-adherence to chronic pain medication is common…



But rates vary substantially from study to study

Broekmans S *et al. Eur J Pain* 2009; 13(2):115-23.

Strategies to Improve Adherence

- **S**implify regimen
- **I**mpart knowledge
- **M**odify patient beliefs and human behavior
- **P**rovide communication and trust
- **L**eave the bias
- **E**valuate adherence

Atreja A *et al*. *Medacapt Gen Med* 2005; 7(1):4.

Key Messages

- Pain is a common yet complex biopsychosocial phenomenon that affects every aspect of a patient's life
- Pain can be classified into 3 main types according to pathophysiology (found separately or together/mixed type):
  - Pain due to inflammation or tissue damage (nociceptive pain)
  - Pain due to lesion or disease of somotosensory system (neuropathic pain)
  - Pain due to "central sensitization/dysfunctional pain" (terminology in flux)
- The type of pain pathophysiology can guide us to select rational, mechanism-based treatment options
- Optimal management often requires: identifying the red flags, treating the cause and combining pharmacological, biological, psychological/social and interventional techniques