

Sickle Cell Disease Pain Management

Victoria L. Thornton, MD, MBA
Consulting Associate
Duke University School of Nursing

Sickle Cell Disease:
Breaking Down the Myths and
Barriers

Disclosure Statement

I, nor my spouse/partner, have no relevant financial relationship in any amount with a commercial interest to disclose.

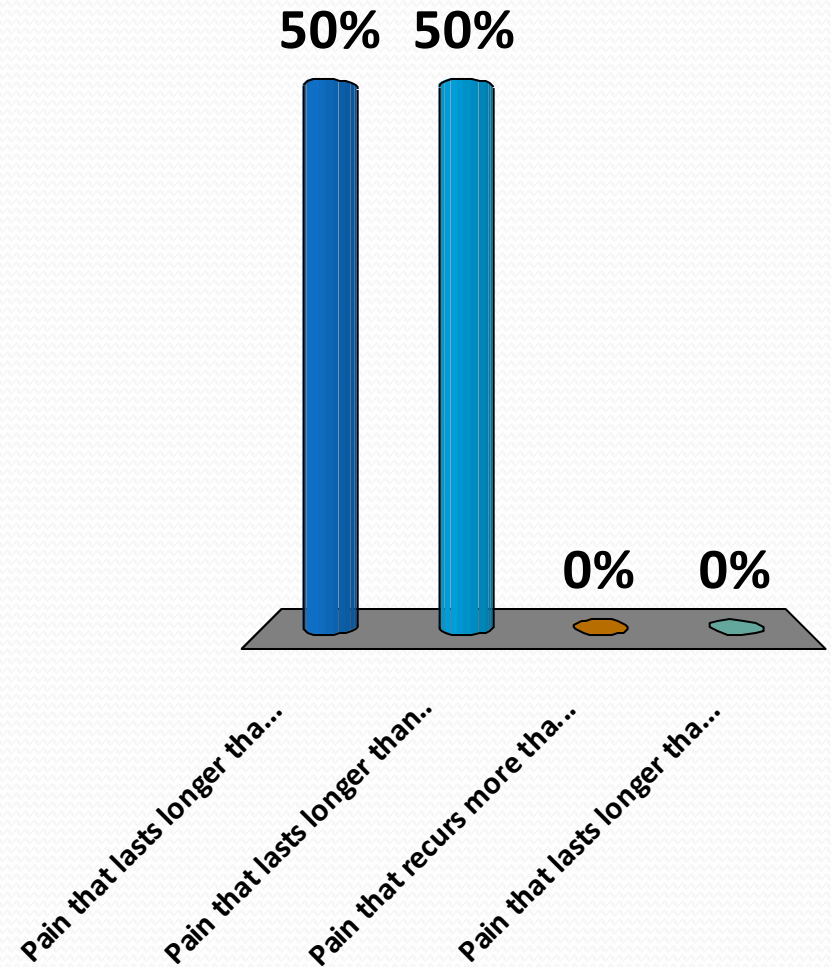
I do not intend to discuss any off-label use of the products or drugs cited in this lecture.

Objectives

- Provide course participants with approaches to manage SCD patients with acute, chronic, and combination pain syndromes.
- Identify ways of providing more consistent, effective and comprehensive pain relief to patients, through understanding of therapeutic profiles and synergistic pathways of common analgesics.
- Understand distraction and non-pharmacologic techniques for managing pain

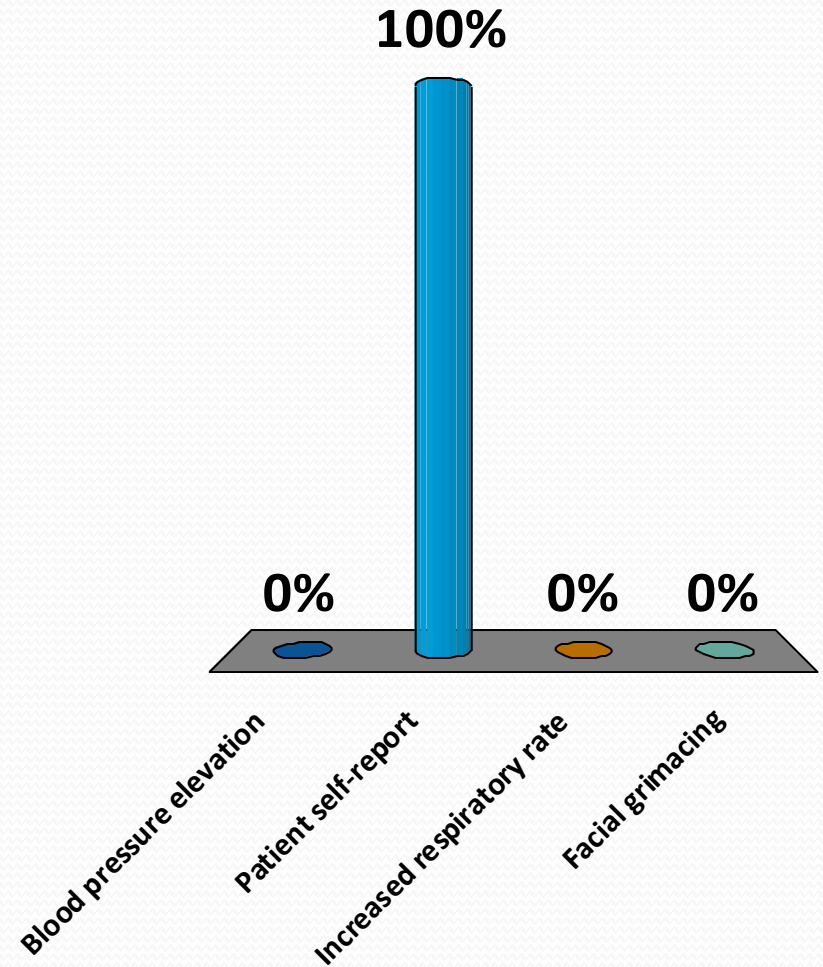
Chronic pain is best defined as:

- A. Pain that lasts longer than three months
- B. Pain that lasts longer than 6 months
- C. Pain that recurs more than four times per year
- ✓ D. Pain that lasts longer than the usual time period expected for tissue healing



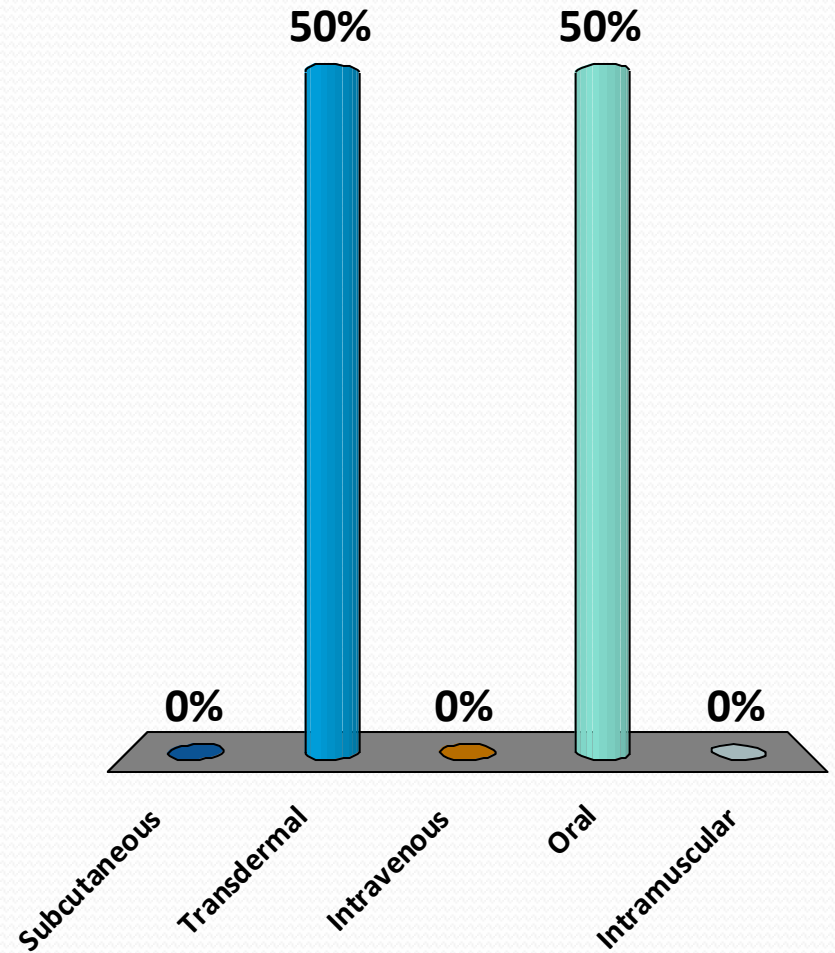
What is the best measure of a patient's pain?

- A. Blood pressure elevation
- ✓ B. Patient self-report
- C. Increased respiratory rate
- D. Facial grimacing



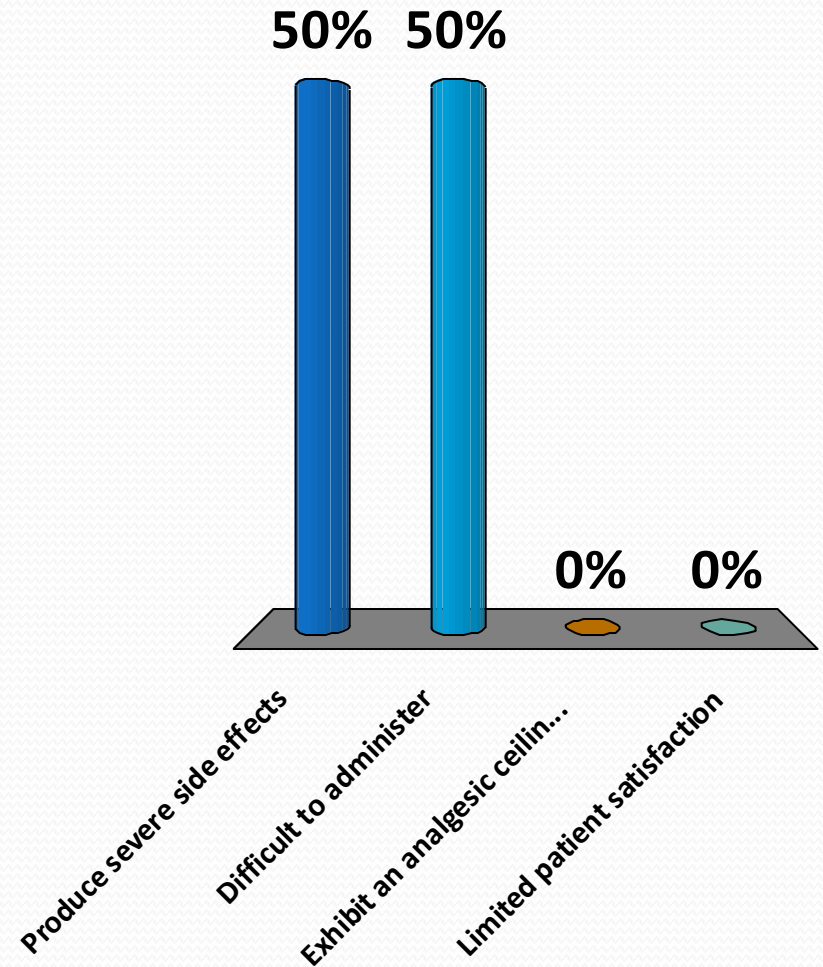
For rapid titration, analgesics are best administered by which of the following routes?

- A. Subcutaneous
- B. Transdermal
- ✓ C. Intravenous
- D. Oral
- E. Intramuscular



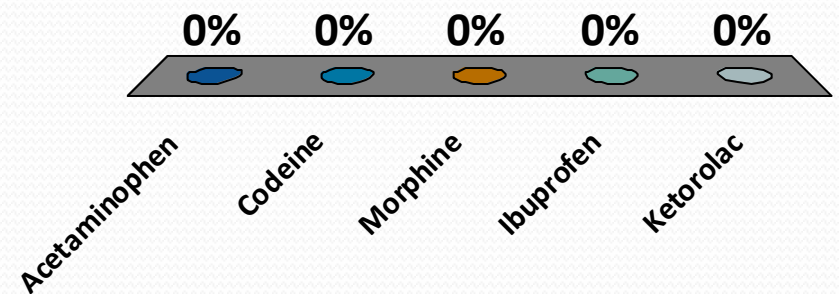
Why is the usefulness of non-opioid agents limited in the setting of severe or fluctuating pain?

- A. Produce severe side effects
- B. Difficult to administer
- ✓ C. Exhibit an analgesic ceiling effect and cannot be titrated to effect
- D. Limited patient satisfaction



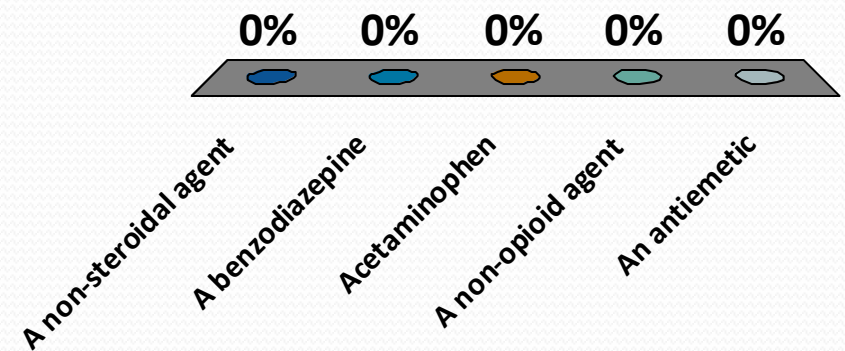
Which of the following is the mainstay of therapy for severe pain?

- A. Acetaminophen
- B. Codeine
- ✓ C. Morphine
- D. Ibuprofen
- E. Ketorolac



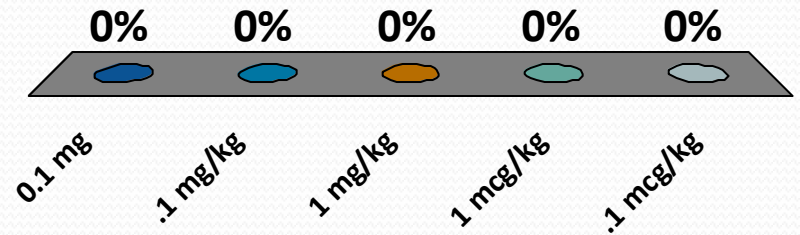
In general, all opioid analgesic regimens should include which of the following?

- A. A non-steroidal agent
- B. A benzodiazepine
- C. Acetaminophen
- ✓ D. A non-opioid agent
- E. An antiemetic



What is the correct weight based dose of fentanyl for an adult SCD patient in severe pain?

- A. 0.1 mg
- B. .1 mg/kg
- C. 1 mg/kg
- ✓ D. 1 mcg/kg
- E. .1 mcg/kg



Consequences of Untreated Pain

- **Undertreated or untreated pain** leads to delayed discharge and readmission of patients = \$\$\$
- **Untreated acute pain leads to chronic pain syndromes** because of pain-induced changes in the CNS (neuronal plasticity)
- **Most common reason for unrelieved pain is failure to routinely assess pain and pain relief**

What is Pain ?

- IASP definition:
 - “unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”
- Definition emphasizes the subjective nature of pain, the involvement of *nociception* – process by which information about injury is conveyed to the CNS - and *emotion* – the perception of the painful event.

Pain and Suffering

- Suffer (verb) :
 - To feel pain or distress; sustain loss, injury, harm, or punishment
 - To tolerate or endure evil, injury, pain, or death
- Clinicians need to
 - assess and treat pain as both an emotional and sensory experience.
 - recognize pain and suffering, feel compassion for the patient, comfort the patient and then alleviate pain and suffering.

What is Chronic Pain?

- Chronic pain is now recognized as pain that extends beyond the period of healing, with levels of identified pathology that often are low and insufficient to explain the presence and/or extent of the pain
- Also defined as a persistent pain that “disrupts sleep and normal living, ceases to serve a protective function, and instead degrades health and functional capability.”

Examples of Chronic Noncancer Pain (CNCP)

- Low back pain
- Fibromyalgia
- Chronic recurrent headaches/migraine
- Sickle Cell Disease
- Phantom Limb Pain
- Trigeminal and post-herpetic neuralgias

Nociceptive Pain

- Adaptive and protective
- Nociceptors transduce chemical, thermal and mechanical stimuli into action potentials
- CNS interprets as pain

Inflammatory Pain

- Response to tissue damage which potentiates pain through inflammatory changes
- Damaged tissue releases proinflammatory mediators which lower threshold of primary sensory neurons: **peripheral sensitization**
- Inflammation alters properties and functions of neurons: **phenotypic switch**
- Inflammation increases the excitability and responsiveness of neurons in the CNS: **central sensitization**

Neuropathic Pain

- Results from a lesion to the PNS
- Primarily nerve-injury related
- Abnormal signal processing in the PNS and the CNS
- Inflammatory features such as upregulation of central COX-2 and prostanoid levels contribute to abnormal central sensitization
- Continuous, paroxysmal or abnormal skin sensitivity characterized by hyperalgesia, hyperesthesia, dysethesia, cold sensitivity

Neuropathic Pain

Associated with chronic pain and:

- Metabolic disorders such as diabetes, hyperkalemia
- Toxins such as alcohol, chemotherapy agents
- Infections such as HIV, Zoster
- Trauma, Stroke and Tumors
- Compressive states, e.g. nerve or muscle entrapment
- Autoimmune and hereditary diseases including sickle cell disease

Importance of Pain Assessment

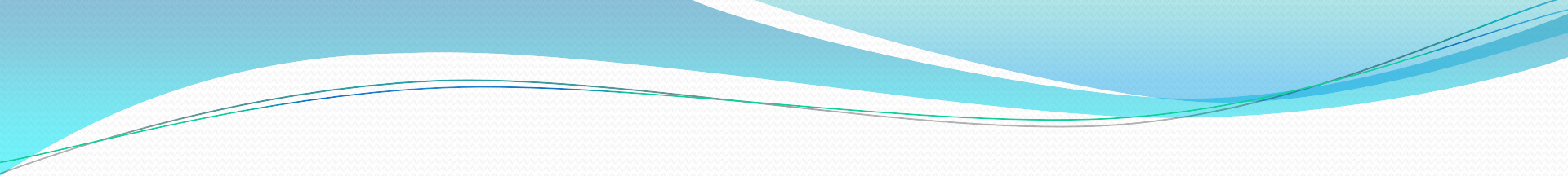
- Can't treat pain adequately if not assessed
- Can't determine effectiveness of pain relief if can't assess and reassess using same parameters, so methods of assessment and reassessment must be comparable

Pain Intensity Scales and Signs of Acute Pain

- Verbal Pain Scores
- Visual Analog Scales
- Numerical Rating Scores
- Pictorial Pain Ratings
- Sympathetic Autonomic Changes in Vital Signs: tachycardia, hypertension, diaphoresis, mydriasis, pallor: *these changes may be absent in chronic pain*
- Behavioral cues: crying, grimacing, disuse of painful areas: *these cues may be absent in chronic pain*

Multimodal Therapy

- Goal is to relieve pain using medications directed to mechanism of pain, and to avoid adverse effects and safety risks such as misuse or abuse.
- Strive to reduce pain by at least 50% of initial pain level.
- Often requires non-pharmacologic approaches combined w/drugs, e.g., weight reduction, physical/occupational therapy, stress reduction
- Synergy of different medications allows for lowering of doses of each agent than dosage that would be used in monotherapy.
 - especially important w/opioids which have significant side effect and safety profiles.



How can pain be relieved without
damaging or eliminating normal
homeostasis and protective
nociceptive responses ?

OPIOIDS

- Act by binding to specific receptors of the mu (OP₃ - limbic system frontal cortex, temporal cortex, amygdala, and hippocampus and GI tract), delta (OP₁) and kappa (OP₂ -spinal cord and cerebral cortex types in both PNS and CNS)
- Stimulation at the mu receptor produces therapeutic effects as well as adverse effects such as euphoria, mental clouding or confusion, urinary retention, respiratory depression, pruritus, nausea, vomiting, constipation, and physical dependence.
- Opioid analgesics are added to non-opioid regimens that are insufficient to control pain alone.
- Individualize route, dosage and schedule of administration

Opioid Sparing Effects

- Local anesthetics
- Nonspecific NSAIDs (NS-NSAIDs)
- Acetaminophen
- Decreased opioid requirements reduce risk of adverse effects
- Active research to better understand relationship between decreased opioid requirements and decreased side effects such as N/V, fatigue, sedation, ADL function, hospital LOS

Route of Administration

- Oral
 - Convenient, flexible, steady blood levels
 - Liquid, immediate release and controlled release tablets or capsules
 - Onset of action 45 minutes, peak drug effect 1-2 hrs for most immediate release preps
 - Repeat dose of immediate controlled dosage if no significant pain relief or adverse effects at time of peak drug effect
 - Repeat dosing of controlled release dosage results in significant overdosing

Route of Administration

- SC
 - Intermittent or continuous
 - Slightly slower onset, longer offset, lower peak effect than IV
 - Local histamine release w/SC morphine so better with hydromorphone or fentanyl at high concentrations
- IM
 - Painful, wide fluctuations in absorption, time to peak effect, rapid offset, potential nerve injury, sterile abscesses, fibrosis of muscle/ST

Route of Administration

- IV bolus
 - Peak effect dependent on lipophilicity of drug:
 - Fentanyl 1-5 minutes
 - Hydromorphone 5-6 minutes
 - Morphine 15-30 minutes
 - Duration of action slightly less than IM

Route of Administration

- IV bolus
 - Repeat dose if no significant pain relief (reduce pain by 50%) or side effects at time of peak effect
 - For patients in severe acute pain or exacerbated cancer or chronic pain, may need repeated boluses q 10-20 min until 50% reduction in pain
- IV Infusion
 - Provide consistent blood levels
 - May be provided as infusion or in combination w/PCA
 - Hourly maintenance dose based on loading doses and elimination half-life

Route of Administration

- Transdermal
 - Lipophilic drugs readily absorbed through skin
 - Fentanyl: convenient, expensive, avoid in opiate naïve patients
 - **Lag time of 12-16 hours** before substantial therapeutic effect
 - Not indicated for acute procedures as Fentanyl can accumulate when pain stimulus is removed
 - Less constipation than equianalgesic CR oral preps

PCA

- Meta-Analysis of 15 randomized trials
 - 787 adults (aged 16-65)
- Superior analgesia
- Improved satisfaction
- Trend to reduced analgesia
- Trend to decrease length of stay

Ballantyne J, *Clinical Anesthesia*, 1993

Dosage

- Optimal dose varies widely
- Age, gender and ethnic variation
- Reduce dosage to 25-50% of usual doses and titrate accordingly if > age 70, opiate naïve, hepatic impairment
- Do not use morphine or its derivatives if renal insufficiency or renal failure is present
- Serial trials of dosages or trial of different opioid from the same class depending on effect or side effects

Parental Opioid Dosing for Opioid Naive Patients

IV Opioid	Weight Based Dosing	Time to Onset of Action	Duration of Action	Side Effects
Fentanyl	1mcg/kg	1-5 minutes	30-45 minutes	Rigidity at high doses
Hydromorphone	0.02mg/kg	5-6 minutes	2-3 hours	Least vagal effect; Significant euphoria
Morphine	0.15mg/kg	15-30 minutes	3-4 hours	Vagal symptoms; Histamine release; Dose adjustment in patients with renal insufficiency

Multimodal Therapy

- Non-opioid analgesics:
 - Acetaminophen
 - NSAIDs: ibuprofen, diclofenac, celecoxib, naproxen; ketorolac (Toradol TM) 30mg IV, subsequent 15 or 30 mg IV comparable to range of 6-12mg morphine; may precipitate renal failure in dehydrated patients; reduce dose in elderly to 10-15mg IV q 6hrs
 - duloxetine (Cymbalta TM) SNRI used for depression, anxiety, diabetic neuropathy, fibromyalgia, chronic musculoskeletal pain
- Analgesic dose-ceiling above which additional analgesia does not occur, however adverse effects profile escalates

Non-pharmacologic techniques

- music, meditation, eating, exercise, heat
- activity pacing,
- time-dependent analgesia dosing vs. pain-dependent prn dosing

Key Points



- Know the dose and time course of several opioid analgesics
- Use & recommend multimodal treatments, including non-pharmacologic interventions
- Remember to treat the emotional component of pain

Pain Resources

- American Pain Society, www.ampainsoc.org
- International Society for the Study of Pain, www.iasp-pain.org
- American Academy of Pain Management, www.aapainmanage.org
- American Chronic Pain Foundation, www.painfoundation.org
- American Chronic Pain Association, www.theacpa.org