PAIN MANAGEMENT

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Session outline

- Introduction
- Epidemiology
- Pathophysiology
- Pain classification
- Clinical presentation
- Treatment

Introduction

- The accepted current definition of pain is:
- "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.“
- Pain often is so subjective, however, that many clinicians define pain as whatever the patient says it is.
- Humans have always known and sought relief from pain.
- Today, pain's impact on society still is great, and indeed pain complaints remain a primary reason patients seek medical advice.

Epidemiology

- One in 4 Americans have suffered pain that lasts for more than 24 hours in the previous month
- In those reporting pain, 42% state that it lasted more 1 year.
- 76.5 million Americans report they are in chronic pain;
- this is more than the number of patients with heart disease, cancer, and diabetes combined.
- The annual cost of pain to U.S. society can be estimated to be in the billions of dollars

Con`t…

- In 1 year, an estimated 25 million Americans will experience acute pain due to injury or surgery,
- One-third of Americans will experience severe chronic pain at some point in their lives.
- These numbers are expected to rise, as increasingly more Americans work beyond age 60 years and survive into their 80s.
- Despite much public attention, considerable focused education, and a number of consensus guidelines, pain often remains underestimated and undertreated.

Pathophysiology

- The Pathophysiology of pain involves a complex array of neural networks in the brain that are acted on by afferent stimuli to produce the experience we know as pain.
- In acute pain, this encounter is short lived; but in some situations, the changes may persist, and chronic pain develops

Con`t…

Nociceptive Pain

- Nociceptive pain typically is classified as either

  Somatic pain

- pain arising from skin, bone, joint, muscle, or connective tissue
- often presents as throbbing and well localized,

  Visceral pain

- Pain arising from internal organs such as the large intestine or pancreas
- visceral pain can manifest as pain feeling as if it is coming from other structures (referred)
- or as a more localized phenomenon..

Con`t…

- Nociception occur in terms of stimulation, transmission, perception, and modulation

Stimulation

- The first step leading to the sensation of pain is stimulation of free nerve endings known as nociceptors.
- These receptors are found in both somatic and visceral structures.
- They distinguish between noxious and innocuous stimuli,
- They are activated and sensitized by mechanical, thermal, and chemical impulses

Con`t…

- The underlying mechanism of these noxious stimuli may be the release of :
  - Bradykinins, hydrogen and potassium ions
  - Prostaglandins, histamine, interleukins,
  - Tumor necrosis factor alfa, serotonin, and substance P
- These sensitize and/or activate the nociceptors.
- Receptor activation leads to action potentials that are transmitted along afferent nerve fibers to the spinal cord

Con`t…

Transmission

- These afferent, nociceptive pain fibers synapse in various layers of the spinal cord's dorsal horn,
- Releasing a variety of neurotransmitters, including glutamate, substance P, and aspartate
- These pain-initiated processes reach the brain through a complex array of a number of ascending spinal cord pathways, which include the spinothalamic tract

Con`t…

- Information other than pain is also carried along these pathways.
- Thus, pain is influenced by many factors supplemental to nociception and precludes simple schematic representation
- It is postulated that the thalamus acts as a relay station,
- These pathways ascend and pass the impulses to central structures where pain can be processed further

Con`t…

Perception

- At this point in transmission, pain is thought to become a conscious experience that takes place in higher cortical structures.
- The brain may accommodate only a limited number of pain signals, and cognitive and behavioral functions can modify pain.
- Relaxation, distraction, meditation, and guided mental imagery may decrease pain by limiting the number of processed pain signals.
- In contrast, a change in our neuro biochemical makeup that results in states such as depression or anxiety may worsen pain

Con`t…

Modulation

- The body modulates pain through a number of complex processes.
- One, known as the endogenous opiate system,
- Consists of:

  - Neurotransmitters (e.g., enkephalins, dynorphins, and –beta endorphins) and

  - Receptors (e.g.μ ðand k) that are found throughout the CNS

Con`t…

- Like exogenous opioids, endogenous opioids bind to opioid receptor sites and modulate the transmission of pain impulses
- Other receptor types also can influence this system.
- Blockade of N-methyl-D-aspartate (NMDA) receptors, found in the dorsal horn, may increase theμ -receptors' responsiveness to opiates

Con`t…

- There are three classes of opioid receptors : mu, delta and kappa
- All three are widely distributed in the brain
- There are also three major classes of endogenous opioid peptides
- They interact with opiate receptors

Con`t…

- The opioid peptides modulate nociceptive input in two ways:
- ✓ Block neurotransmitter release by inhibiting ca2 +influx into presynaptic terminal
- ✓ Open K+ channels which hyperpolarize neurons and inhibit spike activity

Con`t…

- The CNS also contains a highly organized descending system for control of pain transmission.
- This system can inhibit synaptic pain transmission at the dorsal horn and originates in the brain.
- Important neurotransmitters here include endogenous opioids, serotonin, norepinephrine, and GABA

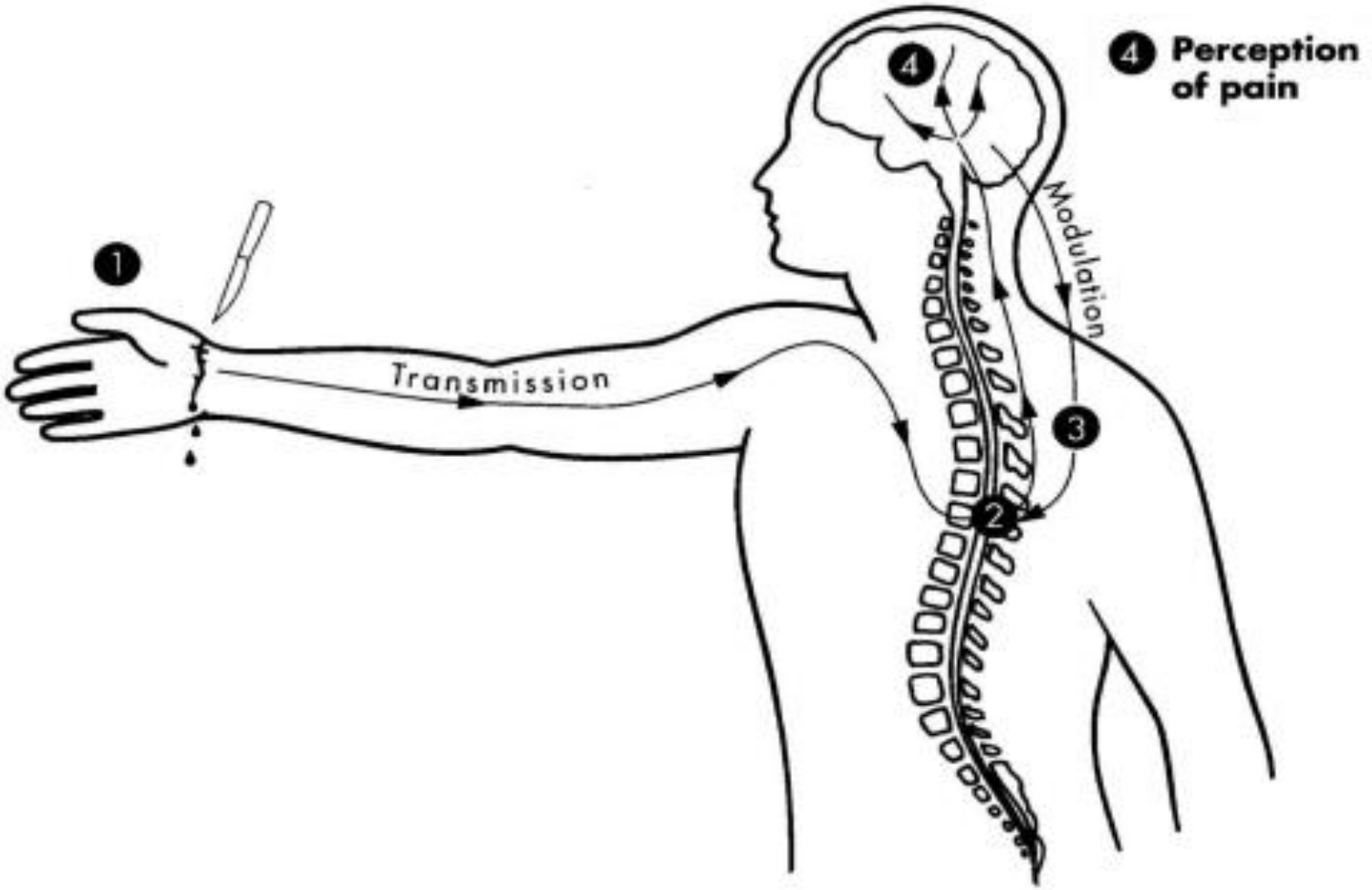
Con`t…

Adaptive Inflammation

- Inflammatory pain can be thought of as the body's shifting from preventing tissue damage to the promotion of healing
- As a result of the inflammatory process, the pain threshold is reduced and the injured area becomes more sensitive to pain.
- This process decreases our contact with and movement of the injured area, thus promoting the progression of healing.
- When this course of action outlives its functionality it can move from an acute to a chronic problem

Con`t…

- In response to tissue damage and inflammation, a significant alteration occurs in the chemical composition and properties of the neurons
- These alterations reflect the nature and levels of the different proteins expressed by the sensory neurons.
- Altered production of these proteins may modify the phenotypes of the neurons,
- Changing their transduction and transmission properties.
- Then increase in the excitability or responsiveness of neurons within the CNS, referred to as central sensitization.


4 Perception of pain
4
Modulation
1
Transmission
3
2

Neuropathic and Functional Pain

- Is distinctly different from nociceptive pain in that it becomes disengaged from noxious stimuli or healing
- Often is described in terms of chronic pain.
- Neuropathic pain is a result of nerve damage,
- Eg. Post herpetic neuralgia, diabetic neuropathy
- Functional pain can be thought of as abnormal operation of the nervous
- E.g., Irritable bowel syndrome, sympathetic induced pain, tension-type headaches

- The mechanism responsible for neuropathic and functional pain may be the nervous system's endogenous dynamic nature.
- Nerve damage or certain disease states may evoke changes seen in inflammatory pain, ectopic excitability, enhanced sensory transmission, nerve structure reorganization, and loss of modulatory pain inhibition.
- Pain circuits rewire themselves both anatomically and biochemically.

Con`t…

- This produces a mismatch between pain stimulation and inhibition, and a potential progressive increase in the discharge of dorsal horn neurons
- Clinically, patients present with episodic or continuous pain transmission , hyperalgesia and/or allodynia
- This change over time may help to explain why this type of pain often manifests long after the actual nerve related injury or when no actual injury is identified.

Classification

Acute Pain

- Acute pain can be a useful physiologic process, warning individuals of disease states
- Severe, unremitting, undertreated acute pain,, can produce many deleterious effects.
- Aside from unnecessary suffering, untreated acute pain has also been shown to increase one's risk for the development of chronic pain syndromes.
- Acute pain is usually nociceptive in nature with common causes, including surgery, acute illness, ,,

Con`t…

Chronic Pain

- Under normal conditions, acute pain subsides quickly as the healing process decreases the pain-producing stimuli;
- However, in some instances, pain persists for months to years, leading to a chronic pain state with features quite different from those of acute pain
- This type of pain can be nociceptive, neuropathic/functional, or mixed.
- Chronic pain can be classified as either being associated with cancer (cancer pain) or from noncancer etiologies (chronic noncancer pain).

Table 69-1 Characteristics of Acute and Chronic Pain		
Characteristic	**Acute Pain**	**Chronic Pain**
Relief of pain	Highly desirable	Highly desirable
Dependence and tolerance to medication	Unusual	Common
Psychological component	Usually not present	Often a major problem
Organic cause	Common	May not be present
Environmental/family issues	Small	Significant
Insomnia	Unusual	Common component
Treatment goal	Cure	Functionality
Depression	Uncommon	Common

Data from Stimmel[2] and Jacobson and Mariano.[60]

Con`t…

Cancer Pain

- Pain associated with potentially life-threatening conditions is often called malignant pain or simply cancer pain.
- This type of pain includes both chronic and acute components and often has multiple etiologies.
- It is pain caused by the disease itself, treatment or diagnostic procedures

Clinical presentation

Acute pain

- General
- Obvious distress (e.g., trauma),
- infants may present with changes in feeding habits, increased fussiness.
- Those with dementia may exhibit changes in eating habits, increased agitation, calling out..

Symptoms

- Can be described as sharp, dull, shock like, tingling, shooting, radiating, fluctuating in intensity, and varying in location .

Con`t…

Signs

- Hypertension, tachycardia, diaphoresis, mydriasis, and pallor, but these signs are not diagnostic.
- In some cases there are no obvious signs.
- Comorbid conditions usually not present.
- Outcome of treatment generally predictable.

Laboratory Tests

- Pain is always subjective.
- There are nonspecific laboratory tests for pain.
- Pain is best diagnosed based on patient description and history

Con`t…

Chronic pain

- General
- Can appear to have no noticeable suffering.
- Attention also must be given to mental/emotional factors that alter the pain threshold.

Symptoms

- Can be described as sharp, dull, shock-like, tingling, shooting, radiating, fluctuating in intensity, and varying in location
- Over time, the pain stimulus may cause symptoms that completely change (e.g., sharp to dull, obvious to vague

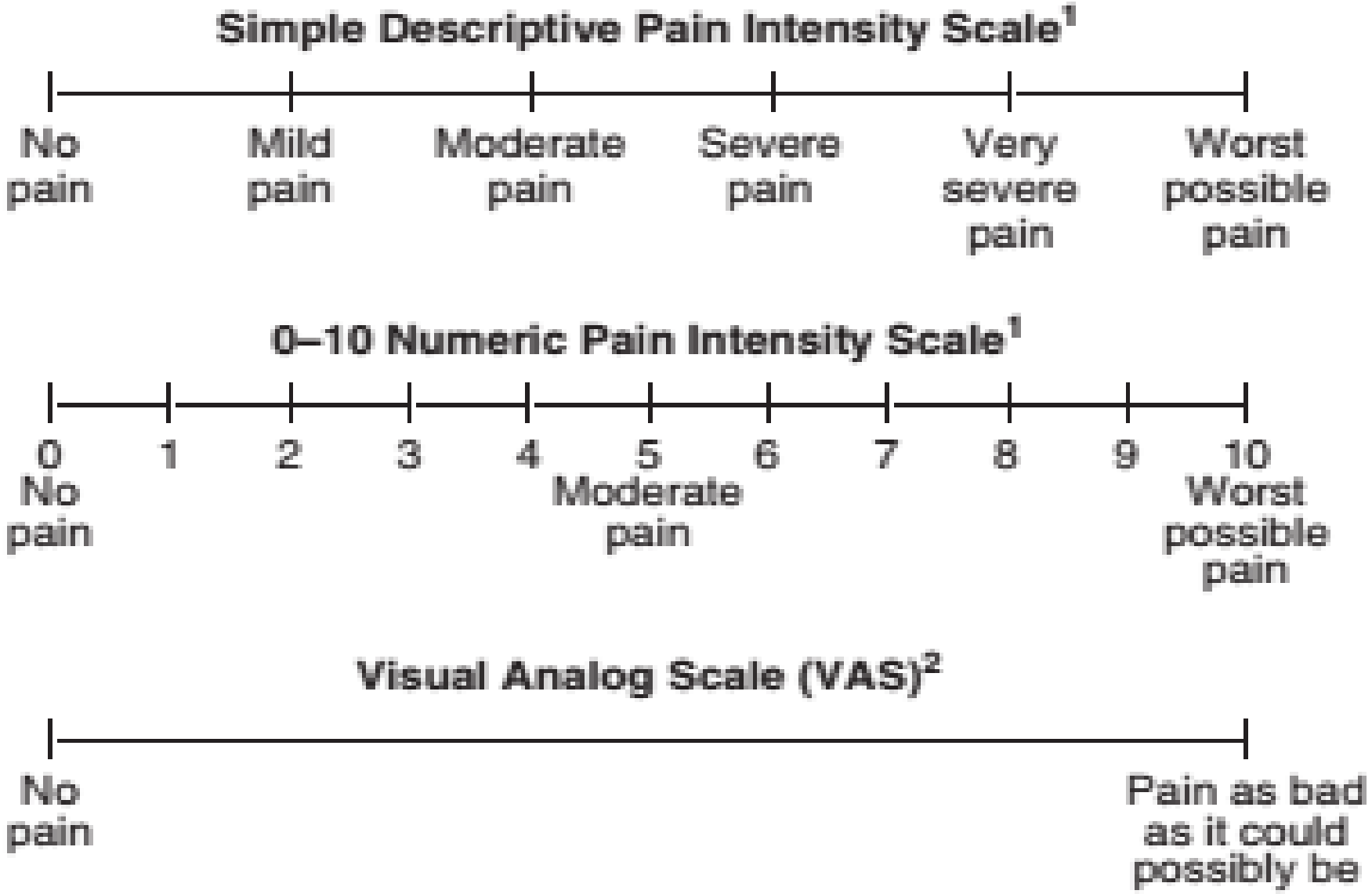
Con`t…

Signs

- Hypertension, tachycardia, diaphoresis, mydriasis, and pallor are seldom present.
- In most cases there are no obvious signs.
- Comorbid conditions often present
- Outcome of treatment often unpredictable.

Laboratory Tests

- Pain is always subjective.
- Pain is best diagnosed based on patient description and history.
- There are no specific laboratory tests for pain; however, history and/or diagnostic proof of past trauma



[1] If used as a graphic rating scale, a 10 cm baseline is recommended.
[2] A 10-cm baseline is recommended for VAS scales.

Treatment algorithm

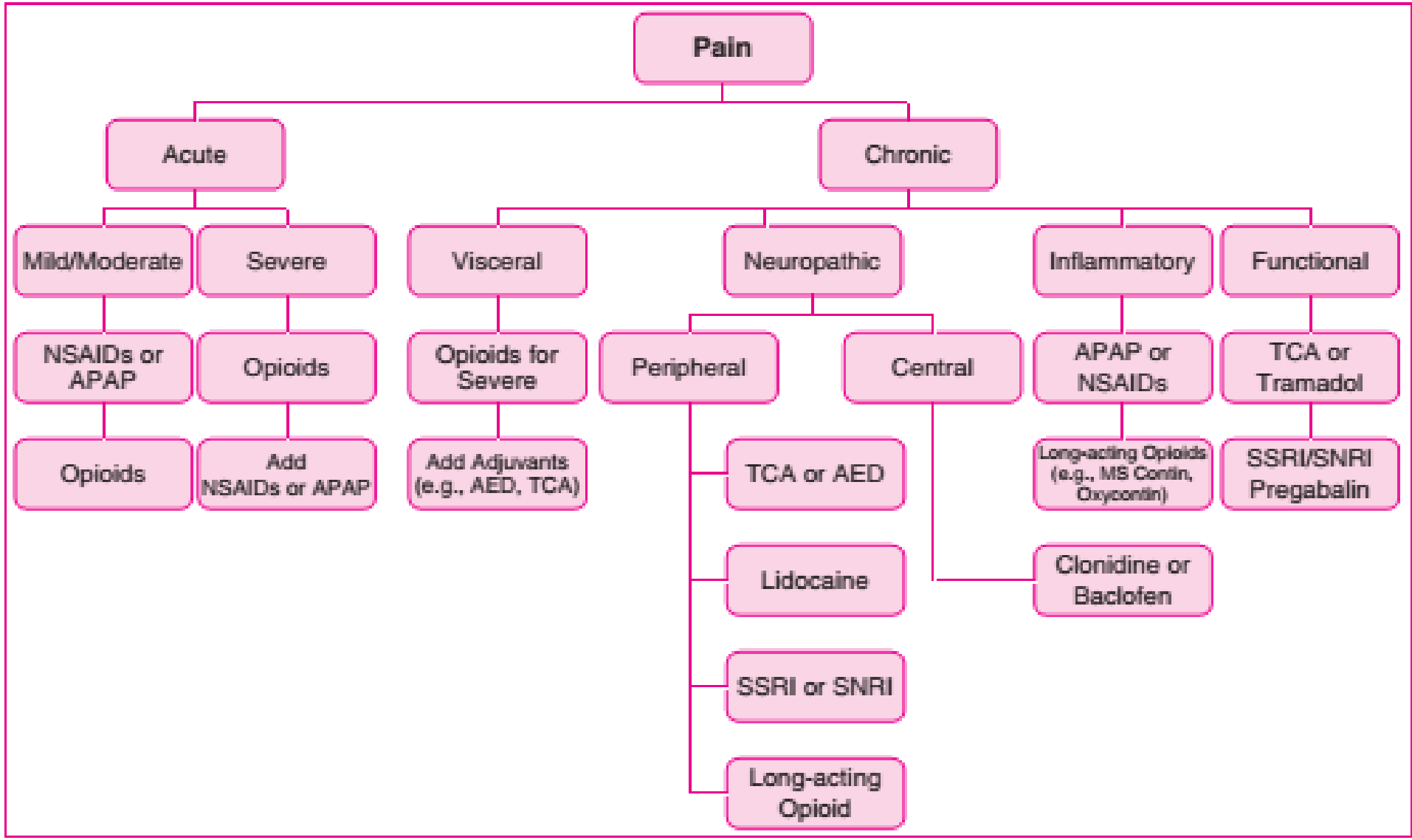


FIGURE 30–2. Pain algorithm. AED, antiepileptic drug; APAP, acetaminophen; NSAID, non-steroidal antiinflammatory drug; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

Treatment

Pharmacologic Treatment

- Many consider pharmacologic treatment to be the cornerstone of pain management.

Nonopioid Agents

- Analgesia should be initiated with the most effective analgesic agent having the fewest side effects.
- Asprin, Acetaminophen, NSAIDs often are preferred over opiates in the treatment of mild-to-moderate pain
- NSAIDs may be particularly useful in the management of cancer-related bone pain

Con`t…

- Studies comparing the efficacy of these agents have been inconsistent.
- Therefore, the choice of a particular agent often depends on availability, cost, pharmacokinetics, pharmacologic characteristics, and the side-effect profile
- Switch to another member of this class if there is inadequate response after a sufficient therapeutic trial of any single agent is considered

Pain Intensity	Corresponding Numerical Rating	WHO Therapeutic Recommendations	Examples of Initial Therapy	Comments
Mild	1–3/10	Non-opioid analgesic; regular scheduled dosing	Acetaminophen 1000 mg every 6 hours; Ibuprofen 600 mg every 6 hours	Consider adding an adjunct or using an alternate regimen if pain is not reduced in 1–2 days
Moderate	4–6/10	Add an opioid to the non-opioid for moderate pain; regular scheduled dosing	Acetaminophen 325 mg + codeine 60 mg every 4 hours; Acetaminophen 325 mg + oxycodone 5 mg every 4 hours	Consider step-up therapy if pain is not relieved by greater than or equal to 2 or more different drugs
Severe	7–10/10	Switch to a high-potency opioid; regular scheduled dosing	Morphine 10 mg every 4 hours; Hydromorphone 4 mg every 4 hours	

Opioid Agents

- Opioids are often the next logical step in the management of acute pain and cancer-related chronic pain.
- They also may be an effective treatment option in the management of chronic noncancer pain;
- however, this continues to be somewhat controversial. Many times a trial of opioids is warranted,

Con`t…

- But such a trial should not be done without a complete assessment of the pain complaint, patient's functionality and risk factors for opioid misuse and abuse
- Opiate choice should be based on patient acceptance; analgesic effectiveness; and pharmacokinetic, pharmacodynamic, and side-effect profiles

Con`t…

- The pharmacologic activity of opioids depends on their affinity for opiate receptors.
- Therapeutic activities and side effects range from those exhibited by the opiate agonists to those seen with the opiate antagonists
- Partial agonists and antagonists (e.g., pentazocine) compete with agonists for opiate receptor sites and,
- Exhibit mixed agonist–antagonist activity.

Con`t…

- Morphine can stimulate μ1-, μ2-, and κ-receptors,
- perhaps this ability to stimulate multiple receptors accounts for morphine's mixed analgesic and side effect profile.
- Pure opiate antagonists (e.g., naloxone) occupy
- opiate receptors without eliciting a direct response
- It block the access of opiate agonists, such as morphine, to these receptors.

Con`t…

- As a result, pure narcotic antagonists block both the desired and undesired opiate effects
- Opioids produce analgesia by three main mechanisms:
- ✓ Presynaptically, opioids reduce the release of inflammatory transmitters (e.g., tachykinin, excitatory amino acids, and peptides) from the terminals of afferent C-fiber neurons after activation of opioid receptors

Con`t…

- ✓ Opioids also can reduce the activity of output neurons, interneurons, and dendrites in the neuronal pathways by means of postsynaptic hyperpolarization.
- ✓ Opioids also inhibit neuronal activity via GABA and enkephalin neurons in the substantia gelatinosa.

Con`t…

- Mixed agonist–antagonist agents with analgesic activity appear to exhibit selectivity for analgesic receptor sites.
- This may result in analgesia with fewer undesirable side effects.
- Efficacy and side effects also may further differ among agents because of receptor subtype variability.
- This -receptor subtype variability may explain why some patients respond differently to certain opioids, specifically receptor agonists

Con`t…

- The effects of the opioids analgesics are relatively selective, and at normal therapeutic concentrations, these agents do not affect other sensory modalities,
- Such as sensitivity to touch, sight, or hearing; undesirable side effects may increase as the dose is escalated
- Patients in severe pain may receive high doses of opioids with no unwanted side effects, but as the pain subsides, patients may not tolerate even very low doses.

Con`t…

- Frequently, when opioids are administered, pain is not eliminated, but its unpleasantness is decreased.
- Patients report that although their pain is still present, it no longer bothers them
- Opioids share related pharmacologic attributes and exert a profound effect on the CNS and gastrointestinal tract.

Con`t…

- Mood changes, sedation, nausea, vomiting, decreased gastrointestinal motility, constipation, respiratory depression, dependence, and tolerance are evident in varying degrees with all agents.
- Tolerance to side effects (except to constipation) often develops over time.
- Some differences exist between the opioids in regards to incidence of side effects.
- Consideration of these differences assists in selection of the most appropriate agent.

Con`t…

- The route of administration depends on individual patient needs.
- In patients who have oral access, the oral route is preferred.
- However, the onset of analgesic effects for oral medications is approximately 45 minutes, and the peak effect usually occurs 1 to 2 hours after administration.

Con`t…

- This delay must be a consideration when immediate relief is needed in the management of acute pain.
- Therefore, in some scenarios, such as acute severe pain (i.e., pain crisis) or when the patient is unable to take oral medications, alternative routes of therapy
- The relative potency, defined by the equianalgesic dose, of opioids differs greatly
- True opioid allergies are rare

Con`t…

- Most reactions to opioids, such as itching or rash, are due to the associated histamine release from cutaneous mast cells.
- Reactions due to histamine release may be reduced by choosing agents shown to have less effect on histamine release
- Morphine has been associated with the greatest histamine release,
- whereas agents such as oxycodone and fentanyl typically cause fewer histamine-related reactions

Con`t…

- In the initial stages of acute pain, analgesics should be given around the clock.
- This should commence after administering a typical starting dose and titrating up or down,
- As-needed schedules often produce wide swings in analgesic plasma concentrations that create wide swings in pain and sedation.
- This may initiate a vicious cycle where increasing amounts of pain medications are needed for relief.

- As the painful state subsides and the need for medication decreases, as-needed schedules may be appropriate.
- As-needed schedules also may be useful in patients who present with pain that is intermittent or sporadic in nature
- When opioid are used in the management of persistent chronic pain, around-the-clock schedules should be utilized.
- PRN opioids should be used in conjunction with around-the clock regimens and when patients experience breakthrough pain.

Con`t…

- A barrier that consistently causes clinicians to misjudge and mistreat pain is the misunderstanding of opioid tolerance, physical dependence, addiction, and pseudo addiction
- Tolerance is the reduction of drug effect over time as a result of exposure to the drug.
- It develops at different rates and with great patient variability. However, with stable disease, opioid use often stabilizes, and tolerance does not lead to addiction.

Con`t…

- Physical dependence is defined by the occurrence of an abstinence syndrome following administration of an antagonist drug or abrupt dose reduction or discontinuation.“
- Clinicians must understand that physical dependence and tolerance are not equivalent to addiction; however, with chronic opioid use, dependence and tolerance are likely to develop
- Addiction is best defined as a behavioral pattern characterized as loss of control over drug use, compulsive drug use, and continued use of a drug despite harm."

Con`t…

- When opioids are being used, these behaviors must be evaluated continually.
- However, caution is advised when using the term addiction because of its many negative connotations,
- which can lead to a compromised clinician–patient relationship and resulting ineffective pain control.
- In addition, clinicians must be aware that an individual's behaviors may suggest addiction,

Con`t…

- when in reality the behaviors noted are a reflection of unrelieved pain, this is termed pseudo addiction
- The incidence of addiction varies depending on the patient population.
- In patients with no history of addiction, the risk of addiction is relatively small
- In patients with a higher risk for opioid misuse, treatment strategies should be modified.

Con`t…

- Modifications include baseline and random urine drug screens, patient–provider treatment agreements, a smaller prescription supply, and regular assessment of aberrant behaviors.
- Combining these approaches with regular and ongoing assessments of pain and functionality may result in improved outcomes.

Con`t…

Morphine and Congeners

- Despite the availability of several newer agents, morphine remains the prototype opiate analgesic.
- As new opioid and nonopioid compounds are developed, their efficacy and side-effect profiles are typically compared against morphine as the standard.
- Many clinicians consider morphine the first-line agent when treating moderate-to-severe pain.
- Morphine can be given parenteral, orally, or rectally

Con`t…

- Side effects can be numerous, particularly when morphine is first initiated or when doses are significantly increased.
- Morphine causes nausea and vomiting through direct stimulation of the chemoreceptor trigger zone.
- Opioid-induced nausea subsides over time.
- Although euphoria and dysphoria have been reported, morphine's unpleasant effects are more prominent when administered to patients not experiencing pain

Con`t…

- As doses of morphine are increased, the respiratory center becomes less responsive to carbon dioxide, causing progressive respiratory depression.
- This effect is less pronounced in patients being treated for severe or chronic pain.
- Respiratory depression often manifests as a decrease in respiratory rate
- And is further compounded because the cough reflex is also depressed

Con`t…

- Morphine-induced respiratory depression can be reversed by pure opioid antagonists, such as naloxone.
- Morphine used cautiously in
  - Underlying pulmonary disease
  - When CNS depressants used
- Therapeutic doses of morphine have minimal effects on BP, HR , or cardiac rhythm when patients are supine

Con`t…

- However, morphine does produce venous and arteriolar vessel dilation, and orthostatic hypotension may result.
- Hypovolemic patients are more susceptible to morphine-induced cardiovascular changes
- Because morphine prompts a decrease in myocardial oxygen demand in ischemic cardiac patients,
- It is often considered the drug of choice when using opioids to treat pain associated with MI

Con`t…

- Morphine also affects the hypothalamus inhibiting the release of gonadotropin-relasing hormone,
- Thus decreasing plasma testosterone and cortisol.
- Although the clinical meaning has not clearly been elucidated, morphine and other opioids also appear to be immunosuppressive
- Other drugs of the class:
  - Hydromorphone, Oxymorphone,Levorphanol
  - Codeine, Hydrocodone ,Oxycodone

Con`t…

Meperidine and Congeners (Phenylpiperidines)

- Meperidine, has a pharmacologic profile comparable with that of morphine;
- However, it is not as potent and has a shorter analgesic duration.
- Meperidine offers no analgesic advantage over morphine, has greater toxicity and should be limited in use.
- In particular, avoid long-term usage, and use in patients at greatest risk for toxicity(elderly, renal impairment)

Con`t…

- Fentanyl is a synthetic opioid structurally related to meperidine that is used often in anesthesiology as an adjunct to general anesthesia.
- This agent is more potent and faster acting than meperidine
- It can be administered parenterally, transmucosally, and transdermally.

Methadone and Congeners

- Methadone has oral efficacy, extended duration of action, and ability to suppress withdrawal symptoms in heroin addicts.
- With repeated doses, the analgesic duration of action of methadone is prolonged, but excessive sedation may also result.
- Although effective for acute pain, it is usually used for chronic cancer pain.

Con`t…

Opioid Agonist–Antagonist Derivatives

- This class produces analgesia and has a ceiling effect on respiratory depression and lower abuse potential than morphine.
- However, psychotomimetic responses (e.g., hallucinations and dysphoria with pentazocine),
- Aceiling analgesic effect, and the propensity to initiate withdrawal in opioid-dependent patients have limited their widespread use

Con`t…

Opioid Antagonists

- Naloxone is a pure opioid antagonist that binds competitively to opioid receptors but does not produce an analgesic response.
- It is used to reverse the toxic effects of agonist and agonist-antagonist opioids.

TABLE 30–2. Equianalgesic Doses of Selected Opioids[26,45,49,51]

Opioid	Dose Equianalgesic to 10 mg of Parenteral Morphine (mg)	
	Parenteral (mg)	Oral (mg)
Mild-Moderate Pain		
Codeine	120	200
Hydrocodone	N/A	30
Oxycodone	N/A	20
Meperidine (Demerol)	100	400
Propoxyphene (Darvon)	N/A	65–130
Moderate-Severe Pain		
Morphine	10	30
Hydromorphone (Dilaudid)	1.5	7.5
Oxymorphone	1	N/A
Levorphanol	2	4
Fentanyl (Duragesic)	0.1–0.2	N/A[a]
Methadone (Dolophine)	10[b]	3–5[b]

[a]Transdermal: 100 mcg/hour = 2–4 mg/hour of IV morphine.
[b]Dosage calculations when converting from morphine to methadone are not linear. The equianalgesic dose of methadone will decrease progressively as the morphine equivalents increase (Table 30–4).

TABLE 30–3. Managing Opioid Side Effects

Adverse Effects	Drug Treatment/Management
Excessive sedation	Reduce dose by 25% or increase dosing interval
Constipation	Casanthranol-docusate 1 cap at bedtime or twice daily; senna 1–2 tabs at bedtime or twice daily; bisacodyl 5–10 mg daily + docusate 100 mg twice daily
Nausea and vomiting	Prevention: hydroxyzine 25–100 mg (PO/IM) every 4–6 hours as needed; diphenhydramine 25–50 mg (PO/IM) every 6 hours as needed; ondansetron 4 mg IV or 16 mg PO Treatment: prochlorperazine 5–10 mg (PO/IM) every 3–4 hours as needed or 25 mg per rectum twice daily; ondansetron 4–8 mg IV every 8 hours as needed
Gastroparesis	Metoclopramide 10 mg (PO/IV) every 6–8 hours
Vertigo	Meclizine 12.5–25 mg PO every 6 hours as needed
Urticaria/itching	Hydroxyzine 25–100 mg (PO/IM) every 4–6 hours as needed; diphenhydramine 25–50 mg (PO/IM) every 6 hours as needed
Respiratory depression	Mild: Reduce dose by 25% Moderate–severe: naloxone 0.4–2 mg IV every 2–3 minutes (up to 10 mg) for complete reversal; 0.1–0.2 mg IV every 2–3 minutes until desired reversal for partial reversal; may need to repeat in 1–2 hours depending on narcotic half-life
CNS irritability	Discontinue opioid; treat with benzodiazepine

Con`t…

Central Analgesic

- Tramadol, a centrally acting analgesic for moderate to moderately severe pain, binds to μ opiate receptors and weakly inhibits norepinephrine and serotonin reuptake.
- Tramadol has a side-effect profile similar to that of other opioid analgesics.
- It may also enhance the risk of seizures.
- It may be useful for treating chronic pain, especially neuropathic pain, but it has little advantage over other opioid analgesics for acute pain.

Con`t…

Adjuvant Analgesics

- Adjuvant analgesics are pharmacologic agents with individual characteristics that make them useful in the management of pain but that typically are not classified as analgesics.

Examples of adjuvant analgesics include:

- Anticonvulsants (e.g., gabapentin, which may decrease neuronal excitability),
- Tricyclic antidepressants,
- Serotonin and norepinephrine reuptake inhibitor
- Topically applied local anesthetics

Con`t…

Regional Analgesia

- Regional analgesia with properly administered local anesthetics can provide relief of both acute and chronic pain
- These agents can be positioned by injection or topically.
- Lidocaine in the form of a patch has proven effective in treating focal neuropathic pain.
- Regional application of local anesthetics relieve pain by blocking nerve impulses.

Con`t…

- High plasma concentrations can cause signs of CNS excitation and depression,
- Cardiovascular effects include myocardial depression, hypotension, decreased cardiac output, heart block, bradycardia, arrhythmias, and cardiac arrest.
- Disadvantages of such methods include the need for skillful technical application, need for frequent administration, and highly specialized follow up procedures

TABLE 30–5. Selected Adjuvant Analgesics and Suggested Dosing[54–58]

Agent	Dosing Guidelines	FDA-Approved Indication
Amitriptyline (Elavil)	10–25 mg at bedtime with weekly increments to a target dose of 25–150 mg of amitriptyline or an equivalent dose of another TCA	
Duloxetine (Cymbalta)	60 mg daily	DPN
Gabapentin (Neurontin)	Initially, 300 mg three times daily up to a maximum of 3600 mg daily, in divided doses[a]	PHN
Pregabalin (Lyrica)	DPN: Initially, 50 mg three times daily; may be increased to 100 mg three times daily within 1 week based on efficacy and tolerability[a] PHN: Initially 75 mg twice daily or 50 mg three times daily; may be increased to 100 mg three times daily within 1 week based on efficacy and tolerability[a]	DPN and PHN
Lidocaine 5% (Lidoderm patch)	Up to three patches may be applied directly over the painful site once daily; patches are applied using a regimen of 12 hours on and 12 hours off	PHN

Pain Level Description	Typical Corresponding Numerical Rating (0 to 10 Scale)	WHO Therapeutic Recommendations	Example Medicines for Initial Therapy	Comments
"Mild" pain	1–3	Nonopioid analgesic: taken on a regular schedule, not as needed (prn)	• Acetaminophen 650 mg every 4 hr • Acetaminophen 1,000 mg every 6 hr • Ibuprofen 600 mg every 6 hr	• Consider adding adjunct analgesic or using an alternate regimen if pain not reduced in 12 days • Consider step up if pain not relieved by two different regimens
"Moderate" pain	4–6	Add opioid for moderate pain (e.g., moderate potency analgesic). Use on a schedule, not prn	• Acetaminophen 325 mg/codeine 60 mg every 4 hr • Acetaminophen 325 mg/Oxycodone 5 mg every 4 hr • Tramadol 50 mg every 6 hr	• Consider adding adjunct analgesic or using an alternate regimen if pain not reduced in 12 days • Consider step up if pain not relieved by two different regimens
"Severe" pain	7–10	Switch to a high potency (strong) opioid; administer on a regular schedule	• Morphine 15 mg every 4 hr • Hydromorphone 4 mg every 4 hr • Morphine controlled release 60 mg every 8 hr	• Consider alterrate regimen (e.g., different strong opioid) if pain not reduced in 12 days • Consider increased dose of strong opioid, or addition of nonopioid agents, if pain not adequately relieved by two regimens

THANK U