A PHARMACIST'S ROADMAP To Pain Management

NEW DIRECTIONS
To Improved Patient Care

Thursday, September 15, 2011
10:00 - 11:30 AM

ICHP Annual Meeting

Drury Lane Theatre and Conference Center
Oakbrook Terrace, Illinois

▶ PRACTICE GAP AND EDUCATIONAL NEED

Pain represents a major crisis in today's healthcare environment with over 70 million Americans experiencing chronic pain each year. Poor management of pain has been linked to reduced quality of life and patient satisfaction of care. During hospitalization, inadequate management of pain leads to longer length of stay and higher readmission rates, resulting in overall higher healthcare costs. Pain places a heavy financial burden on society and is a leading cause of disability and lost work days.

Adequate pain management requires clinicians to make rational decisions regarding analgesic selection, dosing, titration, and administration. A thorough understanding of pain pathophysiology is essential to guide clinical decision-making. Despite the availability of effective analgesics, several barriers to adequate pain management continue to exist. These barriers include failure to assess scope of pain, concerns for abuse, fear of adverse events, and a lack of knowledge about pain and analgesics.

Healthcare providers must recognize the impact of pain on their patients and advance their efforts to better manage pain. Pharmacists, as part of a interdisciplinary team, can play a leading role in these efforts to address the current practice gaps.

▶ TARGET AUDIENCE

This continuing pharmacy education activity is planned to meet the needs of pharmacists in a variety of practice settings, including large and small health systems, outpatient clinics, managed-care organizations, long-term care facilities, and academia. This activity would be especially beneficial for pharmacists, clinical specialists, managers, leaders, and educators who are interested in pain management, new drug therapies, and improving the care of patients experiencing moderate to severe pain.

▶ LEARNING OBJECTIVES

After participating in this educational activity, learners should be able to

- Optimize pain management decisions based on pain pathophysiology
- Select an appropriate analgesic and dosing regimen to effectively treat moderate to severe pain
- Incorporate evidence-based strategies to minimize adverse events and toxicity associated with analgesics
- Utilize pain assessment tools and communication techniques to accurately evaluate pain

▶ EDUCATIONAL DESIGN

This interactive Initiative is designed to incorporate a multifaceted-activities approach in order to build the skills and competencies of health-system pharmacists and to facilitate application of these competencies in clinical practice. Health-system pharmacists will have the opportunity to participate in the live activity followed by an online tutorial series with cases and Internet Point of Care.

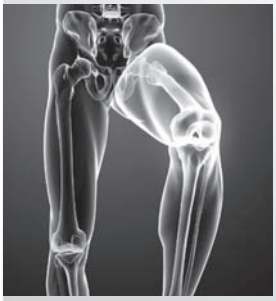
The **live activity** consists of evidence-based presentations focusing on leading issues facing pharmacists when managing patients with chronic pain. This will be followed by a Case Study Forum discussing the application of clinical tools through faculty-learner dialogues in two virtual cases.

The **online tutorial series** with cases will reinforce practical application of tools and competencies acquired during the live activity. Each tool is a combination of faculty commentary on essentials in clinical practice, links to relevant scientific publications, and printable handout material for reference. Cases following the online tutorials will give the learners an opportunity to earn extra CE credit upon completion.

As health-system pharmacists attempt to implement principles and strategies learned, they will continue to have questions regarding how to incorporate them into clinical practice. Therefore, through **Internet Point of Care** activity, participants will have access to resources necessary to search for answers to their specific clinical questions.

Please visit the Vemco MedEd website for these upcoming educational opportunities: www.vemcomeded.com.

▶ 10 STATE ANNUAL SHP MEETINGS



1. **Texas**
2. **Louisiana**
3. **Washington**
4. **Arkansas**
5. **Georgia**
6. **Florida**
7. **New York**
8. **Illinois**
9. **Minnesota**
10. **California**

Educational Program

10:00 - 10:10 AM **Welcome and Introduction**
Recognizing the Current Crisis in Pain Management
Gregory L. Holmquist, PharmD

10:10 - 10:55 AM **Back to Basics: Understanding and Assessing Pain**
Joseph B. Straton, MD

Drug Selection, Administration and Dosing: The Rationale
Charles E. Argoff, MD

10:55 -11:25 AM **Case Study Forum**
All Faculty and Participants

11:25 - 11:30 AM **Learning by Sharing: Q&A**
All Faculty and Participants

Faculty

Gregory L. Holmquist, PharmD, CPE (Moderator)

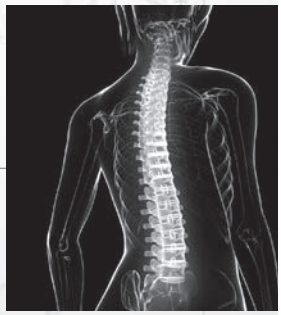
Pain and Palliative Care Specialist
Certified Pain Educator
Palliative Care Strategies
Seattle, Washington

Joseph B. Straton, MD, MSCE

Medical Director
VITAS Innovative Hospice Care
Philadelphia, Pennsylvania

Charles E. Argoff, MD

Professor of Neurology
Albany Medical College
Director of the Comprehensive Pain Program
Albany Medical Center
Albany, New York



CE ACCREDITATION

Pharmacists

The University of Kentucky College of Pharmacy is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

This knowledge-based activity has been assigned ACPE # 022-999-11-024-L04-P and will award up to 1.5 contact hours (0.15 CEUs) of continuing pharmacy education credit in states that recognize ACPE providers.

Statements of credit will indicate hours and CEUs based on participation and will be issued online at the conclusion of the activity. Successful completion includes signing in at registration, attending the entire session for which credit is claimed, completing the activity evaluation and requesting credit online at conclusion of the activity. The College complies with the Accreditation Standards for Continuing Pharmacy Education.

Instructions For Credit

1. Attend activity in its entirety

2. Post program, go to www. CECentral.com/getcredit

3. Enter activity code PLN11109

4. Choose the date of the session you attended

5. Login or register for a free account

6. Complete evaluation

7. Get credit. A printable certificate will be issued.

Disclosure Of Conflicts Of Interest
University of Kentucky and Vemco MedEd require faculty, planners, and others who are in a position to control the content of continuing education activities to disclose to the audience any real or apparent conflict of interest related to the activity. All identified conflicts of interest are reviewed and resolved to ensure fair balance, objectivity, and scientific rigor in all activities. The faculty is further required to disclose discussion of off-label uses in their presentations.

Disclosure: Planning Committee Members
Employees of University of Kentucky and Vemco MedEd have no relevant financial relationships to disclose.

Disclosures: Faculty
In accordance with policies set forth by the Accreditation Council for Continuing Medical Education (ACCME) and the Accreditation Council for Pharmacy Education (ACPE), University of Kentucky UK HealthCare CECentral (UKHCCEC) require all faculty members and spouses/significant others with an opportunity to affect the content of a continuing education activity to disclose any relevant financial relationships during the past 12 months with commercial interests. A commercial interest is any entity producing, marketing, re-selling or distributing health care goods or services consumed by or used on patients. Relationships with commercial interests and conflicts of interest resulting from those relationships must be revealed to the audience and resolved prior to the activity.

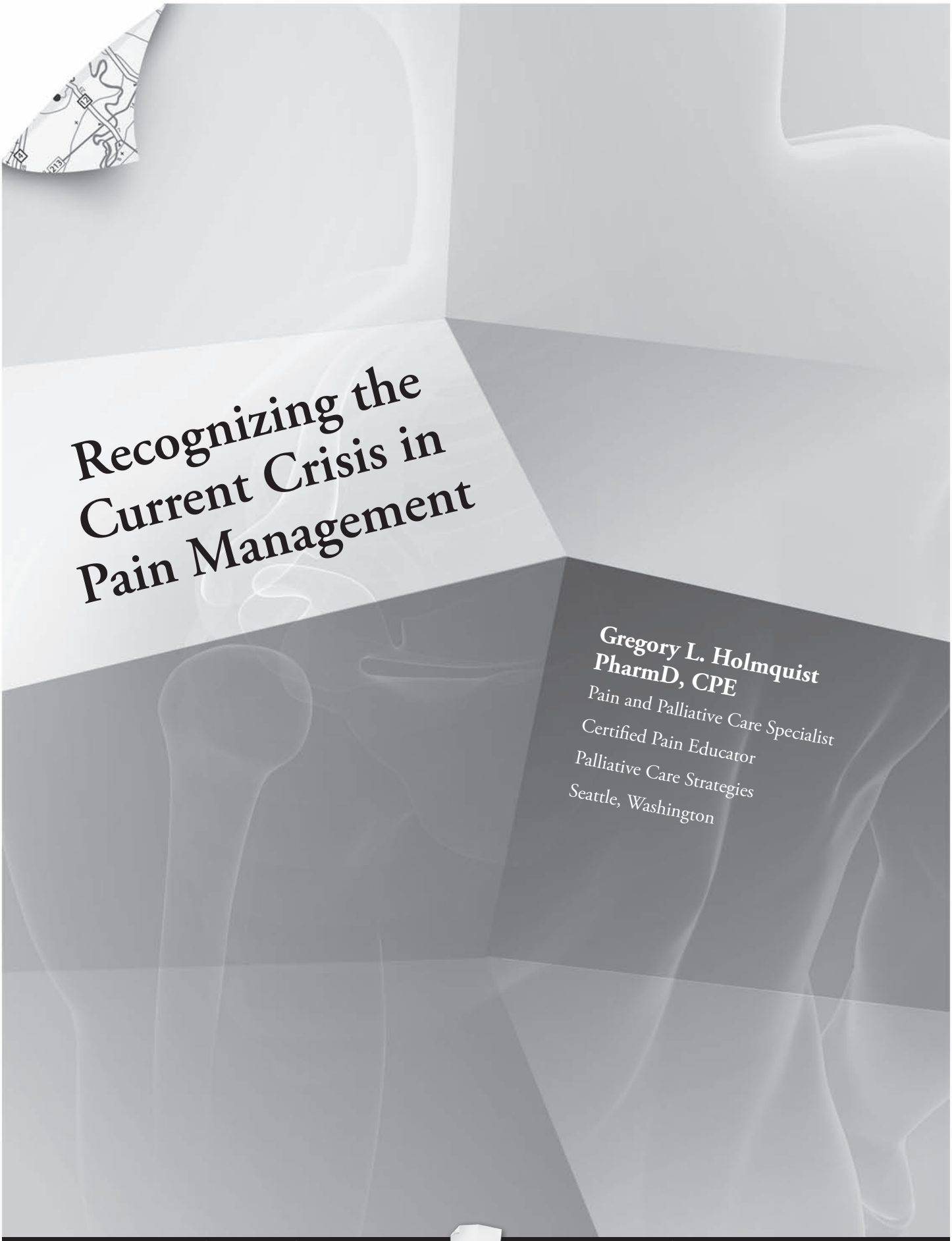
Relevant relationships include roles such as speaker, author, consultant, independent contractor (including research), employee, investor, advisory committee member, board member, review panelist, and investigator. If a potential speaker or author indicates a possible conflict of interest, the conflict will be resolved by choosing another speaker or author for that topical area, or the slides, handouts, and/or monograph will be reviewed and approved by a qualified commercially-disinterested peer.

Disclosure of a relationship is not intended to suggest or condone any bias in any presentation, but is made to provide participants with information that might be of potential importance to their evaluation of a presentation.

Faculty/Spouse/ Significant Other	No relevant financial relationships in past 12 months	Intend to discuss off-label use of a product	Commercial Interest	Role	Received	Conflict(s) resolved
Gregory L. Holmquist, PharmD	not applicable	No	King Pharmaceuticals	Speaker	Yes	Yes
Joseph B. Straton, MD	Yes	No	not applicable	not applicable	Yes	Yes
Charles E. Argoff, MD	not applicable	Yes	Endo Pharmaceuticals, Forest Laboratories, King Pharmaceuticals (Pfizer), Lilly, PriCara, Depomed, Covidien, Cephalon, and Nuvo Research	Speaker, Grantee and a Consultant	Yes	Yes

Discussion Of Off-Label Uses
The following off-label use of pain medications will be discussed during this activity: venlafaxine for management of neuropathic pain; lamotrigine for central post-stroke pain and diabetic poly-neuropathy.

Commercial Support
This activity is supported by an educational grant from Janssen Pharmaceuticals, Inc., administered by Janssen Scientific Affairs, LLC.



Recognizing the Current Crisis in Pain Management

Gregory L. Holmquist PharmD, CPE
Pain and Palliative Care Specialist
Certified Pain Educator
Palliative Care Strategies
Seattle, Washington

Gregory L. Holmquist, PharmD, CPE

Dr. Gregory L. Holmquist earned his Doctor of Pharmacy degree from the University of Washington in Seattle and has been a practicing clinical pain management and palliative care pharmacist for over 20 years. In addition to being the Director/Owner of Palliative Care Strategies, Dr. Holmquist currently provides direct patient care and consultative services for the chronic non-cancer pain and hospice teams at Group Health in Seattle.

Dr. Holmquist is currently certified by the American Medical Association as an Educator for Physicians on End-of-Life Care (EPEC), by the American Society of Pain Educators as a Certified Pain Educator (CPE), and by the Board of Pharmaceutical Specialties as a Board Certified Oncology Pharmacist (BCOP). Dr. Holmquist is a frequently requested lecturer and has been invited to present over 1000 CME/CE sessions on pain management across the country over the past decade.

Dr. Holmquist has acted as Principle Investigator on numerous clinical trials and has served on the Editorial Board of *Journal of Pharmaceutical Care in Pain and Symptom Control*. Most recently, Dr. Holmquist accepted a position to the Board of Advisors of the American Society of Pain Educators.

Bill's Story

- Bill is a 52-year-old warehouse worker who has been suffering from low back pain for the past 7 years
- Bill is married with 2 teenage sons
- He describes the pain as "like a screwdriver twisting in my lower back that can last for hours"
- When pain was not present, Bill had a constant fear that the pain would return
- All of Bill's life activities would revolve around the presence of pain

Bill's Life with Pain

- Pain significantly impacts Bill's work performance
- On a good day, he could work 2-3 hours before he would have to find a quiet place in the storehouse to lie down until the pain subsided
- He was afraid to let his co-workers know about the pain for fear of losing his job
- Bill could not get more than 2-3 hours of sleep at a time since the pain returns during the night

- As a result, he is always exhausted

Managing Bill's Pain

- Bill has changed physicians several times over the years without improved results
- He has tried several different pain medications but the side effects limit their use

- Mainly nausea, vomiting, reflux, and abdominal pain

- Basically, Bill had to choose between dealing with the pain or the adverse effects of medication
- Bill believes that everything possible is being done to control his pain

Is Bill receiving the best possible care available?

How can health-system pharmacists help patients like Bill?

Pain is Prevalent

- Pain impacts an estimated 70 million Americans[1]
  - 59 million experienced low back pain in previous 3 months[2]
- 50 million experience chronic pain[1]
  - Osteoarthritis impacts 27 million[2]
  - Fibromyalgia impacts 5 million[2]
- Chronic pain conditions result in 50 million lost workdays[3]
- Total health expenditures by patients with back pain are over $90 billion[4]

1. U.S. Department of Health and Human Services. Health, United States, 2006. Available from: http://www.cdc.gov/nchs/data/hus/hus06.pdf. Accessed April 13, 2011.
2. Lawrence RC, et al. *Arthritis Rheum*. 2008;58:26-35.
3. Stewart WF, et al. *JAMA*. 2003;290(18):2443-2454.
4. Luo X, et al. *Spine*. 2004;29:79-86.

Pain is Poorly Managed

In a survey of 988 terminally ill patients at 6 US sites:[1]

- 50% reported suffering moderate to severe pain

A survey from a random sample of residents in Olmstead County, MN showed:[2]

- 64.4% reported having chronic pain (>3 months duration)
- Over 21% of chronic pain sufferers reported dissatisfaction with current care
- 28% rated their effectiveness of treatment as poor/fair

1. Weiss SC, et al. *Lancet*. 2001;357:1311-1315.
2. Watkins EA et al. *Pain Med*. 2008;9:166-174.

PainSTORY Results

- **PainSTORY** (Pain Study Tracking Ongoing Responses for a Year) monitored how chronic pain impacts the lives of patients over 1 year
- **Results after 1 year of treatment:**
  - 6 in 10 patients feel that pain controls their life
  - 95% report that they are suffering from moderate to severe pain
  - 19% feel that their pain is getting worse
  - Yet, 64% feel that they are receiving the most appropriate treatment
    - Only 12% were being prescribed a strong opioid medication

PainSTORY. Available at: www.painstory.org. Accessed February 11, 2011.

Barriers to Pain Management

- **A**buse concerns by clinicians, patients, family
- **B**elief or lack thereof by all parties
- **C**apability of the prescriber and patient
- **D**angers – adverse effects, management, awareness
- **E**nforcement – laws and regulations, constraints
- **F**inancial implications
- **G**aining clinical access
- **H**earing patient – not listening
- **I**ncomplete prescribing
- **J**udgmental issues
- **K**nowledge of polymodal treatment plan
- **L**ack of patient specific-, centered-, focused-pharmacotherapy personalized care
- **M**eaning of pain to the patient
- **N**eed for follow-up
- **O**ther

Pain Management Beliefs

- **Some pain is good for you**
  - One-third of patients believe that pain builds character[1]
- **Pain is to be "expected"**
  - Over 70% of patients believe that pain is part of "having cancer"[2]
- **No one dies from pain**
  - True, but they may wish they did
  - EPIC study revealed that 33% of patients reported their pain is sometimes so bad that they feel like they want to die.[2]
- **I can judge pretty well how much pain a patient is having**
  - Pain is very subjective

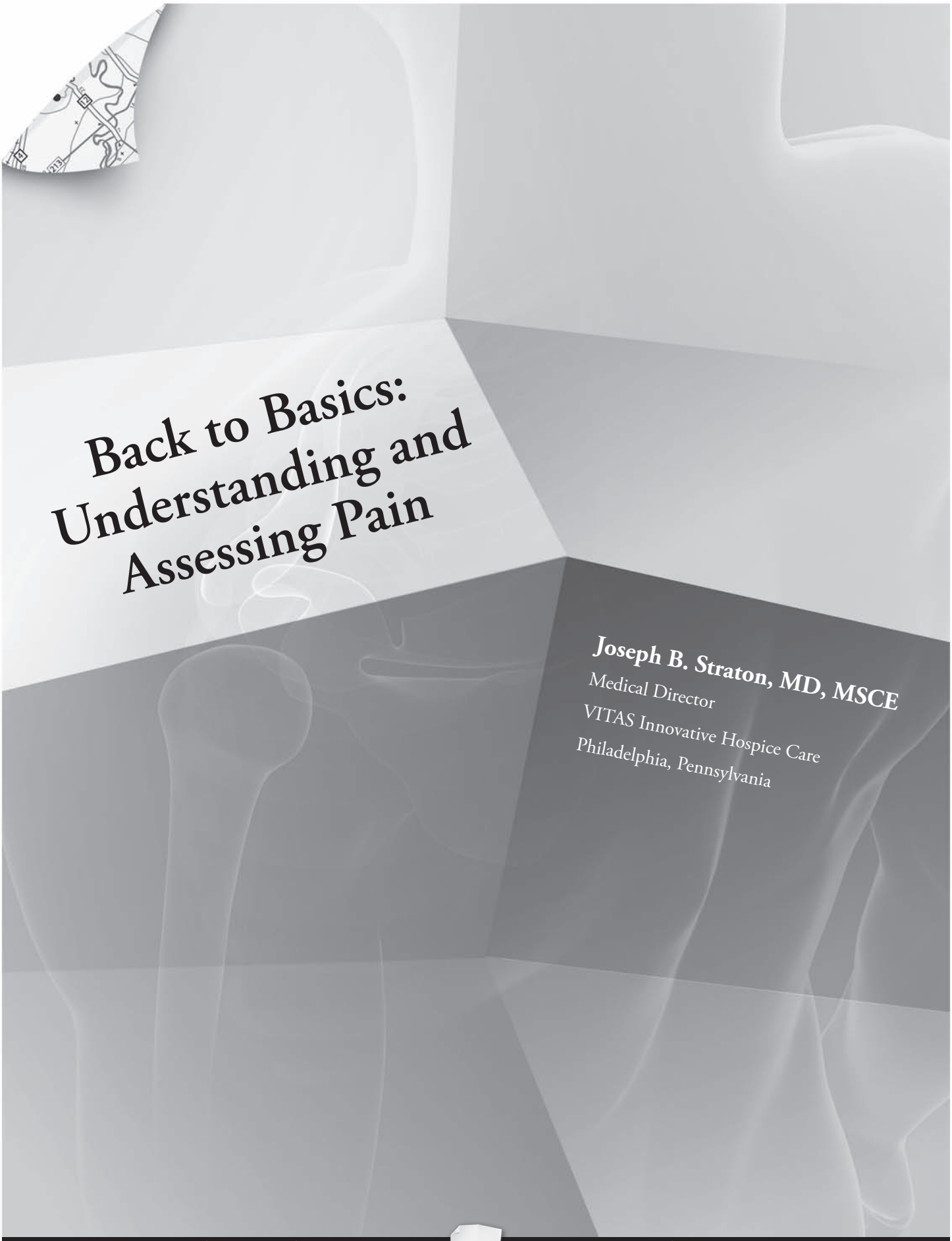
1. Weis OF et al. *Anesth Analg*. 1983;62:70-74.
2. EPIC Study. Available at: http://www.ecco-org.eu/binarydata.aspx?type=doc/PL5_-_J_Foubert.pdf. Accessed on February 11, 2011.

What is the Role of the Health-System Pharmacist in Pain Management?

Are pharmacists responsible for:

- Ensuring pain is adequately addressed (HIPAA)?
- Assessing pain? (Which assessment tools to use?)
- Knowing the treatment options and how to utilize them?
- Managing adverse events?

Notes



Back to Basics: Understanding and Assessing Pain

Joseph B. Straton, MD, MSCE
Medical Director
VITAS Innovative Hospice Care
Philadelphia, Pennsylvania

Joseph B. Straton, MD, MSCE

Dr. Joseph B. Straton is a Medical Director at VITAS Innovative Hospice Care. Prior to recently joining VITAS, Dr. Straton was Assistant Professor of Family Medicine and Community Health, as well as Assistant Professor of Anesthesiology and Critical Care at the University of Pennsylvania School of Medicine in Philadelphia, Pennsylvania. Dr. Straton is double board certified in Family Medicine and Hospice and Palliative Care Medicine.

After receiving his medical degree from Jefferson Medical College and completing his residency from Thomas Jefferson University Hospital, Dr. Straton went on to earn his Master of Science in Clinical Epidemiology from University of Pennsylvania. He is a member of numerous societies including American Academy of Family Physicians, Pennsylvania Academy of Family Physicians, and American Academy of Hospice and Palliative Medicine. Dr. Straton has served as a reviewer for several journals including *JAMA, Journal of Palliative Medicine, Journal of American Geriatric Society, Psychological Medicine,* and *Journal of General Internal Medicine*. He has authored numerous journal articles, editorial reviews, and book chapters with a particular focus on palliative care approaches in older patients.

Objectives

- Differentiate among the various types of pain
- Utilize pain assessment tools to accurately evaluate pain

"On the plus side, you've cured my back pain."

Acute vs. Chronic Pain

Acute Pain	Chronic Pain
▪Duration < 6 months	▪Duration > 6 months
▪Signals disease process (arthritis pain flare)	▪No useful function (degenerative joint pain)
▪Obvious cause (direct injury, surgery)	▪Unclear cause (chronic abdominal pain)
▪Abates with treatment of underlying cause	▪Persistent pain despite medical diagnostic workup
▪Significant relief with analgesic medication	▪Incomplete relief with analgesic medication

Differentiating Types of Pain

	Nociceptive Pain		Neuropathic Pain
	Somatic Pain	Visceral Pain	
Location	Localized	Generalized	Radiating or specific
Patient Description	Pinprick, stabbing, or sharp	Ache, pressure, or sharp	Burning, prickling, tingling, electric shock-like, or lancinating
Mechanism of Pain	A-delta fiber activity Located in the periphery	C Fiber activity Involved deeper innervation	Dermatomal (periphery), or non-dermatomal (central)
Clinical Examples	•Periosteum, joints, muscles •Sickle cell •Superficial laceration •Superficial burns •Intramuscular injections, venous access •Otitis media •Stomatitis •Extensive abrasion	•Colic and muscle spasm pain •Appendicitis •Kidney stone •Chronic pancreatitis •IBS •Angina •Menstrual cramps	•Trigeminal neuralgia •Avulsion neuralgia •Posttraumatic neuralgia •Peripheral neuropathy (diabetes, HIV) •Limb amputation •Herpetic neuralgia

Institute for Clinical Systems Improvement (ICIS). *Assessment and Management of Acute Pain*. Sixth Edition, March 2008. www.icis.org

Breakthrough Pain of Chronic Pain Syndromes

- Fluctuation in pain intensity that interrupts a tolerable background level of pain
- May occur spontaneously, after some incident, or due to end-of-dose failure
- Episodes are generally of rapid onset, short duration, high intensity, with similar features to background pain

Greco MT, et al. *Clin J Pain*. 2011:27:9-18.
Chou R, et al. *J Pain*. 2009;10(2):113-130.
American Pain Society. *Principles of analgesic use in the treatment of acute pain and cancer pain*. 6th Edition, 2008.

Back to the Case (Bill)

- What's going on with Bill?
- How can we use the information he's provided to guide care?

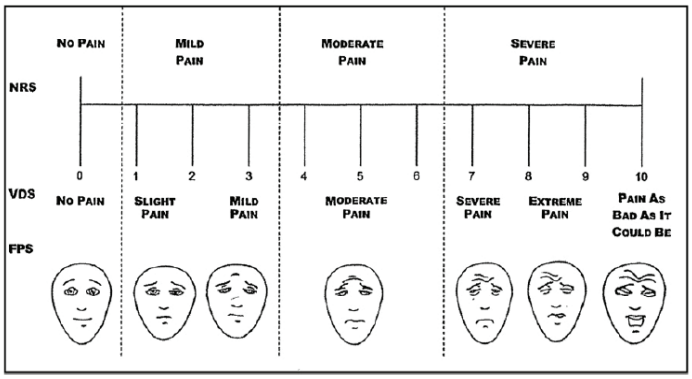
Pain Assessment

"You say it's a sharp, stabbing pain. Hmmmm ... sharp ... stabbing pain."

Assessment

- **Why?**
  - Unrecognized pain will not be treated
  - Underestimated pain will not be treated aggressively enough
- **How?**
  - Lots of methods

Self-Report Pain Tools



NRS, numerical rating scale; VDS, verbal descriptor scale; FPS, faces pain scale (revised)

Herr K. *Pain Manag Nurs*. 2010;11:S1-S10.
Tomlinson D, et al. *Pediatrics*. 2010;126;e1168.
Bailey B, et al. *Pain*. 2010;149:216-221.

Behavioral Pain Tools

Item	Score 0	1	2
Face	No particular expression or smile	Occasional grimace, frown, withdrawn or disinterested	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal position or relaxed	Uneasy, restless, or tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, or tense	Arched, rigid, or jerking
Cry	No cry	Moans, whimpers, or occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or being talked to; distractible	Difficult to console or comfort

Voepel-Lewis T, et al. *Am J Crit Care*. 2010;19:55-61.

Validity of Pain Tools

- **Self-report by children ≥5 yrs of age**
  - 0-10 numerical rating scale
  - Faces Pain Score – Revised
  - Oucher Pain Scale
  - Wong-Baker Faces Pain Rating Scales
- **Cognitively impaired adults**
  - Checklist of Nonverbal Pain Indicators (CPNI)
  - Pain Assessment in Advanced Dementia (Pain AD)
- **FLACC for both adults and children**

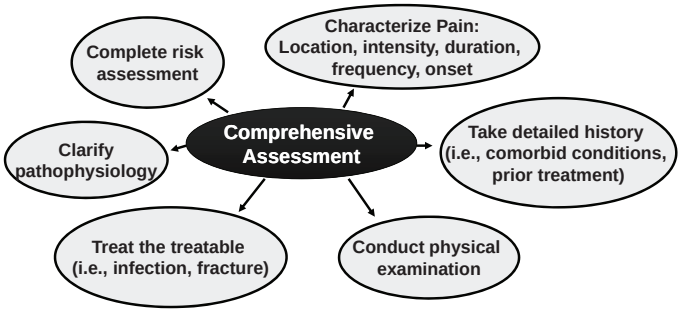
Voepel-Lewis T, et al. *Am J Crit Care*. 2010;19:55-61.

Pain Assessment is Not Always as Easy as it Looks

While intensity is the most salient dimension of pain, a single dimension will always fail to capture the many qualities of pain

…**so what do we do?**

Comprehensive Pain Assessment



1. Turk D, Melzack R. *Handbook of Pain Assessment, 2nd Edition*. Guilford Press, 2001.
2. JCAHO. *Pain: Current Understanding, Assessment, and Treatment*. December 2001. Available at: http://www.npcnow.org/App_Themes/Public/pdf/Issues/pub_related_research/pub_quality_care/Pain-Current-Understanding-of-Assessment-Management-and-Treatments.pdf .

Assessing Pain: Use 'OLD CARTS'

Pain Characteristic	Questions to Ask
Onset	Did the pain begin acutely or gradually? Did it occur after an injury?
Location	Where do you feel the pain? Is the pain isolated to certain points or generalized? Is the pain unilateral or bilateral?
Duration	How long have you been having the pain?
Character	Is the pain knifelike or cutting, prickly, pinching, burning, itching, or throbbing? Is the pain provoked or unprovoked? Does the pain radiate to other areas?
Aggravating/ Associated Factors	If the pain is provoked, what are precipitants?
Relieving Factors	What have you tried? Did anything help?
Temporal Factors	Is the pain constant? Are there pain-free periods?
Severity	On a scale of 1 to 10, with 10 being the worst pain you can imagine, rate the pain.

Seidel H, et al. *Mosby's Guide to Physical Examination*. St. Louis, MO: Mosby, 2003.

Reassessment of Pain: Global Subjective Efficacy Scale

- Person rates how effective their treatment was, on a numeric or verbal scale
- Person is asked if their pain is half gone
  - Not sensitive to intermediate levels of analgesia
  - 20-33% decrement may be clinically important to persons with pain, depending on starting point

Salaffi F, et al. *Eur J Pain*. 2004;8:283-291.

Patient Satisfaction

- Joint Commission study to improve hospital pain management – what matters to patients
  - Staff asking about pain
  - Staff level of care and concern about pain
  - Prompt response to pain medication requests
- Cancer patient core aspects of satisfaction
  - Being treated right
  - Having a safety net
  - Being in a partnership with their health care team
  - Having pain treatment that was efficacious

DuPree E, et al. *Joint Commission Journal on Quality and Patient Safety*. 2009;35:343-350.
Beck SL, et al. *J Pain Symptom Manag*. 2010;39:100-115.

What Will Be Most Useful Here?

- For the patient?
- For the clinician?

Notes

Drug Selection, Administration and Dosing: The Rationale

Charles E. Argoff, MD
Professor of Neurology
Albany Medical College
Director of the Comprehensive Pain Program
Albany Medical Center
Albany, New York

Charles E. Argoff, MD

Charles E. Argoff, MD is Professor of Neurology at Albany Medical College and Director of the Comprehensive Pain Program at Albany Medical Center in Albany, New York.

Dr. Argoff received his medical degree from Northwestern University Medical School in Chicago, Illinois. After completing an internship in the Department of Medicine and a residency in the Department of Neurology at the State University of New York in Stony Brook, Dr. Argoff went on to complete a fellowship in developmental and metabolic neurology at the National Institutes of Health/National Institute of Neurological Disorders and Stroke (NIH/NINDS).

Dr. Argoff is a member of numerous professional organizations including the International Association for the Study of Pain, the American Academy of Pain Medicine, and the American Academy of Neurology. He serves on the editorial board for the *Clinical Journal of Pain* and as a reviewer for several journals including the *Journal of Pain, Brain, Journal of the American Medical Association, Journal of Musculoskeletal Pain,* and *Journal of Pain and Symptom Management.* He is co-editor of the Neuropathic Pain Section of *Pain Medicine.*

Dr. Argoff has served as a guest editor for and published articles in the *Clinical Journal of Pain* and Current Pain and Headache Reports, among other peer-reviewed journals. He has written on many types of pain, including myofascial pain, spinal and radicular pain, and neuropathic pain. Dr. Argoff had an active role in the development of the diabetic peripheral neuropathic pain guidelines published in *Mayo Clinic Proceedings*, and he has contributed to other published neuropathic pain treatment guidelines. He is one of the editors of the published textbook *Raj's Practical Management of Pain*, Fourth Edition.

Objectives

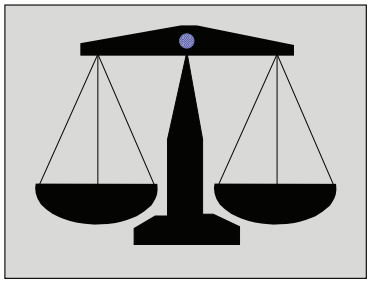
- Select an appropriate analgesic to effectively treat moderate to severe pain
- Incorporate evidence-based strategies to minimize adverse events and toxicity associated with analgesics

Balancing Medication Use in Patients

√ Non-pharmacological strategies

√ Pain modulation

√ Patient satisfaction



√ Improving functionality

√ Minimizing side effects

√ Medical / legal guidelines for opioid use

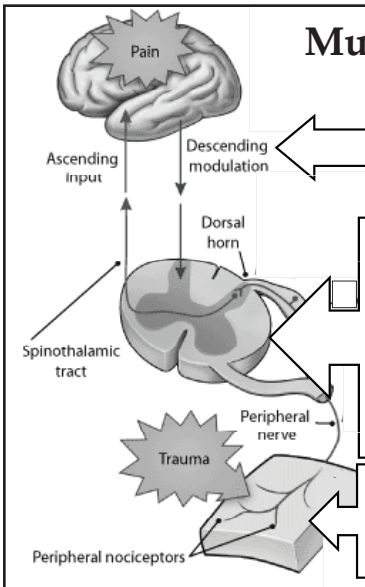
√ Ethical issues

Chronic Pain Management

- **Goal:** decrease pain while improving function and reducing psychosocial suffering while minimizing adverse events
- **Multimodal:** interventions that constitute the use of more than one type of therapy (e.g. opioid and co-analgesic/adjunctive medication)
- **Multidisciplinary:** interventions that include more than one discipline (e.g. physical therapy and psychological treatment)

American Society of Anesthesiologists. *Anesthesiology*. 2010; 112:810-835.

Multimodal Drug Therapy



Descending Modulation
-Opioids
-Antidepressants (e.g. tricyclic and SNRI)
-Alpha-2 agonists (e.g. clonidine)
-Tapentadol and tramadol

Central Sensitization
-Neuraxial local anesthetics
-Alpha-2 agonists (e.g. clonidine)
-NMDA-receptor antagonists (e.g. methadone)
-Anticonvulsants (e.g. gabapentin, pregabalin, topiramate)
-Antidepressants (e.g. tricyclic and SNRI)
-Tapentadol and tramadol
-Opioids
-Acetaminophen

Peripheral Sensitization
-Topical local anesthetics, opioids, capsaicin, and tricyclic antidepressants
-Non-steroidal anti-inflammatory drugs

Adapted from Gottschalk A, Smith DS. *Am Fam Phys*. 2001;63:1979-1986.

Acetaminophen

- **Benefits**
  - Weak anti-inflammatory activity (COX-1 inhibitor)
  - Central pain mechanism: good evidence to suggest activity in descending serotonergic inhibitory pain pathway
- **Risks**
  - Hepatotoxicity
    - Increased risk with acute or chronic alcohol ingestion
    - Chronic daily use ≥4000 mg/day (risk-benefit of chronic daily use of ≥2600 mg/day being considered)
  - Evidence of COX-1 inhibition*
  - Limited evidence on renal toxicity

Harvey WF. *Clin Geriatr Med*. 2010;26:503-515.
*Oscier CD, Milner QJW. *Anaesthesia*. 2009;64:65-72.

NSAIDs

- **Benefits**
  - Strong anti-inflammatory activity with oral NSAIDs but need to be prescribed with a proton pump inhibitor or misoprostol
  - Multiple clinical trials demonstrating safety and efficacy of topical NSAIDs for superficial joint pain in elderly with minimal evidence of adverse effects (e.g. renal impairment, hypertension, bleeding)
- **Risks**
  - Adverse effects including GI bleeding, platelet inhibition, hypertension, renal toxicity, aspirin cardioprotection interference
  - Drug interactions with SSRIs, diuretics, ACE inhibitors, corticosteroids
- **A review of RCTs on the use of NSAIDs showed:**
  - For Low Back Pain: Strong efficacy evidence (placebo controlled)
  - For Fibromyalgia: Weak evidence from clinical studies
    - —Not recommended in fibromyalgia guidelines

RCTs, randomized controlled trials
Harvey WF. *Clin Geriatr Med*. 2010;26:503-515.

Antidepressants

- **Serotonin norepinephrine reuptake inhibitors (SNRIs)** are the cornerstone in treatment of fibromyalgia, post-herpetic neuralgia, painful poly-neuropathy, and chronic musculoskeletal pain
  - Duloxetine: FDA-approved for diabetic neuropathy, fibromyalgia, and chronic musculoskeletal pain (strong evidence from clinical trials)
  - Milnacipran: FDA-approved for fibromyalgia
  - Venlafaxine: neuropathic pain (unlabeled use; modest evidence)
- **Tricyclic antidepressants (TCAs)**
  - Multiple clinical trials confirming efficacy of amitriptyline and nortriptyline for treatment of neuropathic pain
  - Anticholinergic side effects with high doses

Finnerup NB, et al. *Pain*. 2010; 150:573-581.

Anticonvulsants

- **Gabapentin and Pregabalin**
  - Alpha-2-delta calcium channel antagonists
  - Randomized, controlled trials demonstrate efficacy in the treatment of neuropathic pain ranging from 5-12 weeks
  - Pregabalin: FDA-approved for treatment of fibromyalgia
- **Lamotrigine**
  - Evidence of effectiveness for central post-stroke pain and diabetic poly-neuropathy
- **Inconclusive results from large trials on treatment of neuropathic pain with topiramate, levetiracetam, valproate and oxcarbazepine**

Finnerup NB, et al. *Pain*. 2010; 150:573-581.

Tramadol

- **Mechanism of action:**
  - Weak mu-opioid receptor agonist
  - Inhibits norepinephrine and serotonin reuptake
- **Moderate quality efficacy data for:**
  - Neuropathic pain
  - Low back pain
  - Fibromyalgia
- **Limitations**
  - Ceiling dose to minimize risk of seizures
  - Potential for serotonin syndrome when used in combination with SNRIs and SSRIs

Rosenberg MT. *Int J Clin Pract*. 2009;63:1531-1543.

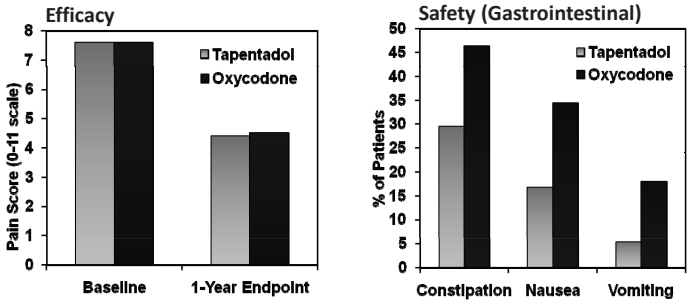
Tapentadol

- **Mechanisms of action**
  - Mu-opioid receptor agonist
  - Norepinephrine reuptake inhibition
- **FDA-approved for moderate to severe acute and chronic pain**
- **Randomized, open-label trials with chronic low back pain or osteoarthritis pain**
- **Limitations**
  - Seizure risk not systematically studied (prescribe with care in patients with history of seizure disorder)
  - No evidence from clinical trials and post hoc analysis for serotonin syndrome when used alone or in combination with drugs associated with serotonin syndrome risk

Prommer EE. *J Opioid Manag*. 2010;6:223-226.
Wild JE, et al. *Pain Pract*. 2010;10:416-427.

Tapentadol ER vs Oxycodone CR

Randomized open-label study of tapentadol ER vs oxycodone controlled release for management of chronic low back pain or osteoarthritis pain (N=1117)



Discontinuations due to GI-related adverse events:
- **Tapentadol: 8.6%**
- **Oxycodone: 21.5%**

Wild JE, et al. *Pain Pract*. 2010;10:416-427.

Opioid Therapy Recommendations

- **First-line therapy**
  - Moderate to severe acute pain
  - Chronic pain unresponsive to acetaminophen, NSAIDS and co-analgesics
  - Cancer pain
- **Second-line therapy**
  - Osteoarthritis
  - Neuropathic pain
- **Incompletely recommended**
  - Fibromyalgia
- **Not recommended**
  - Patients actively engaging in aberrant opioid behaviors

Chou R, et al. *J Pain*. 2009;10(2):113-130.
Zhang W, et al. *Osteoarthritis Cartilage*. 2008;16:137-162.
Smith HS, Barkin RL. *Am J Ther*. 2010;17:418-439.
American Society of Anesthesiologists. *Anesthesiology*. 2010; 112:810-835.

Addiction, Tolerance and Dependence

Addiction
Characterized by behaviors that include impaired control over drug use, craving, compulsive use and continued use despite harm

Tolerance
Characterized by regular use of a drug in which an increased dosage is needed to produce a specific effect, or a reduced effect is observed with a constant dose over time

Physical Dependence
State of adaptation that often includes tolerance and is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.

Heit HA. *J Pain Palliat Care Pharmacother*. 2003;17(1):15-29.

Role of Short-Acting Opioids

- **Supported in clinical practice**:
  - Initiating opioid therapy at low doses
  - Titration to an effective dose in conjunction with long-acting opioid
  - End-of-dose breakthrough pain with long-acting opioids (typically with end-of-life pain)
- **Lack of data to support:**
  - Large quantity and frequent dosing of short-acting opioid without a long-acting opioid
  - Chronic daily use of short-acting opioid exceeding the long-acting opioid dose
- **Potential benefits of transitioning to long-acting opioids include:**
  - More consistent control of pain
  - Improved adherence

Fine PG, et al. *Pain Med*. 2009;10(S2):S79-S88.
Chou R, et al. *J Pain*. 2009;10(2):113-130.

Long-Acting Oral Opioid Formulations

Name	Dosing Interval	Administration
Kadian (morphine)	q12h or q24h	Capsule, sprinkle, G-tube
Avinza (morphine)	q24h	Capsule, sprinkle
OxyContin (oxycodone)	q8-12h	Tablet
MS Contin (morphine)	q8h or q12h	Tablet
Opana ER (oxymorphone)	q12h	Tablet
Exalgo (hydromorphone)	q24h	Tablet
Nucynta ER (tapentadol)	q12h	Tablet

Tamper-Resistant Oral Opioids

Name	Formulation	Status
OxyContin (OP)	Controlled-release oxycodone HCl designed to resist fracturing and to produce a gel substance when exposed to solvents	FDA-approved 4/5/10 – label does not include abuse deterrent language
Embeda	Encapsulated beads of extended-release morphine sulfate with a sequestered core of naltrexone HCl	Recalled from the market 3/16/11
Oxecta	Immediate-release oxycodone HCl that utilizes AVERSION Technology – a unique composition of commonly-used pharmaceutical ingredients	FDA-approved 6/20/11
COL-003	Extended-release oxycodone encapsulated in a micropartical matrix (DETERx)	Phase III clinical trials

Minimizing Adverse Events with Opioid Use

Opioid-Induced Hyperalgesia (OIH)

- Three forms of OIH can be distinguished
- All can result in either increased sensitivity to pain, aggravation of pre-existing pain, or expression of novel pain symptoms
  - **OIH_1: Opioid maintenance therapy**
    - Involves up-regulation of pain facilitating neuronal pathways at multiple levels of the central and peripheral nervous system
    - Stimulation of excitatory amino acid neurotransmitter system
  - **OIH_2: Very high and escalating doses of opioids**
    - Usually implicated with high doses of morphine or hydromorphone
    - Severe allodynia (e.g., pain response to a normally non-painful stimulus), myoclonus noted
    - Thought to be due to metabolites inhibiting glycine at spinal cord level inducing a strychnine-like excitatory intoxication
  - **OIH_3: Observed in animals on ultra-low doses**

Angst MS, Clark JD. *Anesthesiology*. 2006;104:570-587.

Prevention Strategies for Opioid-Induced Hyperalgesia

- Use of adjuvant therapies for "opioid sparing" effect
  - ❑ Anticonvulsants
  - ❑ Antidepressants
- Opioid rotation to take advantage of "incomplete cross tolerance"
- Combination of opioid and low-dose mu receptor antagonist (e.g. buprenorphine and naltrexone)
- Blockade of the NMDA receptor (e.g. ketamine)

Silverman SM. *Pain Physician*. 2009;12(3):679-684.

Prevention of Opioid Adverse Effects

- Clinicians should anticipate, identify and treat common opioid-associated adverse effects
- Strong recommendation, moderate quality evidence
  - ❑ Constipation
  - ❑ Nausea and vomiting
  - ❑ Sedation
  - ❑ Sexual dysfunction
  - ❑ Pruritus
  - ❑ Myoclonus

Chou R, et al. *J Pain*. 2009;10(2):113-130.

Methadone Monitoring Recommendations

- **Disclosure:** Clinicians should inform patients of arrhythmia risk when they prescribe methadone
- **Clinical History:** Clinicians should ask patients about any history of structural heart disease, arrhythmia, and syncope
- **Screening:** Obtain a pretreatment electrocardiogram for all patients to measure the QTc interval and a follow-up EKG within 30 days and annually.
  - Additional EKG is recommended if the methadone dose exceeds 100 mg/day or patients have unexplained syncope or seizures.
- **Drug Interactions:** Clinicians should be aware of interactions between methadone and other drugs that possess QT interval prolongation properties or slow the elimination of methadone

Krantz MJ, et al. *Ann Internal Med*. 2009;150:387-395.

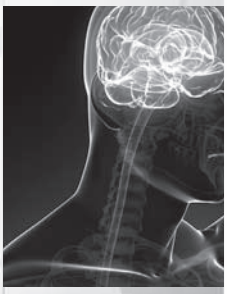
Summary

- **High quality evidence to support first-line recommendations for:**
  - Use of acetaminophen and NSAIDs for osteoarthritis (oral and topical)
  - SNRIs for poly-neuropathy, peripheral neuropathy, fibromyalgia, and chronic musculoskeletal pain
  - Tricyclic antidepressants, gabapentin and pregabalin for peripheral neuropathic pain
- **Low to moderate quality evidence to support recommendations for:**
  - Chronic opioid therapy for non-cancer related conditions
  - Opioid switching to reduce tolerance and hyperalgesia
  - Use of controlled substance agreements and urine drug testing
  - Monitoring for adverse effects from opioids

Notes

Case Study Forum

Individualizing Treatment to Maximize Effectiveness and Safety



All Faculty and Participants

Led by:
Gregory L. Holmquist, PharmD, CPE

CASE 1

Meet the Patient BH

- **Patient History**
  - 73-year-old male; Height - 71”; Weight - 246 lbs; Chronic case of low back pain for 9 years (radicular)
    - Pain scale: 8.5/10 for bilateral lower extremities
    - Pain described as burning on dorsum and plantar surface of feet
    - Confusion, urinary retention
- **Patient Medical History**
  - Hypertension, hypercholesterolemia, type 2 diabetes, obesity, lumbar DJD, osteoarthritis (hips)
- **Surgical History:** Appendectomy, left hip replacement
- **Past Psychiatric History**: Denies
- **Social History**
  - Denies: tobacco, alcohol, and SRDU
  - Retired, grandparent

SRDU, self-reported drug use

BH Medical History

- **Test Results:**
  - GU: hematuria
  - MRI: L_4L_5 canal narrowing due to protruding disc
  - EMG: bilateral neuropathy in lower extremities
- **Prescription History:** lisinopril, HCTZ, amlodopine, simvastatin, glipizide, metformin, hydrocodone/APAP (10/325 mg; 10 tablets/day for 3 years), celecoxib
- **OTC Medications:** NSAIDs, APAP, diphenhydramine (sleep)
- **Herbals:** garlic, ginger, ginkgo biloba, feverfew, ginseng, lutein, lycopene
- **Chemistry (general):** Cl_{Cr} 29 mL/min, ↑ MCV, ↑ GGT, ↑ transaminases, HgbA1c 9.2% ~1 month ago
- **Vital Signs:** BP- 168/97 mmHg; Pulse Rate – 90/min
- **State Prescription Monitoring Program:** by pharmacist reveals 2 clinicians prescribing the opioids (~15 tablets/day use)
- Pharmacist asks for clinical urine drug testing (CUDT)

EMG, electromyogram; HCTZ, hydrochlorothiazide; MCV, mean corpuscular volume; GGT, gamma-glutamyl transpeptidase

CLINICAL CONSIDERATION

What is your primary concern for this patient?

Impression

1. Chronic low back pain with radiculopathy; uncontrolled with aberrant opioid use (multiple prescribers)
2. Osteoarthritis – status post hip arthroplasty
3. Hypertension - uncontrolled above goal
4. Type 2 diabetes mellitus – Uncontrolled
   - Question appropriateness of metformin given renal function
5. Stage III chronic kidney disease – stable
6. Macrocytic anemia
7. Potential EtOH abuse (elevated MCV and GGT)

CLINICAL CONSIDERATION

For this patient, would you discontinue the use of NSAIDs?

Course of Action

- **Management Plan:**
  - ❑ Stop all NSAIDs
  - ❑ Discontinue hydrocodone/APAP
  - ❑ Improve diabetes management
  - ❑ Pain center consult
  - ❑ Stop herbals
- **Pharmacist:** CUDT; evaluate medication treatment plan, symptom analysis & create new plan / recommendations

CLINICAL CONSIDERATION

Is this patient a candidate for long-acting opioid therapy?

CLINICAL CONSIDERATION

Is this patient a candidate for adjunctive therapy?

Case 1 Discussion

Pharmacists can be involved!

- Round-the-clock availability of MD, nurse, outpatient pain center, controlled substance agreement
- Use one pharmacist/pharmacy/Pain Center
- No additional use of opioids from any source
- Follow-up with pharmacist for diabetes testing and prescriptions
- Encourage medication compliance/adherence
- No OTC medications for pain; no sharing of medications

CASE 2

Meet the Patient MC

- **Patient History**: 38-year-old female; 65"; 173 lbs
  - **Vital Signs:** within normal limits
  - Chronic case of "pain all over"; poor sleep; daytime drowsiness; fatigue; pain of shoulder, lower back, buttocks, knee and hip; myalgia; progressive weight gain; peripheral edema; memory issues
- **Medical History**: FMS, migraine w/aura, IBS, TMJ, GERD
  - Sensitivities: environmental and medication
- **Collateral Treatment:** dental appliance
- **Surgical History:** 2 births/C-section; appendectomy; cholecystectomy; knee, hip & shoulder surgery (bicycle injury); wrist trauma (sports injury)

IBS, irritable bowel syndrome; TMJ, temporomandibular joint; FMS, fibromyalgia syndrome; GERD, gastroesophageal reflux disease; WNL, within normal limits; CMP, comprehensive metabolic panel

Meet the Patient MC (cont'd)

- **Social History:** ~3 cigarettes/day on/off; social drinker; SRDU–marijuana 1-2x/week
  - Married, mother of 2 children (16-yo twins)
  - Vocation: real estate sales
  - Avocation: cycling
- **Labs:** CBC – WNL
  CMP – WNL
- **CT scan (head):** no anomalies
- **MRI:** WNL
- **Tests:** No ↑ ESR or CRP
  - EKG: some QTc prolongation

CBC, complete blood count; WNL, within normal limits; CMP, complete metabolic profile; PPI, proton-pump inhibitor; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

CLINICAL CONSIDERATIONS

When asked to rate her pain, the patient indicates 10/10 on the pain scale. Do you believe her?

Prescription History

sumatriptan 50mg PO (2x/month)
metoclopramide (PRN, 2x/mo)
dicyclomine 20mg Q6H
cyclobenzaprine 10mg Q8H
pregabalin 75mg Q12
trazodone 100mg QHS
topiramate 100mg QHS
omeprazole 20mg QD
methadone 20mg Q8H
oxycodone 5mg Q6H PRN
tramadol 50mg 2 tabs Q6H PRN
carisoprodol 350mg PRN

CLINICAL CONSIDERATION

What is your primary concern with her current medications?

MC Treatment Plan

- **Pain Management Physician, Nurse Practitioner, and Pharmacist collaborate in a patient care conference**
- **Decisions:**
  - FMS – SNRI (venlafaxine, milnacipran, duloxetine)
  - Discontinue / wean cyclobenzaprine, carisoprodol
  - Discontinue tramadol and methadone
  - Optimize pregabalin dosing
  - Topical diclofenac for knee and shoulder
  - Equianalgesic dose of CR morphine in place of methadone
  - Exercise/weight reduction by PM&R, increased range of motion, nerve blocks, SIJ injections (low back pain, buttocks)

SNRI, serotonin-norepinephrine reuptake inhibitor; PM&R, physical medicine and rehabilitation; SIJ, sacroiliac joint; ADL, activities of daily living

CLINICAL CONSIDERATION

For this patient, would you prefer an agent with dual modes of action to treat breakthrough pain?

CLINICAL CONSIDERATION

What are your most prominent pharmacotherapy concerns with the new treatment plan?

Summary: Responsible and Ethical Prescribing of Pain Medications

- **Select the right patient**
  - Reliability issues, history, preferences
- **Select the right pain syndrome**
  - Type, intensity, quality, expected duration of pain
- **Select the right molecule**
  - Severity of pain, side effect profile, abuse/diversion risks
- **Select the right way to deliver the medication**
  - Blood levels, crescendo pain, risk of adverse effects
- **Select the right way to assess for outcomes**
  - Believe the patient, regular assessments, pain levels, diaries, agreements, urine drug testing, functional status

ABBREVIATIONS

ACE	angiotensin-converting enzyme
ADL	activities of daily living
AED	anti-epileptic drug
APAP	N-acetyl-para-aminophenol (acetaminophen)
CBC	complete blood count
CMP	complete metabolic profile
CRP	C-reactive protein
CUDT	clinical urine drug testing
DIRE	Diagnosis, Intractability, Risk, and Efficacy
ECG	electrocardiogram
EMG	electromyogram
ESR	erythrocyte sedimentation rate
FMS	fibromyalgia syndrome
GERD	gastroesophageal reflux disease
GGT	gamma-glutamyl transpeptidase
IBS	irritable bowel syndrome
HCTZ	hydrochlorothiazide
MCV	mean corpuscular volume
NMDA	N-methyl-D-aspartate
NRS	numeric rating scale
NSAID	non-steroidal anti-inflammatory drug
OIH	opioid-induced hyperalgesia
ORIF LE	open reduction internal fixation in the lower extremities
ORT	Opioid Risk Tool
PM&R	physical medicine and rehabilitation
PPI	proton-pump inhibitor
SIJ	sacroiliac joint
SNRI	serotonin norepinephrine reuptake inhibitor
SOAPP	Screener and Opioid Assessment for Patient with Pain
SRDU	self-reported drug use
SSRI	selective serotonin reuptake inhibitor
T/A	tonsils/adenoids
TCA	tricyclic antidepressant
TMJ	temporomandibular joint
UTI	urinary tract infection
VAS	visual analog scale
VRS	verbal categorical rating scale
WNL	within normal limits

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