Pre-opioid Screening Prior to Treatment

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SPS, New Orleans
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Disclosures

• Nothing to disclose

Outline

• Patient selection
• Treatment goals and monitor
• Guidelines
Patient Selection

- Failed non-opioid, if appropriate
- LDN, SA (4/day), buprenorphine, Hemp oil extract (CBD) (<0.3% THC)
- PT: modalities, body mechanics, HEP
- Risk assessment/psych factors
Patient Selection

- PDMP
- UDS
- Opioid responsive pain: do a ‘trial’
- Aware and supportive significant others
- Impulse: A/D history, periods of incarceration, moving violations, recreational gambling, etc. i.e. acting-out behaviors; 22 pills vs 21 pills
- Cognitive functioning
- Willingness to trial non-opioid and/or non-medical therapy

Aberrant Drug Behavior

First year escalation of dose is a warning sign!
Escalating Group: increase in daily dose of > 30 mg ME
Characteristics: younger, white, 16 additional outpatient encounters (3 additional office visits, 5 additional telephone, 4 additional)

Addiction/Abuse Questionnaires:
SOAPP and ORT

- The Screener and Opioid Assessment for Patients with Pain (SOAPP and SOAPP-R) predicts possible opioid abuse in chronic pain patients: 14 items, 5 point scale, <8 minutes to complete.
- How often do you smoke a cigarette within an hour after you wake up?
- How often have any of your close friends had a problem with alcohol/drugs?
- The Opioid Risk Tool (ORT) assesses the risk of aberrant behaviors when patients are prescribed opioid medication for chronic pain: 5 items, <1 min.
- Age (36-45), Sexual abuse, Psychiatric disease, Family history substance abuse, Personal history substance abuse
### Outcome Prediction: Patient Characteristics

<table>
<thead>
<tr>
<th>Unfavorable</th>
<th>Favorable</th>
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<tbody>
<tr>
<td>• Abuse victim</td>
<td>• Pathology matches complaints</td>
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<tr>
<td>• Primary depression</td>
<td>• Record of compliance</td>
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<tr>
<td>• Diffuse complaints</td>
<td>• Internal locus of control (accept responsibility)</td>
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<tr>
<td>• High pain focus</td>
<td>• Self efficacy</td>
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<tr>
<td>• Active addiction</td>
<td>• Optimism – expectancy</td>
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<tr>
<td>• Blame</td>
<td>• Resilience</td>
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<td>• Poor support system</td>
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### Addiction

- Is a primary chronic **neurobiological disease**, with genetic, psychosocial and environmental factors influencing its development and manifestation.
- Characterized by the **5 Cs**:
  - Chronic
  - Compulsive use
  - Craving
  - Control–impaired
  - Continued use despite harm

Savage et al., JPSM, 2003, 26, 655-667.

### Select Goals and Monitor
### Pain as 5th Vital Sign: Abandoned

"How often did the hospital or provider do everything in their power to control your pain?"

This question embedded pain as the 5th vital sign

Unintended consequence of encouraging opioid administration in response to patients' self-reported NPR

Result: “pain as the 5th vital sign” with its reliance on the NPR directly contributed to the prescribed opioid epidemic


### Informed Consent vs Agreement

- The patient’s diagnosis, if known
- The nature and purpose of a proposed treatment or procedure
- The risks and benefits of a proposed treatment or procedure
- Alternatives (regardless of their cost or the extent to which the treatment options are covered by health insurance)
- The risks and benefits of the alternative treatment or procedure
- The risks and benefits of not receiving or undergoing a treatment or procedure


### Agreement Violations: Possible Consequences (Exit Strategy)

- Discontinue treatment
- Report to the authorities
- Counsel and continue
- Ph.D. evaluation
- Addiction evaluation
- Discontinue opioid(s)
- 1:1 treatment
Drug Security: Nonmedical Users

- 2014 National Survey on Drug Use and Health (NSDUH):
  - 54% got opioids for free from friends or relatives
  - 16% bought/stole pills from friends/relatives
  - 4% bought from strangers
  - 6% online purchases, forged prescriptions, and theft from doctors' offices or pharmacies
  - 20% obtained opioids through prescriptions written for them

*You Have a Responsibility to Prevent Diversion*

Post-operative Opioid Use: Factor Associated With Immediate and Long term (90 days)

- The Problem: Up to 13% pre-op opioid naïve patients continue to use 90 days post-op
- Causes:
  - Pre-op opioid use: > 75 MEE/day
  - Increased risk of misuse with refill/duration vs dosage
  - Catastrophizing
  - Anxiety
  - Depression
  - Social Support
  - Solicitous spouse
  - Disability
- Recommendation:
  - Wean as low as possible pre-op
  - Coping strategies
  - Carefully monitor post-op use

Opioids and Children: “1 Pill Can Kill”

- Hospitalizations for prescription opioid-related poisonings increased 165% for children ages 1-19, between 1997-2012
- Prescription opioid poisoning among adolescents 15-19 years increased 176%
- The largest percentage increase in prescription opioid poisonings was among the 1-4 year-olds; 205%.
- The vast majority of these poisonings are unsupervised ingestions; children got into opioids prescribed for a family member

Drug Security Risk Profile

- Age
- Age co-dwellers
- Psych diagnosis
- Legal history
- A/D history
- Cognitive functioning
- Living environment (high crime area/affluent)
- Naltrexone (OTC)

Nearly 20% of teens can get prescription drugs (in order to get high) in an hour. More than 33% can get prescription drugs within a day.

70% of teens get the prescription drugs from family or friends.

Factors Associated with Patient ‘Injury’

1. Faulty communication: When patients feel they clinician cares and has their best interests in mind, they tend to be more forgiving of errors.
2. Lack of informed consent: A big area where claims can come into play
3. Failure to stay up-to-date on standards and training: Be aware of new and revised developments in areas of practice and specialties
4. Inadequate follow-up of diagnostic tests and specialist referrals
5. Variations in policies and procedures: There should be one set of rules that all staff understands and follows
6. Avoidance behavior: Compassionate gestures count. Do not avoid bad outcomes or difficult patients

Overdose: What’s Your Liability?

- Adherence to licensing board requirements
- Following what a reasonably prudent practitioner would do in the same or similar circumstance.
- What licensing board wants documented
  
  **Risk and evaluation**
  - Rationale for prescribing opioid
  - Rationale for amount of opioid

- Follow the plan
- Educate patients.
- Prepare for more requirements from medical licensing boards regarding overdose events

Accessed 6/22/18
Treatment Goals and Monitoring

10 steps of universal precautions in pain medicine
• Make a diagnosis with appropriate differential
• Psychological assessment including risk of addiction
• Informed consent
• Treatment agreement
• Pre-post assessment of pain level and function
• Appropriate trial of opioid therapy +/- adjuvants
• Reassessment of pain and function
• Apply the 5 'As': analgesia, activity, adverse events, aberrant behavior, affect

10 universal steps (cont.)
• Review Pain Diagnosis, comorbid conditions/ addiction
• Documentation including doctor-patient relationship
• Triage:
  - I PCP: No a/d hx in patient or family, lack of any major or untreated psychopathology.
  - II PCP w/ specialist support: ?a/d hx but not active, past or concurrent psychiatric disorder, ‘co-managed’.
  - III Specialty Pain Management: complex cases

(Gourlay, Heit, Almahrezi, Pain Medicine, 2005, 6, p107-112)
5As of Pain Management

- Analgesia: verbal report, rating scales
- Affect: MSE, significant others, Beck Depression Inventory
- Activities of daily living: Oswestry D.I., 3-5 new activities
- Adverse effects: check-list, exam, labs
- Aberrant drug related behavior: chart review, PDMP, office staff

Treatment Expectations

- Pain as a chronic “disease” not unlike diabetes; thus the need for education & joint responsibility (Siddal & Cousins; Anesth Analges, 2004)
- QOL (i.e. increased function) > Pain relief
- Evidence-based long term percent improvement in pain approximates 40-60%
- Estimated maximum dosing: patients may need to adjust to our medicine verses our adjusting medicine to patient
- “Chemical Coping” i.e. “Life is NOT a chemical deficiency” (author unknown)

Aberrant Drug Taking Behavior Will Happen: Be Prepared to Address

- Addiction: Multiple unsanctioned doses escalation; multiple prescribers; self injecting PO formulations
- Psychiatric Co-morbidity: Impulsive – Personality Disorders; Self-medicating symptoms of anxiety, depression et
- Cognitive: Dementia, TBI, IQ
- Criminal Intent: For purpose of diversion
- CONCLUSION: Aberrant behavior does not equal addiction. It is a matter of type and extent.

Management Tips to Consider

• 72 hour “medication diary” pre UDS
• UDS + GS/MS confirmation
• Pill count with or without “extra” dose
• Automated/ locked dispenser
• Friendly toxicologist/ M.R.O.
• Random UDS/ pill count
• Frequent visits especially initially
• Significant other dispense
• Knowledgeable/experienced psychologist or psychiatrist

Patient Abandonment: Recommendations (cont)

1. Give patient written notice of termination
2. Provide brief explanation for the reason, presumably valid, for the termination
3. Agree to provide treatment and access to service for a reasonable period of time, e.g. 30 days
4. Provide a resource to help the patient locate another provider of like specialty
5. Offer to transfer records to the new physician. The chart should contain a copy of the termination letter and any related documentation such as conversations with the pt.

(J.L. Griffin J.D., B’ham Medical News, 4/05)

Know What The Board of Medical Examiners Expects

• Required UDS x 2/year at about 30-90 MMEs and/or based on level of risk
• Risk assessment prior to prescribing opioids
• PDMP prior to first Rx; regular there after
• Stratify treatment
• Document plan
Guidelines

- Federal
- State
- Local
- Standard of Care

CDC: Assessing Risk and Addressing Harms of Opioid Use

- Evaluate risk factors for opioid-related harms.
- Incorporate strategies to mitigate risk, e.g. naloxone
- Review the patient's history of controlled substance use (PDMP)
- Review PDMP: may vary based on risk level
- Use urine drug testing: before starting opioid therapy and according to guidelines and risk level for prescribed medications, other controlled drugs, and illicit drugs.
- Avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
- Offer or arrange evidence-based treatment: MAT combination with behavioral therapies) for patients with opioid use disorder.


Standards: Legal, Community, Professional

- Legal Standards: DEA’s role under the Controlled Substances Act (CSA) is to ensure that controlled substances are prescribed, administered, and dispensed only for legitimate medical purposes by DEA-registered practitioners acting in the usual course of professional practice and otherwise in accordance with the CSA and DEA regulations.
- Community Standards of Care: Each State also has its own laws (administered by State agencies) requiring that a prescription for a controlled substance be issued only for a legitimate medical purpose by State-licensed practitioners acting in the usual course of professional practice.
- Professional Standards/Guidelines: Professional societies/organizations, expert panel/consensus guidelines, community standards

The Tenets of Lawful Prescribing

• A lawful prescription for a controlled substance must be
  • issued for a legitimate medical purpose
  • by an individual practitioner acting in the usual course of his or her professional practice
  • physician–patient relationship exists
  • documented in the medical records

This requirement has been construed by the courts to mean that the prescription must be issued “in accordance with a standard of medical practice generally recognized and accepted in the United States.”

Who will testify on your behalf

*United States v. Moore
423 U.S. 122 (1975)*

Applying criminal sanctions to doctors

“Registered physicians can be prosecuted under [21 U.S.C.] 841 when their activities fall outside the usual course of professional practice.”

(United States v. Moore 423 U.S. 122, 1975)

**HOWEVER:** Less than 0.1% of practicing physicians have been charged with opioid-related offenses (Goldenbaum et al., Pain Medicine, 2008;9)
Personnel Precautions/Screening

• The DEA registrant shall not employ, as an agent or employee who has access to controlled substances, any person who has been convicted of a felony offense relating to controlled substances or who, at any time, had an application for registration with the DEA denied, had a DEA registration revoked or has surrendered a DEA registration for cause.

• Local inquiries. Inquiries should be made by name, date and place of birth, and other identifying information, to local courts and law enforcement agencies for records of pending charges and convictions.

• Regional Inquiries: identifying information should be furnished to DEA Field Division Offices along with written consent from the concerned individual for a check of DEA files for records of convictions. The regional check will result in a national check being made by the Field Division Office.

http://www.deadiversion.usdoj.gov/21cfr/cfr/1301/1301_76.htm

Key Concepts

• Opioid therapy is like Arnold Palmer’s view of golf: ‘Deceptively simple, yet endlessly complex’

• Chronic pain is not an opioid deficiency

• “Life” is not a chemical deficiency

• Don’t say yes, if you can’t say no

• ‘NO’ is a complete sentence

• Function trumps pain relief

SUMMARY
You ARE obligated to treat pain. BUT...

You are NOT obligated to:
• Prescribe on the first visit
• Treat in the absence of adequate work-up; physical/ psychological
• Treat with opioids
• Treat as patient specifies
• To use only pharmacological treatment
• Treat without requiring patient involvement and responsibility
OK to Prescribe When You Know:

- The medications
- The condition
- The patient
- The context
- Yourself

Be the clinician your patients needs; not just the one they want

Thank You
(Overlooked)
Psychopharmacology in the Management of Pain
The Southern Pain Society — Sunday, September 15th, 2019 — 8:50 to 9:30 AM
Mordecai Potash, M.D.
Associate Professor of Clinical Psychiatry, Tulane University
Associate Professor of Physical Medicine & Rehabilitation, LSU HSC

Psychopharmacology in the Treatment of Chronic Pain

• Almost every pain practitioner, whether prescribing or not, is familiar with some aspects of psychopharmacology in the treatment of chronic pain. For example, there are gobs of practitioners who use psychopharmacology as their FIRST LINE treatment in chronic pain.
• Don’t believe me? How many primary care referrals have you received where the sole treatment for chronic pain initiated was 25mg or 50mg of Amitriptyline at bedtime for pain? That is a psychopharmacological treatment often prescribed with the hope that it will quell the entire chronic pain experience.
• I would like to use our time together reviewing some overlooked aspects of psychopharmacology for chronic pain, including drug choice and drug dosing.

The Atypical Anti-Psychotics in the Treatment of Chronic Pain

• Atypical anti-psychotics are the expanding group of newer anti-psychotics agents that have less side effects than older anti-psychotics and have an expanding repertoire of uses beyond the treatment of schizophrenia.
• These medications are being used to treat depression, anxiety, PTSD, and sleep disorders.
• Atypical anti-psychotics have a much more complex psychopharmacology compared to older anti-psychotics. They do share blockade of dopamine receptor that older anti-psychotics have, but they also alter receptor abilities at a range of serotonin receptor subtypes, as well as binding to alpha receptors, histaminic receptors, muscarinic receptors.
• There have been expanding case reports and case series on using these medications for chronic pain mitigation. Besides these reports, there was also a review article on this topic last year in the Clinical Journal of Pain.

Olanzapine / Zyprexa

- As described in the article by Jimenez, Olanzapine/Zyprexa is the atypical anti-psychotic with the most studies in chronic pain treatment. At least eleven studies have explored olanzapine’s response in diminishing pain from fibromyalgia, headaches, cancer pain, chronic pain, and glossodynia. Ten of the eleven studies found olanzapine to be effective, including the largest study of 87 chronic headache sufferers.

- All these publications prescribed dosages of Olanzapine that were a fraction of the dose used to treat schizophrenia.

- A three-case series authored by Dr. Gorski and Dr. Willis give typical results— with all three patients giving dramatic improvements in numeric rating scale and also voicing great improvements with sleep and mood.

Quetiapine / Seroquel

- At least five publications with the use of Quetiapine for chronic pain including fibromyalgia, migraine, glossodynia. The largest case study – 120 cases of fibromyalgia recruited by McIntyre and colleagues — found quetiapine to be very helpful for pain and mood.

- Doses of Quetiapine used in schizophrenia is typically 300-700mg. Doses of quetiapine used for pain mitigation are much lower – 50mg to 300mg.

- Consistent with Quetiapine’s enduring use as a sleep aide, quetiapine seemed to work particularly well for patients with disordered sleep.

- However, a 2016 Cochrane Review found that the studies were poorly designed and with a high drop-out rate that calls into question whether quetiapine can help people with chronic pain. They recommend an 8-12 week trial and then a re-evaluation of its effectiveness in your particular patient.

Risperidone / Risperal

Aripiprazole / Abilify

Ziprasidone / Geodon

- Each of these antipsychotics have several publications of case-series with a low number of subjects in each of the case series. However, patients voiced significant improvement with pain and treatment with these medications was continued for patients in the case series.

- On the basis of these studies, it appears that efficacy of certain atypical anti-psychotics seems concentrated in headache/migraine and fibromyalgia conditions.

- Both headache/migraine and fibromyalgia conditions have high rates of psychiatric co-morbidity and central sensitization. So do other difficult to manage conditions such as irritable bowel syndrome.

- Although results are preliminary and tentative, atypical antipsychotics may offer an avenue to symptom reduction in traditionally very hard to treat and confounding disorders.
The SNRI’s in the treatment of chronic pain

- Serotonin-Norepinephrine re-uptake inhibitors (SNRI’s) remain the popular anti-depressants for chronic pain control.
- They are easier to tolerate, with far less toxicity in overdose, compared to much older tricylic anti-depressants.
- They are also much more potent inhibitors of ascending pain signaling pathways compared to serotonin-specific reuptake inhibitors (SSRI’s).
- For these reasons, SNRI’s are really popular in the treatment of chronic pain syndromes, especially syndromes with strong depressive affect components or are associated with suicidal ideation due to prolonged physical pain.
- Cochrane Library has been following published literature on this topic for many years, with a comprehensive update being published last February.

Five SNRI’s are on the market

- There are currently five SNRI’s on the market:
  1. Duloxetine / Cymbalta 30mg to 120mg with specific indications for neuropathic pain, fibromyalgia, chronic musculoskeletal pain.
  2. Milnacipran / Savella 50mg to 200mg with specific indication for fibromyalgia
  3. Desvenlafaxine / Pristiq / Khedezla 50mg to 100mg for depression
  4. Venlafaxine/ Effexor 75mg to 375mg for depression, anxiety, PTSD, & headache prevention
  5. Levomilnacipran / Fetzima 40mg to 120mg for depression

Response to Fibromyalgia

- 18 studies with nearly 8,000 participants reviewed.
- Duloxetine and milnacipran had a clinically relevant benefit over placebo in patient's global impression to be much or very much improved.
- Duloxetine and milnacipran had a clinically relevant benefit compared to placebo for pain relief of 30% or greater.
- There were no differences between either duloxetine or milnacipran and placebo in reducing sleep problems.
- Duloxetine and milnacipran had no clinically relevant benefit compared to placebo in improving health-related quality of life.
- A minority of people with fibromyalgia might experience substantial symptom relief without clinically relevant adverse events with either duloxetine or milnacipran.
- The authors did not find placebo-controlled studies with other SNRIs than desvenlafaxine, duloxetine and milnacipran.
**Response to Fibromyalgia**

- Bottom line was that the evidence showed that patients could expect about a 30% decrease in pain symptoms—it did not often show greater than 50% symptom reduction but would frequently show a more modest reduction in symptom intensity of about 30%.
- None of the studies have looked at SNRI rotation in case a patient cannot tolerate an SNRI or has to change SNRI's due to insurance or formulary reasons or issues.
- However, there is no reason to suspect that a rotation would be poorly tolerated if it became necessary, especially rotations to venlafaxine or desvenlafaxine.
- Although study was with fibromyalgia, also no reason to expect that the same rate of response would not been seen for other chronic pain conditions with high rates of depression / emotional dysregulation.

**What about SSRI’s?**

- Serotonin-specific reuptake inhibitors remain the most commonly prescribed anti-depressants world-wide since their introduction in the 1980’s.
- They tend to be very easily tolerated at a range of doses and very effective for treating diverse depressive disorders, anxiety disorders, and traumatic stress disorders.
- They are not commonly thought of as part of the pain armamentarium and patients with chronic pain are often switched from their SSRI to Duloxetine as part of their pain management plan.
- Is there any evidence that SSRI’s could be helpful in chronic pain?
- A team of biochemists and pharmacologists at Emory University and Ahvaz Jundishapur University in Iran looked at that very issue in a paper published in April.
  
  "Fluoxetine increases analgesic effects of morphine, prevents development of morphine tolerance and dependence through the modulation of L-type calcium channels expression in mice."  

- They investigated the effects of fluoxetine on morphine-induced analgesia, as well as preventive effects of it on morphine induced tolerance and dependence in mice.
- Results showed that co-administration of fluoxetine with morphine increased morphine’s acute analgesia effect and prevented the induction of morphine antinociceptive tolerance and physical dependence in mice.
- Their data indicated that co-administering of fluoxetine with morphine could potentiate the antinociceptive effect of morphine, prevent morphine analgesia tolerance and attenuated the morphine withdrawal signs during induction phases.
- However, this is animal data and clinical review studies points out that TCA’s and SNRI’s are more potent inhibitors of pain—especially neuropathic pain—and this superior efficacy is mediated by norepinephrine reuptake inhibition in the synaptic cleft. The NNT are consistently lower in SNRI’s compared to SSRI’s.
Evidence for Buproprion for pain control and other symptom management

- Buproprion / Wellbutrin is an anti-depressant that is a reuptake inhibitor of norepinephrine and dopamine – or a NDRI.
- It is FDA approved for major depressive disorder, seasonal affective disorder, smoking cessation, and attention-deficit hyperactivity disorder.
- Because of its norepinephrine reuptake inhibition, there has been periodic interest in its use for pain.
- Several years ago, a review on the use of buproprion for the treatment of pain was published in the American Journal of Hospice and Palliative Medicine.
- Authors found some studies that suggested that buproprion was helpful for neuropathic pain. They also found studies that showed it was not helpful for somatic pain states.
- In patients responding for neuropathic pain, the improvement was real, but modest. Average decrease in numeric pain score on buproprion was 1.7 compared to placebo.

Evidence for Buproprion for pain control and other symptom management

- Interest in the use of buproprion for the treatment of pain remains – with periodic studies being published up to present. The studies continue to demonstrate that buproprion is well tolerated and reasonably effective for neuropathic pain reduction.
- In addition to neuropathic pain, buproprion has also shown some effectiveness in treating chronic pain that is caused by inflammatory bowel disease (IBD). IBD is a group of relapsing incurable diseases of the gastrointestinal tract and is comprised of two major disorders; ulcerative colitis and Crohn's disease that have two distinct pathological processes.
- Furthermore, buproprion has been shown to be very helpful in combating fatigue, whether it is cancer fatigue or sedation as a side effect of pain treatment.

Any role for good ol’-fashioned Lithium in pain treatment?

- Lithium is still a mainstay indispensable treatment in psychopharmacology. It is FDA approved for acute and maintenance treatment in bipolar mood disorder and schizoaffective disorder. It is also frequently used as an adjunct anti-depressant. Patients can respond to lithium when they would not respond to anything else.
- Have there been any studies or trials on the use of lithium for pain control in any pain condition?
- It turns out that there have both been trials and systemic reviews on the use of lithium to prevent and manage chronic cluster headache (CCH).
- Lithium was compared to many other treatments for CCH such as methysergide and ergotamine and found to be equally effective.
Any role for good ol’-fashioned Lithium in pain treatment?

- One other important role of lithium in the treatment of pain is a little more indirect. For years, the research of Dr. David Fishbain, Dr. Melanie Racine, and others have found robust evidence that chronic pain itself, regardless of type, was an important independent risk factor for suicidality.
- Other situations that frequently happen in chronic pain – such as chronic poor sleep and chronic unemployment due to disability – further aggravates the risk of suicide to the point that suicide is a frequently occurring outcome from the chronic pain experience.
- Lithium is one of our best treatments for the prevention of suicide, with patients often needing only ½ or 1/3rd the dose needed in bipolar mood disorder in order to effectively deter suicidal thoughts or behaviors.
- Therefore, lithium should be considered in the chronic pain patient exhibiting suicidal ideation or tendencies.


Rates of Depression and Anxiety in Pain States

- Our discussion on chronic pain, suicide, and anti-depressants should also serve as a reminder of the very high rates of chronic depressive and chronic anxiety disorders in chronic pain conditions.
- Dr. Michael Hooten authored a comprehensive review on depression, anxiety and chronic pain for a special issue of Mayo Clinic Proceedings.
- He found very high rates of depression and anxiety for range of pain states.

**DEPRESSION**
- Spinal pain 2%-56%, Fibromyalgia 21%-83%, Pelvic pain 19%-22%
- Abdominal pain 9%-54%, Arthritis 3%-39%

**ANXIETY**
- Spinal pain 1%-26%, Neuropathic pain 5%-27%, Fibromyalgia 18%-60%
- Pelvic pain 12%-41%, Abdominal pain 21%-51%, Arthritis 1%-35%


Rates of Depression and Anxiety in Pain States

- Dr. Hooten stresses the importance of using many of the medications we will discuss in this presentation – antidepressants, anxiolytics, and mood stabilizing agents.
- One point well made is to try to use the full anti-depressant dose when using tricyclic anti-depressants TCA's for chronic pain control. Amitriptyline and nortriptyline are popular TCA's used for pain and sleep. But, they are often prescribed at just a fraction of their anti-depressant dose.
- The co-morbidity between psychiatric symptoms and pain symptoms would argue that full anti-depressant strength is necessary for both sets of symptoms.
- For both amitriptyline and nortriptyline, that would mean titrating the medication to at least the 50mg dose, and perhaps as high as 150mg – this is much higher than the usual 10mg to 25mg used for pain.
- Most patients can tolerate an increase in side effects if happens (dry mouth) and it is often worth it to get the full benefit from the TCA in treating both the pain state and the psychiatric issues.
Oral Gabapentinoids for Chronic Pain Management

- For many years the two oral gabapentinoids have been very popular medications for pain control:
  - Gabapentin 900mg-3,600mg per day for post-herpetic neuralgia, neuropathic pain, fibromyalgia
  - Pregabalin 150-600mg per day for diabetic neuropathic pain, spinal-cord injury associated neuropathic pain, post-herpetic neuralgia, fibromyalgia.
- There is an abundance of data from around the world that these two medications remain popular for all types of chronic pain – whether neuropathic or not. This has led to a very high discontinuation rate seen in some studies in 80% to 90% because gabapentin/pregabalin are being so ubiquitously used for all types of pain conditions.


Oral Gabapentinoids for Chronic Pain Management

- Gabapentinoids (gabapentin and pregabalin) and antidepressants (tricyclic antidepressants and serotonin noradrenaline reuptake inhibitors) use the same descending noradrenergic inhibitory system from the locus coeruleus (LC) to the dorsal horn of the spinal cord to induce its anti-pain effects.
- In particular Gabapentinoids activate the LC by inhibiting the release of γ-aminobutyric acid (GABA) and inducing the release of glutamate, thereby increasing noradrenaline levels in the spinal cord. Antidepressants increase noradrenaline levels in the spinal cord by inhibiting reuptake, and accumulating noradrenaline inhibits chronic pain through α₂-adrenergic receptors in the spinal cord.


Oral Gabapentinoids for Chronic Pain Management

- Many articles suggest that Gabapentin and Pregabalin are equally efficacious in treating neuropathic pain complaints, at least in general. More studies have been published recently put these two medications head-to-head.
- One recent head to head trial looked at patients attending a specialist neurosurgery clinic with unilateral chronic sciatica were considered for trial recruitment. Chronic sciatica was defined as pain lasting for at least 3 months radiating into 1 leg only to, at, or below the knee level.
- Both medications appeared equally efficacious at reducing pain. Gabapentin had better compliance because it had fewer adverse reactions / side effects and this was significantly better tolerated by study patients.

Oral Gabapentinoids for Chronic Pain Management

• Many of the articles on comparisons of Gabapentin to Pregabalin – or the use of Gabapentin by itself – point out that it is important to use full strength dosing of these medication if you expect any positive anti-nociceptive response at all.

• I frequently encounter patients who are maintained on just 300mg of Gabapentin per 24 hours because they develop dizziness, somnolence, ataxia or another side effect at higher dosages. Often this 300mg dose is given at bedtime as a quasi sleep aid.

• Studies would strongly suggest that this low dose of Gabapentin – or a comparably low dose of Pregabalin – would not alleviate pain.

• Minimal responsive dose of Gabapentin for pain is 900mg/24 hours

• Minimal responsive dose of Pregabalin for pain is 150mg/24 hours

Ketamine-based anti-depressant for chronic pain control

• Esketamine / Spravato is an intranasal form of Ketamine that is FDA approved for treatment resistant major depression that has already failed several oral anti-depressants.

• It is used by delivering 56mg of intranasal Ketamine twice during the first week and then between 56mg to 84mg for weekly maintenance treatment.

• IV Ketamine is approved for moderate to severe acute pain. The availability of an intranasal format would make it easier to dispense Ketamine as a pain treatment to patients – they would not necessarily need to get an IV infusion in clinic.

• Like IV Ketamine, Esketamine is postulated to work by antagonism of the N-methyl-D-aspartate (NMDA) receptor.

• As noted in a 2016 review of Ketamine, the nasal absorption delivery format gives therapeutic plasma levels of Ketamine almost as quickly at IV delivery.

Ketamine-based anti-depressant for chronic pain control

• One major drawback to Spravato is that it almost always requires a lengthy prior authorization process for approval from patients’ insurance.

• No commercial health insurance has it available without prior authorization review – often including a complete case review and peer to peer discussion between patient’s doctor and insurance review doctor.

• At this point, the makers of Spravato stress that it is to be used for depression only, even though there is tremendous interest in using Spravato for the treatment of pain because its bio availability and plasma levels so closely match the IV format.

• I expect case reports and small case series to begin to get published in the years to come. If results are strongly encouraging, it may motivate more formal research on Esketamine and pain to be done by its manufacturer.

Esketamine’s website is https://www.spravato.com
Anti-convulsants / Mood stabilizers in the treatment of pain

• There is now established an extensive history of using certain anti-convulsants / mood stabilizing agents for pain control.
• Especially used as a first line agent in neuropathic pain but being added more and more often as an “opioid sparing agent” in a wide array of pain conditions.
• Medications employed in this way include valproate/Depakote, carbamazepine/Tegretol, lamotrigine/Lamictal, and topiramate/Topamax.
• These medications are often combined with SNRI or TCA anti-depressants as a way of further reducing the intensity of pain without using opioid medications.

Valproate/Depakote

• Numerous articles on the use of valproate / Depakote to treat all manner of headache pain. Overall consensus of articles appears to be that valproate is especially useful for treating cluster headache.
• In using valproate for chronic pain control, it is relatively easy to titrate the medication to give the blood level that the clinician desires due to easily available plasma testing. Most clinicians try to get a target level of 60 to 100 nanograms per milliliter.
• Basic science research with animal models show that valproate also reduces inflammation in the nervous system and should be a pain reliever for conditions well beyond headache.
• But clinical studies have not born that out. The VIPER trial was completed and due to be published this year. It looked at the administration of valproate to reduce pain after limb amputation in 107 veterans. The authors found no difference in post-amputation pain control whether or not valproate was used.

Carbamazepine / Tegretol

• Carbamazepine is of such enduring interest in chronic pain management that it has periodic reviews of effectiveness studies published in the Cochrane Database.
• High quality evidence shows that carbamazepine is a first-line treatment for chronic headache and chronic facial pain – two conditions that respond poorly to opiates.
• The Cochrane Reviews also shows that carbamazepine has been extensively studied for pain from diabetic neuropathy, post-stroke pain syndrome, and fibromyalgia.
• All the studies, taken together, included hundreds of patients in cross-over treatment design.
• Carbamazepine clearly shown to be an effective pain-relieving treatment for all these conditions!
• Cochrane database would like the duration of these studies to be much longer than presently – to evaluate long term effectiveness.
Lamotrigine / Lamictal

- The same pain research group at Cochrane has also been publishing periodic reviews on the evidence for lamotrigine for pain management.
- The University of Oxford's Pain Research and Nuffield Department of Clinical Neurosciences found that lamotrigine has been tried for the treatment of pain in truly a wide array of pain conditions: central post-stroke pain, chemotherapy-induced neuropathic pain, diabetic neuropathy, HIV-related neuropathy, mixed neuropathic pain, spinal cord injury-related pain, and trigeminal neuralgia.
- These large, high-quality, long-duration studies reporting clinically useful levels of pain relief for individual participants provided no convincing evidence that lamotrigine is effective in treating neuropathic pain and fibromyalgia at doses of about 200 to 400 mg daily.
- Despite the Cochrane results, lamotrigine continues to be used for pain control in both clinical and research settings.

Topiramate / Topamax

- Topiramate is extensively used in both neurological and psychiatric treatments as it is FDA approved for migraine headache prophylaxis, sleep-related eating disorder, and for nightmares associated with PTSD.
- Numerous original publications and review studies on Topiramate as a very effective preventive medication for headache.
- There have been studies that investigated other uses of Topiramate for other types of pain control. Dr. Joshua Will and his group looked at using topiramate for acute mechanical back pain in active duty soldiers at Fort Benning, GA. They were specifically interested if topiramate provided enough pain relief to be an alternative to the use of opiates in acute mechanical back pain states.
- They found that topiramate was moderately helpful in acute back pain – and often more helpful than muscle relaxants, lidocaine patches, and TENS units.
- Other studies have found no improvement in back pain relief. Therefore, best that can be stated is that topiramate can help chronic pain in selected patients, particularly when paired with other interventions like SNRIs or physical therapy.

Sublingual Buprenorphine/Naloxone for Pain Management

- Everyone practicing in our field is familiar with growing articles and news stories on the use of Buprenorphine/Naloxone for the treatment of opiate addiction and dependence.
- It has also long been recognized and exploited that buprenorphine has antinociceptive/anesthetic effects on its own that makes it a potentially powerful pain medication for patients with a better safety profile than full mu agonists.
- In fact, transdermal buprenorphine / Butrans patch has been available for many years for the treatment of moderate to severe chronic pain.
- Last year, Dr. Rohit Aiyer and his colleagues published a comprehensive review of all studies that have examined buprenorphine for pain control.
- They found twenty five studies – with fourteen of the studies showing significant pain relief from buprenorphine.
Sublingual Buprenorphine/Naloxone for Pain Management

- Surprisingly, only three of the studies used SL buprenorphine/naloxone for pain control. All three showed positive results.
- Most of the buprenorphine studies employed Butrans and these studies also demonstrated good pain relief.
- An accompanying editorial in Anesthesia & Analgesia points out the buprenorphine might be the fabled “silver bullet” in pain management – providing adequate treatment of pain and associated with a low risk profile.
- They agree with Aiyer that there simply have not been enough studies done to make a recommendation of buprenorphine over other opiates for the treatment of pain.
- But, the opioid crisis is such an urgent national issue, that more studies on the use of SL buprenorphine/naloxone for chronic pain should be funded promptly.

Concluding Thoughts

- There has always been a great amount of interest in the use of psychopharmacology for the treatment of chronic pain – with articles on this topic going back to the 1960’s.
- With the present attention on alternatives to opiates for chronic pain control, there is more interest in psychopharmacology for pain control than ever.
- Despite our great interest in this area, no psychopharmacological medication has turned out to be “the silver bullet” – and not for lack of investigators trying to find one!
- Rather, these medications can deliver a measurable, modest decrease in the pain experience that most patients quantify as a 2 or 3 point reduction in 0-10 numeric pain score.
- It also appears that it is important to use full dosages of these medications to maximize attained pain relief.
- These medications can be employed with other non opioid medications – such as anti-inflammatories or topical analgesics.
- They can also be used as opioid-sparing agents to provide pain relief while decreasing opioids dosages.

Concluding Thoughts

- Most importantly, it appears important to be flexible in your use of different psychopharmacological medications for pain control.
- For example, you may have a patient who responds well to an SSRI like fluoxetine for chronic pain control. Studies would suggest that most patients will respond to SNRI’s better, but your patient can have an individualized superior response to an SSRI.
- The same is true of lamotrigine – published studies would suggest that it is not helpful for chronic pain control but there are certainly cases where patients do respond to it for pain control, which is why its use in this area endures.
- So, a flexible approach that builds a foundation of pain control using different psychopharmacological medications combined with medications of other classes based on the patient’s individualized response is the approach most likely to attain a good outcome.

Thank You!
HORMONAL CARE IN CHRONIC PAIN PATIENTS

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COURSE DESCRIPTON

Hormone administration in a variety of forms has permanently entered pain care. Oxytocin is a direct pain reliever and being used as non-opioid, analgesic agent. Neurosteroids are a class of hormones produced by the brain and spinal cord which the central nervous system uses for neuroprotection and neuroregeneration. Animal experiments and early clinical trials indicate these hormones reduce pain severity and lower the need for potent analgesic agent are positive additions to standard pain care. Anabolic hormones including human chorionic gonadotropin and nandrolone appear palliative in the wasting stages of Ehlers-Danlos Syndrome, adhesive arachnoiditis, and RSD/CRPS. Both severe chronic pain and opioid administration may reduce serum levels of some hormones and require replenishment to maintain analgesic potency. Some corticosteroids are potent suppressors of neuroinflammation and can be safely and effectively administered in select clinical situations.
Educational Objectives

OBJECTIVES

1. How to prescribe oxytocin for short-term relief.
2. Identify which neurosteroids and anabolic hormones may be effective for specific pain disorders.
3. How to prescribe hormones for replenishment purposes.
4. How to identify clinical situations for safe use of corticosteroids.

Two Major Discoveries

• Glial Cell Activation and Neuroinflammation

• CNS Produces Neurosteroids

Major Neurosteroids

- Pregnenolone
- Progesterone
- Allopregnanolone
- Dehydroepiandrosterone (DHEA)
- Estradiol

Definition: Made in CNS independent of adrenal and gonadal function.
Functions of Neurosteroids

- Neuroprotection from Damage
- Suppression of Neuroinflammation
- Neuroregeneration

**NOT A DIRECT ANALGESIC**


### Key References


### Painful Conditions

<table>
<thead>
<tr>
<th>Centralized (&quot;Constant&quot;) Pain</th>
<th>Genetic Collagen Disorders</th>
<th>Autoimmune Disorders</th>
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<tr>
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Candidates for Hormone Administration

- Constant pain requiring multiple analgesic agents (Example: opioids and neuropathic agents)
- Impairment and difficulties with daily living (Example: eating, hygiene, sleep)
- Tissue wasting and weakness
- Immobility, fatigue, house-couch bound

Steroid

Any of a group of lipids that contain the cyclopentanoperhydrophenanthrene ring system.

Steroids Include

- Cholesterol
- Adrenal steroids: cortisol, pregnenolone
- Gonadal steroids: progesterone, testosterone
- Neurosteroids
- Anabolic steroids: synthetic testosterone
- Corticosteroids
Special Characteristics of Hormones in Pain Care

- Not direct analgesics (Exception: oxytocin)
- Not a substitute for symptomatic analgesics, neuropathic agents, and antidepressants
- Not replacement therapy
- Not to be taken daily to maintain safety and efficacy
- Are an essential treatment for some chronic, painful conditions

Clinical Trials

- Only controlled studies with DHEA and HGH
- Trials can be 1 to 2 months
- Look for increased: Pain reduction, Energy, Activity, Sleep
- Decrease in symptomatic drug use

Pregnenolone

- 200 to 400 mg, start 25 to 50 mg
- 3 to 5 days a week
- Converts to progesterone, allopregnanolone, and mineral corticoids
- NMDA suppressor

DHEA

- 200 to 400 mg
- 3 to 5 days a week
- Converts to estradiol and testosterone
- Peripheral pain conditions: SLE, psoriasis, EDS


Progesterone

- Multiple stroke, trauma, and pain trials – mixed results
- No oral dosage established
- Medroxyprogesterone (MDP) appears effective in open trials.
  Dosage is 10 mg BID on 3 to 7 days a week
- MDP may have considerable potential


Corticosteroids

- Essential for some special uses
- Potent suppressor of glial cells, neuroinflammation, and central hyperactivity
- Most corticosteroids don’t cross the blood brain barrier or act on central receptors to produce clinical effects

Most Potent Central-Acting Corticosteroids

- Methylprednisolone (Medrol®) (oral, depo-injection, short-acting injection)
- Dexamethasone
- Prednisone

Special Clinical Situations

- Pain and bladder/lower extremity impairment after spinal procedures (potential arachnoiditis)
- Pain flares, can use with ketorolac and opioids
- Ongoing suppression of central neuroinflammation
  - Adhesive arachnoiditis
  - RSD/CRPS
  - Lyme
  - EDS
- Standard uses are intralesional, topical, acute neuropathic conditions

Therapeutic Trial and Testing

- Best “test” for neuroinflammation
- Example: 6-Day methylprednisolone dose pak or injection of 10-20 mg on 1 to 3 consecutive days
Safe and Effective Long-Term Use

- Do not use daily
- Use low dosage 1 to 3 days a week
  - Example: Methylprednisolone, 2.0 to 4.0 mg
  - Dexamethasone, .50 to .75 mg
  - Prednisone, 2.5 to 5.0 mg
- Options: Injection, 1 to 2 times a month
  - Example: methylprednisolone 10-20 mg

Anabolic Hormone Therapy

- Term may "frighten" but tissue regeneration may be essential
- Clinical indications are:
  1. Wasting, debilitating disease ("catabolism")
  2. Pain uncontrolled by standard therapy dosages
  3. Intractable, severe pain with these symptoms/findings

  - Symptoms/Findings:
    - Bed-home bound
    - Tissue wasting
    - Anorexic
    - Weight loss
    - Unable to do activities of daily living

Anabolic Agents

- Human chorionic gonadotropin (HCG), 250 to 500 units (injection, sublingual)
- Nandrolone 25 mg, 1 to 2 a day
- Human growth hormone (HGH) (injection)

Use on 3 to 5 days a week.
**Oxytocin**

- One hormone with direct analgesic activity
- Uses are intra-NASAL, sublingual, or troche
- Dosage is 40 to 80 units every 4 to 6 hours
- Can be used with neuropathic agents, opioids, and ketamine


**Pain and Opioid Suppression**

- Both can suppress testosterone, cortisol, DHEA, and pregnenolone
- Replenishment reported to reduce pain and opioid dosages
- Periodic serum testing recommended to document normalization


**OTC Dietary Supplements**

- Adrenal extracts
- Gonadal extracts (Orchex® or other)
- Colostrum
- Deer antler velvet
Hormone Laboratory Testing

**Screening Panel:** cortisol, DHEA, estradiol, progesterone, testosterone, CRP-HS, ESR

**Pain Control Markers:** ACTH, prolactin

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**Summary**

- The function of neurosteroids are neuroprotection and neuroregeneration
- Severe chronic pain causes glial cell activation and neuroinflammation
- Centralized ("constant") pain conditions are best treated with symptomatic agents (neuropathic, opioids, ketamine) in conjunction with hormonal agents that suppress neuroinflammation and promote neuroregeneration
- Hormonal agents in the steroid (neuro, cortico, anabolic) classes should not be used daily to maintain effectiveness and safety
- Patients with severe, uncontrolled pain due to a wasting, catabolic disease will require anabolic hormones
Compassion Fatigue Resilience

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Greetings from my City and University
1. School of Social Work
2. Disaster Resilience
3. Leadership Academy
4. Tulane Traumatology Institute

Raise your hands

• How many of you are work with patients who are in pain?
• How many years have you been doing this?
This final session is for you: Focusing on THE

- **Costs of caring** and its impact on you as a person and as a provider.
- The impact of your work on you and **your family**.
- **Risk and protective factors** that enable you to thrive and succeed in your work and life.

Background work: Compassion Fatigue

Have studied compassion fatigue in
- medical professionals,
- trauma and disaster workers,
- veterinarians,
- trauma psychotherapists,
- and refugee workers

Among Physicians

- Addressed the high suicide rate of physicians and the general lack of self care
- about physician stress resilience and how to improve our medical education for practitioners to focus more on self care and institutional support
Motto:
First do no SELF HARM

• Aware of your secondary traumatic stress reactions
• Aware of the impact on capabilities and effectiveness
• Aware of the signs of compassion fatigue and
• your special risk and protective factors.

What happens to us?

• Impact is a spectrum of adaptation to either direct or indirect trauma exposure, or both
• Primary Traumatic Stress Injuries from the demands of the job – the strain, wear and tear managing direct threats and fear.
• Secondary Traumatic Stress Injuries from the demands of being compassionate.
Compassion Fatigue

- **Compassion fatigue** is the inability to adapt to the impact of secondary traumatic stress from exposure to the suffering of others.
- A caregiver's reduced capacity or interest in being empathetic or bearing witness to the suffering of others.

Compassion Fatigue (cont.)

- Can result from placing the care of others over self-care.
- Can result from using empathy and dispensing compassion, day after day, week after week, year after year.
- Can diminish the quality of compassionate care especially by those critical to the recovery of clients medically or mentally.

How do we build Compassion Fatigue Resilience? (prevention!)
Compassion Fatigue Resilience

1. Building the **capacity to bounce back** following a stressful incident/period using 8 measurable risk and protective factors.
   a. To guide effective preparation.
   b. Monitor these factors in self and others

Compassion Fatigue Resilience (cont.)

2. **Protective Factors** that increase resilience and lower secondary traumatic stress levels are:
   a. good **Self-Care**
   b. effective **Detachment**
   c. high sense of **Compassion Satisfaction** and
   d. good **social support**

Compassion Fatigue Resilience (cont.)

3. **Risk Factors** that increase secondary traumatic stress levels and decrease resilience:
   a. **Empathic Response** increases the risk of exposure to client suffering
   b. **Prolonged exposure** to suffering
Risk Factors (Cont.)

c. **Traumatic memories** provoked by client suffering
d. **Other life demands** that increase stress and detract from self care and other protective factors

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The Compassion Fatigue Resilience Model

1. **Map to building resilience** by knowing the critical (risk and protective) factors to measure and develop.
2. Low resilience is associated with inadequate compassion that leads to poor performance in helping the traumatized.
3. High resilience is associated with an exquisite form of empathy that is protective and invigorating.

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Figure 1: The Compassion Fatigue Resilience Model
The Empathic Response – Key to Effective Human Services

Empathic Response effective in human services work, requires:

- Exposure to the suffering
- Empathic Ability
- Empathic Concern for the suffering

Secondary Traumatic Stress

Self-care and self-care plan

- Detachment from distress
- Sense of Satisfaction as a caregiver
- Sense of Satisfaction with being a caregiver

Social Support

Other Life Demands

- Compassion Fatigue
- Resilience Level

Traumatic memories that distract from doing our job

risk factors for Compassion Fatigue

- Empathic Response to Client Suffering
- Prolonged Exposure to the Suffering
- Trauma memories
- Other life demands
**Conclusion (cont.)**

• Compassion is a learned behavior that benefits both the receiver of compassion but also the compassion provider.
• But it requires working at it, starting with a self care plan (do it for your family).

**Conclusion (cont.)**

• Self-care – develop a written plan and use it

**Reaction Panel**

• Please talk about how best to help members of the SPS
• Include me on plans to improve the prevention of compassion fatigue in organizations and specialties
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• Tulane Trauma Courses
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• All my journal articles are at ResearchGate.net