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Treatment of Pain Opioid Choices and Issues for Patient and Practitioner

Greg Caldwell, OD, FAAO

Mid-Winter Getaway
Optometric Education Consultants
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Disclosures- Greg Caldwell, OD, FAAO

All relevant relationships have been mitigated

- Lectured for: Alcon, B&L, BioTissue, Dompé
  - Disclosure: Receive speaker honorariums
- Advisory Board: Dompé, ImmunoGen, Iveric
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- I have no direct financial or proprietary interest in any companies, products or services mentioned in this presentation
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- Healthcare Registries – Chairman of Advisory Council for Diabetes and AMD
- The content of this activity was prepared independently by me - Dr. Caldwell
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My Practice

I am a clinician first then a scientist

- Some are scientists first then clinician
- I need to simplify for patient and patient care.
- Science is great, but not good if there isn't a clinical application.
- Some lecturers are science based without clinical application.
- My lecture will be a hybrid. Showing clinical applications of the science

It is wonderful to have someone who's juggling so many aspects of optometry. [scientific, clinical experience, teacher & lecturer]. It is refreshing and very informative. -Sarah

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Agenda

- The opioid crisis
- Pain definition
- Pathways of pain and the receptors
- Types of pain
- Grading pain – pain scales
- The opioids – opioids, semisynthetic, and synthetic
- Formulation changes to help prevent ease of abuse
- Allergies to opioids and the alternatives
- Opioid adverse drug reactions
- Opioid antagonists
- Tolerance
- True Addiction
- Alternatives or additions to opioids
- Ocular cases where opioids where used
- Questions and answers

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NIH: National Institute on Drug Abuse

As of March 2018

- Every day, more than 115 people in the United States die after overdosing on opioids
- The misuse of and addiction to opioids
  - Prescription pain relievers, heroin, and synthetic opioids such as fentanyl
- Serious national crisis that affects public health as well as social and economic welfare
- The Centers for Disease Control and Prevention estimates that the total "economic burden" of prescription opioid misuse alone in the United States is $78.5 billion a year
  - Including the costs of healthcare, lost productivity, addiction treatment, and criminal justice involvement

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What do we know about the opioid crisis?

NIH: National Institute on Drug Abuse (March 2018)

- Roughly 21 to 29 percent of patients prescribed opioids for chronic pain misuse them
- Between 8 and 12 percent develop an opioid use disorder
- An estimated 4 to 6 percent who misuse prescription opioids transition to heroin
- About 80 percent of people who use heroin first misused prescription opioids
- Opioid overdoses increased 30 percent from July 2016 through September 2017 in 52 areas in 45 states
- The Midwestern region saw opioid overdoses increase 70 percent from July 2016 through September 2017
- Opioid overdoses in large cities increase by 54 percent in 16 states

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What are HHS and NIH doing about it?

- In the summer of 2017, NIH met with pharmaceutical companies and academic research centers to discuss:
  - Safe, effective, non-addictive strategies to manage chronic pain
  - New, innovative medications and technologies to treat opioid use disorders
  - Improved overdose prevention and reversal interventions to save lives and support recovery

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Pain

- Pain is very important to our survival
- Pain is defined as the perception of a noxious (harmful) stimulus
- Pain can also occur in the absence of injury or long after an injury has healed
- Pain provides humans with information about:
  - Tissue-damaging stimuli
  - Thus enables them to protect themselves from greater damage
- Pain is protective in two ways:
  - It removes a person from stimuli that cause tissue damage through withdrawal reflexes
  - Learning associated with pain causes the person to avoid stimuli that previously caused pain
- Pain often initiates the search for medical assistance and helps us to pinpoint the underlying cause of disease

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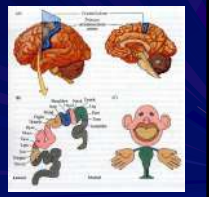
Somatosensory System

- Diverse sensory system composed of the receptors and processing centers to produce the sensory modalities:
  - Touch
  - Temperature
  - Proprioception (body position)
  - Nociception (pain)
- The system reacts to diverse stimuli using different receptors
  - Thermoreceptors
  - Nociceptors
  - Mechanoreceptors
  - Chemoreceptors



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Pain

- Pain is an unpleasant sensory experience associated with actual or potential damage to the body, or perception of such damage. It is a subjective experience
- Subjective experience
- Memories of events associated with extreme pain persist for a long time
- Mental state is known to have a powerful influence over pain
  - An athlete may not notice a twisted ankle until after the competition is over.
  - Soldiers in battle often continue to fight even after sustaining serious injury, and they may report afterwards that they experienced no pain until after battle
- The scientific explanation for this phenomenon is that the brain not only receives pain messages, but also has a descending system of neurons that suppresses pain messages

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Pharmacology of Pain Management

- Peripheral acting agents
  - Prevent sensitization of receptors to substance P
  - Example: NSAIDs, ibuprofen
- Signal inhibiting agents
  - Prevent pain signal from travelling to cortex
  - Example: Anesthetics, proparacaine
- Central acting agents
  - Act on pain perception centers in the cortex (CNS)
  - Example: opioids/narcotics

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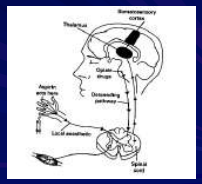
Descending Pathway

- This system inhibits cells in the spinal cord that transmit pain signals
- A pathway for natural pain modulation
- Opioids that occur naturally such as the endorphins are important neurotransmitters in some of these descending pathways



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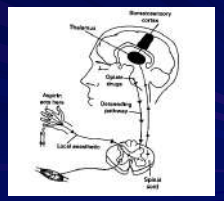
Peripheral versus Central Acting



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Question?

What type of pain does not respond well or at all to opioid pharmaceuticals?

A. Nociceptive pain
B. Neuropathic pain

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Four Major Types of Pain

- Nociceptive Pain
  - Typically the result of tissue injury
- Inflammatory Pain
  - An abnormal inflammation caused by an inappropriate response by the body's immune system
- Neuropathic Pain
  - Pain caused by nerve irritation
- Functional Pain
  - Pain without obvious origin but can cause pain

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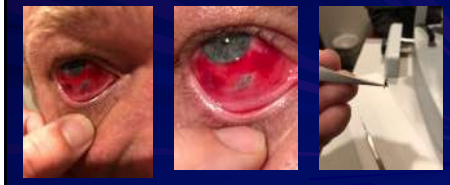
Nociceptove Pain- I was hit in the eye with a tree branch, and I think my eye is scratched



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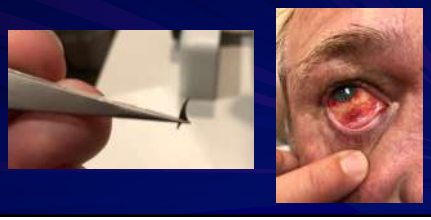
Nociceptive Pain- Healing Well



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Pain is Complex and Confusing

Nociceptive Pain and Neuropathic Pain

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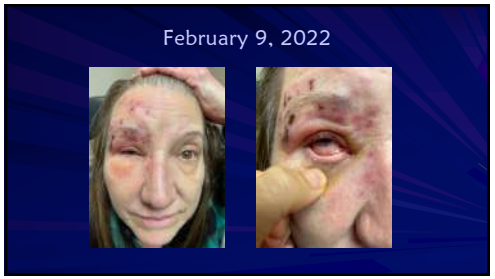

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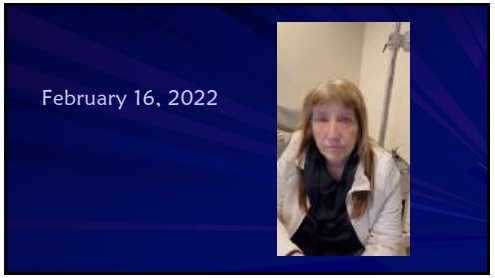

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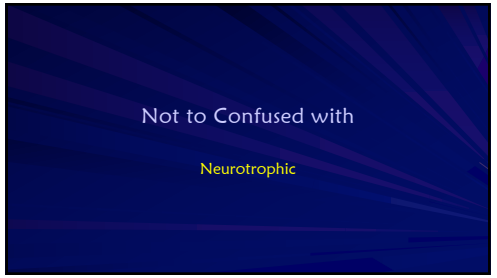

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Cornea Sensitive Testing – Another Patient

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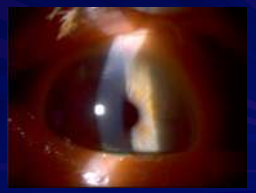
Cornea Sensitive Testing – Yet Another Patient



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Drug Treatment Options… Neuropathic Pain

- Not the focus of today's discussion…
- Why is this relevant?
- Adjuvants – means "add on" medications
  - Some of them have addiction potential
    - Anti-seizure medications that address nerve damage/inflammation
      - MOA: work on the GABA system – similar to benzodiazepines (ex. Xanax)
      - Gabapentin (Neurontin) – controlled substance in multiple states
      - Pregabalin (Lyrica) – controlled substance in all 50 states
    - Anti-anxiety and sleep medications
      - Zolpidem (Ambien)
      - Alprazolam (Xanax), Lorazepam (Ativan), Diazepam (Valium)

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Neuropathic Pain

Chronic Pain

- Trigeminal neuralgia
- Post-herpetic neuralgia
- Diabetic neuropathy
- Phantom limb pain following an amputation
- Multiple sclerosis
- Pain following chemotherapy
- HIV infection
- Alcoholism
- Tension headache
- Migraine
- Fibromyalgia
- Low back pain

- Tricyclic antidepressants for pain
  - The most effective type of antidepressant used for pain
  - Imipramine — Tofranil
  - Clomipramine — Anafranil
  - Nortriptyline — Pamelor
  - Desipramine — Norpramin
- Anticonvulsants for pain
  - Gabapentin — Neurontin
  - Topiramate — Topamax
  - Pregabalin — Lyrica
  - Carbamazepine — Tegretol
  - Oxcarbazepine — Trileptal

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Acute versus Chronic Pain

- Acute
  - Where we are most of the time as optometrists
  - Acetaminophen
  - NSAIDS
  - Opioid
- Chronic
  - Acetaminophen
  - **NSAIDS**
  - **Opioid**
  - **Tricyclic antidepressants**
  - **Gabapentin (Neurontin)**

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Goals of Pain DO Differ…

The goal for managing **acute pain** is to keep the patient as comfortable as possible while minimizing the ***adverse drug reactions (ADRs)*** from the pain meds.

The goals for managing **chronic pain** are to keep the patient as comfortable as possible (this may not mean the patient is pain free) and integrating the patient back into a "normal life" and activities of daily living, while minimizing the ADRs from the pain meds.

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Pain Assessments and Scales

- Adds objective data to a patient's feeling of pain
  - It is a subjective problem to assess!
  - Remember…no patient should needlessly suffer!
- "Does the injury or wound or diagnosis fit the patient's presentation?
  - It is important to be able to assess the degree of pain in a patient.

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Question?

Do you use a pain scale when prescribing narcotics?

A. Yes
B. No
C. I don't prescribe narcotics
D. I will place a comment in the chat box

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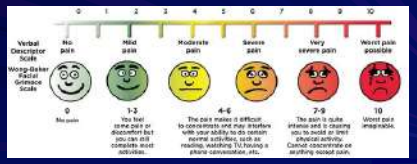
Combination Pain Scale…



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Drug Treatment Options… Nociceptive Pain

Groups of analgesics

- Non-opioids
  - Acetaminophen (Tylenol)
  - NSAIDs (Ibuprofen, naproxen sodium)
  - Glucocorticosteroids (methylprednisolone, prednisone)
- Opioids
  - Codeine (Tylenol with codeine)
  - Hydrocodone (Vicodin)
  - Tramadol (Ultram)

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Question?

Marijuana is allowed to be used in Colorado for recreational usage. It is still considered illegal by the FDA in Colorado?

A. Yes
B. No

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Controlled Substance Schedules

Schedule I – not considered to be medically necessary, research only
- Heroin
- "Medical" Marijuana
  - State control of marijuana and CBD
- LSD
- Mushrooms
- Ecstasy

Schedule II – **more likely to be abused (as compared to Schedule III, IV, V)**
- **Opioids, AKA "Narcotics"**
  - **Oxycodone (OxyContin)**
  - Hydrocodone (Vicodin, Lorcet, Norco)
  - Morphine (MSContin, MSIR)
  - Hydromorphone (Dilaudid)
  - Methadone
  - Fentanyl (Duragesic)
- ADD/ADHD meds:
  - Methylphenidate (Ritalin)
  - Mixed amphetamine salts (Adderall)

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Controlled Substance Schedules

Schedule III - Safer, less likely to be abused (as compared to Schedule II)
- Combination products with APAP or ASA (codeine)
- Esketamine – nasal spray for treatment resistant depression

Schedule IV – Safer, less likely to be abused (as compared to Schedule II and III)
- Tramadol (Ultram)
- Benzodiazepines (lorazepam, diazepam, oxazepam)
- Sleep agents (zolpidem, etc.)

Schedule V – safest, least likely to be abused
- Expectorants with codeine

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State-By-State Restriction

- Marijuana
  - Still considered to be "C1" or "Schedule I"
  - Federal government "ignores" it
- Hydrocodone products
  - C3 to C2 as of 2014
  - "hydrocodone exception"
    - NJ, etc.

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Opioids "narcotics"

- Mainstay of therapy for the treatment of pain
- NO maximum daily dose limitation
- Useful for acute and chronic pain
- They mimic the actions of endogenous opioid compounds:
  - Enkephalins, dynorphins, endorphins

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Mechanisms of Action

- Relieve pain and induce euphoria by binding to the opioid receptors (mu, kappa, delta) in the brain and spinal cord:
  - Mu, kappa, delta receptors in other places = ADRs
    - Mu: analgesia, euphoria, miosis, sedation, constipation, respiratory depression, addiction
    - Kappa: analgesia, diuresis, sedation, miosis, dysphoria, psychomimetic effects, respiratory depression, constipation
    - Delta: analgesia

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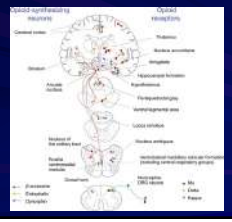
Mu, Delta, and Kappa Receptors



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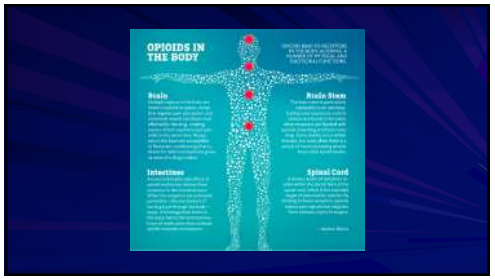

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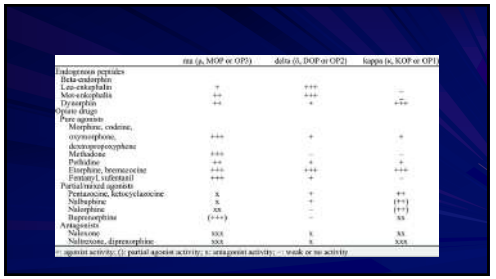

	mu (μ, MOP or OP3)	delta (δ, DOP or OP2)	kappa (κ, KOP or OP1)
Endogenous peptides			
Beta-endorphin	+	+++	–
Leu-enkephalin	++	+++	–
Met-enkephalin	++	+	+++
Dynorphin			
Opiate drugs			
Pure agonists			
Morphine, codeine, oxymorphone, dextropropoxyphene	+++	+	+
Methadone	+++	–	–
Pethidine	++	+	+
Etorphine, buprenorphine	+++	+++	+++
Fentanyl, sufentanil	+++	+	–
Partial/mixed agonists			
Pentazocine, ketocyclazocine	X	+	++
Nalbuphine	X	+	(++)
Nalorphine	XX	–	(++)
Buprenorphine	(+++)	–	XX
Antagonists			
Naloxone	XXX	X	XX
Naltrexone, diprenorphine	XXX	X	XXX

+ agonist activity; (): partial agonist activity; x: antagonist activity; –: weak or no activity

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Opioid Drugs That Bind to Opioid Receptors

- Opiates
  - Morphine, codeine
- Semi-synthetic
  - Oxycodone, hydrocodone
  - Naloxone, Naltrexone
- Synthetic
  - Non-morphinians
    - Fentanyl
    - Methadone
    - Tramadol

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Formulations

- **Immediate release**
  - AKA short-acting
  - Uses: acute pain
    - Percocet, Tylenol w/ codeine, tramadol, Vicodin
- **Controlled release:**
  - AKA long-acting; sustained release; extended release
  - Uses: basal control of chronic pain
  - Typically NOT for acute pain nor in opioid naïve patients!
    - OxyContin, MS Contin, Duragesic patch

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Morphine Products

- Standard for comparison of other agents
- Used for severe pain
- Multiple Brand/Trade names for long-acting morphine products, with very diverse delivery and release systems
  - **MSIR** (IR caps) (q 3-4 hours prn)
  - **MS Contin** (CR tabs) (q 8–12 hours)
  - **Kadian** (CR caps) (q 12 – 24 hours)
  - **Avinza** (CR caps) (q 24 hours)

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Hydromorphone Products

- **Hydromorphone (Dilaudid)** tablets – immediate release
  - Take 1 – 2 tablets every 4 to 6 hours as needed for pain
- **Hydromorphone ER (Exalgo)** tablets – extended release
- Used for severe pain
- Very potent
  - Compare to morphine
    - 30mg PO morphine = 8mg PO hydromorphone

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Codeine-Based

- Codeine – C3; Schedule III
  - Naturally occurring opioid
- Hydrocodone – C2; Schedule II
  - Semi-synthetic derived from codeine
  - More potent than codeine
  - Retains cough suppression
- Oxycodone – C2; Schedule II
  - Semi-synthetic derived from codeine
  - Pain only, no cough suppression

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Codeine tablets

- WEAK analgesic: 30mg PO morphine = 200mg PO codeine
  - Weakest of morphine, hydrocodone, and oxycodone
- Add acetaminophen/aspirin – Schedule III
  - Tylenol #2 = 300 mg acetaminophen & 15 mg codeine
  - **Tylenol #3** = 300 mg acetaminophen & 30 mg codeine
  - Tylenol #4 = 300 mg acetaminophen & 60 mg codeine
  - 1 – 2 tablets every 4 – 6 hours as needed for pain
    - Not to exceed **3 grams** of APAP per day
- Add expectorant – Schedule V

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Oxycodone Products

- **Long-Acting, Extended-Release**
  - OxyContin
- **Immediate Release; short-acting tablets**
  - **OxyIR** (IR cap)
  - **Roxicodone** solution
- Combination with acetaminophen
  - **Percocet** and Endocet (oxycodone/APAP dose)
- Take 1 – 2 tablets by mouth every 4 to 6 hours as needed for pain
  - Not to exceed 3 grams of APAP per day

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Oxycodone Products

- **Percodan** (oxy + asa) – no one uses this product
- Percocet
  - Oxycodone is combination with acetaminophen
  - Various strengths
- 30mg PO morphine = 20mg PO oxycodone

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Hydrocodone Products

- As of August 2014, hydrocodone products are ALL CII
  - Moved from schedule III to schedule II
- Immediate-Release Products
  - **Hydrocodone 7.5 mg + IBU 200 mg**
    - **Vicoprofen**
  - **Hydrocodone + acetaminophen:**
    - **Vicodin** = 5/300; 7.5/300; 10/300
    - Lortab = 2.5/300, 5/300, 7.5/300, 10/300
    - Norco = 5/325, 7.5/325, 10/325
- Take 1 – 2 tabs/caps every 4 – 6 hours as needed for pain
  - Not to exceed 3 grams of APAP per day
- 30mg PO morphine = 20mg PO hydrocodone

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Tramadol – another great choice

Tramadol (Ultram) tabs

Tramadol with 325 mg APAP (Ultracet), Tramadol ER tabs

- tramadol (50 – 100 mg q 4 – 6 hours; do not exceed 400 mg/day)
  - Dual action: **mu** receptors & inhibits neuronal uptake of **serotonin** & **norepinephrine**
  - Lowers seizure threshold; increases serotonin levels
    - Watch drug interactions with other meds that ↑ serotonin
      - Selective serotonin reuptake inhibitors (SSRIs): fluoxetine/Prozac
      - Migraine meds ("triptans"): sumatriptan/Imitrex
  - Not controlled
    - AS OF AUGUST 2014, NOW A C4 (Schedule IV)
    - "tramies" = abuse potential; helps decrease withdrawal symptoms

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Question?

When you see a patient in your office on Methadone be kind to them as they are trying to recover or have recovered from opioid abuse:

A. True
B. False

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Miscellaneous

- **Fentanyl Patch** (Duragesic)
  - MOST potent opioid
  - Black Box Warning against use in acute pain and in opioid naïve patients
- **Meperidine** (Demerol)
  - ACTIVE metabolites = undesirable
- **Methadone**
  - Typically reserved for morphine/codeine allergic patients

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Methadone tidbits…

- Chronic pain or opioid abuse deterrent
- 2-phase elimination
  - Alpha phase = 8 hrs
    - Offers pain control
  - Beta phase = 16+ hrs
    - Mitigates withdrawal symptoms
- Patient 1: On a short-acting pain med = likely being used to treat chronic pain
  - Twice per day dosing
- Patient 2: On methadone ONLY; lower doses
  - Once daily dosing

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Analgesic Medications in Pregnancy

- Acetaminophen (Tylenol)
  - Analgesic of choice in pregnancy
- NSAIDs should generally be avoided in pregnancy
  - Despite Category B
  - Miscarriage risk in first trimester
    - Ibuprofen
  - Second trimester use is likely safe
    - Ibuprofen
  - Third trimester avoid ALL NSAIDs
    - Premature Ductus Arteriosus closure in third trimester
- Opioids should be avoided in pregnancy unless there is no viable alternative
  - First trimester use is associated with heart defects and spina bifida

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Opioid Allergies

- If a patient states "codeine allergic" ask appropriate questions
  - "You have indicated that you have an allergy to codeine, can you describe what happens when you take codeine?"
- If a patient is truly allergic to codeine
  - Most likely allergic to morphine, hydromorphone, oxycodone, hydrocodone, and tramadol
- And…if they had an opioid IV after surgery, then their "reaction" may have been due to histamine release
  - NOT always an allergic reaction

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Opioid Allergies

- Do you know what a patient can take if true codeine allergy?
  - Fentanyl
  - Methadone
  - Meperidine
- Assessing "allergies" appropriately helps practitioner sort through Actual allergy potential and "placebo allergies"
  - Fear versus drug seeking

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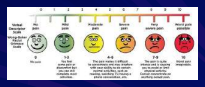
Specific Medications Using Numeric Pain Scale

Mild pain = 1 – 3
- Acetaminophen (APAP; Tylenol)
- Ibuprofen (Advil, Motrin)
- Naproxen sodium (Aleve)
- Tramadol (Ultram) - low dose



Moderate pain = 4 – 6
- Tramadol (Ultram) – mid to high dosing
- Tylenol with codeine (Tylenol #3)
- Acetaminophen with oxycodone (Percocet)
- Acetaminophen with hydrocodone (Vicodin) – lower dosing

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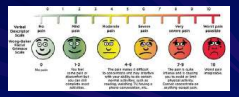
Specific Medications Using Numeric Pain Scale

Severe pain = 7 – 10
- Tylenol with hydrocodone
  - Vicodin, etc. – higher doses
- Tylenol with oxycodone
  - Percocet, etc. – higher doses
- Morphine (MSIR)
- Hydromorphone (Dilaudid)
- Fentanyl (Duragesic patch; Actiq lozenge on a stick)



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Question?

One of the main problems with an opioid is:

A. The low ceiling effect
B. The high ceiling effect
C. The lack of a ceiling effect

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"Ceiling Effect"

- Commonly used when discussing *analgesics*
- Phenomenon in which a drug reaches a maximum effect
  - Increasing the drug dosage does not increase its effectiveness
- Central Nervous System Agents
  - No ceiling effect
  - Part of the problem
- Peripheral Nervous System Agents
  - Has a ceiling effect

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Tolerance

- Escalation of dose to maintain effect
  - Analgesia or euphoria
  - Happens to everyone
- Regarding euphoria = may be life threatening because respiratory depression does not show much tolerance

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Opioid Effects/ADRs

- CONSTIPATION-anticipate it!
  - All patients should receive a stool softener + stimulant
  - Combo: docusate + senna/Senna+S
- Sedation
- Euphoria – mu receptors
- Dysphoria/Hallucinations – kappa receptors
- Pruritis – allergy versus normal release of histamine
- Nausea/vomiting
  - Triggers CTZ
  - Codeine "allergy"

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Opioid Effects/ADRs

- Confusion
- Miosis
- Respiratory depression
  - This is what kills a patient
  - ***Mixing opioids with other CNS depressants***
    - **Alcohol**
    - **Benzodiazepines**
    - **Muscle relaxers**
    - **Sleep agents**
    - **Antihistamines**
    - **Anti-seizure medications**

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Opioid Effects/ADRs

- Withdrawal symptoms:
  - Short half-life agents are more likely to cause abrupt withdrawal symptoms
  - Sweating
  - High sympathetic tone: increase in heart rate and blood pressure, mydriasis
  - Agitation
  - Irritation
  - Irrational behavior
  - Symptoms disappear with (immediate) use of an opioid

71

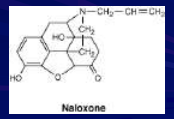
Respiratory Affects

- Inhibition of cough reflex
- Respiratory depression
  - This is what kills a patient
  - **Important to make sure that the patient doesn't**
    - **Increase dose on their own**
    - **Add another CNS depressant with it!**

72

Overdosing

- Opioid antagonists
- **Naloxone (Narcan) & Naltrexone (ReVia)**
  - Used to treat opioid overdose



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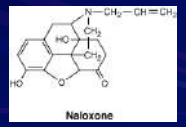
Opioid Antagonist

Naloxone (Narcan) & Naltrexone (ReVia)

- Used to treat opioid overdose



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Mixed Opioid Agonist-Antagonist For the Treatment of Abuse/Addition

- Exhibit partial agonist or antagonist activity at the opioid receptors
- **Agonist/Antagonist combinations for the treatment of opioid abuse/addiction**
  - **Buprenorphine (Buprenex)**
  - Buprenorphine/Naloxone (Suboxone)
- **Schedule III**
- Adverse effects
  - Less respiratory depression & less abuse potential?
- Precipitate withdrawal in an opioid-dependent patient

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Mixed Opioid Agonist-Antagonist for the Treatment of Chronic Pain

- Exhibit partial agonist or antagonist activity at the opioid receptors
- **Agonist/Antagonist combinations for the treatment of chronic pain**
  - **Not appropriate for the treatment of acute pain**
  - **Morphine/Naltrexone (Embeda)**
  - **Oxycodone/Naltrexone (Troxyca ER)**
- **Schedule II controlled substance**

76

Substance Abuse History

- Avoid all opioids in a patient with a history of heroin use
  - This includes tramadol
  - May trigger dopamine reward and the drug "need"
  - Stick with higher doses of a NSAID +/- acetaminophen
- Patients with abuse history for other substances
  - Ex. Benzodiazepines, alcohol, amphetamines?
  - It is a judgement call
  - Some evidence to suggest that all addictive meds should be avoided!

77

"True Addiction" formerly "Psychological Dependence"

- Compulsive use despite harm
- Quality of life is not improved by the medication and eventually it becomes compulsive
  - "Wanting without liking"
- Relapse is very common even after "successful" withdrawal
  - It is a relapsing disease that is incredibly hard to treat

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Identifying Behaviors of Abuse/Addiction

- "Fast talkers"
- Strange allergies
- Excuses for "loss" of meds
- Excuses why they need "a strong pain medication"

79

Ways to respond

- Avoid getting "bullied"
- Avoid acting like you are judging the patient
- Use the tools that are available
  - Call your local pharmacy/pharmacist
  - State databases
    - **PDMP** = **P**rescription **D**rug **M**onitoring **P**rogram
- Legal/ethical issues
  - If you didn't write it down, then it didn't happen!

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Prescription Monitoring Program (PMP)

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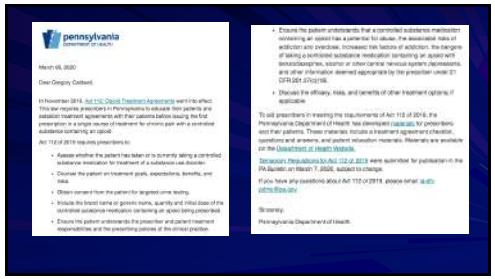

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Ways to Combat Abuse

Drug Company Approaches

83

OxyCONtin (Controlled release tablets (q 12 hours…once in a while q 8 hours); new formulation is out to help control abuse

Manual Crushing Followed by Dissolution

Crushed New Formulation | Crushed Original Formulation

84

Tampering for IV Abuse

- New formulation results in gelatinous material which cannot be drawn into a syringe for injection (the syringe is empty)

New formulation | Original formulation

85

Alternatives/Additions to Opioids

86

Alternatives for Pain Control

- NSAIDs
- COX-2 Inhibitors
- Corticosteroids
- Integrative approach
  - Acupuncture
  - Surgical interventions
  - Nerve blocks
  - Spinal cord stimulators
- Benefits: "SYNERGY" = better control because the combination is working at multiple receptor sites!

87

Bandage Contact CL 92071

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Medrol Dose Pack (Methylprednisolone)

Convenient for patient
6 day "automatic taper"

Sometimes it is not HIGH enough of a dose or LONG enough of a treatment duration

4mg methylprednisolone = 5mg prednisone

MDP equivalent (to prednisone):
Day 1: 30mg
Day 2: 25mg
Day 3: 20mg
Day 4: 15mg
Day 5: 10mg
Day 6: 5mg

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Millipred Dose Pack (Prednisolone)

5mg prednisone/prednisolone = 4mg methylprednisolone

An alternative to a Medrol dose pack
COST/AWP: **Medrol** = $30
Millipred = $ 400
Just give "free" **prednisone** tabs!

Clinical Pearl: The mineralocorticoid (salt and H2O retaining properties of methylprednisone versus prednisone/prednisolone is NOT IDENTICAL!

Methylprednisolone is LEAST LIKELY to cause salt and H2O retention = LESS LIKELY to exacerbate blood pressure

90

Adverse Reactions: Steroids

- Loss of glycemic control
  - Watch in patients with diabetes!
- Drug-Drug interaction with warfarin (Coumadin)
  - Typically ↑ INR
- GI upset: take with food!
- Fat redistribution, osteoporosis, cataracts, muscle wasting = long-term effects

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Acetaminophen (Tylenol)

- Mechanism: largely unknown
- Mild to moderate pain
- No anti-inflammatory potential
- Available in 325mg, 500mg, and 650mg tablets/capsules
- Dosing: 1,000mg every 6 to 8 hours OR 650mg every 6 hours
  - Max daily dose: DO NOT EXCEED 3,000 to 4,000mg in 24 hours
  - OK to use ALONG with or ALTERNATING with ibuprofen or naproxen
- ADRs: avoid in patients who consume > 3 alcoholic beverages per day

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NSAIDs – Ibuprofen (Advil/Motrin)

- Mechanism: prostaglandin inhibitors = decrease in inflammatory mediators
- Good for pain and inflammation
- Mild to moderate pain

- Available in 200mg (OTC) and 400mg, 600mg, and 800mg tablets (RX only)
- Dosing: 200mg to 800mg every 6 to 8 hours
  - Max daily dose: do not exceed 3,200mg in 24-hour period
  - MUST reach 1,200mg daily to achieve anti-inflammatory potential

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NSAIDs – Naproxen Sodium (Aleve)

- Mechanism: prostaglandin inhibitors = decrease in inflammatory mediators
- Good for pain and inflammation
- Mild to moderate pain

- Available in 220mg, 275mg, 375mg, and 550mg tablets
- Dosing: 220 to 440mg every 8 to 12 hours OR 660mg every 24 hours OR 550mg every 12 hours
  - Acute pain: more often is BETTER
  - Maximum daily dose is 1,000 to 1,100mg in 24 hours period
    - OK to dose 1,375mg to 1,500mg on DAY 1 ONLY!
  - Anti-inflammatory potential: dose at HIGHER END of range

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NSAIDs – Adverse Effects

- Take with food – tough on the stomach
- May cause vasoconstriction in the kidneys
- Inhibits platelet aggregation, so ibuprofen interacts with warfarin (Coumadin) = ↑ INR
- May increase risk of heart attack and stroke in patients at "high risk" and with "regular use"
- May increase blood pressure and IOP

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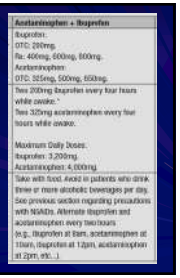
SYNERGY…

It is acceptable to use an ALTERNATING dosing regimen OR an ADDITIVE dosing schedule

Good in moderate to severe pain



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Pain Reliever Help

Know your maximum daily allowances:

- APAP 3000 mg (4000 mg*) — 2 ibuprofen and 2 Tylenol
- ASA 6000 mg — 4 ibuprofen and 2 Tylenol
- Ibuprofen 3200 mg
- Naproxen Sodium 1650 mg (Aleve/Anaprox)
- Naproxen 1500 mg (Naprosyn)

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Alternative?

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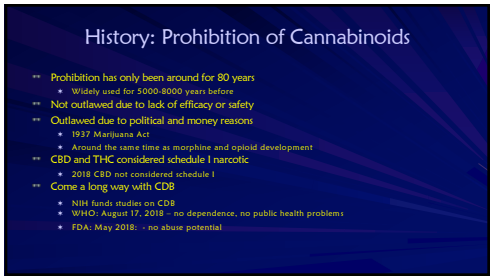

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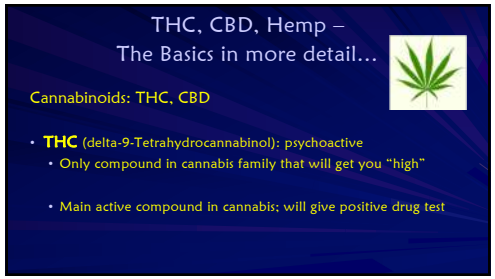

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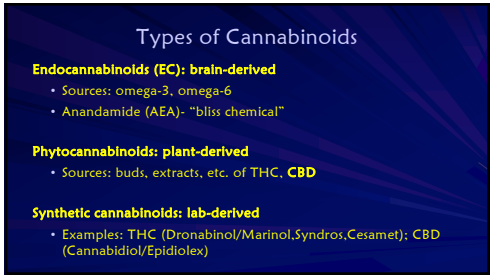

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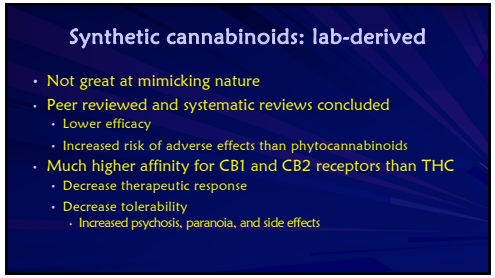

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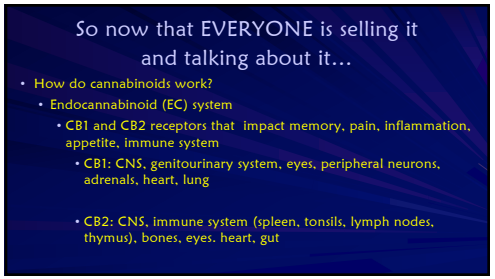

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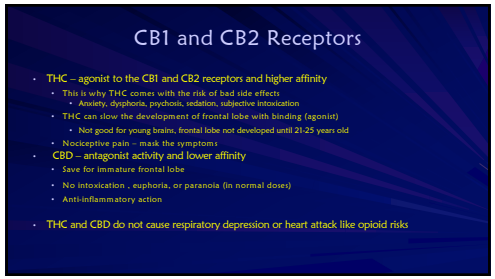

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3 Types of Products in the Market

- Full Spectrum CBD
  - Contains trace amounts of THC (delta 9 THC)
  - Should include other cannabinoid compounds
  - Multiple cannabinoids and terpenes
  - Lower dose than isolate by 5-10 times
  - Stable shelf life
  - Might fail a work or drug recovery program drug test – avoid
- Broad Spectrum CBD
  - No detectable THC
  - Other phytocannabinoids, terpenes
  - Won't fail a drug test
- Isolate CBD
  - Only CBD
  - Least medical benefits
  - Won't fail a drug test
  - Need high doses – 5-10 times more than full spectrum
  - Unstable shelf life

Doesn't work for everyone and everything
But CBD has a broad spectrum of uses

105

Starting to See Outcomes of Studies

Remember illegal until 2018

106

Fibromyalgia

- Allopathic way to treat is Cymbalta, Lyrica, and Savella
  - 8-10% say really effective
- Full spectrum cannabinoids – 62% very effective

107

Hemp Derived CBD Full Spectrum with Opioids

- 97 patients
- 15 mg softgels, average dose 30 mgs
- 53% of patients stopped or decreased opioid use in 8 weeks
- 94% reported better sleep or decrease pain
- CBD could significantly reduce opioid use and improve sleep quality

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CBD with Drug Addiction

- Decreases reward facility effect and seeking behavior in opioid dependence
  - Not cocaine
- Decreases opioid seeking behavior
- Potential for relapse prevention in cocaine and alcohol

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CBD to Recommend Need

- Dosing
- Delivery
- Interactions
- Monitoring
- Side effects
- Tolerability
- Risks
- Product selection

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What to Look in a Company

- "Medical grade CBD"
- Certificate of Analysis (COA) – ask questions
  - Lot specific, comprehensive, is the lab iso-certified for cannabinoids
  - Checking heavy metals
  - Checking for molds, fungus, and bacteria
  - Manufacturing process
  - Planting process
    - Indoor or outdoor
    - Using pesticides
- The spectrums they have
  - If have isolate – does they do stability testing

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Practical Application- Side Effects

- Elevated LFTs (liver function tests)
  - AST and ALT – why *THESE?!?*
  - High doses of CBD
- Drowsiness/Dizziness
- Diarrhea
- Dry mouth
- Hypotension
- Increase in IOP
- Change in appetite

Generally, side effects are most often seen in people taking HIGH doses of CBD

112

Our Associations Fought Hard

We took this course for a reason

113

Cases Where I Recently Used My DEA

114

Conditions Which May Require Pain Management

- Large cornea abrasions
  - Cornea burn
  - PRK/PTK
- Orbital trauma
- Orbital blowout fractures
- Scleritis

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A "bit" Too Close

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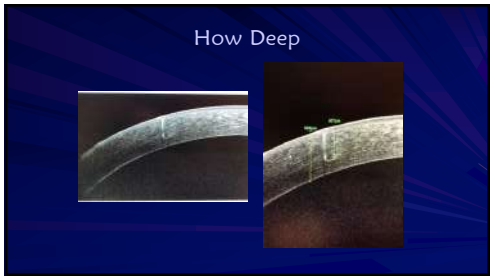

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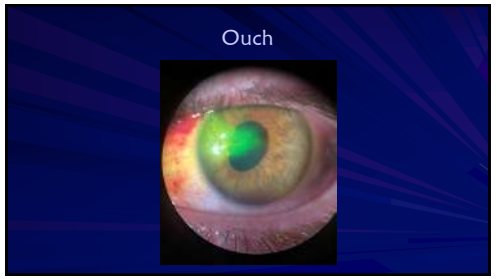

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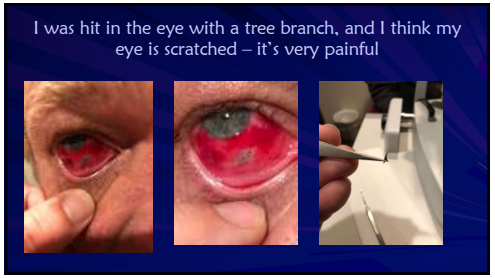

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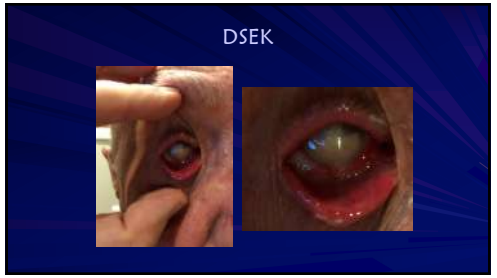

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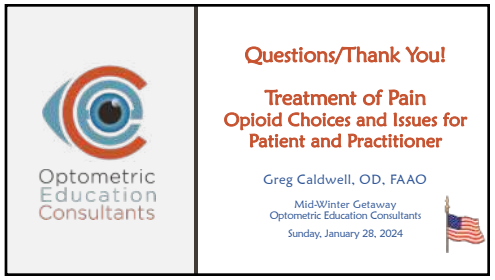

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