Optometric Education Consultants

Treatment of Pain
Opioid Choices and Issues for Patient and Practitioner

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Disclosures- Greg Caldwell, OD, FAAO

All relevant relationships have been mitigated

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Financial Obligations






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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 lectures 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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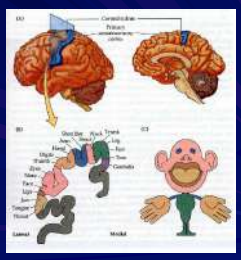
Somatosensory System

- 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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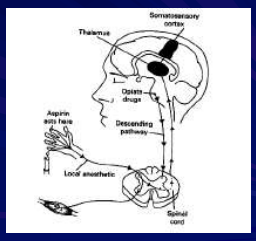
Descending Pathway

- 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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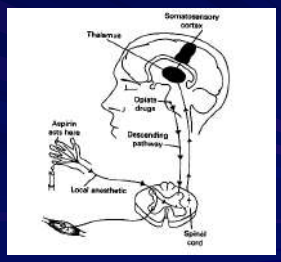
Peripheral versus Central Acting



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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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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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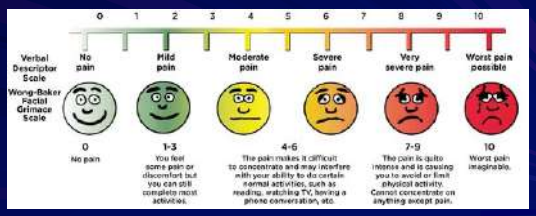
Combination Pain Scale…



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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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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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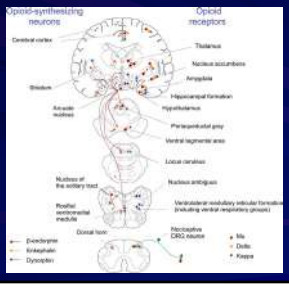
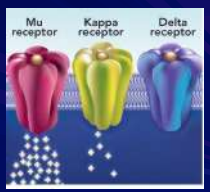
Mu, Delta, and Kappa Receptors





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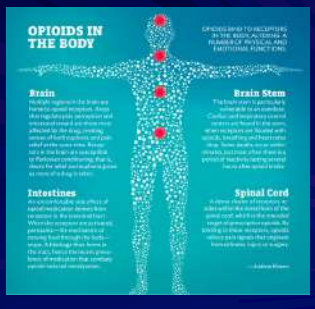

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	mu (μ, MOP or OP3)	delta (δ, DOP or OP2)	kappa (κ, KOP or OP1)
Endogenous peptides			
Beta-endorphin			
Leu-enkephalin	+	+++	–
Met-enkephalin	++	+++	–
Dynorphin	++	+	+++
Opiate drugs			
Pure agonists			
Morphine, codeine, oxymorphone, dextropropoxyphene	+++	+	+
Methadone	+++	–	–
Pethidine	++	+	+
Etorphine, bremazocine	+++	+++	+++
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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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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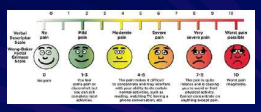
Specific Medications Using Numeric Pain Scale

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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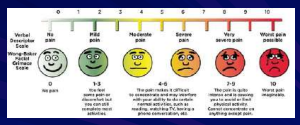
Specific Medications Using Numeric Pain Scale

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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"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

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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!**

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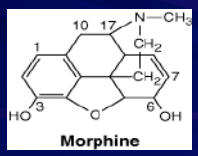
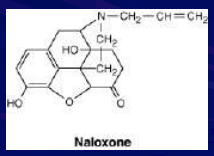
Overdosing

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





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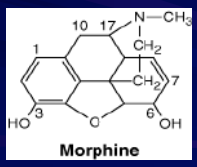
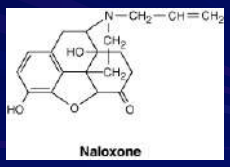
Opioid Antagonist

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**

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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!

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"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"

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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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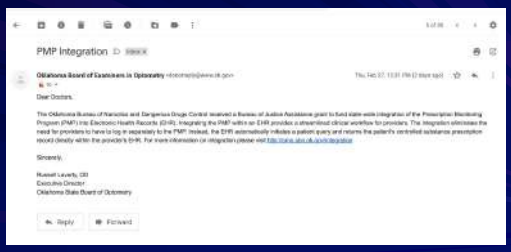
Prescription Monitoring Program (PMP)



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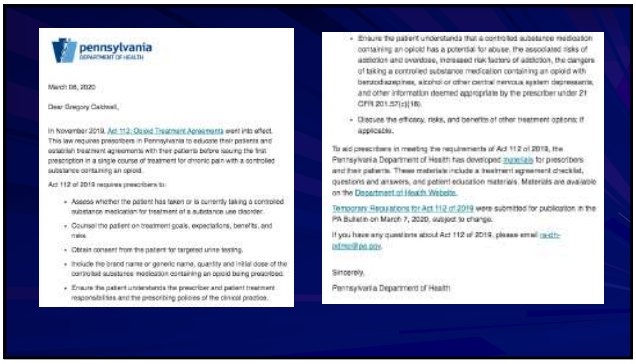

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Ways to Combat Abuse

Drug Company Approaches

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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

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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

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Alternatives/Additions to Opioids

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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!

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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

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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

Acetaminophen + Ibuprofen
Ibuprofen: OTC: 200mg. Rx: 400mg, 600mg, 800mg. Acetaminophen: OTC: 325mg, 500mg, 650mg.
Two 200mg ibuprofen every four hours while awake.* Two 325mg acetaminophen every four hours while awake.
Maximum Daily Doses: Ibuprofen: 3,200mg. Acetaminophen: 4,000mg.
Take with food. Avoid in patients who drink three or more alcoholic beverages per day. See previous section regarding precautions with NSAIDs. Alternate ibuprofen and acetaminophen every two hours (e.g., ibuprofen at 8am, acetaminophen at 10am, ibuprofen at 12pm, acetaminophen at 2pm, etc...).

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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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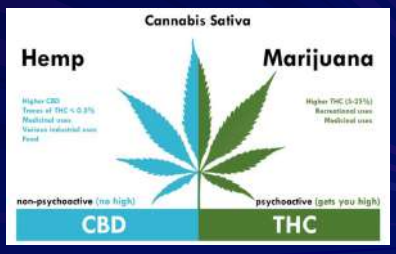
Alternative?



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History: Prohibition of Cannabinoids

- Prohibition has only been around for 80 years
  - Widely used for 5000-8000 years before
- Not outlawed due to lack of efficacy or safety
- Outlawed due to political and money reasons
  - 1937 Marijuana Act
  - Around the same time as morphine and opioid development
- CBD and THC considered schedule I narcotic
  - 2018 CBD not considered schedule I
- Come a long way with CDB
  - NIH funds studies on CDB
  - WHO: August 17, 2018 – no dependence, no public health problems
  - FDA: May 2018: - no abuse potential

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THC, CBD, Hemp – The Basics in more detail…

Cannabinoids: THC, CBD

- **THC** (delta-9-Tetrahydrocannabinol): psychoactive
  - Only compound in cannabis family that will get you "high"
  - Main active compound in cannabis; will give positive drug test

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Types of Cannabinoids

Endocannabinoids (EC): brain-derived
- Sources: omega-3, omega-6
- Anandamide (AEA)- "bliss chemical"

Phytocannabinoids: plant-derived
- Sources: buds, extracts, etc. of THC, **CBD**

Synthetic cannabinoids: lab-derived
- Examples: THC (Dronabinol/Marinol,Syndros,Cesamet); CBD (Cannabidiol/Epidiolex)

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Synthetic cannabinoids: lab-derived

- Not great at mimicking nature
- Peer reviewed and systematic reviews concluded
  - Lower efficacy
  - Increased risk of adverse effects than phytocannabinoids
- Much higher affinity for CB1 and CB2 receptors than THC
  - Decrease therapeutic response
  - Decrease tolerability
    - Increased psychosis, paranoia, and side effects

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So now that EVERYONE is selling it and talking about it…

- How do cannabinoids work?
  - Endocannabinoid (EC) system
    - CB1 and CB2 receptors that impact memory, pain, inflammation, appetite, immune system
      - CB1: CNS, genitourinary system, eyes, peripheral neurons, adrenals, heart, lung
      - CB2: CNS, immune system (spleen, tonsils, lymph nodes, thymus), bones, eyes. heart, gut

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CB1 and CB2 Receptors

- THC – agonist to the CB1 and CB2 receptors and higher affinity
  - This is why THC comes with the risk of bad side effects
    - Anxiety, dysphoria, psychosis, sedation, subjective intoxication
  - THC can slow the development of frontal lobe with binding (agonist)
    - Not good for young brains, frontal lobe not developed until 21-25 years old
  - Nociceptive pain – mask the symptoms
- CBD – antagonist activity and lower affinity
  - Save for immature frontal lobe
  - No intoxication , euphoria, or paranoia (in normal doses)
  - Anti-inflammatory action
- THC and CBD do not cause respiratory depression or heart attack like opioid risks

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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

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Starting to See Outcomes of Studies

Remember illegal until 2018

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Fibromyalgia

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

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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

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Our Associations Fought Hard

We took this course for a reason

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Cases Where I Recently Used My DEA

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Conditions Which May Require Pain Management

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

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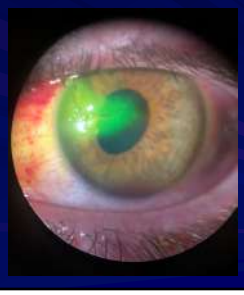
A "bit" Too Close

99

How Deep

100

Ouch



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Optometric Education Consultants

Questions? Thank You!

Treatment of Pain
Opioid Choices and Issues for Patient and Practitioner

Greg Caldwell, OD, FAAO
Nashville – Music City Fall Classic 2022
Optometric Education Consultants
Sunday, October 23, 2022

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