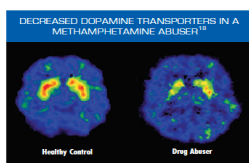


Prescription Drug Abuse

- Prescription medications, including opioid pain relievers (such as OxyContin® and Vicodin®), anti-anxiety sedatives (such as Valium® and Xanax®), and ADHD stimulants (such as Adderall® and Ritalin®), are commonly misused to self-treat for medical problems or abused for purposes of getting high or (especially with stimulants) improving performance

Impaired Brain Function with Long Term Drug Abuse

- Long term drug use decreases the normal dopamine production or receptors making patients feel "flat"
- Patients' require the drug in order to feel that high and in increased levels to obtain the previous "high"



National Institute of Drug Abuse: Drugs, Brains and Behaviour: The Science of Drug Addiction

Opioid Abuse

- Opioid pain relievers are frequently abused by being crushed and injected or snorted, greatly raising the risk of addiction and overdose.
- there is a common misperception that because medications are prescribed by physicians, they are safe even when used illegally or by another person than they were prescribed for.

Withdrawal

- The withdrawal syndrome may be very severe (except for codeine) and includes intense dysphoria (state of unease), nausea or vomiting, muscle aches, lacrimation, rhinorrhea, mydriasis, piloerection, sweating, diarrhea, yawning, and fever.
- Beyond the withdrawal syndrome, which usually lasts no longer than a few days, individuals who have received opioids as analgesics only rarely develop addiction. In contrast, when taken for recreational purposes, opioids are highly addictive.
- The relative risk of addiction is 4 out of 5 on a scale of 1 = nonaddictive, 5 = highly addictive.

Opioid Abuse/Overdose

- The most common drugs involved in prescription opioid overdose deaths include:
 - Methadone (long acting opioid for heroin abuse)
 - Oxycodone (such as OxyContin®)
 - Hydrocodone (such as Vicodin®)
- Overdose rates were highest among people aged 25 to 54 years.
- Overdose rates were higher among non-Hispanic whites and American Indian or Alaskan Natives, compared to non-Hispanic blacks and Hispanics.
- Men were more likely to die from overdose, but the mortality gap between men and women is closing.

<https://www.cdc.gov/drugoverdose/data/overdose.html>

Opioid Abuse/Overdose

- Prescription opioids can be used to treat moderate-to-severe pain and are often prescribed following surgery or injury, or for health conditions such as cancer.
- there has been a dramatic increase in the acceptance and use of prescription opioids for the treatment of chronic, non-cancer pain, such as back pain or osteoarthritis, despite serious risks and the lack of evidence about their long-term effectiveness.

<https://www.cdc.gov/drugoverdose/data/overdose.html>

Opioid Abuse/Overdose

- Research shows that some risk factors make people particularly vulnerable to prescription opioid abuse and overdose, including:
 - Obtaining overlapping prescriptions from multiple providers and pharmacies.
 - Taking high daily dosages of prescription pain relievers.
 - Having mental illness or a history of alcohol or other substance abuse.
 - Living in rural areas and having low income.

<https://www.cdc.gov/drugoverdose/data/overdose.html>

Opioid Abuse/Overdose

- Anyone who takes prescription opioids can become addicted to them
 - as many as one in four patients receiving long-term opioid therapy in a primary care setting struggles with opioid addiction.
 - In 2014, nearly two million Americans either abused or were dependent on prescription opioid pain relievers.
- Taking too many prescription opioids can stop a person's breathing—leading to death.

<https://www.cdc.gov/drugoverdose/data/overdose.html>

Opioid Abuse/Overdose

- Prescription opioid overdose deaths also often involve benzodiazepines.
- Benzodiazepines are central nervous system depressants used to sedate, induce sleep, prevent seizures, and relieve anxiety.
 - Examples include alprazolam (Xanax®), diazepam (Valium®), and lorazepam (Ativan®).
- Avoid taking benzodiazepines while taking prescription opioids whenever possible.

<https://www.cdc.gov/drugoverdose/data/overdose.html>

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Oral Pain Management

Pain Management: Oral Analgesics

- Conditions potentially requiring us of oral analgesics:
 - Corneal ulcers
 - Herpes simplex/zoster
 - Post-surgical
 - Trauma
 - Thermal burns

Oral Analgesics: Guidelines

- Make the proper diagnosis first (ie. Don't prescribe without knowing what you are prescribing for!)
- Treat the underlying cause for the pain
- Treat the pain at presentation..don't wait!
- Treat pain continuously over a 24 hour schedule
- Non-prescription drugs should be first choice and tend to be low cost
- Treat patients with the simplest and safest means to alleviate pain

Oral Analgesics: Guidelines

- Mild to moderate pain is often successfully treated with acetaminophen or NSAID
- Moderate to severe pain is best treated with opioid analgesics
- Adjunctive treatments are very valuable in pain management:
 - "RICE": rest, ice, compression and elevation
 - Mydriatic/cycloplegic useful for ocular pain
 - Bandage CL or pressure patch

Systemic NSAID's

- NSAID's are the drug of choice for treating mild to moderate ocular pain.
 - Very beneficial for treating systemic inflammation as well.
- All NSAID's are rapidly absorbed from the GI tract, highly bound in the plasma, and capable of crossing the blood-brain barrier.
- Exhibit a "ceiling effect" – there is a dosage beyond which no further analgesia occurs.
 - Produce no tolerance or dependence, increasing their safety profile.
- Variability exists in patient responses to NSAID's
 - No definitive recommendation on treatment can be given.
 - If one NSAID does not work – TRY ANOTHER.

Aspirin (ASA)

- Weak organic acid.
- Oldest non-opioid analgesic available today.
 - Reduces pain by inhibiting synthesis of the prostaglandin E_2 by irreversible acetylation and inactivation.
 - Has some CNS effect on pain by acting on the hypothalamus.
- Very good anti-inflammatory and antipyretic properties.



Aspirin



- Commercially available in multiple formulations and dosages.
 - Formulations include controlled-release tablets, enteric coated, etc.
 - Add buffers to help increase GI tolerance.
 - Adult Dosage: 325 – 650 mg every 4 hours
 - Do not exceed 4 g/day.
 - Most Common use of ASA: Inhibit platelet aggregation in patients with history of heart attacks and heart surgery.
 - Most common dosing is 81 mg/day



2019 Aspirin Recommendations

- American College of Cardiology:
 - *Aspirin should be used infrequently in the routine primary prevention of ASCVD because of lack of net benefit.*
 - low-dose aspirin should not be routinely given as a preventive measure to adults 70 years and older or to any adult who has an increased risk of bleeding

Acetaminophen



- Mechanism of Action is not well understood.
 - Possibly some CNS component
 - Very weak inhibitor of prostaglandin synthesis
- One of the most commonly used analgesics for mild to moderate pain.
 - Equal analgesic properties to ASA unless associated with inflammation, where it is less effective.

Take home: Good for pain; Good for fever;
No effect on inflammation

Acetaminophen



- Typical Adult Dosage (FDA Based):
 - 650 mg every 4 - 6 hours for Regular Strength (2 X 325)
 - Cannot take more than 10 caplets in 24 hours.
 - 1000 mg every 6 hours for Extra Strength (2 X 500)
 - Cannot take more than 6 caplets in 24 hours.
 - 1300 mg every 8 hours for Extended Release (2 X 650)
 - Cannot take more than 6 capsules in 24 hours.
- Daily dose of Extra Strength Tylenol should not exceed 3 grams!
 - This has been recently changed from 4000 mg which can be done with doctor approval.
- Should only be used for short term therapy
- Exhibits a ceiling effect, like NSAIDs and ASA.

Acetaminophen Contraindications

- Must be used in caution in all patients with chronic alcoholism or with preexisting liver impairment.
 - Should also avoid if using medications such as barbituates, phenytoin, or rifampin due to toxicity.



Dangers of Acetaminophen

- Acetaminophen overdose is the leading cause of liver failure in the U.S.
 - It sends 56,000 people to the emergency room annually and causes approximately 400 deaths yearly.
- Acetaminophen is used in so many products, people are often unaware that they are taking it, leading to more overdoses.
 - Combined with agents to get wide range of symptom coverage.
 - Antihistamines such as diphenhydramine – Tylenol PM
 - Diuretics such as Pyrilamine maleate – Midol Complete
 - Cough Suppressants such as Dextromethorphan - Nyquil

Combining Meds for More Severe Pain Relief

- Acetaminophen and Aspirin are often combined with each other and various agents to increase their analgesic effect.
 - Frequently seen in combination with narcotic analgesics.
 - Caffeine is also commonly used, especially in the treatment of migraines.
 - Excedrin Migraine
 - Acetaminophen 250 mg
 - Aspirin 250 mg
 - Caffeine 65 mg



Ibuprofen

- Adult analgesic dose: 200-400mg q4hours
 - Maximum Dosage: 2400 mg/day for pain (approved for 3200 mg/day in arthritis treatment)
- OTC: 200 mg tabs
- Rx: 300, 400, 600, 800mg tabs
 - Can prescribe 800 mg q8hrs
- Peak levels 1-2 hours
- Most renal toxic of all the NSAID's
- Brand Names: Motrin, Advil, and Nuprin



Consider Combining APAP with NSAID's for Mild to Moderate Pain Relief

- 1:00 pm: Two 325mg Tylenol
- 3:00 pm: Two 200mg Ibuprofen
- 5:00 pm: Two 325mg Tylenol
- 7:00 pm: Two 200mg Ibuprofen

Alternated every 2 hours while awake
 – Each medication is q 4 hours.



Naproxen and Naproxen Sodium

- Sodium speeds up the absorption over Naproxen (Naprosyn) alone causing it to be used more frequently.



Naproxen Sodium

- Type of Medication Determines Dosage (This is for Naproxen Sodium):
 - OTC: 220mg tablets (Aleve)
 - Rx: 275 and 550 mg tablets (Anaprox and Anaprox DS)
- Adult Dose:
 - OTC: 220 or 440 initial dose followed by 220 mg q 8 – 12 hours.
 - Rx: 550 initial dose, followed by 275mg q6-8h or 550mg q12hours.
 - Maximum Dose: 1375mg/day.

Indole Acetic Acids: Indomethacin

- Rx Only
- Available as 25, 50, 75 ER, and IV
- Adult Dosage: 25 - 50 mg TID
- Mainly used as a short term anti-inflammatory especially for conditions that do not respond to less toxic NSAIDs.
 - Indomethacin has a very high level of intolerance compared to other NSAID's.



NSAIDS Black Box Warning

- **BLACK BOX WARNING:**
 - May increase the risk of serious thrombotic events, MI, and stroke.
 - Increase risk of serious GI adverse effects such as bleeding, ulcer, and perforation.

Contraindications to NSAIDs

- Avoid in:
 - Pregnancy (especially the late trimesters)
 - Active Peptic Ulcer Disease
 - Cross Sensitivity to ASA
 - Previous Hypersensitivity to NSAIDs
 - Chronic Renal Insufficiency
- At Risk Patients Include:
 - Dehydration
 - HTN or CHF
 - Use of ACE Inhibitors
 - Advanced Age

Cox-2 Inhibitors

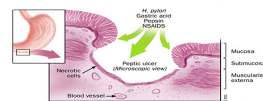
- Selective agents for only COX-2 designed to protect the GI system from the side effects seen with NSAID's.
- Major agent available on the market is Celecoxib (Celebrex).
 - Other agents Valdecoxib (Bextra) and Rofecoxib (Vioxx) were removed from the market due to increased risk of heart attacks and strokes.
- It is approved for the treatment of osteoarthritis and rheumatoid arthritis.
 - Dosage: 100 mg BID or 200 mg daily

COX-2 Selective Agents

- Must avoid use in patients with cardiovascular risk factors.
 - Studies have shown that the greater the Cox-2 selectivity the greater the risk for hypertension from NSAID's.
- Celebrex has still been shown to cause GI bleeding in patients at risk and should not be consider "safe".

Stomach disease: peptic ulcer

- There are two major causes of peptic ulcer disease: NSAIDs and chronic H pylori infection.
- Evidence of H pylori infection or NSAID ingestion should be sought in all patients with peptic ulcer.
- Alcohol, dietary factors, and stress do not appear to cause ulcer disease.
- Less than 5–10% of ulcers are caused by other conditions



Stomach disease: peptic ulcer

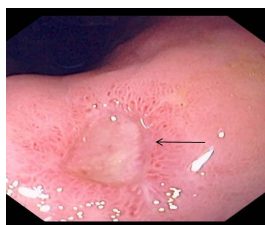
- Traditional NSAIDs inhibit prostaglandins through reversible inhibition of both COX-1 and COX-2 enzymes.
- Aspirin causes irreversible inhibition of COX-1 and COX-2 as well as of platelet aggregation.
- Coxibs (or selective NSAIDs) preferentially inhibit COX-2—the principal enzyme involved in prostaglandin production at sites of inflammation—while providing relative sparing of COX-1, the principal enzyme involved with mucosal cytoprotection in the stomach and duodenum

Peptic Ulcers: Signs and Symptoms

- Epigastric pain (dyspepsia), the hallmark of peptic ulcer disease, is present in 80–90% of patients.
 - However, this complaint is not sensitive or specific enough to serve as a reliable diagnostic criterion for peptic ulcer disease.
- Pain is typically well localized to the epigastrium and not severe. It is described as gnawing, dull, aching, or “hunger-like.”
- Approximately 50% of patients report relief of pain with food or antacids (especially those with duodenal ulcers) and a recurrence of pain 2–4 hours later.

Peptic Ulcers: Signs and Symptoms

- Upper endoscopy is the procedure of choice for the diagnosis of duodenal and gastric ulcers



NSAID-related ulcers

- COX-2 inhibitors such as celecoxib (Celebrex) are less likely to cause ulcers than aspirin
- Proton pump inhibitors (e.g. Prevacid® or Prilosec®) help to offset the risk of NSAID-related stomach ulcers
 - patients should be treated with concomitant proton pump inhibitors once daily, which results in ulcer healing rates of approximately 80% at 8 weeks in patients continuing to take NSAIDs

Oral Analgesics: Guidelines

- Never exceed maximum recommended dosages:
 - ASA: 8 grams/day
 - Acetaminophen: 4 grams/day?? (3000 likely safer limit)
 - Naproxen sodium: 1375 mg/day
 - Ibuprofen: 1200 mg/day OTC and 2400 mg/day prescription
 - Codeine: 360 mg/day



Anesthetics

- Topical Ocular Anesthetics should not be used for pain relief outside of the clinical setting.
- However, topical skin creams do have one possible use in optometry – treatment of skin lesions caused by herpes zoster.
 - Cannot be used on open wounds – only once scabs have formed.

Anesthetic Agents for Pain Relief

- OTC Option: Zostrix Cream (Capsaicin)
- Prescription Option: EMLA Cream (lidocaine 2.5% and prilocaine 2.5%)
- Must use caution near the eye.



Narcotic Analgesics

- Also known as:
 - Opiates (Any agent derived from opium)
 - Opioids (Compounds that possess morphine-like analgesic properties)
- Morphine is the standard med used to compare the effects of all other opioids.



Opioids Information

- Drug of first choice for the treatment of **severe** acute pain.
 - Block the body's natural protective mechanism for protecting areas in pain – thus never prescribe unless you know the direct cause of the pain.
- Often administered in combination with acetaminophen or aspirin to enhance the analgesic effect.
 - FDA recommended in 2011 that all prescription narcotics containing acetaminophen standardize and limit the dosage to 325 mg.
 - This is to be slowly phased in over three years (just required in January 2014).

Tolerance to Opioids

- Patients experience shorter durations of analgesia from similar dosages, followed by increased levels of pain. Requires dosages to continually be adjusted to provide desired effects.
- Withdrawal can occur if long term use is discontinued abruptly resulting in increased heart rates and blood pressure, nausea, vomiting, dilated pupils, photophobia, shivering, etc. These symptoms peak approximately 2 to 3 days after the last dose and will subside over weeks.

Patient Education

- Avoid all depressants – especially using along with alcohol.
- Must educate all patients of risks of these symptoms and caution them for driving or operating dangerous machines.
- Stomach upset can be helped by consuming the medication with food.
- Watch for signs of breathing difficulty or changes in blood pressure.

Opioids Contraindications

- Avoid in patients with history of hypersensitivity to narcotics.
 - True allergic reactions are rare and often involve skin rashes or contact dermatitis.
- Avoid in patients with acute bronchial asthma or COPD.
- Avoid in patients with a history of depression or suicidal tendencies.
- Avoid in patients with history of addiction.
- Avoid in pregnancy (Most opioids are pregnancy category C).
 - Drug Effects seem to be insignificant in nursing infants, but should recommend waiting at least 4 – 6 hours to nurse.
- Use caution in kidney or liver dysfunction due to increased accumulation of the medication.
- Must be very cautious of drug interactions and always review medications with your patient prior to prescribing.

Scheduled Medications – Most Opioids

Schedule	Description	Optometric Medications
I	Not commercially available; no approved indication	
II	Very addictive medications that are accepted for medicinal use	Oxycodone = OxyContin, Oxyfast Oxycodone + APAP = Percocet or Tylox Oxycodone + ASA = Percodan Oxycodone + NSAID = Combunox Hydromorphone (Dilaudid) Codeine Sulfate = Codeine Generic Meperidine (Demerol) Hydrocodone + APAP = Lortab or Vicodin Hydrocodone + Ibuprofen = Vicoprofen
III	Significant abuse risk, but less potent than I or II. May still contain narcotics.	Codeine + APAP = Tylenol 3 and Tylenol 4
IV	Relatively low abuse potential and limited risk	Propoxyphene (Darvon) Propoxyphene with APAP = Darvocet (Removed from Market in November 2010). Pentazocine + APAP (Talacen) Tramadol
V	Very limited abuse potential. May be OTC in some states.	Acetaminophen

Schedule III Opioids: Codeine



- Prodrug that relies on the cytochrome P-450 system to be metabolized to active drug morphine.
 - Schedule II medication if prescribed alone (Codeine Sulfate 15, 30, 60 mg generic.)
- Analgesic effect occurs within 20 minutes of ingestion and reaches a maximum at 1 – 2 hours.
 - Ceiling effect occurs.

Schedule III Opioids: Codeine

- Usually administered in combination with .
 - Tylenol 3 = Codeine 30 mg and Acetaminophen 300 mg
 - Dosage: 1-2 tablets every 4 hours.
 - Tylenol 4 = Codeine 60 mg and Acetaminophen 300 mg
 - Dosage: 1 tablet every 4 – 6 hours
 - Also available as generic with 15, 30, or 60 mg of Codeine with 300 mg of Acet. or elixer of 12 mg codeine + 120 mg Acet. per 5 mL.
 - Elixer can be used in children for pain management if >3 years.

The FDA has mandated that all prescription medications have no more than 325 mg of Acetaminophen in each capsule/tablet by January 2014.

Schedule II Opioids: Hydrocodone

- Approximately 6X more potent than codeine.
- Milder Side Effects than Codeine: Less constipation and sedation.
- Clinically believed to cause more euphoria than codeine, but this is not backed by clinical studies.

Schedule II Opioids: Hydrocodone

- Used in combination with APAP and Ibuprofen.
 - Lortab: Hydrocodone 5, 7.5, and 10 mg with APAP 325 mg
 - Dosage: 1-2 tablet every 4-6 hours
 - Lortab Elixer: Hydrocodone 10 mg with APAP 300 / 15 mL
 - Dosage: 3 tsp every 4-6 hours
 - Vicodin: Hydrocodone 5 mg with Acetaminophen 300 mg
 - Vicodin HP: Hydrocodone 10 mg with Acetaminophen 300 mg
 - Dosage: 1 tablet every 4-6 hours
 - Vicodin ES: Hydrocodone 7.5 mg with Acetaminophen 300 mg
 - Dosage: 1 tablet every 4 – 6 hours
 - Vicoprofen: Hydrocodone 7.5 mg with Ibuprofen 200 mg
 - Dosage: 1 tablet every 4-6 hours
 - Norco: Hydrocodone 5, 7.5, and 10 with 325 mg APAP

Schedule II Opioids: Oxycodone

- Approximately 10-12X more potent than codeine
 - As potent as parenteral morphine when given orally.
- Lower level of side effects in comparison to morphine, but high level of euphoria produced, thus higher level of abuse risk.



Schedule II Opioids: Oxycodone

- Available in combination with APAP, ASA, or Ibuprofen.
 - Percocet Tablets
 - 2.5, 5, 7.5 or 10 mg Oxycodone with 325 mg Acetaminophen
 - Dosage: 1 tablet every 6 hours
 - Tylox Capsules
 - 5 mg Oxycodone with 300 mg Acetaminophen
 - Dosage: 1 tablet every 6 hours
 - Percodan Tablets
 - 4.5 mg Oxycodone HCl
 - 0.38 mg Oxycodone terephthalate
 - 325 mg Aspirin
 - Dosage: 1 tablet every 6 hours
 - Combunox
 - 5 mg Oxycodone with 400 mg Ibuprofen
 - Dosage: 1 tablet daily to QID

Newly Schedule IV: Tramadol (Ultram)

- Central acting narcotic
 - Synthetic analogue of codeine.
 - Binds to mu receptors and inhibits norepinephrine and serotonin reuptake.
 - Potential for abuse is very low, but has occurred.
- Available as 50 mg tablets.
- Dosage: 50 – 100 mg q4 – 6 hours.**
 - Analgesia occurs after 1 hour.
 - Maximum dose: 400 mg/day



Tramadol Extended Release (Ultram ER)

- Available dosages of 100, 200, and 300 mg extended.
 - Begin taking 100 mg daily X 5 days
 - Increase by 100 mg if relief not met to 200 mg X 5 days.
 - 300 mg maximum daily.
- Does not work on all patients – some need heavy doses every 4-6 hours.
- More for chronic pain control.



Tramadol + APAP (Ultracet)

- Combination of:**
 - 325 mg of APAP
 - 37.5 mg of Tramadol
- Dosage: 2 tablets every 4 – 6 hours**
- Max: 8 tablets daily**



Tramadol

- Must use with extreme caution in patients taking MAO inhibitors.
- Despite low risk for addiction should still use caution in patients with history of problems.
- Similar side effects to all opioids such as dizziness, nausea, dry mouth, and sedation.
- Avoid in patients with liver or renal impairment.
- Inferior pain relief with risk of side effects has limited Tramadol's use clinically.

- First Step in Managing Acute Pain: Acetaminophen
 - If inadequate analgesia with 1000 mg TID
- Consider NSAID:
 - Ibuprofen 400 mg every 4-6 hours
- If NSAID inadequate or contraindicated:
 - Hydrocodone + APAP
- If inadequate consider in combination with Ibuprofen or may need to consider stronger options/comanagement.

Opioids

- The short-term effects may include:
 - drowsiness
 - constipation
 - light-headedness and dizziness
 - mild anxiety
 - dry mouth
 - headaches
 - nausea
 - reduced appetite
 - Confusion
- may experience the following:
 - vomiting
 - rash and itchiness
 - pinpoint pupils
 - difficult urination
 - burning sensation on the skin
 - cold clammy skin
 - trouble with breathing, such as slow or shallow breathing