

## Ocular Pain Management



Delaware Optometric Association  
February 10, 2018  
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Text NICHOLASCOLA090 to 22333 once to join

## Disclosures

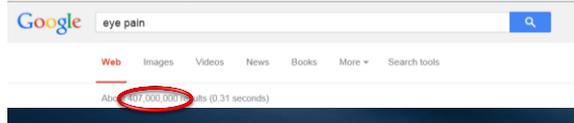
- Allergan Pharmaceuticals Speaker's Bureau
- Bio-Tissue
- BioDLogics, LLC
- Katena/IOP
- Seed Biotech
- Johnson and Johnson Vision Care, Inc.
- Shire Pharmaceuticals

## Live Survey

- Text NICHOLASCOLA090 to 22333 once to join
- Then text A, B, C, D, E to answer
  - Live
  - Immediate
  - Accurate

## Why?

- Licensure allows us to treat these patients
  - Non-steroidal anti-inflammatory agents
  - Analgesics
  - Approved controlled substances
    - Schedule II hydrocodone combination products
    - Schedule III controlled substances
    - Schedule IV controlled substances
    - Schedule IV anti-anxiety/sedative agents
    - Schedule V controlled substances
- These patients are in our chair



## Delaware

- Prescription for controlled substances
  - Schedule II controlled substances containing Hydrocodone, with a limitation on maximum 72-hour supply.
  - Schedules III, IV, and V controlled substances, with a limitation on maximum 72-hour supply.
- Prescription for the use of an oral steroid with a limitation not to exceed a single 6-day methylprednisolone dose pack.
  - Excludes the prescription of any substance delivered intravenously or by injection.
- Excludes any medication used solely for the treatment of systemic conditions outside the scope of an optometrist.

## Resources



## Course Topics

- Definition of Pain
- Types of Pain
  - Acute
  - Chronic
  - Neuropathic
- Pathophysiology of Pain
- Psychological Aspects of Pain
- Subjective Assessment of Pain
- Choices of Drugs (topical, oral, OTC, Rx)

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## Goal of Pain Management

- Prescribe the least amount of medication required to adequately control the patient's pain and have them return to normal function.
- While being careful not to interfere with the clinical picture
  - Microbial keratitis
  - Endophthalmitis

## Ocular Causes of Eye Pain



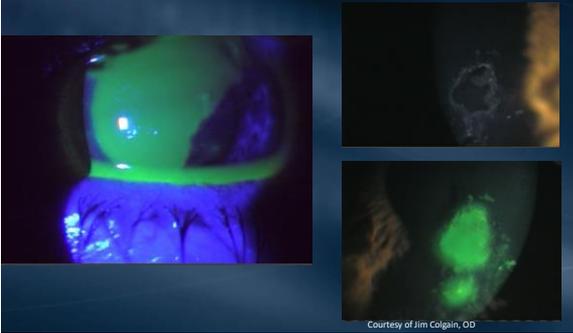
## Ocular Causes of Eye Pain



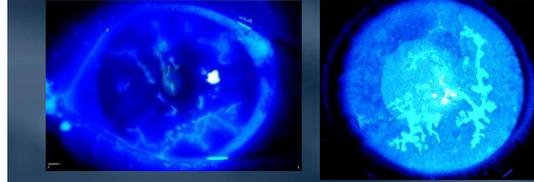
## Ocular Causes of Eye Pain



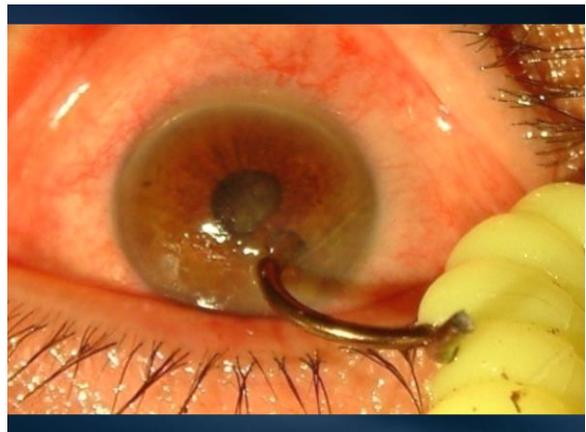
### Ocular Causes of Eye Pain



### Ocular Causes of Eye Pain



### Ocular Causes of Eye Pain



## Ocular Causes of Eye Pain

- Posterior Segment
  - Posterior Scleritis
  - Orbital Tumor ?????
  - Orbital Pseudotumor
  - Optic Neuritis
- Surgical
  - PRK / PTK
  - Penetrating Keratoplasty
    - Exposed sutures
  - Superficial Keratectomy
- Blind painful eye

## Non-ocular Causes of Eye Pain

- Sinusitis
- Meningitis
- Carotid Cavernous Fistula
- Cranial Arteritis
- Trigeminal Neuralgia
- Post-herpetic Neuralgia
- Temporal Arteritis

## Ocular Pain

- Frequently undertreated by practitioners
  - Underestimation of patient's discomfort level
  - Inadequate comprehension of pain management
  - Hesitation to prescribe controlled substances
  - Fear of addiction to pain medications
- Pain Management
  - #1- treat the cause
  - #2- treat the pain

## Definition of Pain

- usually localized physical suffering associated with bodily disorder (as a disease or an injury)
  - a basic bodily sensation induced by a noxious stimulus, received by naked nerve endings, characterized by physical discomfort and typically leading to evasive action
  - acute mental or emotional distress or suffering
  - "unpleasant sensory and emotional experience associated with actual or potential tissue damage"
- International Association for the Study of Pain (1994)

## Ocular Pain Clinical Anatomy and Pathway

- Nociceptors in peripheral tissues - i.e. skin, blood vessels, mucous membranes, cornea, etc.
  - Localization possible where nerves and nerve endings densely distributed, i.e. cornea
  - Localization not possible where nerves and nerve endings sparse or diffusely distributed, i.e. uveal tract, sinuses

## Pain

- Acute and chronic pain afflict 20-30% of population
- More than 550 million work days are lost each year in the US
  - Costs society \$560-\$635 billion / year
- New clinics solely dedicated to pain management

Condition	Number of Sufferers
Chronic Pain	100 million Americans
Diabetes	25.8 million Americans (diagnosed and estimated undiagnosed)
Coronary Heart Disease (heart attack and chest pain)	16.3 million Americans
Stroke	7.0 million Americans
Cancer	11.9 million Americans

## Four concepts of Pain Management

1. Pain is a symptom, not a disease
2. Difficult to assess objectively
3. Emotional components can be used to enhance the treatment of pain
4. Pain does have a purpose

## Types of Pain

- Acute
  - Associated with injury
  - Clear description of onset, duration, location
- Chronic
  - Defined as persisting for more than 6 months
  - Can cause changes in personality, lifestyle, etc...
  - Treatment is challenging
- Visceral
  - Diffuse, typically referred
- Neuropathic
  - Result of damage to sensory pathways
  - Described as dull, burning, or aching

## Pain

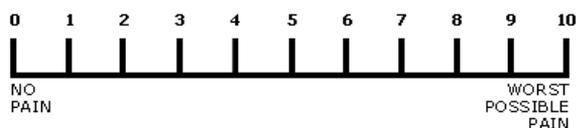
- Important to take a thorough history
  - Location
    - Surface
    - Deeper structures
  - Quality
  - Severity
  - Timing
  - Aggravating/relieving factors
  - Other medications
  - Systemic health
    - allergies

## Subjective Assessment

- Descriptive
  - Sharp
  - Dull
  - Ache
  - Stinging
  - Tingling
  - Pressure
  - Burning
  - Episodic

## Subjective Assessment

- Numerical
  - 0 = No pain
  - 1 to 5 = Mild pain
  - 6 to 7 = Moderate pain
  - 8 to 9 = Severe pain
  - 10 = Worst pain possible



## Subjective Assessment

- Visual

Wong-Baker FACES® Pain Rating Scale



## Subjective Assessment

- Verbal

No Pain      Mild Pain      Moderate Pain      Severe Pain



## Subjective Assessment

- Activity Tolerance Scale

NO PAIN      CAN BE IGNORED      INTERFERES WITH TASKS      INTERFERES WITH CONCENTRATION      INTERFERES WITH BASIC NEEDS      BEDREST REQUIRED

## Types of Pain

- Acute Pain
  - Follows a specific tissue injury or damage
  - Has a well-defined onset
  - Has obvious physical signs
  - Disappears when body heals
  - Easy to localize

## Types of Pain

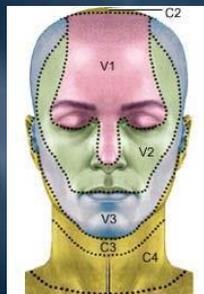
- Chronic Pain
  - May not have well-defined onset
  - Can last months to years
  - May not have any physical signs
  - May require higher doses of medications for same effect
  - May be accompanied by or lead to depression

## Types of Pain

- Neuropathic pain
  - complex, chronic pain state that usually is accompanied by tissue injury
  - nerve fibers might be damaged, dysfunctional, or injured

## Origins of Ocular Pain

- Pain fibers from head and neck are carried in CN V, VII, IX, X
  - Primary route to orbit and adnexa is ophthalmic Div CN V1



The primary sensory innervation to the orbit and adnexa is through the ophthalmic division V1 of the trigeminal nerve. The maxillary division V2 supplies most of the lower eyelid via the infraorbital branch.

Any impingement upon cranial nerve V by trauma, compression, infection, inflammation or ischemia, has the potential to initiate a direct or referred ocular sensation of pain.

## Origins of Ocular Pain

- Deep aching ocular pain originates from the uveal tract
  - Innervated by sensory division of CN V (V1)
  - Pain caused from stretching of the uveal tunics as result of acute rises in IOP from inflammation or secondary irritative spasm of EOM
- Due to the eye's neural network with many pain sensitive structures, pain is often referred.
  - Eye and frontal pain has been documented in posterior occipital lobe lesions, intracranial hemorrhages and cerebellar infarctions

## How to Manage Pain

- Emotionally
- In-Office Care
- Pharmacologically
- Alternative Methods



## How to Manage Pain

- Emotionally
  - Reassurance
  - Empathy
- In-office care
  - Immediate anesthetic
  - Cycloplegic
  - Pressure patch
  - Bandage CL

## In office Management

- Bandage Contact Lenses
  - Used for patients with corneal damage
  - Promote healing, reduce discomfort
  - Allows for topical medication application
  - Limit friction on corneal surface
  - Designed to relieve pain
  - Protect epithelium from eyelids
  - Options
    - Acuvue Oasys (Vistakon)
    - Air Optix Night and Day (Ciba Vision)
    - Purevision (Bausch and Lomb)
  - CPT Code 92071—Fitting of a contact lens for treatment of ocular surface disease
  - CPT Code 99070 ---Supply and material of lenses
  - Concerns?

## Pain Management

- Pharmacologically
  - Topical
    - Anesthetics
    - NSAIDs
    - Lubrication
    - Steroids
    - Cycloplegics
  - Oral
    - OTC
    - Prescription
      - Opioid (Narcotic)
      - Non-opioid (Non-narcotic)
    - Corticosteroids

## Pain Medication Clinical Pharmacology

- Peripheral agents
  - Direct action on nociceptors
  - Prevent stimulation or discharge of receptor
- Anesthetic agents
  - Block signal between nociceptor and opioid receptor
- Central agents
  - Interrupt pain signals and emotional responses to pain at the brainstem to cerebral cortex level

## Topical Anesthetics

- First used in 1884 in Austria
- Used to suppress corneal sensitivity
- Inhibit Na<sup>+</sup> ion channels, inhibiting nerve impulse initiation and conduction
- Creates an immediate numbing effect
- Overuse can cause deep corneal infiltrates, ulceration and even perforation
- Do not generally see systemic side effects

## Topical Anesthetics

- Tetracaine
  - More toxic to cornea
  - More discomfort upon installation
- Benoxinate
  - Combined with sodium fluorescein
- Proparacaine
  - Less discomfort than others
  - Less corneal penetration than others
  - Less impact when culturing
- *Dilute proparacaine for the management of acute corneal injuries in the emergency department.* Ball IM, Seabrook J, Desai N, Allen L, Anderson S. CJEM. 2010 Sep;12(5):389-96.

## Topical Pain Management

- Increase Lubrication
  - Comfort
  - Relief
  - Reduce surface tension
  - Consider preservative free initially
- High return and reward for simple treatment
  - Tears
  - Plugs
  - Restasis / Xiidra

## Topical Pain Management

- NSAIDs
  - Block prostaglandin synthesis by interfering with the activity of cyclo-oxygenases
    - Controls inflammation and pain post-surgically
  - Offer similar anti-inflammatory efficacy as topical steroids without other adverse effects (Rowen et al)
  - Inhibit prostaglandin release that causes pupillary miosis and are very effective at maintaining mydriasis

## Topical Pain Management

- NSAIDs
  - Diclofenac Sodium
    - Voltaren 0.1%
  - Bromfenac Sodium
    - Prolensa 0.07%
    - BromSite 0.075%
  - Nepafenac
    - Nevanac 0.1%
    - Ilevro 0.3%
  - Ketorolac Tromethamine (Allergan)
    - Acular 0.5%
    - Acular LS 0.4%
    - Acular PF 0.5%
    - Acuvail 0.45%

## Topical NSAIDs

- **Acular:** indicated for the temporary relief of ocular itching due to seasonal allergic conjunctivitis and for the treatment of post-operative inflammation in patients who have undergone cataract extraction
- **Acular LS:** indicated for the reduction of ocular pain and burning/stinging following corneal refractive surgery
- **Nevanac:** indicated for the treatment of pain and inflammation associated with cataract surgery
- **Voltaren:** indicated for the treatment of post-operative inflammation in patients who have undergone cataract extraction and for the temporary relief of pain and photophobia in patients undergoing corneal refractive surgery
- **Prolensa:** indicated for the treatment of post-operative inflammation and reduction of ocular pain in patients who have undergone cataract surgery
- **Ilevro:** indicated for the treatment of pain and inflammation associated with cataract surgery
- **BromSite:** indicated for the treatment of postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery.

## Non-approved Uses

- Foreign Bodies
- Abrasions
- RGP adaptation

## Topical NSAIDs

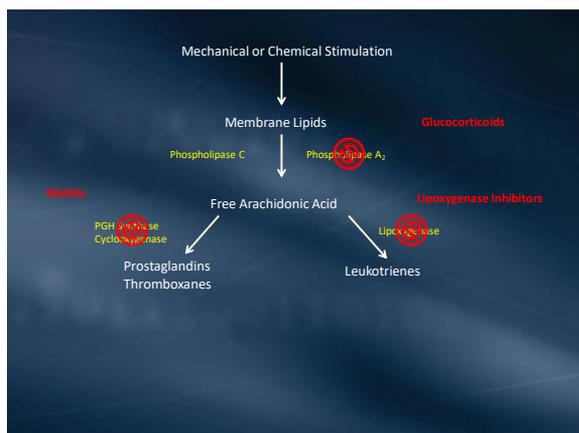
- Study by Weaver et al:
  - Compared topical NSAID to placebo in corneal abrasion patients
  - Patients had similar corneal healing time
  - Quicker pain relief with topical NSAID

## Topical NSAIDs

- Key points
  - Very effective
  - Minimal side effects
- With some non-steroidal anti-inflammatory drugs there exists the potential for increased bleeding time due to interference with thrombocyte aggregation. There have been reports that ocularly applied non-steroidal anti-inflammatory drugs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery.

## Topical Pain Management

- Topical Steroids
  - Generally not considered a true analgesic
  - Most are in suspension form
  - Acetate  $\longrightarrow$  alcohol  $\longrightarrow$  phosphate
  - Blocks phospholipase A2 in the pain pathway



## Topical Steroids

- Avoidance
  - Active herpes simplex epithelial keratitis
  - Acute bacterial or fungal infection
  - Significant corneal epithelial defect
  - Unsure of diagnosis
- Concerns
  - Increased IOP through impeding trabecular outflow
  - Cataracts

## Topical Steroids

- Don't refill or prescribe steroids over the phone
- Use steroids aggressively until inflammation is brought under control
- Consider steroid taper depending on frequency and dosage

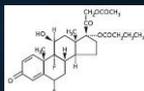
## Topical Steroids

- Approved (2008) for the treatment of inflammation and **PAIN** associated with ocular surgery
  - First steroid to receive a specific indication that includes pain along with inflammation
- First potent steroid approved in more than 3 decades
  - originally developed for dermatology
- original research was conducted in Japan and was compared to betamethasone
  - 6x more potent as an anti-inflammatory to PF
  - Found to be as potent, particularly when tx uveitis.



## Topical Steroids

- Difluorinated derivate of prednisolone purposefully engineered to achieve max efficacy
  - 2 fluorine groups make more potent --- other modifications
  - Increase drug penetration
  - Enhance anti-inflammatory activity
- Formulated as an emulsion for greater bioavailability
  - Provides consistent dosing, especially compared to PF
- No BAK, preserved in Sorbic Acid
- Dosed at half of PF
  - QID as effective as Q2h PF



## Topical Steroids

- Lotemax Ointment
  - The first new prescription ophthalmic single-agent steroid ointment in more than 20 years
- Indications
  - corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery
- Dosage and Administration
  - Apply a small amount (approximately ½ inch ribbon) into the conjunctival sac(s) four times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the post-operative period
  - 100% preservative free



## Lotemax Gel

- Indications
  - corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery
- Dosage
  - Apply one to two drops of LOTEMAX into the conjunctival sac of the affected eye four times daily beginning the day after surgery and continuing throughout the first 2 weeks of the postoperative period.
- Contraindications
  - contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures



## Lotemax Gel

- Muco-adhesive technology
- Dose Uniformity
- Low preservatives with 2 known moisturizers

## Topical Steroids

### ANTI-INFLAMMATORY POTENCY OF TOPICAL OPHTHALMIC STEROIDS

CHEMICAL ENTITY	Common Brand Names	In Vivo Relative Anti-inflammatory Activity	In Vivo Percent Aqueous Protein Reduction	In Vitro Relative GCs Internalization	In Vitro Relative Potency
Difluprednate Emulsion	Durezol	60	NA	NA	1,800
Fluorometholone Acetate	Flarex	40	NA	NA	350
Fluorometholone Alcohol	FML Forte	40	80	53	350
Dexamethasone Sodium Phosphate	Maxidex, Decadron	25	90	27	400
Loteprednol Etabonate	Lotemax, Anex	25	100	100	550
Rimeciclone	Vexol	25	NA	NA	300
Medrysone	HMS	4	NA	NA	200
Prednisolone Acetate	Pred Forte	4	110	58	600
Prednisolone Acetate	Generic	4	5	33	600
Prednisolone Sodium Phosphate	Inflamase Forte	4	NA	NA	600

SOURCES: Sendowski DP et al. Anti-inflammatory drugs. In: Bartlett JD, Jaanus SO, eds. *Clinical Ocular Pharmacology*, 5th ed. St. Louis: Butterworth-Heinemann; 2008:222-264; Samolite SS et al. *J Ocul Pharmacol Ther*. 2004;20(6):533-547.

ABBREVIATIONS: GCs, glucocorticoid receptor; NA, information not available.

## Cycloplegics

- Appropriate for most cases of ocular pain
- Mechanism of Action
  - Block action of acetylcholine (ANS)
    - Receptors located in iris sphincter and ciliary body
- Effective for relieving pain caused by ocular inflammation
  - Relax ciliary spasm
  - Help prevent posterior synechia
  - Stabilize blood-aqueous barrier

## Cycloplegics

- Atropine
  - Most potent
  - 0.5%, 1%, 2% solution
  - 1% ointment
  - Typically dosed BID
- Scopolamine
  - Shorter duration than atropine, but higher anti-muscarinic activity
  - 0.25% solution
  - Typically dosed BID to TID
- Homatropine
  - About 1/10 potent as atropine
  - 2% and 5% solution
  - Typically dosed BID to TID

## Cycloplegics

- Tropicamide and Cyclopentolate
  - Not considered therapeutic
- Risks
  - Acute angle closure
- Adverse Effects
  - Blur, photophobia
  - Neurogenic/psychiatric events

## Oral Analgesics

- Non-narcotics
  - NSAIDs
  - Acetaminophen
  - Peripheral acting
    - Ceiling effect
  - Steroids
- Narcotics (Opioids)
  - Central acting
    - No ceiling effect

## Oral NSAIDs

- Treat pain, inflammation, and fever
- Do not depress CNS like narcotics
- Block pain by inhibiting cyclooxygenase
  - Enzyme responsible for producing prostaglandins
- Some NSAIDs may inhibit migration of inflammatory cells

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## Why NSAIDs?

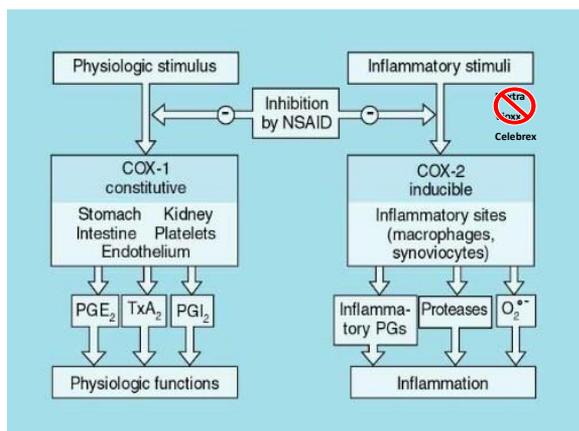
- Some available without Rx
  - Readily available
  - Inexpensive
- Effective

## Oral NSAIDs

- Side effects include
  - GI upset and ulceration
    - Prostaglandins protect GI mucosa
  - Impaired blood clotting
    - Prostaglandins help regulate clotting

## Cyclooxygenase (COX)

- COX-1
  - Mediates production of “normal” prostaglandins that benefit renal function, maintenance of GI mucosa, blood coagulation
- COX-2
  - Mediates production of “pathological” prostaglandins that cause inflammation and pain



## Oral Pain Management

- Oral NSAIDs
  - Salicylate Derivatives
    - Aspirin
  - Propionic Acid Derivatives
    - Ibuprofen, Naproxen, Naproxen Sodium
  - Acetic Acid Derivatives
    - Indomethacin
  - Enolic Acid Derivatives
    - Piroxicam

## Salicylates

- Aspirin
  - Best known oral NSAID
  - Good analgesic effect, but inhibits blood clotting and increases bleeding time
  - Effective anti-inflammatory agent
  - Can lead to GI upset
  - Effective, inexpensive, and OTC
  - Avoid in children, pregnant and nursing mothers

## Propionic Acid Derivatives

- Ibuprofen
- Naproxen
- Naproxen Sodium
- Flurbiprofen

## Ibuprofen

- Motrin, Advil
  - Better analgesia than aspirin
  - OTC, but can get prescription doses
  - Acute ocular pain can be treated with 800 mg q6h (no more than 3x/day)
  - Can cause GI distress and inhibit blood clotting
  - NSAID with lowest propensity to cause bleeding
  - Analgesic vs. anti-inflammatory

## Naproxen

### Naproxen Sodium

- Aleve
  - 1 tablet (220mg) every 8-12 hours
    - First dose can be 2 tablets
  - Available as a prescription in 275 or 550 mg tablets
    - First dose is 550 mg, followed by 275 mg every 6-8 hours

### Naproxen

- Naprosyn
  - Available in OTC or prescription doses
    - 250 mg, 375 mg, 500 mg
  - Longer duration of action
    - every 8-12 hours

## Flurbiprofen

- Ansaid
- 50 mg, 100 mg tablets
- Most potent NSAID in this class
- Scleritis treatment: 100 mg TID



## Acetic Acid Derivatives

- Indomethacin (Indocin)
  - Similar properties as other NSAIDs
  - 30-60% of patients report adverse events

## Acetaminophen

- Tylenol
  - Used for control of mild to moderate pain
  - Does not inhibit peripheral prostaglandin synthesis
    - Can be used in patients with bleeding disorders
  - Not effective for treating pain associated with inflammatory conditions
  - Has anti-pyretic effects
  - Adult dosage: 500-1000 mg q4-6h as needed
  - Adult dosage: 500-1000 mg q6h while symptoms last

## Acetaminophen

- Tylenol
  - Well-tolerated
  - Does not produce gastric irritation or affect kidney or liver function
  - COX-3?
    - Potential site for acetaminophen

## Steroids

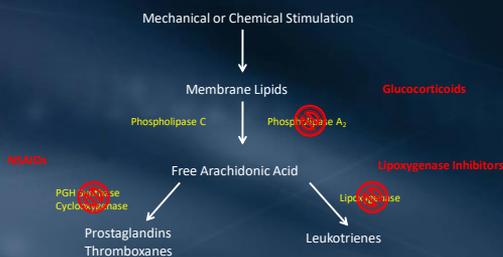
- Not a true analgesic
- Reduce inflammation and pain



## Oral Steroids

Corticosteroid	Relative Anti-inflammatory Equivalent Dose (mg)	Relative Potency
Cortisone	25	0.8
Hydrocortisone	20	1
Prednisone	5	4
Prednisolone	5	4
Triamcinolone	4	5
Methylprednisone	4	5
Dexamethasone	0.75	25
Betamethasone	0.75	25

Courtesy of Jaanus SD, Cheetham JK, Leshner GA.



## Indications

- Endocrine Disorders
- Rheumatic Disorders
- Collagen Diseases
- Dermatologic Diseases
- Allergic States
- Ophthalmic Diseases
- Respiratory Diseases
- Hematologic Disorders
- Neoplastic Diseases
- Edematous States
- Gastrointestinal Diseases
- Nervous System
- Miscellaneous

## Indications

- Ophthalmic Disease
  - Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa
  - Allergic corneal marginal ulcers
  - Herpes zoster ophthalmicus
  - Anterior segment inflammation
  - Diffuse posterior uveitis and choroiditis
  - Sympathetic ophthalmia
  - Keratitis
  - Optic neuritis
  - Allergic conjunctivitis
  - Chorioretinitis
  - Iritis and iridocyclitis

## Oral Steroids

- Potential uses
  - Uveitis
  - Scleritis
  - Arteritic AION
  - Optic neuropathy
  - Optic neuritis



## Oral Steroids

- Prednisone
  - Dosage: 1 mg, 2.5 mg, 5 mg, 10 mg, 20 mg, 50 mg
  - Depends on disease and severity
    - 5-60 mg/day
- Methylprednisolone
  - Dosage: 2 mg, 4 mg, 8 mg, 16 mg, 32 mg
  - Medrol Dosepak
    - Six 4 mg tablets day 1
    - Decrease by 1 tablet every day



## Oral Steroids Adverse Effects

### Ocular

- Cataract formation
- Increased IOP
- Increased susceptibility to infections
- Delayed wound healing

### Systemic

- Suppression of the pituitary feedback loop
- Osteoporosis
- Electrolyte imbalance and fluid retention
- Psychological manifestations of aggression, psychosis, tremors
- Diabetes mellitus
- Increased appetite and weight gain
- GI disturbances
- Increased susceptibility to infections
- Delayed wound healing

- Is there a safer alternative?
- Consult with patient's PCP?

## Schedule I

- The drug or other substance has a high potential for abuse.
- The drug or other substance has no currently accepted medical use in treatment in the United States.
- There is a lack of accepted safety for use of the drug or other substance under medical supervision.
- PCP, Methamphetamine, GHB, Marijuana

## Schedule II

- The drug or other substance has a high potential for abuse
- The drug or other substance has a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions
- Abuse of the drug or other substances may lead to severe psychological or physical dependence
- Hydrocodone combination products
  - Vicodin, Lortab
- Cocaine, Opium, Dilaudid

### Schedule III (Narcotic and Non-Narcotic)

- The drug or other substance has a potential for abuse less than the drugs or other substances in Schedules I and II
- The drug or other substance has a currently accepted medical use in treatment in the United States
- Abuse of the drug or other substance may lead to moderate or low physical dependence or high psychological dependence
- Codeine combination products
  - Tylenol with Codeine
  - ASA with Codeine
- Morphine combination products

### Schedule IV

- The drug or other substance has a low potential for abuse relative to the drugs or other substances in schedule III
- The drug or other substance has a currently accepted medical use in treatment in the United States
- Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule III
- Darvocet (discontinued), Valium, Ativan, Ultram

### Schedule V

- The drug or other substance has a low potential for abuse relative to the drugs or other substances in schedule IV
- The drug or other substance has a currently accepted medical use in treatment in the United States
- Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule IV
- Primarily small amounts of narcotics (codeine) used as anti-tussives or anti-diarrheals

### Opioid Analgesics

- Chemical compounds that have morphine-like pharmacological actions
- Potential for abuse
- Regulated by US Government
  - DEA # required
- Bind opioid receptors in brain and spinal cord
- Provide relief from moderate to severe pain

### Opioid Analgesics

- Contraindications
  - Patients over 75 years old
  - Pregnant women
  - Patients with hepatic or renal disease
- Side effects
  - Nausea/vomiting
  - Drowsiness
  - Respiratory depression
  - Mental clouding/euphoria
  - Miosis (with morphine overdose)
- Caution with addiction

### Opioid Analgesics

- Codeine
  - Usually combined with aspirin or acetaminophen
  - Analgesic effect usually seen at 20-30 minutes
    - Maximum effect at 60-120 minutes
  - Can cause sedation and constipation
- Hydrocodone
  - 6x more potent than codeine
  - Available in combination with aspirin, ibuprofen, or acetaminophen

## Codeine

- Tylenol with Codeine #3
  - 30 mg Codeine with 300 mg Acetaminophen
  - 1-2 tablets every 4 hours
  - Schedule III
- Tylenol with Codeine #4
  - 60 mg Codeine with 300 mg Acetaminophen
  - 1 tablet every 4 hours
  - Schedule III

## Hydrocodone

- Vicodin
  - 5 mg hydrocodone with 500 mg acetaminophen
  - 1-2 tablets every 4-6 hours
  - Schedule II
- Vicodin HP
  - 10 mg hydrocodone with 660 mg acetaminophen
- Vicodin ES
  - 7.5 mg hydrocodone with 750 mg acetaminophen
- Vicoprofen
  - 7.5 mg hydrocodone with 200 mg ibuprofen

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	Non-opioids	Opioids (Narcotics)
Primary Site of Action	Site of the injury	Brain and central nervous system
Require Doctor's Prescription?	Some do, some don't	All require prescription from a doctor
Potency of Pain Relief	Mild to moderate	Moderate to very strong
Interfere with mental activities?	No	Yes
Can reduce emotional distress in addition to pain	No	Yes
Can result in dependence and addiction?	No	Yes
Ceiling Effect?	Yes	No
Interact with alcohol, most sleeping medications, and tranquilizers?	No	Yes
Common Side Effects	Stomach irritation, abdominal pain, gastric ulcers	Constipation, nausea & vomiting, Urine retention, Mental clouding, Dizziness, and sleepiness, Feelings of euphoria

## Ultram

- Indications
  - Management of moderate to moderately severe pain
- Contraindications
  - Acute intoxication with any of the following: alcohol, hypnotics, narcotics, centrally-acting analgesics, opioids or psychotropic drugs
- Useful in corneal abrasions, pain management

## Ultram (tramadol HCl)

- Approved as non-controlled analgesic (1995)
- Indicated for moderate to moderately severe pain
- Central acting analgesic
- Synthetic analog of codeine
- Binds to opioid receptors
- Initially not approved as controlled substance
  - Initially thought to have low abuse potential
  - Opioid-type dependence has been reported
- Mechanism of Action

## Ultram

- Initially thought to have low abuse potential
- Increasing abuse
  - 2005: 6300 ER visits
  - 2008: 11,850 ER visits
  - 2009: 15,349 ER visits
  - 2010: 16,251 ER visits
  - 2011: 21,700 ER visits
- Now labeled as Schedule 4

## Ultram

- Ultram tablets
  - 50-100 mg tramadol HCl
  - 1-2 tablets every 4-6 hours
  - Do not exceed 400 mg/day
  - Safe for geriatric patients
- Ultracet
  - 37.5 mg tramadol/325 mg acetaminophen
  - Indicated for short term management of acute pain
  - 2 tablets every 4-6 hours as needed



## Ultram

- Ultram ER
  - Indicated for the use of chronic pain in patients who need round-the-clock treatment or for extended period of time
- Supplied as 100 mg, 200 mg, 300 mg tablets



## Gabapentin

- Gabapentin (Neurontin, Gabarone)
  - GABA analog
  - initially synthesized to mimic the structure of gamma-aminobutyric acid (GABA)
  - Mechanism of Action: unknown

## Gabapentin

- Indications
  - Epilepsy
  - Post-herpetic neuralgia
- Contraindications/Cautions
  - Impaired renal function
  - Elderly patients
  - Hypersensitivity to drug/class/compound
- Off label uses
  - Migraines
  - Neuropathic pain

## Gabapentin

- Neuropathic pain
  - Post-PRK use
    - 100-300 mg tid x \_\_\_\_\_ days
  - HZO
- Maximum daily dose 3600 mg

## Lyrica (pregabalin)



- Indications
  - Neuropathic pain associated with diabetic peripheral neuropathy
  - Postherpetic neuralgia
  - Adjunctive therapy for adult patients with partial onset seizures
  - Fibromyalgia
  - Neuropathic pain associated with spinal cord injury

## Lyrica (pregabalin)

- Contraindications
  - Known hypersensitivity to pregabalin or any of its components
- Warnings/Precautions
  - Angioedema (e.g., swelling of the throat, head and neck) can occur, and may be associated with life-threatening respiratory compromise requiring emergency treatment.
  - Hypersensitivity reactions (e.g. hives, dyspnea, and wheezing) can occur. Increased seizure frequency may occur in patients with seizure disorders if LYRICA is rapidly discontinued.
  - Antiepileptic drugs, including LYRICA, increase the risk of suicidal thoughts or behavior.
  - LYRICA may cause peripheral edema. Exercise caution when co-administering LYRICA and thiazolidinedione antidiabetic agents.
  - LYRICA may cause dizziness and somnolence and impair patients' ability to drive or operate machinery

## Lyrica (pregabalin)

- Other adverse reactions noted during clinical studies
  - Frequent: Conjunctivitis, Diplopia
  - Infrequent: Abnormality of accommodation, Blepharitis, Dry eyes, Eye hemorrhage, Photophobia, Retinal edema
  - Rare: Anisocoria, Blindness, Corneal ulcer, Exophthalmos, Extraocular palsy, Iritis, Keratitis, Keratoconjunctivitis, Miosis, Mydriasis, Night blindness, Ophthalmoplegia, Optic atrophy, Papilledema, Ptosis, Uveitis

## Lyrica (pregabalin)

- Dosage forms and strength
  - Capsules: 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, and 300 mg
  - Oral Solution: 20 mg/ mL

## Lyrica (pregabalin)

## Lyrica (pregabalin)

## Alternative Pain Management Options

### Acupuncture?

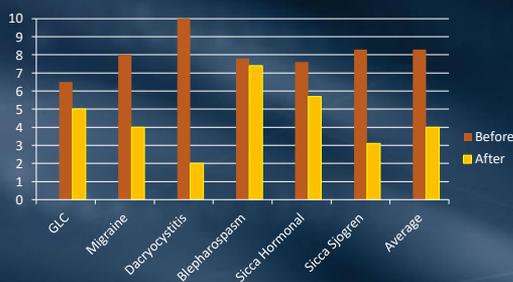
- 2002, N
- Showed reduction in pain
- Ophthalm
- Dry Eye
- Bleph



## Visual Analog Scale (VAS)



## VAS in Ophthalmic Pain



## New technology

- Research published in American Chemical Society Journal (*Langmuir*)
- University of Florida
  - Anuj Chauhan, PhD
- Soaked CL in lidocaine
  - 90% released over period of 2 hours
- Soaked CL in lidocaine (added nanoparticles of Vitamin E)
  - Released over period of 6-11 hours
- Treatment for PRK surgery
- 8 years until market

Peng, CC, Burke, MT, Chauhan, A, "Transport of Topical Anesthetics in Vitamin E Loaded Silicone Hydrogel Contact Lenses", *Langmuir*, 2012 28(2):1478-87

## Future options

- Applying genomics and other technologies to understand pain
  - Advances in basic and clinical genetics are making it possible to both characterize genetic factors related to pain sensitivity and develop novel therapeutic approaches.
- New technologies such as microarray-based assays to better understand the mechanisms of pain and analgesia
- Identify new targets for analgesic drugs
- Test the efficacy and adverse reactions of newly developed or currently used drugs to treat pain

## Future options

- Use computer-assisted technology to capture and quantify pain experiences
  - combined with existing methods to more accurately and consistently measure pain over time and across groups, diseases, and conditions.
- Research will continue identifying biomarkers and biological pathways associated with painful conditions resulting from the use of drugs to treat diseases such as cancer and HIV/AIDS

(<http://www.umgcc.org/research/et.htm>).

## Helpful websites

- [www.epocrates.com](http://www.epocrates.com)
- [www.rxlist.com](http://www.rxlist.com)
- [www.medscape.com](http://www.medscape.com)
- [www.drugstore.com](http://www.drugstore.com)
- [www.medlineplus.gov](http://www.medlineplus.gov)
- [www.drugs.com](http://www.drugs.com)
- [www.dea.gov](http://www.dea.gov)

## Patient Management

- Things to remember:
  - Take thorough history and physical exam to determine underlying source
  - Acknowledge severity of patient's pain
  - Offer sympathy and reassurance
  - Giving prescription gives control back to patient

## Final Thoughts

- Look before you prescribe
  - Thorough health history
    - Ulcers, bleeding conditions, liver or kidney problems, pregnancy, breathing issues
  - Physical exam
  - Allergies, drug interactions
- Consult your local pharmacist



## Thank you



Please feel free to contact us:

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