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Seeing your Way to Diagnosing and Treating Pain

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Disclosures

- Speakers bureau/advisory board:
 - Alcon
 - Aerie
 - Azura
 - Allergan
 - Akorn
 - B&L
 - OCUSOFT
 - Bruder
 - TearLab
 - J&J
 - Sight Sciences
 - Visus Pharmaceuticals
 - Tarsus
 - Sun Pharma

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Feel the pain!!!

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H47TDX

- H47TDX
- Peloton Referral Number!
 - Get one.

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Optometric indications

- For ocular pain, process is usually acute
 - Need for pain relief for only 24-36 hours or less
- Most often, topical only may be enough
 - Cycloplegia
 - Topical NSAIDs
 - Bandage

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Optometric Indications

- Corneal/conjunctival trauma
 - Abrasion
 - Foreign body
- Traumatic hyphema
- Surgery
 - Refractive
 - Cataract
 - Retinal



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Before treatment

- Determine etiology of pain and treat **before** beginning pain management!
- Nature of pain:
 - FOLDAR: frequency, onset, location, duration, association, relief
 - Severity
- What have you done already that helps/doesn't help?



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Before treatment

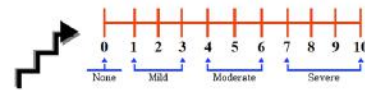
- Assess the level of pain **before** initiating treatment
 - Numerical scale
 - Pictures: Wong-Baker
- Make sure level is **decreasing** with treatment



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Before treatment

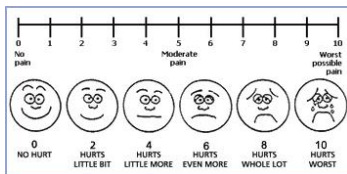
- Numerical Scale



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Before treatment

- Wong-Baker Pain Classification Scale



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Before treatment

- Medical history
 - pregnancy, alcohol use, anti-depressants
- Drug history
 - CNS medications, coumadin, digoxin, **OTC's**, etc.
- Allergy history
 - Esp. ASA etc.



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Topical Pain Relievers

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Topical Pain Relievers

- Cycloplegics
 - Block acetylcholine, a stimulatory neurotransmitter of the ANS
 - Cause pupillary dilation and relaxation of ciliary body
 - Relaxation of ciliary spasm causes pain reduction as well as stabilizes the blood-aqueous, decreasing inflammation

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Topical Pain Relievers

- Cycloplegics
 - Tropicamide: 0.5-1%; qid; 4-6 hrs
 - Cyclopentolate: 0.5, 1, 2%; tid; 2-24 hrs
 - Homatropine: 2, 5%; bid-qid; 1-3 days
 - Scopolomine: 0.25%, bid, 3-7 days
 - Atropine: 0.5,1,2%; bid-tid; 6-12 days

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Topical Pain Relievers

- Cycloplegics
 - Tropicamide: 0.5-1%; qid; 4-6 hrs
 - Cyclopentolate: 0.5, 1, 2%; tid; 2-24 hrs
 - **Homatropine: 2, 5%; bid-qid; 1-3 days**
 - Scopolomine: 0.25%, bid, 3-7 days
 - Atropine: 0.5,1,2%; bid-tid; 6-12 days

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Topical Pain Relievers

- NSAID's
 - Inhibition of prostaglandin synthesis by blockage of cyclooxygenase (COX)
 - Classic Triad effect
 - Reduced inflammation
 - Maintained pupil dilation
 - **Induced analgesic effect**

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Topical Pain Relievers

- Non-steroidal Anti-inflammatory Agents
 - Ketorolac (Acular): 0.5%; qid
 - Diclofenac (Voltaren): 0.1%; qid
 - Bromfenac (Prolensa): 0.07%; QD
 - Bromfenac (Bromsite): 0.075% Bid
 - Nepafenac (Ilevro): 0.3%; QD
 - Flurbiprofen (Ocufen): 0.03%
 - Suprofen (Profenal): 1%
- Steroid options

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Durezol (difluprednate 0.05%)

- First steroid to receive an indication for postoperative pain management
 - Also for postoperative inflammation
- FDA approved June 2008, available early 2009
 - Sirion Therapeutics
 - Acquired by Alcon March 2010
- QID starting day after sx
- ≈\$100 per 5 ml



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New Players and Old Friends

- Lotemax SM
 - (loteprednol etabonate ophthalmic gel) 0.38%
 - tid
- Inveltys
 - (loteprednol etabonate ophthalmic suspension 1%)
 - bid
- Flarex
 - (fluorometholone acetate ophthalmic suspension) 0.1%



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Lotemax 0.5% Ophthalmic Ointment

- Indications
 - Treatment of Post Operative Pain and inflammation following ocular surgery
- ½ inch ribbon qid x 2 weeks starting day after surgery



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Lotemax 0.5% Ophthalmic Ointment

- In 2 studies of 805 patients:
 - less post operative inflammation at post op day 8 vs. vehicle (34-32% vs. 11-14%)
 - Higher rate of complete resolution of anterior chamber cells and flare (34-45%)

Resolution of Anterior Chamber Cells and Flare and Pain at Visit 5: Integrated Intent-to-Treat Population*			
	Lotemax ointment (n=404)	Vehicle (n=401)	Difference (95% CI) P value
Complete resolution of anterior chamber cells and flare	112 (27.7%)	50 (12.5%)	15.2% (9.8%, 20.5%) <0.0001
Grade 0 (no) pain	305 (75.5%)	173 (43.1%)	32.4% (25.7%, 39.2%) <0.0001

*Lotemax, loteprednol etabonate; CI, confidence interval.



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Lotemax 0.5% Ophthalmic Ointment

- Contraindications:
 - Viral disease of cornea/conj (HSV), mycobacterial or fungal infection of eye
 - Should not be used in children
 - May interfere with amblyopia therapy by hindering ability to see out of operated eye
- Adverse effects:
 - AC reaction (25%): conjunctival hyperemia, corneal edema, eye pain (4-5%); HAs (1.5%)
 - IOP increased > 10 mm in 3 pts
 - Check IOP after 10 days of use



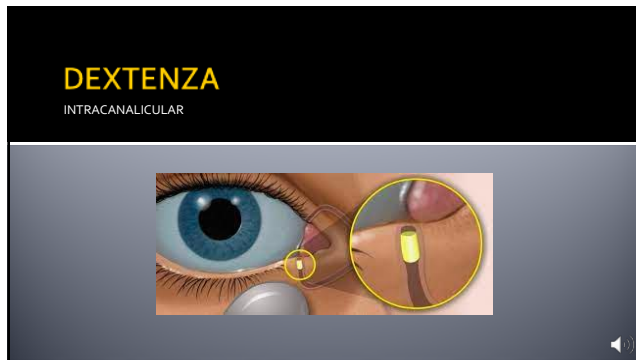
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DEXTENZA (Ocular Therapeutix)

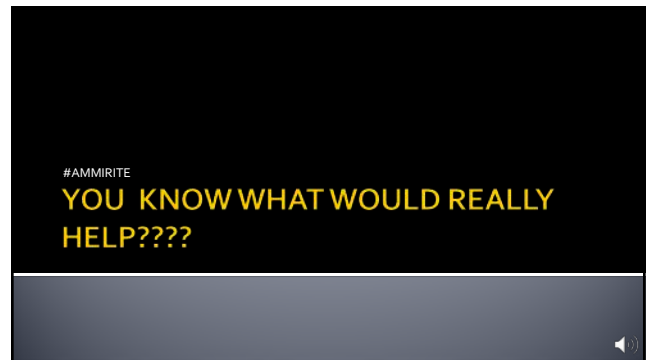
- Dextenza (dexamethasone ophthalmic insert 0.4% mg)
 - Indicated to treat inflammation and pain following cataract surgery
 - Statistically significant level of patients were pain-free on post-op day 8



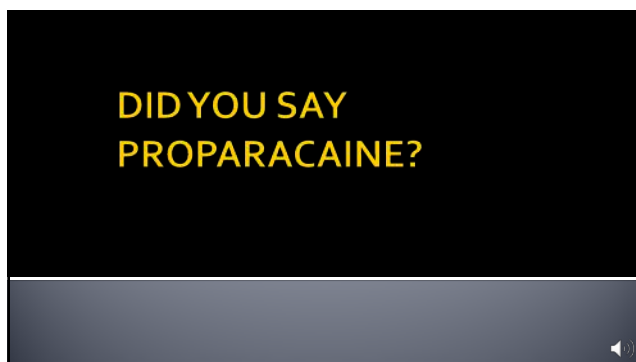
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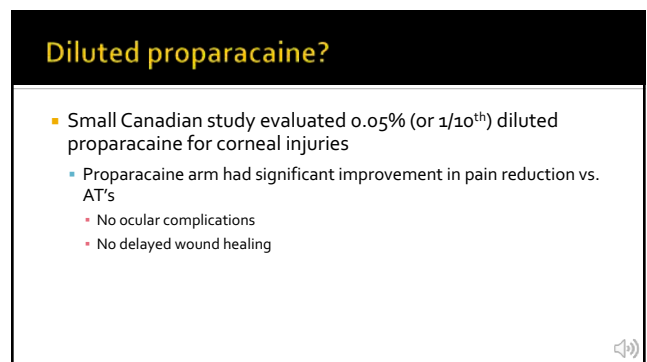
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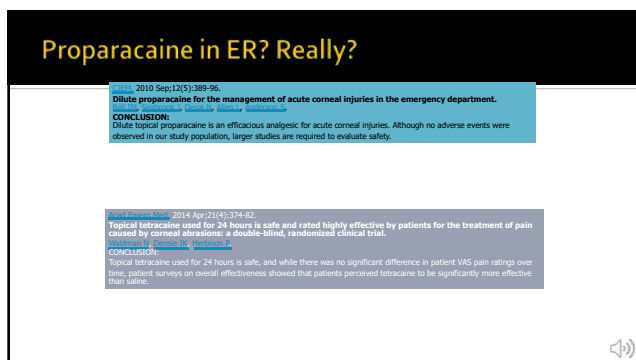
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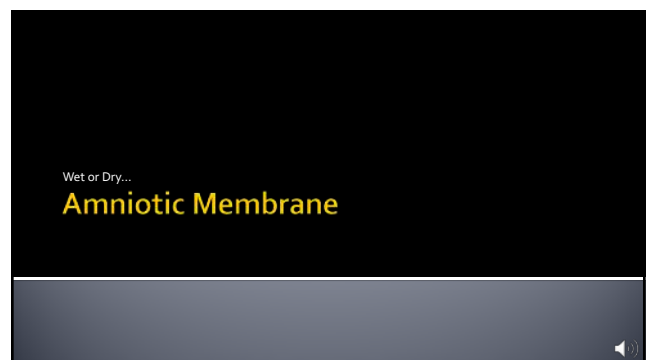
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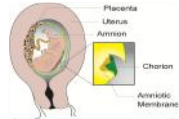
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Amniotic Membrane

- Amniotic membrane is the inner most lining of the placenta (amnion) and shares the same cell origin as the fetus
- Contains cytokines and growth factors
 - Anti-Inflammatory (protease inhibitors)
 - Anti-Angiogenic
 - Aids in rapid wound healing and re-epithelialization
 - Anti-Scarring

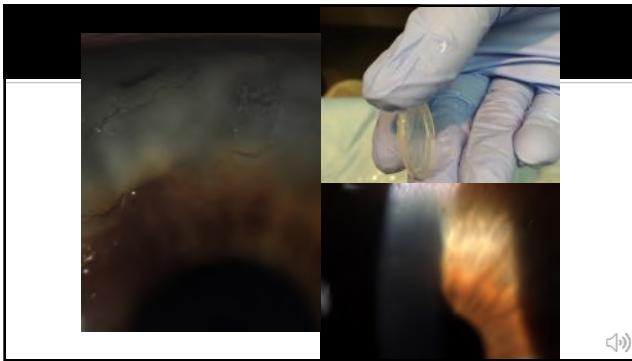


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Cryopreserved amniotic membrane is a biologic therapy that can:

- Promote regenerative healing
- Reduce inflammation
- Minimize scar formation
- Inhibit angiogenesis
- Minimize pain

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Cell_Sci. 2019 Jun 18;1(1):108-136. doi: 10.1016/j.celsci.2017.10.005. Epub 2017 Oct 13.

Efficacy of self-retained cryopreserved amniotic membrane for treatment of neuropathic corneal pain.

Moore AP, Jensen J.
© Author information

Abstract

PURPOSE: Treatment of neuropathic corneal pain (NCP) remains intricate, and involves a long-term combined multistep approach. The self-retained cryopreserved amniotic membrane (PROKERA® Bio-Tissue, Miami, FL) has been utilized for multiple ocular surface disorders. We evaluate the efficacy, safety, and tolerability of Prokera® Bio (PKS) and Prokera® Clear (PKC) in the treatment of NCP.

METHODS: Retrospective case series of 9 patients who received PKSPKVC for the acute treatment of NCP. Patient demographics, prior therapies, clinical examination, duration of PKSPKVC retention, changes in pain severity, corneal subbasal nerve density and morphology by in vivo confocal microscopy (IVCM), HRT3/RCM, Heidelberg Engineering, Heidelberg, Germany), and adverse events were recorded.

RESULTS: PKSPKVC were placed in 10 eyes of 9 patients. Pain severity improved by 72.5 ± 6.4% (from 6.3 ± 0.9 to 1.9 ± 0.6, scale 1–10, p = 0.0025) after retention for 4.4 ± 1.1 days. Despite shorter retention for 4.0 ± 0.7 days in patients with ring dysplasia (6 eyes) or premature implant disengagement (2 eyes), pain severity still improved by 63.1 ± 12.5% (from 6.8 ± 1.0 to 2.4 ± 0.6, p = 0.009). During a follow-up of 3.3 ± 0.8 months, two patients reported recurrence of pain after 2.3 and 8.6 months respectively, treated effectively with additional PKSPKVC. IVCM showed a 36.5 ± 17.8% increase in total nerve density, from 17,700.9 ± 1515.7 to 24,281.5 ± 2043.5 units/mm² (p = 0.047), while the fellow PKSPKVC-untreated eye did not show a significant interval change. Main nerve trunk and branch nerve densities were not statistically different. Dendritic cell density decreased from 48.0 ± 8.2 to 32.0 ± 6.0 cells/mm² (p = 0.01).

CONCLUSIONS: PKSPKVC provide a safe and effective treatment approach to achieve sustained pain control in patients with NCP.
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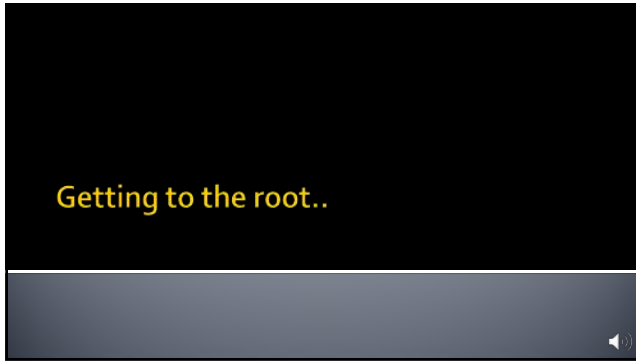
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"Dry" Amniotic Membrane

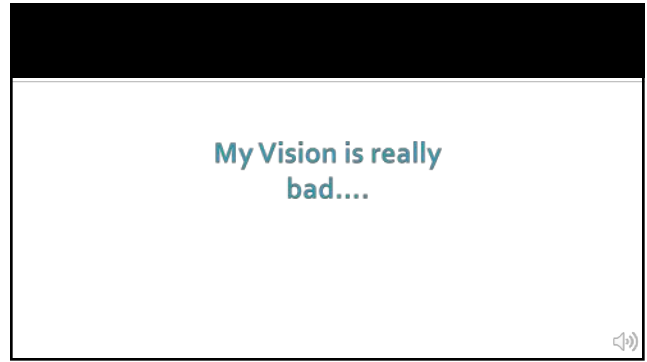
- AcellFX (Thea)
 - Acellular amniotic membrane
 - 5mm
 - Stored at room temperature
 - Up to 5 years



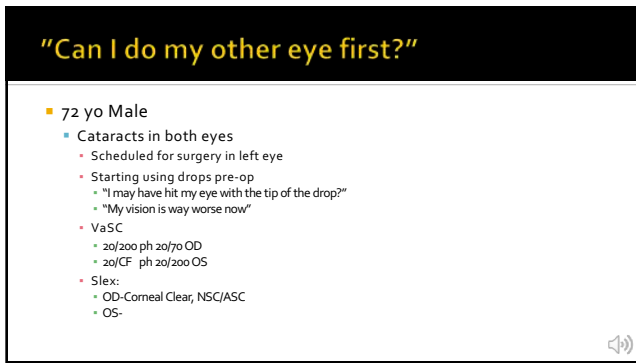
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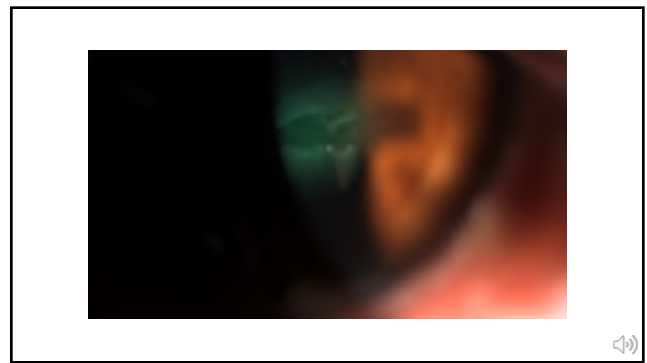
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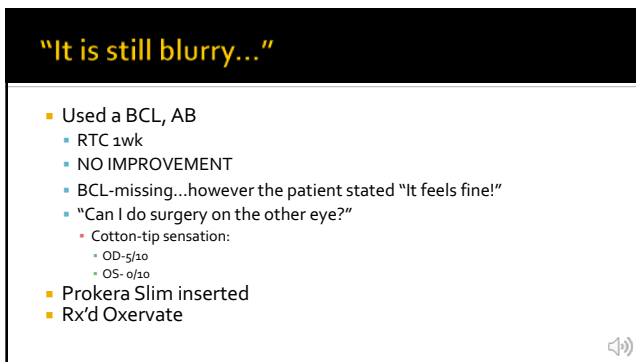
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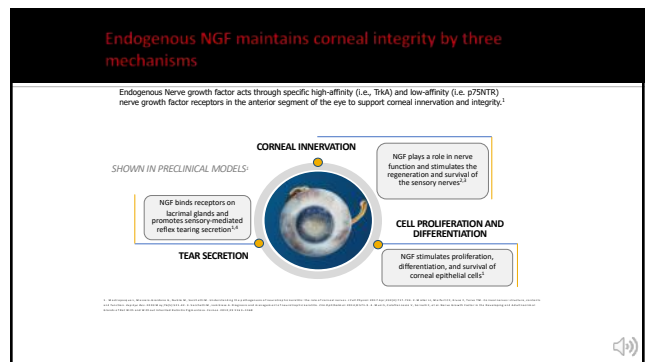
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Active ingredient structurally identical to human nerve growth factor produced in ocular tissues



- Naturally occurring neurotrophin is responsible for differentiation, growth, and maintenance of neurons¹
- The regenerative potential of nerve growth factor (NGF) was discovered by Nobel-prize winning scientists in the early 1950s¹
- Cenegermin-bkbj, a novel recombinant human nerve growth factor (rhNGF), is **STRUCTURALLY IDENTICAL** to the NGF protein²



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Oral Analgesics

- Three main categories
 - Over-the-counter
 - Aspirin, tylenol, advil
 - Non-Narcotic prescription
 - Narcotic prescription



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Over-The -Counter



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Aspirin (Acetylsalicytic acid)

- Over the counter
 - Generic, Bayer, Excedrin etc
- 325 mg, 500 mg
- Dose: 650-975 mg q 4 hr
- Not great for pain relief
- 81 mg for strokeprevention



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Aspirin (Acetylsalicytic acid)

- Contraindications
 - Upper GI disease (ulcers)
 - Bleeding disorders
 - **Kids < 18 with viral illness (flu, pox)**
 - **Reye' s disease**
 - More than 3 alcoholic beverages/day
 - Aspirin allergy
 - pregnancy
 - category D: positive evidence of risk



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Acetaminophen (APAP)

- Tylenol
- Much better pain reliever than ASA
 - no platelet or anti-inflammatory function
- 325 mg, 500 mg (extra strength)
- Dose: 650-975 mg q 4 hr
 - New max: 3000 mg/day
 - 8 regular, or 6 extra-strength
- OK with pregnancy



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Acetaminophen

- Contraindications
 - liver disease
 - alcoholism
 - hypersensitivity to APAP in past
 - Ok to use in pregnancy, kids with viral infections, bleeding disorders, upper GI disease and ASA allergy



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OTC NSAID's

- Ibuprofen
 - Advil, Motrin, Generic
 - 200, 400, 600, 800 mg q 4 hr
 - max dose 2400 mg/day
 - less GI toxicity <1600mg/day
 - Best used for anti-inflammatory control



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OTC NSAIDs

- Naproxen sodium (Aleve, Anaprox)
 - 220 mg q 8-12 hr
 - 2 pills as loading dose
 - No more than 3 pills per 24 hrs
- Ketopriifen (Orudis OTC)
 - 25-75 mg q 4-6 hr



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Excedrin

- Various amounts of ASA and APAP
 - Tension
 - Migraine
 - Extra-strength
- 65 mg caffeine
 - pain reliever aid
- 2 tabs q 6 hr
- Not to exceed 8/24 hrs



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Non-Narcotic Prescription



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Prescription NSAIDs

- **Naproxen (Naprosyn)**
 - **500 mg initial dose, then 250 mg q6-8h**
- Fenoprofen (Nalfon)
 - 200 mg q4-6 hr
- Oxaprozin (Daypro)
 - 600-1200 mg qd
 - For RA only



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Prescription NSAIDs

- **Indomethacin (Indocin)**
 - 25 mg bid-tid
 - no general pain indication
- Ketorolac (Toradol)
 - 10 mg qid
- Etodolac (Lodine)
 - 200-400mg qid



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Prescription NSAIDs

- Diclofenac (Voltaren)
 - 75 mg bid
- Diclofenac Potassium (Cataflam)
 - 50 mg bid or tid
 - 75 mg bid



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Prescription NSAIDs

- Sulindac (Clinoril)
 - 150-200 mg bid
- Nambumetone (Relafen)
 - 500-750 mg bid
 - RA only
- Tolmetin (Tolectin)
 - 400 mg tid or qid



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Prescription NSAIDs

- Flurbiprofen (Ansaid)
 - 50 mg qid
- Piroxicam (Feldene)
 - 10-20 mg qod
 - RA or osteoarthritis only
- Meloxicam (Mobic)
 - 7.5 mg qd
 - RA or osteoarthritis only



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NSAIDs

- Contraindications
 - upper GI disease
 - hypersensitivity to NSAID or ASA
 - diabetics with kidney disease
 - avid alcohol use
 - pregnancy



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Other uses for oral NSAIDs

- Uveitis
 - inflammatory control
 - may prevent rebound when tapering chronic cases
- CME
 - not as good as topical
- Episcleritis
- Scleritis
 - very useful drugs



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Uveitis-Advil

- To shorten or eliminate the use of oral or high-dose topical steroids for anterior uveitic inflammation,
 - Oral ibuprofen
- 2,400 to 3,000mg/day (given standard contraindications)
 - substitute for steroids or used as adjunct therapy.”



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Uveitis-Advil

- Prodromally in certain forms of recurrent uveitis—
 - Fuchs' very prodromal awareness of an acute attack
 - libuprofen proved to be effective in reducing the recurrences and/or the intensity of the recurrence.



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Oral Narcotic Agents



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DEA Schedules

- Schedule I
 - High Abuse potential
 - No approved medical use
 - Only available for investigational use
 - Ex: MJ, LSD, heroin
- Schedule II
 - High Abuse potential
 - **Written prescription only with no refills**
 - Ex: amphetamines, cocaine, **hydrocodone**



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DEA Schedules

- **Schedule III**
 - **Moderately high abuse potential**
 - **Written or telephone prescriptions with refills allowed**
 - **ex: Tylenol with codeine**
- Schedule IV
 - Moderate abuse potential
 - Written or telephone prescriptions with refills allowed
 - ex: phenobarbital



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DEA Schedules

- Schedule V
 - Low abuse potential
 - No prescription needed
 - ex: Robitussin A-C (contains less than 100 mg codeine per 100 ml)



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State Laws

- **PA State Law For Optometrists**
 - Codeine with ASA or APAP: pentazocine; propoxyphene; tramadol
 - Pursuant to Section 2 of the Optometric Practice and Licensure Act, the practice of optometry does not include the use of Schedule I and Schedule II controlled substances. Therefore, starting on October 6, 2014, Pennsylvania optometrists are not authorized to prescribe HCPs.
- **NY State Law For Optometrists**
 - No RX analgesics
- **NJ State Law For Optometrists**
 - III-V
 - No time limit: must be related to eye care



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State Laws

- **South Carolina oral medications** including Schedules II (hydrocodone-combination products) (narcotic), III (narcotic and non-narcotic), IV, and V drugs.
 - Prescribe oral steroids (21 day treatment)
- **CA State Law for Optometrists**
 - Schedule III *if direct indication for ocular pain*
 - *No more than 3 days (72 hrs)!!!*
 - *NEW: Also can request Schedule II for hydrocodone (Vicodin)*



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State Laws

- **GA State Law For Optometrists**
 - Schedule III
 - Over 72 hours may not be done without consultation with the patient's physician
- **FL State Law For Optometrists**
 - Tramadol or tylenol 3
 - 72 hrs max
- **AL State Law For Optometrists**
 - Schedule III with exception of hydrocodone agents
 - 96 hr limit



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State Laws

- **Arizona State Law For Optometrists**
 - Schedule III only
- **Colorado**
 - any controlled substance for ocular pain and inflammation except those specified in schedules I and II
- **New Mexico**
 - Oral analgesic medications, including schedule III through V controlled substances
- **Washington:**
 - Schedule II-V
 - Limited to 7 days per single condition



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State Laws

- **Nevada**
 - Schedule III
 - 72 hours only, no refills
- **Utah:**
 - Schedule III for pain of the eye or adnexa
 - Not to exceed 72 hrs in duration and may not be refilled
- **Oregon:**
 - OD shall consult with MD prior to extending treatment with schedule III analgesics beyond 7 days
- **HI State Law for Optometrists**
 - Currently no controlled substances are allowed



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State Laws

- **SC State Law For Optometrists**
 - Schedule III
- **NC State Law for Optometrists**
 - Schedule II-V
- **TN State Law for Optometrists**
 - Therapeutically certified ODs may utilize any pharmaceutical agent rational to the treatment of eye disease
- **MS State Law for Optometrists**
 - Schedule IV and V only (?)



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State Laws

- MA State Law For Optometrists
 - No RX analgesics
 - Current bill requesting Schedule III-V
- RI State Law For Optometrists
 - Schedule III-V for no more than one 72 hour supply
- CT State Law For Optometrists
 - Schedule II-V for no more than 72 hours
- ME State Law For Optometrists
 - Schedule III-V "with limited formulary"
- NH State Law For Optometrists
 - Schedule III-V
 - Must be for the diagnosis or treatment of disease or conditions of the human eye, adnexa or eyelids



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Morphine

- Standard drug of reference when discussing opioid effects/pain management
- Very poor when administered orally
- Many side effects
- Serious potential for abuse



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Codeine

- Useful for mild to moderate pain
- Can be fairly sedating
- GI effects common, esp. constipation
- Combined with either ASA or APAP
 - w/ APAP, works on separate CNS areas
 - w/ ASA also has anti-inflammatory action
- DEA Class II
 - Potentially causes mild or low physical dependence, but possibility of high psychological dependence if abused



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Codeine

- Tylenol with codeine
 - Tylenol 2: 15 mg codeine/300 mg APAP
 - 1-2 tabs q 4-6hr
 - **Tylenol 3: 30 mg codeine/300 mg APAP**
 - 1-2 tabs q 4-6 hr
 - Tylenol 4: 60 mg codeine/300 mg APAP
 - 1 tab q 4-6 hr
- Max dose: 360 mg codeine and 3000 mg APAP



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Codeine

- Tylenol 3: 30 mg codeine/300 mg APAP
 - 1-2 tabs q 4-6 hr
 - Max: 10 tab/day



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Codeine

- Codeine with aspirin
 - 30 mg codeine/ 325 mg ASA: Empirin with codeine #3
 - 1 tab q 4-6 hr
 - 60 mg codeine/325 mg ASA: Empirin with codeine #4
 - 1 tab q 4-6 hr



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Hydrocodone

- About 6 x more potent than codeine
- May cause less sedation and constipation than codeine
- Available with APAP and Ibuprofen
- Switched from DEA Class III to Class II, effective October 6, 2014
 - Pts will need written prescription and doctors will no longer be able to call in RX



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Hydrocodone

- Switched mainly in response to abuse of prescription painkillers
 - LA times study: of 3,733 prescription drug fatalities from 2006 to 2011, 945 deaths related to hydrocodone
 - Issue is some mid level practitioners (ODs) cannot prescribe, so may limit pts access to needed painkillers
 - Not all groups are advocates of this change



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Hydrocodone

- Trade names
 - NORCO
 - LORTAB
- Hydrocodone: one of most prescribed agents in US
 - 131 million prescriptions for 47 million patients in 2011
- More than #1 antibiotic and HTN med



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Hydrocodone

- Vicodin: hydrocodone 5 mg/300 mg APAP
 - 1-2 tabs q 4-6 hr
 - max dose 8/day
- Vicodin ES: hydrocodone 7.5 mg/300 mg APAP
 - 1 tab q4-6 hr
 - max dose 5/day



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Hydrocodone

- Vicodin HP: 10 mg vicodin/300 mg APAP
 - 1 tab q 4-6 hr
 - max dose 6/day
- Vicoprofen: 7.5 mg vicodin/200 mg IB
 - 1-2 tabs q4-6 hr
 - max dose 5/day



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Oxycodone


- Similar in potency to morphine
- 10-12x more potent than codeine
- Possibly less side effects than morphine or codeine
- Produces euphoria, so serious abuse potential exists
- DEA class II



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Oxycodone

- Percodan: 4.75 mg oxy/325 mg ASA
 - 1 tab q 4-6 hr
- Percocet: 5 mg oxy/325 mg APAP
 - 1 tab q4-6 hr
- Tylox: 5 mg oxy/500 mg APAP
 - 1 tab q 4-6 hr



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Schedule III

- Examples of Schedule III narcotics include: products containing **not more than 90 milligrams of codeine** per dosage unit (Tylenol with Codeine®), and buprenorphine (Suboxone®).

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Pentazocine

- Schedule IV drug used for moderate to moderately severe pain
- Trade names:
 - Talwin NX oral (with naloxone)
 - Fortral (with naloxone)
 - Talacen (with acetaminophen)
- Naloxone helps prevent abuse

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Pentazocine

- Dosage:
 - Depends on level of pain
 - 50 mg q 3-4 hrs
 - may increase to 100 mg if needed
 - No more than 600 mg of pentazocine in 24 hrs



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Propoxyphene

- Synthetic Opioid
- About 2/3 as potent as codeine
- Causes more drowsiness than codeine
- Combined with ASA or APAP
- DEA Class IV
- **Pulled from market in US and Europe due to increased heart attacks**

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Propoxyphene

- Darvon compound 65: 65 mg prop/389 mg ASA/ 32.4 mg caffeine
 - 1 tab q4-6 hrs
- Dorvocet-N 50: 50 mg prop/325 mg APAP
- Darvocet-N 100: 100 mg prop/650 APAP



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Tramadol

- Opioid-like drug
 - synthetic analogue of codeine but non-narcotic
 - binds to opioid receptors
 - prevents re-uptake of serotonin and norepinephrine
- Similar potency to tylenol #3



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Tramadol

- Abuse/addiction potential very low
- Previously, not DEA classified
- Affective August 18, 2014 now DEA schedule IV



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Tramadol

- Minimal side effects:
 - dizziness, N&V, HA, somnolence
- Drug interactions: many
 - tegretol, SSRIs, MAOIs, tricyclics, digoxin, coumadin
- Avoid with h/o seizures



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Tramadol

- Ultram: 50 mg tramadol
 - 1-2 tabs q 4-6 hr
 - max does 400 mg/day
- Ultracet: 37.5 mg tramadol/325 mg APAP
 - 1-2 tabs q 4-6 hr



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Tylenol Plus Ibuprofen

- Some studies suggest that perhaps two tylenol with one IB is *not inferior* to Tylenol # 3 for post operative pain relief
 - More cost effective
 - Fewer side effects
 - Greater patient satisfaction



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Narcotic agents: Side Effects

- Abuse/addiction potential
- CNS effects
- Liver toxicity
- Renal failure/urinary retention
- Nausea and vomiting
- Constipation



101

To consider

- Start with simplest treatment first
 - Topicals
 - OTC APAP or IB
 - Prescriptions
 - Narcotics



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To consider

- Prescribe analgesics on 24 hr basis
 - Tylenol #3
 - sig: 1-2 tab q 4-6 hrs
 - disp #12 (TWELVE)



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```

Rod Cone, O.D.
321 Main Street Columbus, OH (610) 255-1234 Optom Lc. #
12345 DEA Lc. # XXXXXX

Name: John Doh
DOB: 01/01/1980
Address: 74 Evergreen Terrace

Rx:
Tylenol #3
Sig:
1 - 2 tablets p.o. q 4 - 6 hrs
Disp: #12 (TWELVE)
Refills: None Generic substitution: yes
Signature: Rod Cone, O.D.
  
```



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To consider

- Mild: OTC Tylenol or IB
- Mild/moderate pain
 - Tylenol #3 (30 mg codeine/300 mg APAP) 1-2 tabs q 4-6 hrs
 - max 10 tabs/24 hrs
- Moderate/severe pain
 - Vicodin (5 mg hydrocodone/300mg APAP) 1-2 tabs q 4-6 hr
 - max 8 tabs/24 hrs



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To consider

- Severe pain: oxycodone
 - Percocet (5 mg oxy/325 mg APAP) 1 tab q 4-6 hrs
 - Percodan(4.5 mg oxy/325 ASA) 1 tab q 4-6 hrs
 - **CAN'T DO IN MOST STATES!!**



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To consider

- Make sure **only** Rx for eye related pain
- Most states Schedule III
- Check on Schedule II
 - Vicodin
- Most states, 72 hrs max!
- Review laws in your state



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To consider

- Don't be afraid to use opioids if needed
 - ADDICTION AND ABUSE POTENTIAL IS LOW WHEN USED APPROPRIATELY AND FOR SHORT TERM!

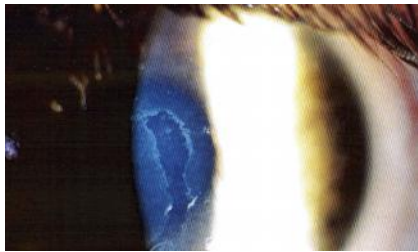
108

Case 1



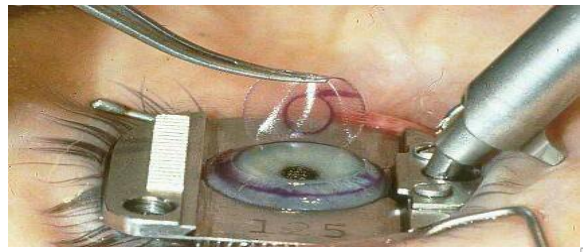
109

Case 2



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Case 3



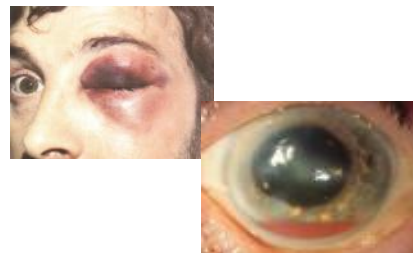
111

Case 4



112

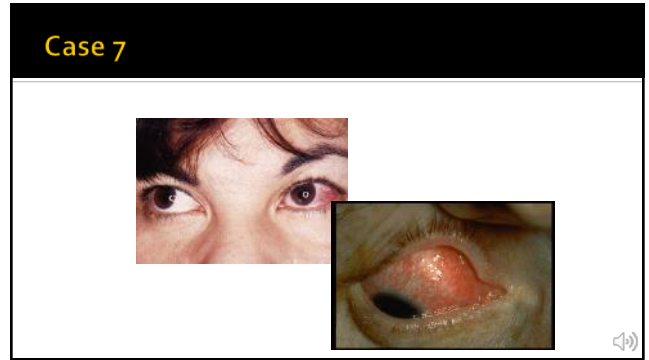
Case 5



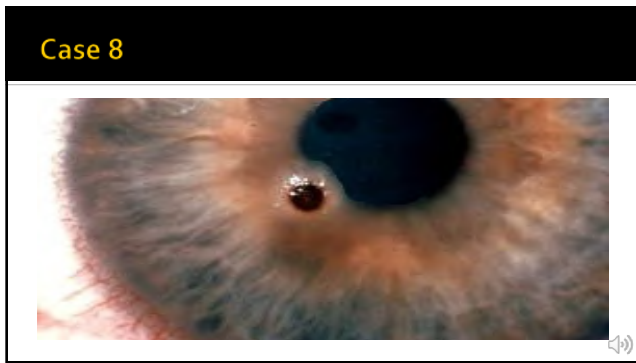
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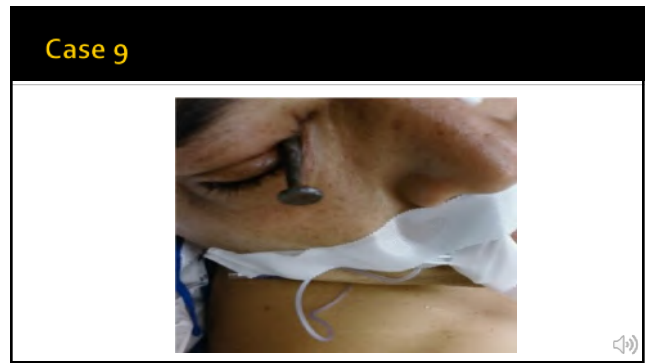
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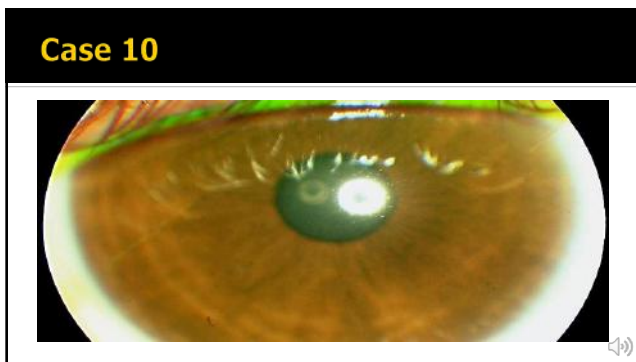
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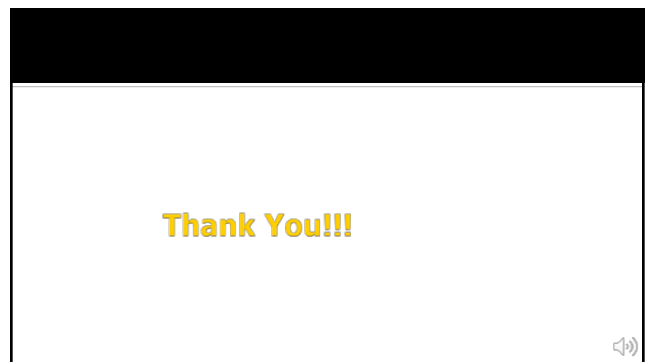
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