Ocular Pain Management for the Primary Care Optometrist

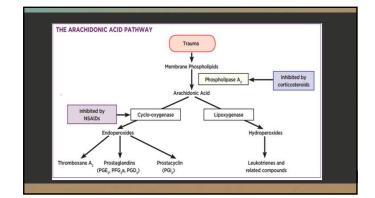
Kimberly D Kohne, OD, FAAO Clinical Professor Indiana University School of Optometry Contributions by Stephanie Klemencic, OD, FAAO, MS

Disclosures

- I have nothing to disclose.

Pain

- Necessary reaction for survival and overall well being
- Pain pathways in every system are redundant
 More than one opportunity to "get out" of the situation
- Sensory nerves in and around the eye are mainly supplied by the trigeminal nerve and its branches
- Cornea one of the most sensitive organs in the body
- 300-600 more receptors per unit area than the skin



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Acute vs. Chronic Pain

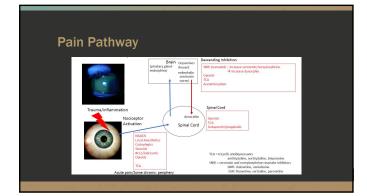
damage

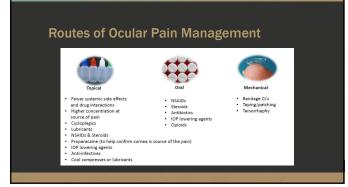
- Life sustaining symptom
- Motivates us to minimize further harm and to heal
- Normal processing of nociceptive stimuli from tissue
- Lasts longer than 3 months, or persists after tissue is healed
 Abnormal, maladaptive, pathologic disorder of pain pathway
 Many genetic and epigenetic factors
 Nociceptive chronic smooth muscle or musculoskeletal injury, disease, inflammation
 Neuropathic damage to nerves resulting in abnormal nerve signaling/processing
 Higher risk of fatal and non-fatal suicide attempts



Opioid Receptors

- Opioid Receptors
 Mu (MOP; MOR); kappa (KOP; KOR); delta (DOP;DOR)
- Found widely in brain and spinal cord
- Lesser extent peripherally
 GI tract, mast-cells
- When bound by opioids (endogenous or exogenous drugs) inhibit neuron firing, blocking pain signals to and from the brain
 endogenous neurotransmitters modulating pain: dynorphin & enkephalin (brain and spinal cord); endorphin (released from pituitary)
- Why opioids can be used for acute moderate-severe pain





Causes of Ocular Pain

- Foreign bodies
- Dry eye
- Corneal/conjunctival abrasions
- Blunt trauma
- Inflammation
- e.g. hordeolum, episcleritis/scleritis, uveitis, keratitis
- Post-surgical

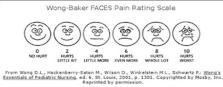
History Is Paramount

- When did this start?
- How often are you feeling the pain? Constant? Intermittent?
- Have you had it in the past?
- Does anything make it better/worse?
- Can you associate the pain with any particular action or time of day?

Pain Scale

- Important to use pain scale
- Many variations
- Gives a starting point/baseline
- On a scale of 1 to 5–5 being the worst pain you have experienced—how would you rate the level of the pain?
- Helps determine how pt progressing through treatment
- Regardless of the scale, remember that pain is subjective

Wong-Baker Classification Scale



History Continued

- Medical History is important:
- Pregnancy
- Allergies to Medication
- Alcohol use
- Other medications that may cause interaction
- Liver function
- Kidney function

Determine Goals

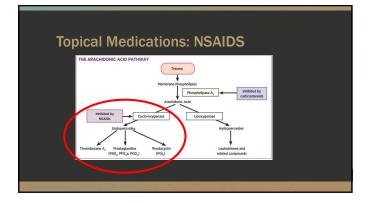
- Determine the goal of pain management
- Treat/manage an obvious inflammation, infection or injury?
- Analgesic effect, i.e. symptomatic relief?
- Symptomatic relief until the hidden source of the pain is identified and eliminated if possible?

Treatment: From the Top Down

- There are ways to treat pain that don't necessarily involve medications
- Removal of some type of foreign body
- Lashes, small fibers or dust, bugs
- Bandage contact lens
- Compression/Pressure patch (rarely used)

Topical Medications: Artificial Tears

- Artificial tears
- Great for lubrication
- Useful for dry eye
- In conjunction with use of other medications
- Assist in healing mild corneal erosions/abrasions
- Usually only a mild sense of relief
- Available OTC, easy to access
- Cost varies



2009 2010 2013 2014 2013 ketorolac 0.45% PF (Acuvail, Allergan) bromfenac 0.09% (Bromday, B&L) bromfenac 0.07% (Polensa, B&L) nepafenac 0.3% (Ilevro, Alcon) bromfenac 0.07% (BromSite, Sun opensite, Sun	05 0.09% &L) 0.1% Ilergan)
(Acuvail, Allergan) (Bromday, B&L) (Prolensa, B&L) (Ilevro, Alcon) (BromSite, Sun	16
QID QD QD QD BID	

Topical NSAIDS Side Effects

Burning

- Stinging
- Hyperemia
- Delayed wound healing

Topical NSAIDS Side Effects

- Rare, but possible corneal ulceration and melt Most cases with generic Voltaren
- Associated with misuse
- Follow FDA dosing
- At risk patients those with decreased corneal sensation and compromised corneas
- · Limit use to short term when patient in pain
- Follow appropriately to ensure proper healing
 Sarcoidosis, rosacea, chemical burns, local radiation around eye, graft vs. host
 disease with epithelial compromise- may not good candidates NSAID use





Commonly Used Topical NSAIDS

- Flurbiprofen: 0.03%, 2.5 mL
- Diclofenac: 0.1%, 5 mL
- Ketorolac tromethamine: 0.5%, 3 mL/5 mL/10 mL
- Ketorolac tromethamine: 0.4%, 5 mL
- Ketorolac tromethamine: 0.45%, PF, 30 vials/box
- Bromfenac: 0.09%, 1.7 mL/2.5 mL/5 mL
- Bromfenac: 0.07%, 1.6 mL/3 mL
- Bromfenac: 0.075%
- Nepafenac 0.1%, 3 mL suspension
- Nepafenac 0.3%, 1.7 mL/4 mL suspension

	LessDrops		
			Costorer Care
http://www.imprimi	srx.com/formulations	/ophthalmology/le	ssdrops/
Formulation		Classification	Strength
MKO. Melt Midazolam/Ketamine. HCP/Ondansetron). L	emon	Oral Medications	3/25/2mg
Mydriatic 3 Tropi Cyclo-Phenyl - 1mc - \$17.00		Topical Medication	1/1/2.5%
Mychanic 4 Tropi Prop. Phenyl-Ketor - 1m \$17.00		Topical Medication	1/0.5/2.5/0.5
Pred-Gati - 3mL - \$25.00		Topical Medication	170.5%
Pred-Gati-Nepat - JmL - \$20.00		Topical Medication	1/0.5/0.1%
Pred-Ketor - 3mL - \$25.00		Topical Medication	170.5%
Pred.Moxi		Topical Medication	1/0.5%
Presi-Mosi-Ketor - 3mi - \$30.00		Topical Medication	1/0.5/0.4%
Pred-Nepal - 3ms \$25.00		Topical Medication	170.1%

Cycloplegic Agents

· Help control inflammation, which in turn helps control pain

How?

Cycloplegics block acetylcholine, therefore stops the contraction of the iris and the ciliary body

Cycloplegic Side Effects

Common:

- Blurred vision, itching, burning, stinging, irritation at application site, photophobia
- Severe:
- Rashes, hives, itching, difficulty breathing, tightness of chest, swelling of mouth, face, lips or tongue, difficulty urinating, dry mouth, eye pain, fever, flushing or dryness of skin, irregular or rapid heartbeat, unsteadiness on your feet.

Interactions

- Review the patient's medical history and current medications and allergies
- Educate patient before starting drops on the following:
- Cardiovascular changes
- GI issues
- Toxicity
- Sudden allergic reactions
- Neurologic changes

-	olegics				
	Atropine	Scopolamine	Homatropine	Cyclopentolate	Tropicamide
Peak Effect	30-40 minutes	20-45 minutes	20-90 minutes	20-45 minutes	20-30 minutes
Duration	1-2 weeks	4-7 days	2-3 days	24 hours	3-6 hours
Uses	Amblyopia <u>Tx</u> Uveitis <u>Tx</u>	Uveitis Tx **for those sensitive to Atropine	l≭ line Uveitis Tx	Most commonly used for cycloplegic refraction	Mydriadic (DFE)
Side Effects	Burned vision Bys irration Dry Mouth Fluiting Part pulse Mental Confusion evilse extron with kick and children with Down's syndrome and CP due to possible CNS effects when used in high doses	Blurred vision Fast Pulse Difficulty Breathing **Higher rate of toxic reactions vs. Atropine—no deaths reported	Blurred vision Eye Irritation Fast Pulse Flushing Tiredness	Blurred vision Transient psychosis in kids when 2% used multiple times **Use cation with kids with Down's, CP and emotional problems	Blurred vision Fast Pulse Flushing Tiredness **Similar SE to Atropine but much less likely

Foreign Body Case

- 35 year old male
- "got something in my right eye yesterday"
- Mechanic
- Working underneath a car and something, "maybe rust" fell into eye while working
- +Pain 2-3 out of 5
- Meds: None
- Medical: None
- Allergies: None

Foreign body case

- VAs: OD: 20/40-, pH 20/25, OS: 20/20-
- Entrance testing: Normal, PERRLA, no APD



Foreign body case

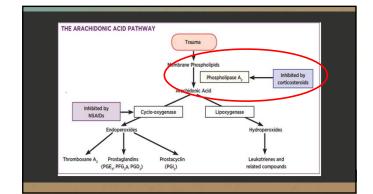
- Assessment: 1. Corneal Foreign Body OD
 - 2. Mild Corneal Edema Secondary to Foreign Body OD
 - 3. Corneal Abrasion OD
 - 4. Secondary Iritis OD due to foreign body

Foreign body case

- 1 gtt proparacaine instilled into OD
- Removed foreign body with spud, followed by use of Alger brush for rust removal
- 1 gtt of Moxeza was given OD in office
- 1 gtt of Prolensa given OD in office
- 1 gtt of 5% HA given OD in office
- Bandage CL AV Oasys was placed in OD 8.4/-0.50 to be worn until next
 appointment. Moxeza QID OD.
- Ibuprofen 400 mg every 4-6 hours prn for pain

Ocular Steroids

- Mimic hormones naturally produced by adrenal gland
- Control pain by:
- suppressing inflammation when introduced at a higher dose than secreted naturally by the body
- suppressing the immune system



Ocular Steroids Side Effects

 Blurred vision, burning, itching, possibly development of glaucoma, cataract formation, photophobia, headaches, ONH damage, visual acuity and field defects, corneal perforation, delayed wound healing, mask other ocular infections, flare up of herpes

Increased IOP

Commonly Used Topical Steroids

- Pred Forte: 1%, 1 mL/5 mL/10 mL/15 mL
- Lotemax: 0.5%, ung/drop/gel
- Durezol: 0.05%, 5 mL emulsion
- As an add on: Tobradex and Zylet



Uveitis Case

- 18 year old female
- Irritation, swelling in left eye, x 1 day
 +tearing, +photophobia, +redness, +foreign body sensation, constant, no vision decrease
- Meds: +Minastrin 24 Fe, +Nexium

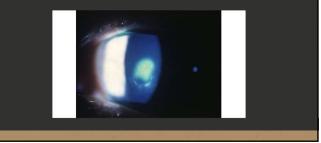
Uveitis Case

- VAs: 0D 20/20-, 0S 20/20-
- Entrance testing: Normal, mild miosis OS, but reactive and no APD
- Anterior Segment: Conj: OD normal, OS gr 1+ ciliary injection
 - Cornea: OD normal, OS normal Anterior Chamber: OD normal, OS gr 1+ cells,
 - mobile, no flare
- Posterior Segment: ONH normal color, distinct margins, 0.3/0.3 OU,
 +FLR, vitreous clear with no cells or flare

Uveitis Case

- Assessment:
- 1. Anterior Uveitis OS
- Plan:
- Pred Forte 1% trade name qid while awake OS for 7 days, shake bottle before each use
- HA 1% 1 gt/day for 5 days

Recurrent Corneal Erosion



Recurrent Corneal Erosion

- "Woke up and it felt like there was a rock in my eye." OS. Saw OD the day before for "tear". Given a bandage lens and told to use FreshKote TID, NaCL ung at night and Moxeza BID OS.
- +pain, 4 out of 5 on severity scale, +photophobia; +watering
- VAs: OD 20/20, OS 20/40- pHNI
- Entrance testing: Normal OU, OS reactive, but sluggish. Pupil sizes asymmetric, but pt was dilated yesterday with 5% HA
- Meds: Metformin, Crestor, Moexipril, Vit D2
- Allergies: Coconut, Adhesive tape

RCE

- Conjunctiva: OD trace injection, OS gr 2+ diffuse injection
- Cornea: OD normal, OS erosion 1mm high X 0.5 mm long, +staining, no edema, no cell or flare

RCE

- Assessment
- 1. Recurrent Corneal Erosion OS
- Plan
- 1 gt 5% HA OS in office
- 1 gt Prolensa 0.07% OS in office for pain
- Continue Moxeza BID OS until follow up with other OD,
- Continue FreshKote TID and new bandage contact lens placed in the OS AV
 Oasys 8.4/-0.50 to be left in until the other doctor evaluates the cornea.
- 400mg Ibuprofen every 4-6 hours prn for pain.

CJEM. 2010 Sep;12(5):389-96.

- Dilute proparacaine for the management of acute corneal injuries in the emergency department. Ball IM¹, Seabrook J, Desai N, Allen L, Anderson S.
- Study done in 1 ER in Canada
- Two groups, 0.005% proparacaine vs. a placebo
- 15 in proparacaine group, 18 in placebo
- The proparacaine group had more pain relief than the placebo
- No wound healing delay or other complications

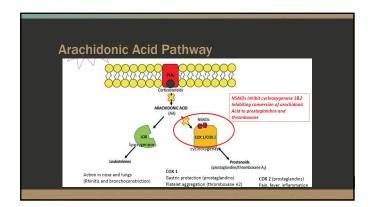
Oral Analgesics

- Three categories
- Over the Counter
- Prescriptions that are Non-Narcotic

Narcotics

1. Analgesic • Relieve pain without sedation 2. Anti-inflammatory • Dose for inflammation tx is higher than pain relief Low information tx is higher than pain relief E.g. ibuprofen pain: 400 mg TID-QID; recurrent episcleritis or scieritis: 600-800 mg TID-QID 3. Anti-platelet **Oral NSAID** Not related to pain Inhibit platelet's to reduce clot formation in MI and CVA prevention

- Activity
- 4. Anti-pyretic Fever treatment
- Drug activity varies and have different side effect profiles



PO NSAIDS: Efficacy the Same but Selectivity Matters for Side Effects



Generic	Brand	OTC/Rx Availability	Cox selectivity	PO Adult Dose	Max Deily Dose	
ibuprofen	Advil, Motrin	OTC (200mg)& Rs(200,400,600, 800 mg)	cox1/cox2	400mg TID-QID	3200 mg	
naproven sodium	Aleve (OTC), Anaprox DS (Rx)	OTC (220mg) & Rx (220,275, 550mg)	cox1/cox2 (leans cox2)	440mg BID 550mg BID	1150 mg	Sodium form preferred for acute pain – faster acting Maybe safer if higher CV risk (on low ASA therapy) Less GI s/e
naproxen	Naprosyn (Rx)	Rx (250, 375, 500mg)	cox1/cox2 (leans cox2)	500mg BID	1000 mg	Less GI s/e
indomethacin	Indocin	Rx (25,50 mg)	cox1/cox2 (leans cox1)	50 mg BID	200 mg	More Gi s/e
meloxicam	Mobic	Rx (7.5-15mg)	cox1/cox2 (leans cox2)	15 QD 7.5 BID	15 mg	Less GI s/e
celecoxib	Celebrex	Rx (50, 100, 200, 400)	cox 2	400 QD-200 BID	400 mg	Less GI s/e
	buprofen naproxen sodium naproxen indomethacin melonikam	aprosen zolum Advil (Motrien naprosen zolum Advil (Motrien naprosen zolum Advil (No) naprosen Naprosen (Ne) naprosen Naprosen (Ne) nabrosen Motoc Nobec	Aurikatiiy Buprofen Advil, Morim Advil, Morim	Autobility Autobility Bugrofen Advl. Mottin Or (2,00mg)B N(200,mg) Gru/Goo2 (adv/Goo2 (ad	Image in the second s	Auslichtity Auslichtity Norm Door bugrohm Akil, Mohm off CX XXmgli, Nu (200 mg) cm.(2002) 400mg TD-Cold 2020 mg XD-Cold 2020 mg TD-Cold 2020 mg XD-Cold 2020 mg XD-Cold



All NSAIDS Boxed Warnings

- Increased Risk of GI ulcerations, bleeding, perforations

 Higher risk in age > 60 y.o. and higher doses
 h(o GI ulcer or bleed pre-NSAID use, 10X higher risk having it again with NSAID use; avaid if has h(o GI ulcer or bleed.
 Increased risk with alcohol, advanced liver disease or other bleeding disorders use
 Increased risk 3(-8) fit and risg anti-coagulants (e.g. aspirin, warfarin, Xarelto etc.)
 Increased rist taking systemic steroids
- 2. Increased Risk of Cardiovascular events: MI & CVA
- More concern with chronic use and higher doses
 If on ASA, need to take ASA dose first wait 30 min before taking NSAID dose
- Contraindicated in peri-operative period of CABG surgery
 ~7 days before and 14 days after

Other NSAID Concerns

Nephrotoxicity

- Acute kildney injury reduce blood flow to kidney; tell patient's to take with water
 More likely to occur if dehydrated or if are on other drugs that can cause pre-renal acute kidney injury (diuretics, Acit inhib /risi/s, ABB 'sartan')
 More likely to occur with chronic NSAID use

Allergy
 If allergic to aspirin must avoid all NSAIDs

- Aspirin Triad + leading to anaphylaxis (avoid all NSAIDs)

 - Aspirin intolerance
 Nasal polyps/rhinitis/chronic sinusitis
 Asthma NSAIDs can worsen asthma (leukotrienes)
 Urticaria (hives)

Counseling the Patient

- Take with food and hydrate to help reduce GI effects and kidney effects
- Best to avoid alcohol (increased GI risks);
- If has issue of GI upset even when take with food
 - Can use proton pump inhibitor (PPI): omeprazole (Prilosec); lansoprazole (Prevacid); pantoprazole (Protonix); esomeprazole (Nexium) Also consider PPI:
 - if > 60 y.o. and on high dose of NSAID
 If on low-dose ASA

Acetaminophen (Tylenol)

abbreviation APAP

- labels also abbreviate: AC, Acetominoph, Acetaminop, Acetamin, Acetam • aka paracetamol
- Mechanism of action unknown
- · Seems to act centrally (brain/spinal cord) pathway
- Works on decreasing fever and pain
- No anti-inflammatory or anti-platelet action

Acetaminophen (Tylenol)

• OTC

• Regular strength 325 mg; 2 tabs q 4-6h while

symptoms last

- Extra Strength 500 mg; 2 caps q 6h
 8HR Arthritis 650 mg; 2 caps q 8h
- Max Dose 4000 mg/day
- 3000 mg/day on labels
- Found in MANY flu/cold/antacids/pain combos • Educate patients to check ingredients
- Ask about use of any other products before prescribing
- Need to be vigilant to avoid accidental overdose

Acetaminophen Side Effects

Irreversible liver damage

- Contraindicated liver disease
- Contraindicated alcoholics
- Can not take with alcohol



Ok if aspirin allergy and in pregnancy/breast feeding

Oral Analgesics for Post Op Pain

COMBINATIONS: control vs. acetaminophe Ibuprofen + APAP 400+1000 1.5 oxycodone or codeine Ibuprofen + oxycodone 400+5 2.3	Analgesic(s)	Dose (mg)	NNT vs Placebo ≥ 50% maximum pain relief over 4-6 hours	~50,000 participants
Bugnom 600 2.7 (mostly denial extraction Kaprown 500 2.7 (mostly denial extraction Celecab 400 2.6 (mostly denial extraction Actaminophone (IAWP) 1000 3.6 (mostly denial extraction Opcodome 15 4.6 (mostly denial extraction Coderine 60 12.0 (buprofem + acctaminophone) Gabageerin 2.90 11.0 works as well or better for oxycodone or codeine Buppofen + A&M 400+1000 1.5 oxycodone or codeine	SINGLE AGENTS:			states block and the studies
Naproen 500 2.7 Celecuiti 400 2.6 Accrannicyben (ANP) 1000 3.6 Oxycodone 15 4.6 Códrie 60 12.0 Gabapentin 250 11.0 Works as well or better fr control ve. acetaminoph bupofien + ASAP control ve. acetaminoph control ve. acetaminoph control ve. acetaminoph control ve. acetaminoph control ve. acetaminoph control ve. acetaminoph control ve. acetaminoph	Ibuprofen	600	2.7	
Actestinisophin (JANP) 1000 3.6 Onycodorne 15 4.6 Codeline 60 12.0 Gabageetin 250 11.0 Common Marco control to better for Common Marco 1000 Common Marco control to better for Common Marco control to better for Common Marco Bupperfore + ARAP 400+1000 1.5 oxycodone or codeline	Naproxen	500	2.7	(mostly dental extractions)
Discodone 15 4.5 Codine 60 12.0 Ibuprofin + acetaminoph works as well or better for communications: COMBINATIONS: control vs. actaminoph buprofin + APAP d00-1000 1.5 oxycodone or codeline oxycodone or codeline	Celecoxib	400	2.6	
Codene 60 12.0 Ibuprofen + acttaminoph Galaperán 250 11.0 worka as well to better fr Communicación + AAM control va. scetaminoph control va. scetaminoph Buprofen + acycobone 400-1000 1.5 oxycodone or codeline	Acetaminophen (APAP)	1000	3.6	
Gabapertin 250 11.0 Works as well or better fr COMBINATIONS: Control vs. acetaminophe Control vs. acetaminophe Control vs. acetaminophe Buprofen + APAP 400+1000 1.5 oxycodone or codeline Daycodone or codeline	Oxycodone	15	4.6	
Gabapentin 250 11.0 works as well or better for control vs. acetaminophe optimum Ibuprofen + ARAP 400+1000 1.5 control vs. acetaminophe oxycodone or codeline Ibuprofen + oxycodone 400+5 2.3	Codeine	60	12.0	Ibuprofen + acetaminonhen
COMBINATIONS: control vs. acetaminophe Ibuprofen + APAP 400+1000 1.5 oxycodone or codeine Ibuprofen + oxycodone 400+5 2.3	Gabapentin	250	11.0	works as well or better for pair
Ibuprofen + oxycodone 400+5 2.3	COMBINATIONS:			control vs. acetaminophen +
	Ibuprofen + APAP	400+1000	1.5	
ADAD - any adapta 205-5 F	Ibuprofen + oxycodone	400+5	2.3	L
APAP + 0XyC0001e 323+3 3.4	APAP + oxycodone	325+5	5.4	
APAP + codeine 300+30 6.9	APAP + codeine	300+30	6.9	
Moore, R. Andrew, et al. The Cochrone Library. 2015	Moore, R. Andrew, et al. The Coch	one Library, 2015		

Acetaminophen + Ibuprofen = Synergy

Analgesic/Pain Dosing

PO Ibuprofen 200mg X 2 = 400 mg 400 mg x TID/**QID = 1600** mg/day

PO acetaminophen 500 mg x 2 = 1,000 mg 1,000 mg x TID/**QID = 4,000** mg/day*

Careful...make sure not taking other things containing acetaminophen if Rx QID, could lead to acute liver failure

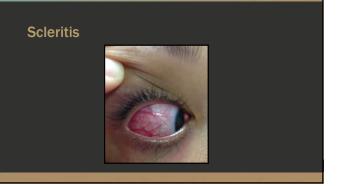
Analgesic & Anti-inflammatory Dosing PO Ibuprofen 200mg X 4 = 800 mg 800 mg x TID/QID = 3200 mg/day

PO acetaminophen 500 mg x 2 = 1,000 mg 1,000 mg x TID/**QID = 4,000** mg/day*

Careful...make sure not taking other things containing acetaminophen if Rx QID, could lead to acute liver failure

Pain Management Tips for the Eye

- Rx lowest effective dose for the shortest duration
- Immediate release formulations should be used for acute pain, not extended release
- NSAID analgesic pain doses lower vs. higher dose needed to treat ocular inflammation
- Know max dose limits to reduce risk for adverse events



Scleritis

• 25 year-old

- Red right eye "several" days ago. No burn, no sting, no tearing, more sensitive to light OD and "throbbing"
- 4 out of 5 on the severity scale.
- Started Pred Forte TID OD for 3 days, BID for 3 days, QD for 3 days. "Drops do give relief" 90% improvement, thinks skin is hot to touch, feels pulfy and swollen. Similar episodes started 3 years ago, has had 6 episodes total.
- · Sees a rheumatologist for unspecified connective tissue disorder
- Meds: Zinc, Vitamin D
- No allergies

Scleritis

- VA's OD 20/20-, OS 20/20 3-
- Entrance testing: Normal
- Adnexa: Puffy appearance to cheeks right
- Conjunctiva: OD bulbar gr 3 diffuse injection, most dense temporal
 - and superior, trace chemosis. Sclera gr 3 diffuse
 - injection temp/superior/nasal with thickening temporal and superior

OS normal

ornea: Clear

Anterior Chamber: Clear

Posterior: ONH good color, distinct margins, OD 0.35/0.35, OS 0.3/0.3, +FLR, No H/B/T 360 OU

Scleritis

- Assessment:
- 1. Anterior Scleritis OD
- Plan
- 1. Spoke with pt's rheumatologist on the phone. Agreed to have pt start lbuprofen 600mg TiD until signs and symptoms resolve. Will follow up in two weeks and reassess at that time. Rheumatologist plans to start the pt on a systemic medication for unspecified connective tissue disorder.

Prescription NSAIDs

- Work the same way Non-Prescription NSAIDs do
- Higher in dose requires a prescription
- The side effects are the same as Non- Prescription NSAID's
- · Contraindications are the same as Non-Prescription NSAID's
- Pregnancy:
- First two trimesters Category C
- Last trimester Category D

Prescription NSAIDs

• Uses:

Episcleritis and Scleritis
 Very useful in these instances

- Uveitis
- To try to help control inflammation
- Cystoid Macular Edema
- Topical is more effective with this

Remember the Scleritis patient???

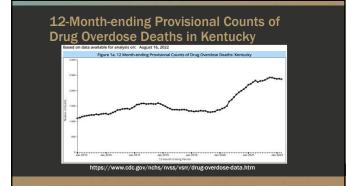
So, it happened again...

Why do an Opioid CE?

Opioid over-prescribing

- Opioid misuse and addiction at epidemic levels
- Public health crisis we work with the public
- March 2016 CDC guidelines for chronic pain management
 - 12 chronic pain recommendations
 1 deals with acute pain
- 2017 opioid overdose deaths declared U.S. National Emergency

12 Month—ending Provisional Counts of **Drug Overdose Deaths in the US** vailable for analysis on: August 1 Figure 1a. 12 Month-ending Prov onal Counts of Drug Overdose Deaths: United States https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm



How Did This Begin?

 Well intentioned, but overzealous advocacy for controlling chronic pain Chronic pain is multi-modal problem, simplified to just take a pill for it: slow releas oxycodone
 Regulatory boards evaluating performance based on pain control satisfaction

- Misleading pharmaceutical claims the new slow release versions made opioid less addictive
- Doctors start Rxing large amounts for lots of things: sprained ankles/backs and chronic pain
 Physicians prescribing were not trained in addiction, even in medical school
 Listening to Pharma and "expert leaders" quoting poor evidence (or no evidence...)
 Eventually claims on not only addiction but also effectiveness of slow release oxycodone found to be false, but cat was out of the bag

Opioid Risks/Effects Even when taken correctly opioids can cause: *Respiratory depression – can be fatal Constipation Analgesia And indifference to pain Pin-point pupils Cough suppressant Itching or bronchoconstriction Release histamine from mast cells Drowsiness/Sedation Euphoria Sweating • Urinary Retention Dysphoria (confusion, anxiety, hallucinations) Immune system alterations Nausea and Vomiting Endocrine Effects Reduced libido in men Menstrual irregularities and infertility in women Physical Dependence Tolerance Addiction

Increased Risk of Respiratory Depression

- Use of other CNIS depressant (sedative) drugs Alcohol or other opiolds Bencidizepines "-lams; pams" Alpracolam (Kanas); diazepam (Valium); lorazepam (Ativan); clonazepam (Klonopin) Barbiturates "-barbitals" Phenobashital (Luminal); thiopental (Pentothal) Muscle relexants cycloherapine (Resarl); carloprodol (Soma) Sleep aldy/Hypnotics Stopp of the company of the company of the company of the company Stopp aldy/Hypnotics Sleep aldy/Hypnotics Sleep aldy/Hypnotics Sleep aldy/Hypnotics Sleep aldy/Hypnotics Sleep aldy/Hypnotics Stopp (Snew, athematic, athematics) Ather the company of the company CMP 2Ak inhibitors (macrolide artibiotics; anti-fungal agents; HIV protease inhibitors) stophomy, athematic, athematics Softyo, Kiner or User Oliseas

- >65vo, Kidney or Liver Diseas

Opioid Side Effects

- Constipation
- Drowsiness
- Confusion
- Nausea and vomiting
- Liver Toxicity
- Addiction/abuse potential
- Itching
- Breathing problems

Opioid Contraindications

- Known allergies/hypersensitivities
- Respiratory diseases (asthma; COPD; sleep apnea)
- Liver and Kidney issues
- Drug metabolism and excretion become an issue
- Pregnancy and Breast Feeding
- History of substance abuse
- Psychiatric illness, anxiety, depression
- Combination with other CNS sedating drugs
- antihistamines, sleeping aids, and some antidepressants
- benzodiazepines

Opioid Metabolism and Genetics

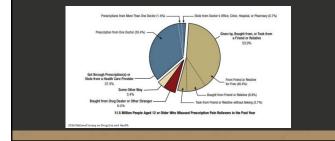
Not all patients respond to the same opioid in the same way

>3,000 polymorphisms in human mu opioid receptor gene
 Single nucleotide polymorphisms (SNPs) identified that affect opioid metabolism, transport across the blood brain barrier, and activity at receptors and ion channels

Broken down in liver by cytochrome P450 (CYP) 2D6 & 3A4 enzymes

- 20-30% may have genetic opioid metabolic defect (GOMD)
 Enzyme too active = metabolized more quickly, pain returns faster
 Require higher than normal dose to manage pain
 Toxic, life-threatening side effects from excessive metabolites building up, even with codeline or
 tramado Enzyme inactive or absent = life threatening allergic reactions or respiratory depression

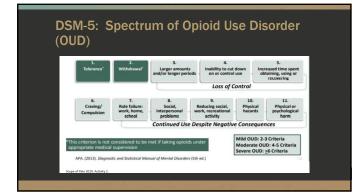
Prescription Opioid Misuse Problem



Lessons Learned over the 20+ of Opioid Epidemic

- Not recommended first line (or 2nd...) for chronic pain treatment
- · Beware of simple solutions for complex problems
- Must evaluate quality of clinical evidence
- Teach health care professionals about addiction and learn from past mistakes
- Some conflicts of interest require a stronger response than disclosure alone Physician speakers admitted to spreading misinformation
 Organizations that took funding from opioid manufacturers;
 Federation of State Medical Boards, American Pain Society, American Griatrics Society, American Academy of Pain Medicine, All supported statements or reports that encouraged physicians to prescribe opioids for chronic pain
- Increase accessibility to medications used to treat Opioid Use Disorder

fstein JM, Olsen Y. Les ned from the Op nic. JAMA 2019; 322(9); 809-810



Opioid Tolerance and Dependence

Happens to everyone: physiologic adaptation to chronic use

Tolerance: Increased dose needed to maintain effect

Physical Dependence: Withdrawal symptoms occur when stopping the opioid, reducing the dose of the opioid, or upon exposure to an opioid receptor antagonist (naloxone, naltrexone) that block opioids from reaching the receptors. Withdrawal symptoms: "like the flu x 1,000!"

Opioid Withdrawal Symptoms

- Rhinorrhea
- Lacrimation
- Yawning
- Chills
- Goosebumps
- Hyperventilation
- Vomiting • Diarrhea

• Mydriasis

• Muscle aches

- Hostility
- Hypothermia
- Anxiety

Feels like you are dying, but is not fatal

Opioid Addiction

Compulsive use despite harm

- Treatable but complex, chronic, relapsing brain disorder Brain changes involved in reward, stress, and self control
 Changes persist even after stopping drug
- Progressive if not treated leading to permanent disability or premature death • Like many chronic diseases, a combination of genetic, environmental, and social factors contribute to a person's vulnerability to addiction and ease of recovery from it

tine 2019. Med rder Save Lives, Wash

Treatment for Opioid Disorder

Treatment

- Long-term pharmacologic therapy
 Non-pharmacologic: psychosocial behavioral therapies, <u>but not required</u> to start pharmacologic therapy
 Only "20% of "2 million with Opioid Use Disorder are receiving treatment
- Three FDA approved medications are effective and save lives
- Inter FDA approved medications are effective and save inves Methadone fullo pioid agonist, only distributed special care facilities Buprenorphine partial opioid agonist, must have "X-waiver" on DEA license; limit on number can RX Brand subsource = buprenorphine + naloxone-rapid acting opioid antagonist Naltrexone long acting opioid antagonist Alleviate withdrawal symptoms, reduce opioid cravings, and decrease the response to future drug use

Treatment for Opioid Disorder Methadone

- Treats multiple things don't automatically assume addiction:
 - Chronic pain
 - Reduce opioid withdrawal symptoms
 - Treat opioid use disorder
 - Pain treatment option in true morphine/codeine allergies
- Wonky drug pharmacokinetics...one of most dangerous opioids Long, variable, unpredictable drug half-life that varies based on length of treatment and dose levels
 - Many other prescription drug-drug interactions

Treatment for Opioid Disorder Buprenorphine

Opioid partial agonist

- Suboxone; Bunavail; Subsolv (buprenorphine + naloxone)
- Often combined with naloxone to decrease likelihood of diversion and misuse, since buprenorphine alone <u>does</u> have opioid effects (just weaker than a full agonist like hydrocodone, heroin, etc.)
- Helps treat pain as well
- Less respiratory depression and abuse potential
- If patient experiencing withdrawal, can send to ER and they can get this started

Treatment for Opioid Disorder Naltrexone (ReVia; Vivitrol)

- Naltrexone: oral tablet (50 mg per day) or IM injection (extended release, IM monthly)
- Also used to treat alcohol use disorder
- Long-acting opioid receptor antagonist
- Used to treat opioid use disorder
- Helps reduce cravings

Treatment of Opioid Use Disorder

- Strongly discouraging simple withdrawal therapy (i.e. just stop drug and get through withdrawal symptoms)
- Simple withdrawal therapy not only ineffective but dangerous
 Often will seek-out street drugs, laced with illicit fentanyl, or turn to IV use, increasing risk HIV and Hepatitis C
- increasing risk HIV and Hepatitis C Return to taking past doses, not realizing they have lost tolerance, more likely to result in fatal respiratory depression/overdose
- to result in fatal respiratory depression/overdose

 Medication therapies are highly regulated, many barriers to access
 - Federal level
 - Many physicians not trained or comfortable prescribing
 - Not enough physicians prescribing or eligible to prescribe to meet demand

Opioid Overdose Reversal with Naloxone

NARCAN Selecter HI

• Opioid antagonist

- Opioid antagonist
 Binds to opiolar receptor, but does not activate if (i.e. no effects). Blocks opiola present in the body from binding and activating opiolar deceptors.
 Rapidiar vestores normal respiration
 "Antagonist Precipitated Withdrawal"
 Rapidiar onet withdrawal symptoms
 Very uncomfortable but not life-threatening
 Very safe, only has a effects if person has opiold in their system
 Three formulations
- Three formulations
 Injectable
 Auto-injectable
 Nasal spray

Naloxone (Narcan; Evzio)

- Many states do not require a prescription for Narcan
- CDC recommends all patients high dose or on extended release formulas have Narcan on hand due to greater risk of accidental overdose or death from respiratory depression
- Narcan = Nasal spray (4mg spray) fast acting
- Tilt head back, give one spray in one nostril, call 911
 Can readminister in other nostril every 2-3 min until emergency services arrive • Evzio = 2, IM auto-injections – fast acting
- Administered like epipen (IM hold for 5 seconds then release), call 911, can give the other one as well
- Naloxone IV/IM/SQ injection fast acting

National Academies of Sciences 2019

BOX S-2 Summary of Conclusions

- Summary of Conclusion
 Oroci and Disorder is a treated front oroce bank desace
 Oroci and Disorder and treatment of DNA-septored medications to treat opoid
 descore are presented interventions in and a secondate
 and the proved actionses.
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AOA Opioid White Paper for Optometry

 Nov 2017: The Opioid Public Health Emergency and How Doctors of Optometry Can Help

 Opioid epidemic prompted re-examination of best practices for using opioids in acute pain – ongoing debate; no consensus

 "It should be noted that long-term opioid use often begins with treatment of acute pain"

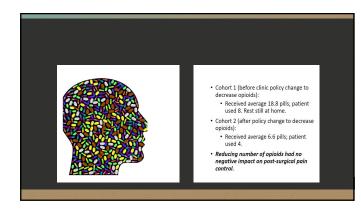
3 general themes: 1. Non-opioid treatment is preferred for acute and chronic pain treatments 2. Use lowest effective dose for shortest duration (usually < 72 hours) 3. Exercise caution when prescribing any opioid and monitor patients closely

Health Policy Institute

JAMA Ophthalmol. 2019 Oct 31:138(1):76-80. doi: 10.1001/jamaophthalmol.2019.4432 Online ahead of print.

Association of Limiting Opioid Prescriptions With Use of Opioids After Corneal Surgery

- PKP, Collagen Crosslinking, Superficial Keratectomy, PRK
- 82 patients surveyed post-surgery; 2 cohorts
 - How many pills actually used?
 - What did they do with leftover pills?
 - How was post-op pain control?



Surgical Procedure	Level 0, 0 Oral Morphine Equivalent	Level 1, <40 Oral Equivale	Morphine nt	Level 2, <80 Oral Morphine Equivalent
Cataract				
Phacoemulsification	x		Significa	ntly reduced
Complex cataract and IOL surgery (large incision)	x			
Comea or ocular surface Prervoiam or conjunctival surrery				opioid prescriptions whil
Pherygium or conjunctival surgery Kenatoplasty (penetrating, lamellar, and endothelial)	x		still main	taining pain control for
Kenatoplasty (penetrating, lamellar, and endothelial) Kenatorefractive excimer survery	X	X	their pat	ionto
Glascoma		A	then pa	ients
Trabeculectomy and bleb revision	x			
Glaucoma dnainage device		X	Urge on	nthalmologists
Cyclophotocoagulation		X		
Retina or ocular oncology				v post-op prescribing
Pars plana vitrectomy	x		patterns	and consider reducing
Scientl buckle		X		
Brachytherapy plaque application or removal				x
Oculoplastics or orbital				
Blepharoplasty, ptosis repair, or eyelid	x			
Brow prosis repair	X			
Orbitotomy	x			x
Encrimal drainage system and DCR Enacleation or eviscention	X			x
Adult strabismus survery		~		X
Trauma, IOFB, or open globe		x		

Collateral Damage of Excess Pills

Young children ingestion and overdose

- Adolescent experimentation leading to overdose or addiction
 Other household contacts (family, visitors)
- Some will misuse extra pills to self-treat pain later on
 Another eye pain episode, migraine, sprained ankle, sinus pain, tooth ache...etc.
- Because of misuse/diversion of opioids, caution should be used even if prescribing only a short-course of opioid treatment and patient's need to be told why it is important to dispose of any leftovers and how to get rid of them.



	Active	Found in Brand Names
	Benzhydrocodone /Acetaminophen	Apadaz
FDA Flush List	Buprenorphine	Belbuca, Bunavail, Butrans, Suboxone, Subutex, Zubsolv
	Fentanyl	Abstral, Actio, Duragesic, Fentora, Onsolis
	Diazepam	Diastat/Diastat AcuDial rectal gel
	Hydrocodone	Anexsia, Hysingla ER, Lortab, Norco, Reprexain, Vicodin,
NIH) U.S. NATIONAL LIBRARY OF MEDICINE		Vicoprofen, Zohydro ER
	Hydromorphone	<u>Dilaudid, Exalgo</u>
	Meperidine	Demerol
	Methadone	Dolophine, Methadose
DAILYMED	Methylphenidate	Daytrana transdermal patch system
DAILINILD	Morphine	Arvmo ER, Embeda, Kadian, Morphabond ER, MS Contin, Avinza
	Oxycodone	Combunox, Oxaydo (formerly Oxecta), OxyContin, Percocet, Percodan, Roxicet,
		Roxicodone, Roxybond, Targinig ER, Kartemis XR, Xtampza ER
https://dailymed.nlm.nih.gov/dailymed/index.cfm	Oxymorphone	Opena, Opena ER
	Tapentadol	Nucynta, Nucynta EB
	Sodium Oxybate	Xvrem oral solution









DEA Authorized Drug Take Back Near You

Controlled Substance Public Disposal Locations - Search Utility									
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Oral Narcotics

Schedule I

- No accepted medical use
 High potential for abuse
- Most dangerous of all the drugs
- Potentially severe psychological or physical dependence
 Heroin, marijuana, LSD, ecstasy
 Marijuana is still considered a Schedule I narcotic even though it is legal in some States

Schedule II

- High potential for abuse, but less than Schedule I
- Potential to lead to severe psychological or physical dependence
- Considered dangerous drugs
 OxyContin, Demerol, Methadone, Adderall

Oral Narcotics

Schedule III

- Low to moderate potential for physical or psychological dependence Dependence less than Schedule I or II
- Testosterone, anabolic steroids, Tylenol with codeine
- Schedule IV
- Low potential for abuse
- Low risk of dependence
 Xanax, Ambien, Tramadol, Valium

Oral Narcotics

- Schedule V
- Lower potential for abuse than Schedule IV
- Generally antidiarrheal, antitussive, analgesic purposes Lyrica, Robitussin AC, Motofen



Prescription Drug Monitoring Program

 PDMP electronic database tracking controlled substance prescriptions • Helps identify patients who may be misusing opioids, receiving

- opioids from multiple providers, or using other prescription drugs (e.g. benzodiazepines) who may be at risk for overdose even with low, short prescription
- What if something looks suspicious on PDMP?
- Confirm the PDMP is correct
- Use the opportunity to provide potentially life-saving communication on risk
 Discuss your concerns and your interest in their safety

Formulations

Immediate Release (IR)

Short Acting

Used in acute pain

- Used in chronic pain (not first line)
- Used in opioid naïve patients

Formulations

Controlled Release (CR) (AKA extended release (ER) or sustained release (SR)

Long Acting

- NOT used in acute pain or in opioid naïve patients
- NEVER disrupt (e.g. chew, break, crush, cut in half, etc.)
- Entire dose released at once can lead to overdose/death by respiratory depression!

Morphine

Morphine is the standard for comparison of other opioid agents

30 mg PO morphine = 200 mg PO codeine 30 mg PO morphine = 20 mg PO oxycodone 30 mg PO morphine = 20-25 mg PO hydrocodone 30 mg PO morphine = 8 mg PO hydromorphone

Fentanyl...so potent dosed in micrograms....

All are estimates, can't account for differences in genetics and pharmacokinetics that vary a lot among individuals

Morphine

- First active ingredient isolated from a plant
- Works on CNS to decrease feeling of pain
- Used in both acute and chronic pain, moderate to mild
- High potential for abuse and dependency
- Frequently used for MI and labor
- Schedule II drug

Codeine

- Used to treat mild to moderately severe pain
- Side Effects:
- Constipation
- Drowsiness
- SweatingMild itch or rash
- Should NOT drink while on codeine
 Can slow or stop breathing

Codeine

- Codeine by itself is a Schedule II drug
- With products containing no more than 90mg of codeine per dosage unit it is a Schedule III drug $% \left({\left| {n_{\rm s}} \right|_{\rm s}} \right)$
- Pregnancy:
- Category C
- However, prolonged use during pregnancy can lead to dependence in neonate
 It is found in breast milk
- Comes in combinations:
- With APAP
- With ASA

Codeine

- Codeine and Tylenol
- Tylenol #2: 15mg codeine/300mg APAP
 1-2 tabs every 4 hours
- Tylenol #3: 30mg codeine/300mg APAP
 1-2 tabs every 4 hours
- Tylenol #4: 60mg codeine/300mg APAP
 1 tab every 4 hours
- Max dose of Codeine in 24 hours: 360mg
- Max dose of APAP in 24 hours: 3000mg

Codeine

Codeine with Aspirin

- Empiric with codeine #3: 30mg codeine/325mg ASA
 1-2 tabs every 4-6 hours
- Empiric with Codeine #4: 60mg codeine/325mg ASA
- 1-2 tabs every 4-6 hours

Hydrocodone

- Used to treat moderate to severe pain and an anti-tussive for cough management
- It is stronger than codeine, but only 59% as potent as morphine in analgesic properties
- The side effects of constipation and sedation are lesser in hydrocodone
- It gives a sense of euphoria, especially in higher doses
- Most common side effects:
- Dizziness and lightheadedness
- Trade names are: Lortab, Norco, Vicodin, Vicoprofen

Hydrocodone

Vicodin

- 5mg hydrocodone/300mg of APAP
 1-2 tabs every 4-6 hours
- Max: 8 tabs in 24 hours
- Vicodin ES
- 7.5mg hydrocodone/300mg of APAP
- 1 tab every 4-6 hours Max: 6 tabs in 24 hours

Hydrocodone

Vicodin HP

- 10mg hydrocodone/300mg APAP
- 1 tab every 4-6 hours
 Max: 6 tabs in 24 hours
- Vicoprofen
- 7.5mg hydrocodone/200mg ibuprofen
- 1 tab every 4-6 hours
- Max: 5 tabs in 24 hours

Hydrocodone

- Effective October 6, 2014 hydrocodone became a Schedule II narcotic Can no longer have refills
- Must have a handwritten paper script for each fill
- Some states can e-scribe if the doctor has the proper technology and electronic signature license Measure adopted in an attempt to reduce drug abuse and ultimately drug related deaths
- This decision was fought by many groups, such as medicine, Pharmacy and the AOA.
- · It limits availability to patients, especially in rural locations

Hydrocodone

- In 2012, hydrocodone was the most prescribed drug
- In 2015, hydrocodone was not even in the top ten
- In 2018, hydrocodone was still not in the top 10
- Acetaminophen/hydrocodone was #13
- In 2020, acetaminophen/hydrocodone was #10...creeping back up

Oxycodone

- Used to treat moderate to severe pain
- It has a greater analgesic effect than morphine
- It is a Schedule II drug
- Produces high levels of euphoria, so very addictive and high abuse potential
- In Pregnancy C

Oxycodone

- Can slow or stop breathing
- DO NOT drink alcohol when taking Oxycodone
- Common side effects:
- Mild drowsiness, headache, dizziness, tired feeling
- Stomach pain, nausea, vomiting, constipation, loss of appetite
- Dry mouth
- Mild itching
- Trade names: Percodan, Percocet, OxyContin

Oxycodone

- Percodan:
- 4.8355mg oxy/325mg ASA
 1 tab every 6 hours
- Percocet:
- Percocet: 2.5mg oxy/325 APAP 1-2 tabs every 6 hours 5mg oxy/325mg APAP 1 tab every 6 hours Most frequently Rx* dose 7.5mg oxy/325mg APAP 1 tab every 6 hours 10mg oxy/325 APAP

- 10mg oxy/325 APAP
 1 tab every 6 hours

Tramadol

- Used for moderate to severe pain
- · Considered to be an "opioid-like" drug
- Works by two mechanisms of action:
- 1. Activates opioid receptors
- 2. Inhibits uptake of serotonin and norepinephrine
- Analgesic efficacy lies between codeine and morphine
- Schedule IV drug

Tramadol

- Should not give to people that have a history of seizures
- Common side effects:
- Constipation
- Itchiness
- Nausea
- Several drug interactions:
- Antidepressants, MAOI's, SSRI's, digoxin, Coumadin and several others
- Pregnancy category C
- Not as addictive as the other narcotics
- Trade names: Ultram, Ultracet

Tramadol

Ultram

- 50mg
 1 tab every 4-6 hours
- Max dose is 300mg/day
- Ultracet
- 37.5mg tramadol/325mg APAP
 1-2 tabs every 4-6 hours
- Max 8 tabs/day

Conjunctiva Rip

- 60 year old white male, severe OS pain.
- Lost right arm at the elbow and wears a prosthesis with a metal piece on the end. He was working on his farm, trying to open a bag of fertilizer with a pair of pliers. The pliers slipped and he scratched his eye. He was wearing a GP lens at the time of the accident. Extreme pain, "7 out of 5" on the severity scale, +tearing, thinks he is photophobic, but can't keep eye open.
- ***drop of proparacaine was given to perform examination
- VAs OD, 20/25, OS >20/200 (no GP)
- Entrance testing: normal

Conjunctival Rip

Anterior Segment:

- ***another drop of proparacaine given, had to hold lids.
- OD: trace injection bulbar, cornea clear (GP still on), chamber dark and quiet.
- OS: gr 3+ diffuse injection, large laceration nasal running slightly superior to edge of cornea both bulbar area and looks to be slightly in sclera, +staining, no fluid coming from wound. Cornea had mild defect in limbal region inferior nasal (possibly due to a secondary cut by GP lens). No cell and flare.

Conjunctival Rip

Assessment:

1. Conjunctival/scleral laceration OS nasal, moving nasal-superior
 No orbital contents leaking/bulging out of wound

Plan

- Call OMD for consult. Pt referred for suturing of wound.
- Consider narcotic for pain?

Disciform Keratitis



Disciform Keratitis

- 38 year old male
- HSK disciform keratitis OD
- Pain 4 out of 5 on the severity scale Pt states the pain varies from day to day
- +redness, +watering, +burning, +visual decrease, +photophobia.
- Has been going on for one month: Using Zirgan 5x/day OD and has recently discontinued Omnipred. Pt just moved to the US 2 months prior from Iran. Pt has a history of contact lens wear, 6 month replacement. Has been out of the lenses since the flare up. Currently wearing glasses.
- Medications: Zirgan OD
- Allergies: None

Disciform Keratitis

- VAs: OD: 20/400 pHNI, OS: 20/400 pHNI
- Entrance testing: Normal
- Anterior Segment: OD: trace diffuse injection, large central dendrite, opacified on edges, mild stromal involvement, mild edema, no cell or flare

OS: normal

Disciform Keratitis

- Assessment: 1. Herpes Simplex Disciform Keratitis OD
 - 2. Secondary Corneal Edema OD
- Plan:
- d/c use of Omnipred until further notice.
- Continue Zirgan 5 times/day
- 400 mg Ibuprofen for the pain

When writing the Rx

- Write for 24 hours at a time
- Reassess after that time
- Write out the number of tabs on the Rx form
- Usually a time limit on how long you can put patient on opioids
 Most states: 72 hours
- Remember if it is a hydrocodone combination:
 No refills
- Needs to be paper, unless you meet the requirements
- Do not write a script for any issue that is not related to the eye

Last thoughts

- We all treat pain on some level
- Don't be afraid to go to the next level when necessary
- Ask for help if you are unsure

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