









Anatomy & Physiology of Pain

- COX enzymes play a key role in inflammation and pain
 - COX-1 is involved in maintenance of GI mucosa
 - COX-2enzyme signals pain and inflammation
- Prostaglandins role

The Inflammatory Cascade Mast Cell Phospholipids Г Membrane Phospholipase A₂ Stabilization L Tryptase Heparin Histamin Chymase PAF Lipo Cvclo ovvaenase nonase l Cyclic L Prostacvclin Thro oxane A₂ Leukotrienes (TXA₂) (LTC4, LTD4, LTE4, LTB4 (PGF2, PGD2, PGE2)

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Pain – One in a Million

- Pain receptors are specific to location and stimuli
 - Sharp immediate pain A-delta fibers
 - Prolonged unpleasant burning pain mediated by smaller unmyelinated C fibers
- These lay dormant until stimulated and are often sensitized by inflammation

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Nociceptors

- In all peripheral tissue
- Distribution will vary
- Stimulated by
 - Heat
 - Energy
 - Trauma
 - Emotion
 - Chemicals

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Pain – Remember ME

- Various stimuli may signal a specific pattern of neuronal response based on a learned response
 - Think "suspicious coincidences" (Horace Barlow) as seen in the visual cortex

Importance of History

- History
 - Medical
 - Family
 - Social
- Any drug allergies
- DOFDAR
- Tell me about your pain
 - Quality
 - Duration
 - Frequency
 - Reproducible factorsAssociated features

Prescribing for Women

Prescribing for Children

- Certain medications are OK in pregnancy
- Breast feeding
- Consult OB-GYN if necessary

 Children 88lbs or 12 years old and older can be dosed as adults unless otherwise noted
 Look up dosage for child

(mg/kg/day)
Determine how many kg child weighs

1 kg=2.2 lbs

NO ASPIRIN
APAP OK

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So What Can Be Used During Pregnancy? • Antibiotics • <u>Analgesics</u>

- Acetaminophen

- Diphenhydramine

– Ibuprofen

- Tylenol #3

- Loratadine

– <u>Vicodin</u>

Allergy

- Amoxicillin
- Amoxicillin/clavulanate
- Azithromycin
- Erythromycin
- Antivirals
 - Acyclovir
 - Valacyclovir
- Anti-inflammatory
- Prednisone

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Chemical Burns

- Emergency!!! Every minute counts
- Do not waste time on Hx and PE
- Alkali burns more common and worse than acid – Alkali
 - Household cleaners, fertilizers, drain cleaners

- Acid

• Industrial cleaners, batteries, vegetable preservatives

Chemical Burns

- Absolute Emergency
- Immediate irrigation
- Check VA
- Check pH if possible

Management of Chemical Burns

- Debride necrotic tissue
- Frequent ATS
- Bandage contact lens
- Quinolone: 1 gtt 4-6x/day (prevents infection)
- Prednisolone phosphate: 1 gtt q 1-2 hr while awake (reduces inflammation)
- Vitamin C: 1-2 gm po QD (reduces corneal thinning/ulceration)
 400(and issue size to a 2 hear bills evenly (shelpton Gaussian)
- 10% sodium citrate: 1 gtt q 2 hr while awake (chelates Ca++ and impairs PMN chemotaxis)
- Scopolamine 0.25%: 1 gtt TID (reduces pain/scarring with AC inflammation)
 10% Mucomyst (n-acetyl-cysteine): 1 gtt 6x/day (mucolytic agent and collagenase
- inhibitor)
- Oral pain meds
- Doxycycline 100 mg po bid (collagenase inhibitor)
- Glaucoma gtts/oral diamox if IOP elevated
- Significant injury may require admission

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Chronic Pain

- 72 YOAAF Referred by OD for Cataract Eval OU. Blurred VA. Occasionally uses ATs prn.
- Med Hx of allergies, acid reflux and HTN
- SLE: 3+ NS OU
- Uneventful cataract sx OU - OD 1/4/12 OS 2/1/12

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Case Study

- 3/27/12 Increased light sensitivity / pain OU

 Dx: Rebound uveitis OU
 - Tx: Restart difluprednate and nepafenac TID OU
- 5/14/12 F/u chronic uveitis OU, FBS OS
 - Dx: Improved Chronic uveitis OU, Dry eye disease OS>OD
 - Tx: Decrease steroid and NSAID to BID OU, ATs BID OU

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Case Study

- 9/7/12 F/u chronic uveitis, FBS OS>OD, Tearing
 - Dx: Resolved uveitis OU, Dry eye disease OU
 - Tx: Start on cyclosporine 0.05% OU, F/u 4-6 mos
- 2/25/13 F/U dry eye disease OU, OS always has a FBS, Chronic tearing
 - Dx: DED OU / See photo
 - Tear Osm: 298 / 301

Contact Dermatitis

Eyelids and Pain

- Typically inflammation induced
- Many capsaicin receptors

Eyelids

- Pain is often inflammation and swelling based
- Decrease swelling = decrease pain
- Cold vs. Hot compress
- Medrol Dosepak
- Lotemax ung

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Corneal Anatomy

- Most richly innervated structure in the body
 - Densely supplied by sensory and autonomic nerve fibers
- Sensory nerves (the vast majority) come from the ophthalmic division of the trigeminal
 - Possess both sensory and efferent functions
 - Mechanical, thermal and chemical stimulation usually is perceived as pain

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TFOS DEWS II Definition

"Dry eye is a multifactorial disease of the ocular surface characterized by a <u>loss of homeostasis of</u> the tear film, and accompanied by <u>ocular symptoms</u>, in which tear film <u>instability</u> and <u>hyperosmolarity</u>, ocular surface <u>inflammation</u> and damage, and <u>neurosensory</u> <u>abnormalities</u> play etiological roles."

Corneal Sensitivity Changes

- Age considerations
- Contact lenses
- Ocular surface disease
- Previous infections

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Corneal Nerve Structure and Function in Patients With Non-Sjögren Dry Eye: Clinical Correlations

- Mean corneal sensitivity was significantly lower in the NSDD group as compared with the control group (P = 0.014).
- NSDD patients have both structural and functional alterations of subbasal corneal nerves and these changes are related to the severity of dry eye.

Antoine Labbé1 2013 ARVO

The Relationship between Subbasal Nerve Morphology and Corneal Sensation in Ocular Surface Disease

 Corneal sensitivity was significantly decreased in dry eye and glaucoma patients compared with controls. The density and number of subbasal corneal nerves were also significantly decreased in dry eye and glaucoma patients compared with controls.

Labbe 2012 IOVS

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What's Happening in Dry Eye

- Sensory nerves may adapt to irritation by decreasing the frequency and intensity of action potentials
- With time this elevates pain threshold, and stronger stimuli is needed to evoke corneal sensation for basal and reflex tearing
- Corneal hypoaesthesia likely plays a role in the pathogenesis of tear deficiency

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n, P. Realm of dry eye therapy expanding. Ophthalmology Times. November 15, 2







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• Transient light sensitivity syndrome

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sensation

Case Example

- 07/06
- 54 YOMW / Referred from OD for K Ulcer
- Started on moxifloxacin Q1h OS
- Pain and Redness started 5 days prior
- SCLW / Denies sleeping in lenses
- VAcc OD 20/60 OS 20/200





Infectious versus Sterile

- Ulcers
 - <u>Rare</u>
 - <u>Painful</u>
 - AC reaction
 - Usually single lesion
 - Discharge
 - Epithelial staining
 - Corneal edema
 - >2.0mm in size

Infiltrate

- <u>Common</u>
- <u>Mild pain</u>
- <u>No AC reaction</u>
- Multiple lesions
- Minimal discharge
- Epithelium intact
- No corneal edema< 2.0mm in size
- 2.01111111312

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Differentials

- CL peripheral ulcer vs. infiltrate
- CLARE
- Fungal keratitis
- Acanthamoeba keratitis
- HSV Keratitis
- Staph Hypersensitivity

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Case F/U

- 7/7 Cloudy since yesterday
- Labs No growth
- SLE
 - Conj 4+ Injection
 - Cornea 3.5 mm ulcer / Haze / 1+edema / WBC
- A/C Rare cell
- Plan
 - Continue present meds
 - Add sub-conjuctival injection of gentamycin
 - Add loteprednol 0.5% tid OS





Steroids for Corneal Ulcer Trial

- Objective: To determine whether there is a benefit in clinical outcomes with the use of topical corticosteroids as adjunctive therapy in the treatment of bacterial corneal ulcers
- Results: No significant difference was observed
 - 3-month BSCVA (P =.82)
 - Infiltrate/scar size (P = .40)
 - Time to reepithelialization (P = .44)
 - Corneal perforation (P > .99)

Strinksan M, Nasrarenhas J, Rajaraman R, Ravindran M, Lältha P, Glidden DV, Ray KJ, Hong KC, Oldenburg CE, Lee SM, Zegans ME, McLeod SD, Letman TM, Acharya NR; Steroids for Corneal Ulcers Trial Group. 49

Treatment

- Primary goal eliminate the pathogens
- Secondary goal prevent host destruction
- Treated as bacterial initially
- Small infiltrates empirically (<1.0mm)
- Discontinue CL wear
- Cycloplegics
 - Homatropine 5% tid
 - Scopolamine 0.25% tid
 - Atropine 1.0% tid if hypopyon present

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Treatment

- Fluoroquinolones standard
 - Broad spectrum
 - Bioavailability
 - Biocompatibility
- Peripheral infiltrates q1-2h
- Medium size q1h w/ loading dose
- Vision threatening Fortified antibiotics
 - Tobramycin/gentamycin (15mg/mL) q1h
 - Cefazolin (50mg/mL) or vancomycin (25mg/mL) q1h

Fluoroquinolone

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- Typical Patient
 - Has progressed as a dry eye patient
 - Has little response to traditional treatment
 - Often doesn't realize lagophthalmos
 - Sandy gritty feeling in the morning
 - Feels the need for artificial tears upon waking
 - Slight photophobia
 - Feels better after a shower

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Case Example

- 44yo Asian American c/o blurred VA, redness, tearing, peri-orbital edema starting 2-3 days prior
- Med Hx: Uncontrolled DM (Dx in 1998)
- Vasc: OD 20/60 PH 20/30 OS 20/80 PH 20/40
- IOP: 21/18

Case Example

- Acute, non-granulomatous, anterior uveitis OS
- Cause???
- Treatment
 - Ordered labs CBC w/diff, ESR, SMA-12, HLA-B27, Urinalysis, FTA-ABS, RPR, Lyme Western Blot
 - Difluprednate q2h OS
 - Homatropine 5% TID OS
 - Doxycyline 100 mg BID po

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Pulse Therapy

- QID to Q 1 Hour for 7 to 10 Days
- Zero Tolerance for AC Cells
- Avoids Surface Toxicity
- Quick & Dirty
- Hit It Hard and Fast: Aggressive

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Doxycycline

- Inhibits bacterial protein synthesis
- Cannot be used for kids <8 and pregnancy/nursing – Category D
- Anti-infective dose: 100 mg BID for 10 days
- Anti-inflammatory dose: 50 mg BID for one month then qd 1-3 months
- Side effects/Contraindications:
 - GI upset: caution patient to take this with food
 - Photosensitivity
 - Pseudotumor cerebri

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Lyme Titer

- Ordered based on suspicion
- Erythema migrans is the only manifestation of Lyme disease in the United States for which clinical diagnosis should be made in the absence of laboratory confirmation
- A patient with a significantly characteristic symptom with the appropriate history of possible exposure should be started on antibiotics after appropriate laboratory studies have been drawn

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Tx for Lyme Disease Early infection or nonspecific symptoms with positive Lyme titers in the adult may be treated with: Doxycycline 100 mg BID x 14 days Amoxicillin 500 mg TID x 14 days Severe infection in adults with definitive ocular, neuroophthalmic, neurological, or cardiac involvement may be treated with penicillin G (24 million units, intravenous, daily in four divided doses for 21 days) or intravenous ceftriaxone (2 g/day in two divided doses for 21 days)

Wormser et. Al. The Clinical Assessment, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis, and Babesios is: Clinical Practice Guidelines by the Infectious Diseases Society of America. *Clinical infectious diseases. Vol.* 43. Issue 9.

When Should Lab Tests Be Ordered? Bilateral cases • Hyperacute cases Atypical age group • Worsens with tapering Recurrent uveitis • VA worsens Recalcitrant cases • Immunosuppressed

Uveitis: Common Systemic Associations

- Most common cause
 Idiopathic : 38-70%
- Other systemic causes
 - HLA-B27 related disease
 - Sarcoidosis
 - Systemic Lupus Erythematosus
 - Rheumatoid Arthritis
 - Behcets Disease





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Classification of Uveitis

- Anatomical / structural location
- Etiology
- Acute vs. Chronic
- Non-granulomatous vs. Granulomatous
- Unilateral vs. Bilateral





Posterior Segment Pain

- Neovascular glaucoma
- Ocular ischemic syndrome
- Optic neuritis
- Posterior uveitis
- Pars planitis



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Managing the Blind Painful Eye

- Topical medication
 - Steroids
 - OHTN
 - Atropine
- Retrobulbar injection
- Corneal anterior stromal puncture
- Cyclophotocoagulation
- Incisional surgery

Ahluwalia, MA, Vold. SD. Managing the Blind, Painful Eye. *Glaucoma Today. July/* August 2013. Access from http://glaucomatoday.com/2013/08/managing-the-blind-painful-eye/

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Headaches

- Migraine
- Cluster
- Tension
- Sinus
- Hemicrania
- Trigeminal neuralgia

Migraine Most common headache disorder that causes ocular pain Characterized by throbbing pain, photophobia

- and sometimes by nausea or visual disturbances
- 1) Are you light sensitive?
- 2) Is the headache disabling?
- 3) Is there nausea or vomiting?

Cluster Headache

- More common in men
- Usually presents in young and middle-aged
- Episodic vs. chronic
- Unilateral pain

 Orbital, supraorbital, or temporal pain
- Lasts 15-180 minutes
- Can occur from once every other day to 8 times a day

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Trigeminal Neuralgia

- Aka "tic doloureux"
- Most severe, chronic ocular pain condition, and it causes extreme, sporadic, burning or shocklike pain
- Daily for several minutes a day or multiple
- Triggers

 Vibration or contact, such as combing hair, brushing teeth, touching the temple or a blast of cold air

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TREATMENT CONSIDERATIONS

Hemicrania

• Most often seen in middle aged women

• Multiple times throughout the day

Continuous pain around face and eye

• Few minutes to 45 minutes

• Tx with indomethacin

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Prescribers Concerns

- Empathy
- Insurance
- DEA #
- Side effects
- Addiction
- Reassurance

Addressing Ocular Pain

- Complete history
- What is underlying cause?
- Time course
- Verbal anesthesia

Artificial Tear Supplements

- Improve comfort
- Reduce irritation and friction
- Improve ocular surface
- Store in the fridge

Analgesics for Pain

Anesthetics

- Blocks action potential signal from nociceptor to brain or spinal cord
- Lidocaine, proparacaine, tetracaine, benoxinate

Central-acting agents

- Interrupts pain signals and emotional responses to pain at the
- brainstem to cerebral cortex level – Opioid (narcotic) analgesics

Peripheral-acting agents

- Blocks peripheral nociceptor stimulation, and the inflammatory pathway that contributes to nociceptor stimulation.
- Non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen,
- Non-steroidal anti-inflammatory drugs (NSAIDs), acetaminopne aspirin

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Topical Anesthetics

- Benoxinate
 - Only available with fluorescein
 - Onset 10-20 seconds
 - Duration 10-20 minutes
- Proparacaine 0.5%
- Poor penetration
- Very little cross sensitivity to tetracaine and benoxinate
- Tetracaine 0.5%
- Onset 10-20 seconds
- Duration 10-20 minutes

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Are Eye Anesthetics Safe for Home Use? Salim Rezaie, MD on August 14, 2014 Published in ER Physician's Monthly

Take Home Message

 To date, the only evidence that topical anesthetics in uncomplicated corneal abrasions causing more harm than benefit come from experimental animal studies, case reports, and case series. Other studies showed superior pain control without delayed wound healing. Based on available evidence, it is most likely reasonable to send patients home with dilute (0.5%) topical anesthetics for a period of no more than 24 – 48 hours as long as these patients do not have complications. Larger, prospective studies would lend more weight to this recommendation.

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• Ball IM, Seabrook J, Desai N, et al. Dilute proparacaine for the management of acute corneal injuries in the emergency department. CJEM. 2010 Sep;12(5):389-96.











Steroid Pulse Therapy
QID to Q 1 Hour for 7 to 10 Days
Zero Tolerance for AC Cells
Avoids Surface Toxicity
Quick & Dirty
Hit It Hard and Fast: Aggressive
Treat and Follow

Dexamethasone 0.4mg Insert

- The treatment of ocular inflammation and pain following ophthalmic surgery.
- The treatment of ocular itching associated with allergic conjunctivitis.
- Sustained release of dexamethasone 0.4 mg for up to 30 days



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- Bromfenac
- Diclofenac
- Ketorolac
- Nepafenac







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Non-Therapeutic Treatments

- Hot compress
- Sunglasses / Hats
- Stay indoors
- Low lighting
- Plus for near
- Patching
- Pressure patch

Bandage Contact Lens

- Not used nearly enough
- Filamentary or severe punctate keratitis
- Allows a bridge for re-epithelialization and establishment of a normal glycocalyx

Amniotic Membranes

- Used to manage ocular surface healing for a variety of indications including:
 - Corneal epithelial defects
 - High-risk corneal transplants
 - Recurrent Corneal Erosion
 - Infectious Diseases (Herpes/Keratitis)
 - Stevens-Johnson Syndrome & Chemical Burns



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Oral Analgesics

- Hydrocodone/acetaminophen is the most frequently prescribed oral medication in the U.S.
- Indicated for:
 - Corneal abrasions
 - Recurrent corneal erosions
 - Severe keratitis
 - Severe uveitis
 - Refractive surgery

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NSAIDS

- Studies have shown NSAIDS to have same analgesic effect as narcotics
 - Some studies show better pain control than morphine (what?.....)
- Almost all have a ceiling effect
- Have cross sensitivities with aspirin, ibuprofen, and other NSAIDS
- Can delay wound healing

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Advil (Ibuprofen)

- Analgesic, antipyretic, anti-inflammatory properties
- Suppresses inflammatory cascade by inhibiting COX pathway
- Pregnancy Category
 - C Prior to 30 weeks gestation
 - D After 30 weeks gestation
- OTC 200 mg tablets/capsules
- Analgesic dosage 1,200 mg / day
- Anti-inflammatory dosage 3,200 mg / day
- Generics available

Case Example

- 74 yowm with blurred VA OS>OD X 1 month / + HA
- Oc Hx: NPDR OU / AMD dry OU / Cat Sx
- Med Hx: DM x 10 yrs, Back Pain, Coronary Artery Disease, Chronic Kidney Disease, Anemia, Sensorineural hearing loss, Cardiomyopathy -Ischemic, Cardiomyopathy - Congestive
- BCVA
 - OD: 20/40-2 PH 30-2
 - OS: 20/60-1 PH 40-2
- (-) APD



Oral Corticosteroid Considerations

- Accurate diagnosis is essential
- Indicated for acute inflammatory eye, orbital and eyelid conditions
- Pregnancy category C
- Dosepaks available
 - 24 mg, 30 mg, 60 mg with taper
- Best taken with meals
- Short term rarely has ocular side effects

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Prednisone

- Suppresses inflammatory cascade and immune response
- Optic neuritis
 - Methylprednisolone 1g/day i.v. for 3 days
 - 60-100mg qd p.o. for 11 days
 - Only after initial IV steroid treatment per ONTT to decrease risk of recurrence
- AION: 60-100mg qd
- Scleritis/Uveitis
 - Not responding to topical treatment
 - 40-80 mg as an initial dose with taper

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Prednisone

- Side Effects/Contraindications:
 - Increased IOP
 - Cataract formation
 - Fluid retention (moon face, buffalo hump)
 - Increase blood sugar levels in diabetics
 - Gastric ulcers
 - Not to be used if pregnant
 - Mood changes
- Advantages:
 - Widely available
 - Inexpensive

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Aspirin

- Pain, inflammation, fever, anti-platelet
- Pregnancy Category D
- OTC 325-650mg every 4-6 hours
- Avoid aspirin 1-2 weeks prior to surgery
- Consider in patients with CRVO, retinal emboli
- Side effects
 - Hypersensitivity
 - Rhinitis
 - Bleeding disorders
 - Reye's syndromePregnancy

Analgesics and antipyretic

Acetaminophen

- Indications:
 - Pain relief associated with corneal abrasions, chemical burns, headaches associated with eye pain, scleritis
- Pregnancy Category B
- Side Effects/Contraindications:
 - Rash, Hives
 - Itching
 - Difficulty swallowing/breathing
 - Overdose may damage liver
 - Do not take with alcohol

Oral Narcotic Analgesics

- Centrally acting opioid receptor blockers
- Safe and effective for acute, short-term pain
- Clinically used in combination with acetaminophen
- Generally prescribed as one tablet po q4-6hours prn
- Onset 20 minutes, peak 1 hour, duration 4-6 hours
- Addiction potential
- Opioid Receptors
 - Mu
 - Delta
 - Карра

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Codeine

- Available with acetaminophen
- Most commonly used
- Works in 20 min, peaks at 2 hours
- Less toxicity
- Less addiction potential
- Less sedation and constipation

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6X more potent than codeine with less sedation and constipation

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Hydrocodone/acetaminophen

- Dosage:
 - Vicodin contains 5mg hydrocodone with <u>300 mg</u> APAP
 - Vicodin ES contains 7.5mg hydrocodone with <u>300 mg APAP</u>
 - Vicoprofen contains 7.5mg hydrocodone with <u>200 mg</u> ibuprofen
 - Pregnancy Category C
- 1 tablet po q4-6 hours
- Indicate how many in writing
- Generics available

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Combos

- Aspirin w/Codeine #3

 30mg of codeine combined with 325mg of aspirin
- Aspirin with codeine #4
- 60mg codeine with 325mg aspirin
- Recommended dose of either is one tablet every four to six hours, with a maximum daily dose of 360mg of codeine



- Available with acetaminophen (Percocet)
- 10X effective than codeine
- Less side effects than codeine
- Higher addiction potential

Controlled Drug Act

- Schedule I drugs with a high abuse risk. These drugs have NO safe, accepted medical use in the United States. Some examples are heroin, marijuana, LSD, PCP, and crack cocaine.
- Schedule II drugs with a high abuse risk, but also have safe and accepted medical uses in the United States. These drugs can cause severe psychological or physical dependence. Schedule II drugs include certain narcotic, stimulant, and depressant drugs.
- Schedule III, IV, V drugs with an abuse risk less than Schedule II. These drugs also have safe and accepted medical uses in the United States. Schedule III, IV, or V drugs include those containing smaller amounts of certain narcotic and non-narcotic drugs. anti-anxiety drugs, tranquilizers, sedatives, stimulants, and non-narcotic analgesics.

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Tramadol hydrochloride

- Moderate to severe pain
- · Non-narcotic opioid receptor agonist
- Pregnancy Category C •
- 50-100mg q4-6 hours
- Side effects
 - Hallucinations
 - Fever
 - Nausea and vomiting
- Seizure
- Skin rash
- Shallow breathing, weak pulse

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Medical Marijuana

- Used for chronic pain in patients

 - Nerve damage
 - Terminal cancer
 - Nausea – Glaucoma
 - Movement disorders

Gabapentin

Exhausted All Options?

- Time to collaborate
 - Neurologists
 - Pain specialists
 - Anesthesiologists
 - Psychiatrists

Conclusions

- Treat the underlying cause
- Consider all treatment options
- Follow up is key
- wwhitley@cvphealth.com

