Ocular and Systemic Pain, and Drug Diversion CDR Chris Cordes, OD FAAO Staff Optometrist Albuquerque Indian Health Center United States Public Health Service

Disclosure Statement Nothing to disclose Course Description:

Course Description:
 This course presents a review of pain, both ocular and systemic. It reviews ocular and local anexthesia and it relationship to pain management. The course then reviews in depth ocular pain and how systemic and topical pain management is used for ocular pain drug diversion and its components with the use/need for opixits and drug diversion and its components with the use/need for opixits and or ocurse Learning Objectives :

- To understand the physiological pathways and components of ocular pain.

pain. - To review how to management ocular and systemic pain with both topical and systemic medications. - To understand drug diversion.





Noun Noun • ohysical suffering or distress, as due to injury, illness, etc. • a distressing sensation in a particular part of the body • mental or emotional suffering or torment Verb (used with object) • to cause physical pain to hurt • to cause (someone) mental or emotional pain distress Verb (used withor object) • to have or give pain



Definition of pain and classification of pain disorders K. Hanoch Kumar, P. Elavarasi- <u>http://jcri.net/elournals/ ejournals/112 Review%20Article.pdf</u>



Pain is the physical sensations or signals (within your body) that tells you something is happening within your body in relation to an event or situation. Suffering is the interpretation or story that you tell yourself about the pain (i.e thoughts, judgements, beliefs etc).

Pain and suffering is the legal term for the physical and emotional stress caused from an injury Some damages that might come under this category would be: aches, temporary and permanent limitations on activity, potential shortening of life, depression or scarring

3 Types Nociceptor Pain Receptors

一个画影 Nociceptor- Mechanical
 Respond to mechanical damage such as cutting, crushing or pinching

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- Nociceptor Thermal
   Temperature extremes (especially heat) Poly-modal Nociceptors Respond to all kinds of damaging stimuli- including irritating chemicals

Fast-Pain vs. Slow-Pain

Fast-Pain vs. Slow-Pain - A-belia Filess - A-belia Filess - Small Myelinated Filess - Small Myelinated Files - Small Myelinated Filess - Share pricing pain, easy to locate - Share pricing pain, easy to locate - Sile V Pain - Small Unmyelinated Filess - Small Unmyelinated Filess - Nath Pricing Status - Small Unmyelinated Filess - Nath Pricing Status -



Ocular Pain- Trigeminal Nerve









Ocular Pain	
• Originates from nociceptors	
Activated by mechanical and chemical stimulations.	
Processed into Trigeminal Nerve Pathway	







Ocular Pain Causes:

Physical
 Tachycardia
 Hypertension
 Peripheral Vasoc
 Tachypnea
 Emotional
 Poor Sleep
 Anxiety
 Uncooperativene







Orugs which produce reversible conduction blockage of nerve imputese.
 Completely reversible with no evidence of structural damage to the nerve fibers
 Loss of sensation without loss of consciousness
 Except Cocaina al (dinicial) year local anesthetics are synthetic and poorly water soluble, weakly basic and aromatic amines.

# Local Anesthetics- "CAINES"





# Aromatic Ring

-xomeset rngs [Jalos Insown as a renmatic compounds or arenes] are hydrocarbons which contain benzane or some other related ring structure. Benzene, CEH6, is often drawn as a ring of six carbon atoms, with alternasing double bonds and single bond

Ester Linkage





Hydrocarbon Chain



#### Tertiary Amine Group

Tertiary amine (3\* amine): An amine in which the nitrogen atom is directly bonded to three carbons of any hybridization which cannot be carbony group carbons. In organic chemistry, amines are compounds and functional groups that contain a basic nitrogen atom with a lone pair.

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B <sup>3</sup>	Content?	Anna PO	Annual (P) and a	Territory (27) anticine	Andrew (P)	

Mechanism of Action

 Prevent both GENERATION and CONDUCTION of nerve impulses. Work on Cell Membrane
 Block the transient increase in membrane permeability to sodium ions which normally occurs during depolarization of the membrane.





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# Duration of Action

- Proportional to the time in contact with the nerve tissue. ases so does pote
- As lipid solubility increased the potency also increased, however so does the toxicity.
- Ester compo hvdrolyzed unds are tonical and ranidh
- processed by the liver





Transition Transition Transition Transition Transition

Topical Ocular Anesthetic efficacy is determined by their ability to suppress corneal sensitivity.
 There is a point at which no further increase in activity of the drug occurs : maximum effective concentration.
 Indexing Sugge above maximum effective concentration only increases risk
 Optimum Effective Concentration

of toxicity.

Optimum Effective Concentration can be less than maximum

Tetracaine 0.5% is less irritating vs. the maximum effective concentration of
1.0%.

1.0%. • TOPICAL APPLICATION OF TWO OR MORE LOCAL ANESTHETICS DOES NOT PRODUCE AN ADDITIVE EFFECT.





Ester of para-aminobenzoic acid (PABA)
 Onset time of 10-20 seconds

- Clists for 10-20 minutes- 0.5%
   Reported 1% can last up to 1 hour and be used for cataract surgery
   Should NOT be injected- potent and potentially toxic over 1.5mg/kg
- Adverse Reactions: Singing Greater Corneal Compromise (microvili, cell membrane) Allergy



### Proparacaine 0.5%

- Ester of para-aminobenzoic acid (PABA)
   Onset time of 10-20 seconds
- Lasts for 10-20 minutes
- Does not penetrate into the cornea or conjunctiva as well as tetracaine
   Unopened bottles may be stored at room temperature
   Discard discolored solutions of Proparacaine

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- Adverse Reactions:
   Stinging- very mild
   Hypersensitivity- rare
   Corneal Thickness changes

#### Ocular Anesthetics Benoxinate 0.4%

- Ester of para-aminobenzoic acid (PABA)
- Similar duration and effect as Tetracaine and Proparacaine 0.5%
   10-20 seconds for 10-20 minutes
- Always combined with a vital dye (Sodium Fluorescein)
   Sodium Fluorescein alone is good Pseudomonas aeruginosa n
   However in combination with Benoxinate it is bactericidal Adverse Reactions:
- Stinging
   Allergy- very low profile
   Can increase or decreased corneal thickness +/- 10um

# Adverse Drug Reactions/Side Effects

- Risk of those over 50 to get Superficial Punctate Keratitis
- More risk for filamentary keratitis and corneal edema
   Repeated administration of topical ocular anesthetics should be
   avoided. It significantly inhibits healing of the corneal epithelium.
- Systemic absorption of topical anesthetics or injection of them, can cause CNS depression, hypotension, low/absent pulse which can result in respiratory failure Allergic/Hypersentivity reactions are uncommon, but mainly with ester compounds. Amine compounds occur at a much lower rate.
   Occur 5-10 minutes after instillation

Adverse Drug Reactions/Side Effects

- No life threatening allergic responses to topically applied ocular anesthetic has ever been reported.
- has ever been reported. In ejected medications have a very rare chance at anaphylactiod responses # syschomotor-Fainting-can happen but mostly it is anxiety driven Contraindications # uppersubity Uture Disease (ipictable) # systemic Arat: coloniestrase gents (high dosages of topical anesthesia) Dry by Ensign Performing Octar Hyuny (BAC) Chances (ipicchionychion)

# Self Administration of Topical Anesthetics

#### DON'T DO IT

- Leads to infiltrative keratitis and lose of eye
- Occurs from 6 days of usage to 6 weeks
   Loss of corneal epithelium
   Inhibits healing of epithelial defects, loss of microvilli



- Stromal Edema Descemet's Folds
- Yellow-White Ring around area of diseased area



 Centrally Acting Agents
 Works on Central Nervous Sys
 Opioids em blocking both pain and emotional response

Ocular Pain Treatment

Peripherally Acting Agents
 Act on peripheral pain recept
 Block Cycloarygenase Pathway
 Anesthetic Agents

 Nociceptive signal interrupted um Chi nel Block i





G disturbance is most common ADR
 Monsailicytae
 Most used for anti-inflammatory but also effective analgesic
 Most used for anti-inflammatory but also effective analgesic
 Propoinci Acd and COX2 inhibitor classes
 Primarily works by inhibitior classes
 Primarily works by inhibitior classes
 Promotion Acd COX2 inhibitor classes
 Proto-based and COX2 inhibitor classes
 Portunative and Por









- Ibuprofen
   Motrin, Advil, etc
- Naproxen
   Naproxen
   Specifically dev
- eloped to reach peak plasma level rapidly Naproxen Sodium
   Aleve



 Aleve
 Celecoxib
 Celeberex
 ADR's: Decreased Attention, confusion, headache, GI risks Avoid in Renal Patients, Pregnancy and breast feeding

Acetaminophen

Superior safety profile



Safe in pregnancy and breastfeeding in proper dosages

# Cycloplegia

- Inhibit the actions of acetylcholine on muscarinic sites Anticholinergics
- Specifically the Iris Sphincter Muscle and Ciliary Body
- minervauon originates at the Edinger-Westphal Nucleus Pre-Ganglionic parasympathetic fibers travel within CNIII Proceed to the Cliary Ganglion and synapse with postganglionic fibers and enter the globe through short cliary nerves Short cliary reverse run to the second states
- Short ciliary nerves run to the muscarinic receptors (acetylcholine) in the Iris Sphincter and Ciliary Body
   Thus, decreasing the activity the sphincter and ciliary body

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# Cycloplegics

- Atropine
   Naturally occurring alkaloid from bellad
- Homatropine
   Partially synthetic , partial natural Scopolamine
   Alkaloid from plants, shorter duration of action-



Alkaloid from plants, shorter duration of action- Ang
 Cyclopentolate
 Water Soluble Ester introduced in 1951
 Tropicamide
 Synthetic derivative of Tropic Acid, available in 1959

# Opioids

 Opioids/Opiate
 Codeine
 Oxycodone
 Hydrocodone
 Propoxyphene Hydrom
 Tramado





Analgenicippield	Strength' (merphics)	Equivalent dose (78 mg reception)	Strength (codeline)	Equivalent dess (30 mg codelas)
Aspin (hen-spicid)	1/363	eil .	1.06	1080 mg
Diffusioni (NSAD, non-opioid)	1/163	1600 mg	1/95	400 mg
Dectroproper yphene <sup>210</sup>	1140	400 mg	14	120 mg
Codeine	1/10	100 mg	00	(00 mg)
Turnedal	1/10	100 mg	1	30 mg
Anilei den <sup>21</sup>	114	40 mg	2.6	12 mg
Pethidee	0.36	27.8 mg	2.6	8.2 mg
Methodora <sup>E1</sup>	52	20 mg	6	6.mg
Hydrocodone	0.6	16.67 mg	6	5-mg
Maghine (and)	05	(10 mg)	10	2 mg
Oxycothee	15-2	45-0 mg	15-20	15-2 mg
Marghine (V/M)	4	25.mg	43	0.75 mg
Discontringuine - hensis (holbs) <sup>24</sup>	4.3	2.25 mg	43	0.7 mg
Hydromorphone <sup>RII</sup>	5	2 mg	50	0.6 mg
Oxymoshare	7	1.4 mg	23	0.4 mg
Larophang <sup>(R)</sup>	8	0.8 mg	00	0.26 mg
Burrenuphine <sup>(F)</sup>	40	0.25 mg	400	0.075 mg
Ferting	50-100	01-02 mg	500-1000	0.03-0.06 mg
Substanyl	500-1,000	10-30 /4	5000-10,000	3-6 yg
El sophere <sup>4</sup>	1,000-3.000	10.48	13.000-30.000	1-3 ya
Cadestani	10,000,100,000	0.1.1 va	100-000-1 000-000	30-300 m

Opioid	Strength (Codeine)	Equivalent Dose (30 mg codeine)	Strength (Morphine)	Equivalent Dose (10 mg morphine mg)
Aspirin	13150	1080 mg	1/360	3600 mg
Difusinal	35811	480 mg	1/160	1600 mg
Dextroproposyphene	35799	120 mg	14611	400 mg
Codeine	1	30 mg	35805	100 mg
Tramadol	1	30 mg	35805	100 mg
Anileridine	2.5	12 mg	35799	40 mg
Demerol	3.6	8.3 mg	0.36	27.8 mg
Hydrocodone	6	5 mg	0.6	16.67 mg
Morphine	10	3 mg	1	10 mg
Oxycodone	15-20	1.5-2 mg	1.5-2	4.5-6 mg
Morphine IV/IM	40	75 mg	4	2.5 mg
Hydromorphone	50	6 mg	5	2 mg
Oxymorphone	70	0.4 mg	7	1.4 mg
Levorphanol	80	0.26 mg	8	8 mg
Buprenophine	400	0.075 mg	40	25 mg
Fentanyl	500-1000	0.03-0.06 mg	50-100	0.1-0.2 mg



UDIOID ADK S • Numerous • Sedition • Confusion • Cunstipation • Cough Suppression • Circulatory Depression • Biurred Vision • Minosis • Diplopia • Addiction





DEA Schedule

 Schedule I
 Schedule I drugs, substances, or chemicals are defined as drugs with no currently occepted medical use and a high potential for abuse. Some examples of Schedule I drugs are: heroin, lysegic acid diethylamide (LSD), marijuana (cannabis), 3,4-methylenedioxymethamphetamine (ecstasy), methaqualone, and peyote

Schedule II

Schedule II drugs, substances, or chemicals are defined as drugs with a high potential fo abuse, with use potentially leading to severe psychological or physical dependence. These drugs are also considered dangerous. Some examples of Schedule II drugs are: Combination products with less than 15 milligrams of hydrocodone per dosage us (Vicodin), cocaine, methamphetamine, methadone, hydromorphone (Dilaudid), meperidine (Demerol), oxycodone (OxyContin), fentanyi, Dexedine, Adderall, and Ritallin DEA Schedule

- Schedule III Annount and - Annount annonnonnont annount annount annont annount a
- Annouse IV
   Schedule IV drugs, substances, or chemicals are defined as drugs with a low potential for abuse and
   bornk of dependence. Some examples of Schedule IV drugs are:
   Xanax, Soma, Darvon, Darvocet, Valium, Ativan, Talwin, Ambien, Tramadol
   Schedule V
- Schools V (specializations, or chemicalis are defined as drugs, with lower potential for elbodic Schools V drugs are generally used for netidiartheal, antitustee, and analysis purposes. Some complex of Schools V drugs are couply progradions with less than 200 milligans of codeline or per 100 millitlers (poblessin AL) consol, Marchin, Virst, Ampericalin

- Optometry and Opioids (02/2020)

- Optometry and Opioids (02/2020) Cannot RV: DC, Guam, HI, MD, MA, NY, PK, VI, CNMI Schedule IV United: NINT anadol, NM, MS Schedule II United: AIR, Ter, ME, ND, MH, PA, TX\*, VT, VY TX can administer Schedule II, FL, MAP with Codeme and Tramadol Schedule II NOILY HYDROCODON: AK, AR, AZ, CO, DE, GA, IL, KY, MI, NM, NI, OH, OK, OR, RJ, SC, UT, VA, WA, WY, WI Schedule II Norestricted: CT, ID, IA, LA, KS, MO, MT, NC, NE, NV, SD\*, TN Schedule II Norestricted: CT, ID, IA, LA, KS, MO, MT, NC, NE, NV, SD\*, TN
- SD Limited to 30 day supply
- October 6th, 2014- DEA reclassifies Hydrocodone

Drug Diversion

- https://www.deadiversion.usdoj.gov/
   The use of prescription drugs for recreational purposes
   the diverting of predrugtions for other than it's intended purpose.
   From CMS:
   One of the diverting of the divertin
- From CMS: Orug diversion is the illegal distribution or abuse of prescription drugs or their use for purposes not intended by the prescriber (1) The diversion of prescription drugs may occur at any point as prescription drugs are pharmackis, and ultimately to the patient (2) Members of the medical profession may also be involved in diverting prescription drugs are recreational purposes, relief of addictions, monetary gain, self-medication for pain or siles, or the allevation of withforwas profons.

# Drug Diversion- Common Types

	Pharm	nacy th	efts, Ma	ine and	the U.S.	
Selling prescription drugs	Maine ;	Marmacy	thefts	U.S. pha	macy the	ifts
Dector shopping Illegal Internet pharmacies Drug theft Prescription pad theft and forgery Illicit prescribing	68% Armed soldery 57 tools Maine p in desay	23% bagdopes philosope Jitroth	9% Hight Institut Institut	26% amed elibery 2.070ech	46% trapinge pilicope 130° acts remary the pr units	28% National Sciences Sciences
A series of the	43%	37%	20%	11% and abley control desp	44%	45%
		ing below man a	-		-	ALC: NOT A

# Drug Diversion- Opioids





#### Drug Diversion

- Inical Practices That Can Minimize Drug Diversion Exercising caution with patients who use or request combination or Tayered drugs for enhanced effects (for example, anti-psychotics with Documenting Incoughly when prescribing narcotics or choosing not to prescribe

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- ping a DEA or license number confidential unless disclosure is uirord
- required Moving to electronic prescribing so that paper prescriptions are not required

Drug Diversion – REPORT IT!

Local law enforcement and local fraud alert networks

DEA, for reporting theft or loss of controlled substances: https://www.deadiversion.usdoj.gov/webforms/\_dtllogin.jsp
 U.S. Department of Health and Human Services, Office

- of Inspector General (HHS-OIG) by e-mail at <u>HHSTIDS@oig.hhs.gov</u> Telephone at 1-800-HHS-TIPS (1-800-447-8477) TTY: 1-800-377-4950

# Drug Diversions- Turn ins Drug Turn Ins



# Case Study

• 48 yo Native American Male- Assaulted with Fist x 3 days ago Lost Glasses (i.e. never got them)
 All entrance testing normal

Refraction:
 OD: -6.00-2.50x177 20/25
 OS: -6.50-1.75x010 20/25-



#### Acetaminophen and NSAID

ACE Calmin Op I et al di NSAID 4 Ierraria 007 cmedicison consistenti bus ondro provide adequate acute pain retief 5 start with etter at initial dosage 4 Start with etter at initial dosage 5 User geno Storegen Twent to Start (am) 5 Start geno Storegen (Start) 5 Start geno Start geno Storegen (Start) 5 Start geno Start gen

https://www.ada.org/en/publications/ada-news/2020-archive/march/fda-ap combination-ibuprofen-acetaminophen-drug-tor-us

### Any NSAID

 Naproxen BID Ibuprofen 400mg, 600mg, 800mg TID
 Acetaminophen 500/325mg q4-6 hours

Should be your "workhorse" medication for any acute short term pain relief.

# ICE PACKS

 Don't forget about ICE! Every 2 hours for 15-20 minutes for 72 hours.



A bit of everything...

·76 year old Pueblo Male presents with Swollen Left Upper Polyela Ola 7 delation water presents with swolien Left op Evelial (May 2015)
 Established patient, multiple co-morbidities
 Diabetes, Chronic Pain (opioid management), Hypertension, Neuralgia, Sleep Apena, Obesity and Asthma



# CASE HISTORY

76 year old Pueblo Male presents to the ER/Urgent Care
 Upper Respiratory Infection
 Augmentin
 Prednisone 40mg PO



# URTI Background

 The upper respiratory tract includes: Mouth Nose Sinus Throat Larynx (voice box) Trackas (windpipe) Construction to construct to const Often referred to as "colds" Viral or bacterial





 Patient returns to the ER, stating no improvement in URTI Patient is given 2 grams of Intramuscular Steroid · Stopped taking Augmentin



# Back to optometry

• 76 year old Pueblo Male presents with Swollen Left Upper Eyelid

 History as presented—2 ER trips • But now...



Sto-clice

Source: 2

# Treatment

 Started on Augmentin 875/125mg BID x 14 days Can alter based on allergies
 Prefer less total dosages (BID)

Started on Acyclovir 800mg
 5x/day x 7 days (formulary)



Zovirax (Acyclovir) 800mg 5x/day PO Famvir (Famciclovir) 500mg tid PO Valtrex (Valacyclovir) 1000mg tid PO

# Follow-up

 Patient returns for 2 day follow up
 Pre-Septal is looking better
 Zoster looks the same, definitely not worse. Pain is WORSE
 Already taking Gabapentin, Percocet daily

· Capsaicin Cream: Pharmacy/Quick Order Amitriptyline 25mg PO TID



Cless	Medication	Dosage	Cost of generic (brand)*	ANT	Adverse effects
Anticonvulsants	Gabaportin (Neurontin)	1,800 to 3,600 mg	\$50 to \$186 (92.02 or \$1862)	2.8-5.3 Somelience, dizzine edima, dry mouth	Somelence, distinua edima, dra marth
	Prepabalin (Syrica)	150 to 600 mg per-day	NA (\$85 to \$192)	4.9	
2pi si di	Controlled-release procedure (Oxycontin)	oe Verable N4-(3223, 15-mp.12- 2.7 Comitgeti systemini hourstatiets) rosena.	Contipution, routing, vomiting,		
	Long-acting morphine	Variable	\$64 (\$84), 15 erg 12-hour tablets	2.7	sellation, dizziness, dependence
	YanadoliUltrani	100 to 400 mg per sky	\$34 (\$142), 100 mg per tity	4.8	Dependence
fopical agents	Copsaicie 0.075% ceaam (Zootto)	Applied three or laur times per day	NA (\$19 to \$25, 2 od)	3.3	Burning skin
	Lidoceine 5% petch (Lidoderm)	Maximum three partitives per day	N4 (\$217, 30 petches)	2.0	Mild skin reaction
Veyele artidoprosants	Amitriptylinet Desipramine (Norpramini Nortriptyline Pamelott	Up to 150 mg per day Up to 150 mg per day Up to 150 mg per day	\$17(NA) \$140(\$180) \$19(\$1,082)	2.6	Sedation, dry mouth, blured vision, constipation, univer referition
un - not applicable	Mill = number seeded to the				
-Extimated retails rice listery in parent	price based on information obt freezo.	ained at http://www.chugate	ee.com-Secreted Aebraary 76	2018. Gen	ext price liand frat, dran

# Over the next 6 Weeks

Severe Post Herpetic Neuralgia
 Cannot sleep at times
 Cannot function daily
 Taking all medications

Pre-Septal Resolved in 7 days

• Eventually referred to pain manag Lost to follow up/referral issues

Steroids—can/did make it worse?
 Small Studies- can be beneficial
 Large Studies- can make it worse



# Conclusion

 Work with your Pharmacist \*\*\*if you don't have one, work to get one!\*\*\* Sometimes modern medicine is pushed for answers

Get background information:
 Case history
 Recent medications



# Thanks!

Feel free to email Questions Comments <u>Christopher.Cordes@ihs.gov</u> Friend me on Facebook, etc.