



PAIN

New York Certification Course
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Dipl ABO

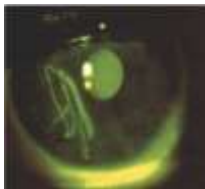
Case Report

- A 22 y/o reports with a CC of a sudden onset of pain in her left eye for the past 8 hours
- The pain is most apparent each time that she blinks and the only relief that she experiences is when she shuts her eyes.
- This occurred after rubbing her eyes after dirt was thrown at her by a child in her care.
- She reports excellent health and NKA's



Case Report

- VA's s 20/15 OD/OS
- Eye exam unremarkable with the following notable exceptions
- Assessment
- Plan
- Follow up



Case Report

- Retained fb on superior palpebral conjunctiva



Treatment Strategies for Trauma

- Get patient to safety
- Treat their pain
- Treat their inflammation
- Promote wound healing
 - Stop bleeding
 - Clean/disinfect wound
 - Close wound (as indicated: bandage, stitch, glue)
 - Immobilize wound (e.g. patch, splint, cast, rest)
- Prevent infection
- Prevent secondary disease/recurrence

Treatment Strategies for Trauma

- Get patient to safety
- Treat their pain
- Treat their inflammation
- Promote wound healing
 - Stop bleeding (e.g. pressure, vasoconstrict, cold, epinephrine)
 - Clean/disinfect wound
 - Close wound (as indicated: bandage, stitch, glue)
 - Immobilize wound (e.g. patch, splint, cast, rest)
- Prevent infection
- Prevent secondary disease/recurrence

Pain Control

- Cold (Ice packs)
- Topical NSAID
 - Controversial
- Topical Anesthetics
- Oral Medications
 - Acetaminophen
 - NSAID
 - Steroids
 - Narcotics
 - Adjuvants
 - E.g. Gabapentine (Neurontin) 400 mg q4 h



Adjuvants

- No direct analgesic effect (as monotherapy)
- Enhance efficacy of analgesic agents
- Tricyclic antidepressants (e.g. amitriptyline)
- Anticonvulsants (e.g. carbamazepine, clonazepam, phenytoin, gabapentin)
- Both have been used to relieve several types of neuropathic pain

In Office Treatment Strategy

Goals

- **Treat their pain**
- Promote Wound Healing
- Prevent Infection
- Prevent recurrence



Let's think about this one

Intervention Examples

- 1 gtt proparacaine oph soln (short term/break cycle/VA)
- Acetaminophen 325 mg q 4-6 hours (PRN)
- Topical NSAID (e.g. ketorolac 0.4/0.5% QID x 3 days)
- Remove retained fb
- Immobilize (patch/cyclo)?
- Close/bandage wound?
- Rx broad spectrum antibiotic gtt
- Safety glasses

Topical NSAIDs for the treatment of pain in traumatic corneal abrasions Cochrane Meta-analysis 2017

- **The findings do not provide strong evidence to support the use of topical NSAIDs in traumatic corneal abrasions**
- This is important, since NSAIDs are associated with a higher cost compared to oral analgesics.
- None of the trials addressed our primary outcome measure of participant-reported pain intensity reduction of 30% or more or 50% or more at 24 hours.

NSAID-induced corneal melt (NICM)

- An intriguing aspect of NICM is the apparent requirement for a compromised cornea for it to occur.
- Cell death seems to be a primary event, and it is likely that "compromised" corneal epithelial cells respond differently to NSAIDs than healthy ones

Rigas B, Huang W, Honkanen R. NSAID-induced corneal melt: Clinical importance, pathogenesis, and risk mitigation. Surv Ophthalmol. 2020 Jan-Feb;65(1):1-11. doi: 10.1016/j.survophthal.2019.07.001. Epub 2019 Jul 12. PMID: 31306671.

If Medication is Indicated in the Management of Eye Pain Oral Analgesics

- Mild Pain
 - Acetaminophen 325 mg q 4-6 hours
 - Ibuprofen 400*-600** mg q 4-6 hours
 - Naproxen 250-500 mg BID
- Moderate Pain
 - Acetaminophen 300 mg/codeine 30 mg q 6 hours (AKA Tylenol 3)
- Severe
 - Acetaminophen 300 mg/hydrocodone 5 mg q 4-6 hr
 - Lorcet, Lortab, Norco, Vicodin
 - Ibuprofen 200 mg/hydrocodone 7.5 mg q 4-6 hr
 - Vicoprofen
 - Acetaminophen 325 mg/oxycodone 2.5-10 mg q 4-6 hr
 - Percocet, Roxicet, Tylox, etc

• * For pain
• ** For inflammation

Course Summary

- Function of pain
- Types of pain
- Transmission of pain signal to brain
- Transmission of modulation signal from brain
- Therapeutic interventions along the pain pathway
- Clinical examples

Function of Pain

- Alert the organism that it is in danger so it will alter the circumstances
 - Withdraw effected region from harm
 - Many similar messengers as our fight-flight response
- Immobilize the organism (effected region) to promote healing



Other pain mediators associated with Injury/Inflammation

- 5-HT (converts to serotonin), kinins, histamine, nerve growth factors (NGF), adenosine triphosphate (ATP), glutamate, nitric oxide (NO), NE and protons
- Some sensitize the receptors
- Others serve as neurotransmitters

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Pain and Inflammation

- Following injury, the localized inflammatory response induces the release of free arachidonic acid (AA) from membrane phospholipids, which are converted into prostaglandins (PG) via the cyclooxygenase (COX) pathways.



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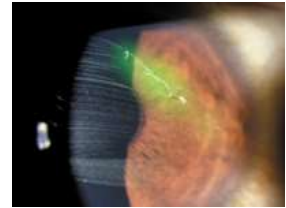
Types of pain

- Acute — injury, inflammation
 - most ocular pain
 - Eg. Corneal abrasion or fb
- Chronic
 - E.g. s/p EOM surgery
- Neuropathic — from diseases of the nerves or from injury to nerves
 - Eg. Corneal Neuralgia
- Cancer — pain related to malignant disease or tumors and their effects on the body



Acute Pain

- Usually a specific and obvious cause (e.g. trauma, surgery)
- Limited duration
- Resolves when the source of pain is detected and treated
- ~ requires topical/local treatment
 - Fewer side effects/complications

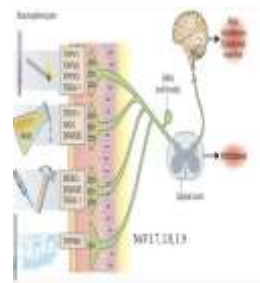


Course Summary

- Function of pain
- Types of pain
- Transmission of pain signal to brain
 - Stimuli that Trigger the Pain Response
 - Pain receptors
 - The ascending pathway
- Transmission of modulation signal from brain
- Therapeutic interventions along the pain pathway
- Clinical examples

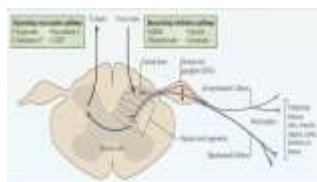
Stimuli that Trigger the Pain Response

- Trauma
- Extreme Heat
- Extreme Cold
- Chemical



Pain Receptors Nociceptors

- Aδ-fibers
 - Acute
 - Myelinated
- C-fibers
 - Chronic
 - Unmyelinated

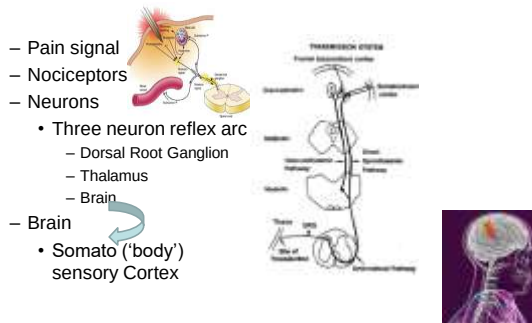


Course Summary

- Function of pain
- Types of pain
- Transmission of pain signal to brain
 - Stimuli that Trigger the Pain Response
 - Pain Receptors (Nociceptors)
 - The Ascending Pain Pathway
- Transmission of modulation signal from brain
- Therapeutic interventions along the pain pathway
- Clinical examples

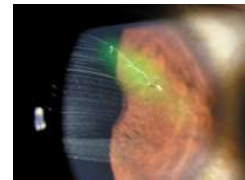


The Ascending Pain Pathway



The Ascending Pain Pathway

- Transmission of pain signal to brain
 - Pain signal clinical examples
 - Mechanical (trauma)
 - Chemical/Thermal



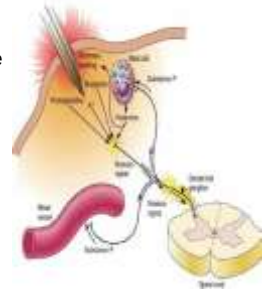
Topical Anesthetic Agents

- Block the nociceptive signal between its peripheral source and its central target by blocking the Na channels (no Na, no action potential)
- Proparacaine
- Tetracaine



Pain Mediators

- Tissue injury causes release of chemicals
- They sensitize or activate receptors
- Neurons release **substance P**, which stimulates mast cells and blood vessels
- Histamine released from mast cells and bradykinin released from blood vessels add to pain stimulus



Nociceptor Activation

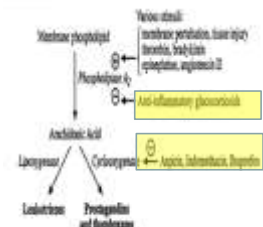
- Mechanical Stimulation
 - E.g. tissue injury
- Release of Chemical Compounds associated with Injury/Inflammation
- ARACHIDONIC ACID METABOLITES
 - PROSTAGLANDINS
 - LEUKOTRIENES

Other chemical mediators:
5-HT (converts to serotonin), kinins, histamine, nerve growth factors, adenosine triphosphate (ATP), glutamate, nitric oxide



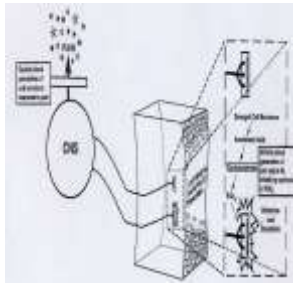
THERAPEUTIC INTERVENTION

- Anti-inflammatory glucocorticoids
- NSAIDs

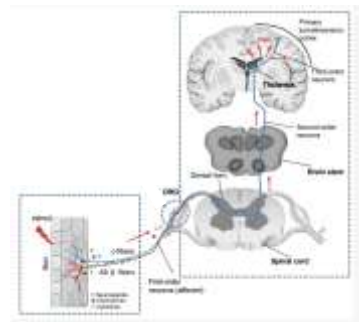


Peripherally Acting Agents

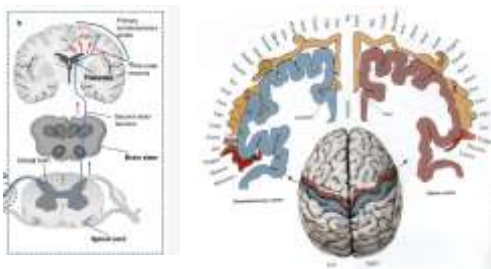
- Prevent sensitization and discharge of the nociceptors
- NSAIDs (including ASA)
 - Block the formation of inflammatory and pain mediatory (e.g. prostaglandins) at the cyclooxygenase pathway



Summary of Ascending Pain Pathway



Cortical Magnification (similar to Visual Cortex)



Pain Pathway of the Eye

- Pain signal is conveyed via CN V to the brainstem (to sensory and spinal nuclei of CN V)
- CN V nuclei sends the pain message to the somatosensory cortical areas

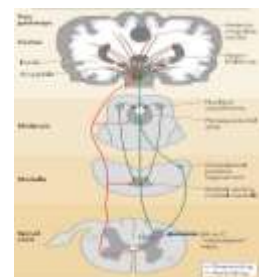


Course Summary

- Function of pain
- Types of pain
- Transmission of pain signal to brain
 - The ascending pathway
- Transmission of modulation signal from brain
 - The descending pathway
- Therapeutic interventions along the pain pathway
- Clinical examples

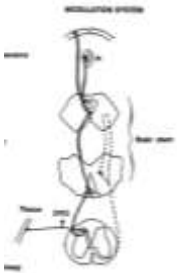
The Descending (modulating) Pain Pathway

- Critical modulator of nociception
- Important role in mediating endogenous and exogenous opioid-induced analgesia



The Descending (modulating) Pain Pathway

Endogenous Opioid System



- Physiological modulation of pain
- Endogenous Opioids
 - B-endorphins – which predominately binds to mu opioid receptors
 - Dynorphins – which predominately bind to kappa opioid receptors
 - Enkephalins – which predominately bind to delta opioid receptors

Role of Opioids in Pain Modulation

- Regulate pain within
 - Brain Stem
 - Cortex
 - Spinal Cord
 - dynorphins and enkephalins reduce the transmission of pain signals in the
 - Dorsal horn
 - » post-synaptic ends of second-order neurons
 - Pre-synaptic ends
 - » first-order neurons



What about the Pain and Anxiety?



Why Opioids Can Produce Analgesia and Euphoria Mu-Opioid Receptors

- Densely concentrated in brain regions that regulate pain perception
 - periaqueductal gray matter
 - thalamus
 - cingulate cortex
 - insula



Why Opioids Can Produce Analgesia and Euphoria Mu-Opioid Receptors



- In addition to pain-induced emotional responses
 - amygdala
- and brain reward regions
 - ventral tegmental area
 - nucleus accumbens
- that underlie the perception of pleasure and well-being.

Bloking Mu-Opioid Receptors Causes

- Analgesia
- Sedation
- Decreased bp
- Itching
- Nausea
- Euphoria
- Decreased respiration
- Effects decline as tolerance develops

Physiologic Effects of Pain

- Tachycardia
- Systemic hypertension
- Tachypnea
- Can exacerbate pre-existing cardiovascular disease

Psychological Effects of Pain

- Poor sleep patterns
- Anxiety
- Uncooperativeness

Physiologic and psychological effects of pain can result in slow and unsatisfactory resolution of the ocular condition initiating the pain

Wong-Baker Faces Pain Rating Scale



Pain severity assessment, as required by The Joint Commission, is intended to improve the quality of pain management.
Provides a baseline which can inform initial treatment and effects of treatment

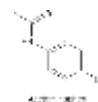
Pain Control

- Cold (Ice packs)
- Topical NSAID (controversial)
- Topical Anesthetics
- Bandage Contact Lenses
- Oral Medications
 - NSAIDs*/Acetaminophen
 - Steroids*
 - Narcotics
 - Adjuvants

* Covered in Inflammation Course

Acetaminophen

- Centrally acting analgesic?
- Well absorbed orally
- Produces analgesia by elevation of the pain threshold
- Produces antipyresis through action on the hypothalamic heat regulating center
- Equal to aspirin in analgesic and antipyretic effectiveness.



Acetaminophen

- **Indications**
 - Pain
 - Fever
 - Temperature >102 degrees Fahrenheit
 - Fever at bedtime
- **Efficacy: Acetaminophen with Codeine**
 - Codeine adds side effects but no benefit to Tylenol
 - Tylenol and NSAIDs are as effective as Tylenol #3
- **Efficacy: Rheumatologic conditions**
 - Scheduled dosing much more effective than prn
 - Tylenol 1000 mg qid is as effective as Tylenol #3

Acetaminophen-When to Use

- Children
- Viral Induced Fever
- Pregnancy
- Nursing Mothers
- Patients with GI disorders
- Patients with Bleeding/Clotting disorders

Acetaminophen-When to Consider Alternatives

- History of liver failure
- Alcoholics (>3 drinks/day)

Acetaminophen

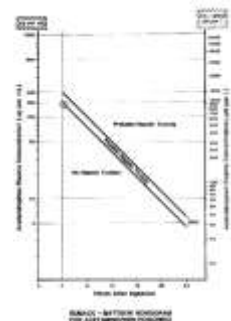
- **Dosing: Adults**
 - Regular Dose: 650 mg PO every 4 to 6 hours prn
 - Higher Dose (Osteoarthritis)
 - Regular Strength Tablet (325 mg)
 - Take 975 mg (3 tablets) PO every 6 hours
 - Extra-Strength Tablet (500 mg)
 - Take 1000 mg (2 tablets) PO every 6 hours
 - Maximum: 4 grams per day
 - Do not exceed 12 regular strength tablets (325 mg)
 - Do not exceed 8 extra-strength tablets (500 mg)

January 13, 2011

- The US Food and Drug Administration (FDA) today announced that it is asking drug makers to limit the amount of acetaminophen in prescription combination pain relievers to no more than 325 mg per tablet or capsule (up to 3 grams/day this year(2012)) to reduce overdoses and the severe liver injury that can follow.

Acetaminophen

- **Risk Factors for hepatotoxicity**
 - Overdosage (over 4 grams in 24 hours)
 - Dehydration or fasting
 - Alcohol Abuse
 - Concurrent use of other medications
 - Isoniazid
 - Zidovudine
 - Barbiturate



Acetaminophen

• Precautions

- Dehydration predisposes to overdosage
- Never exceed maximum daily dosage (hepatotoxicity)

Cases

- Corneal Abrasion
- Corneal Collagen Cross Linking post op
- Pain with no Stain (AKA Corneal Neuralgia)



Post Op Management of Corneal Cross Linking

Day of Surgery			Day 4-7		
Action of medication	Frequency of medication	Additional comments	Action of medication	Frequency of medication	Additional comments
Anti-inflammatory	1 drop every hour	Stings a little	Anti-inflammatory	1 drop every 2 hours	Stings a little
Antibiotic	q-4 times a day		Antibiotic	1 drop 4 times a day	
Tear supplement	every hour	Comfort drop	Tear supplement	1 drop every 2 hours	Comfort drop
Anesthetic drop	prn				

Naproxen (250mg) BID (or Ibuprofen 200mg TID) x 3 days.
Supplement with Acetaminophen 325 mg q 4-6 hours



If Medication is Indicated in the Management of Eye Pain Oral Analgesics

- Mild Pain
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 - Ibuprofen 400*-600**up to 800 mg q 4-6 hours (max daily 2400-3400 mg)
 - Naproxen 250-500 mg BID
- Moderate Pain
 - Acetaminophen 300 mg/codeine 30 mg q 6 hours (AKA Tylenol 3)
- Severe
 - Acetaminophen 300 mg/hydrocodone 5 mg q 4-6 hr
 - Lorcet, Lortab, Norco, Vicodin
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 - Percocet, Roxicet, Tylox, etc
 - * For pain
 - ** For inflammation

NSAID Side Effects, ADRs

- Inhibit platelets (only ASA is irreversible)
- GI upset
- GI ulcer/bleeding/perforation
- Increase risk of serious cardiovascular thrombotic events (MI, CVA): FDA increase warning in 2015



NSAID Precautions

- Asthmatics
- DM relative risk
- Children with fever (no ASA)
- Viral Induced Fever
- Pregnancy
- Nursing Mothers
- Patients with GI disorders
- Patients with Bleeding/Clotting disorders

Pain without Stain

- A patient walks into your office complaining of chronic dry eye symptoms but shows no staining or other signs of tear deficiency.
- Unsure of a diagnosis, you initiate treatment with topical therapies to optimize the ocular surface.
- The patient finds no relief. Now what?

- A clinical diagnosis made for patients with corneal pain that has few-to-no clinical signs and is minimally, if at all, relieved by conventional treatments for DED.
- No standard clinical criteria and no ocular sensory tests that are diagnostic
- Symptom profile of burning and pain associated with wind and light.
- Signs that tend to be associated with neuropathic pain
 - persistent pain after anesthesia (topical proparacaine)
 - a marker of "central sensitization" or centralized neuropathic pain.



Pain with no Stain



- | | |
|---|--|
| <ul style="list-style-type: none"> • The goal of treatment is to reduce pain signaling to <ul style="list-style-type: none"> – provide relief – provide relief • Local support/protection <ul style="list-style-type: none"> – PF ATs • Treat inflammation <ul style="list-style-type: none"> – FML – Cyclosporine – Lifitigrastr | <ul style="list-style-type: none"> • Suppress peripheral sensitization <ul style="list-style-type: none"> – Topical analgesics – PO NSAIDS • System suppression of central sensitization <ul style="list-style-type: none"> – Gabapentin – Tricyclic antidepressants – Serotonin-norepinephrine reuptake inhibitors (SNRIs) |
|---|--|

Adjuvants

- No direct analgesic effect (as monotherapy)
- Enhance efficacy of analgesic agents
- Tricyclic antidepressants (e.g. amitriptyline)
- Anticonvulsants (e.g. carbamazepine, clonazepam, phenytoin, gabapentin)
- Both have been used to relieve several types of neuropathic pain

Discussion on Opioids

- Centrally Acting
 - Inhibits descending pain pathway
- Interrupt pain signal AND emotional response
 - Feel pain, don't care
- Mechanism incompletely understood
 - Mimic Natural Endorphins
- ALLERGIC TO ONE OPIATE: ALLERGIC TO ALL

Before Rxing Opioids

- Discuss substance abuse
- Look for tell tale signs
 - h/o substance abuse
 - Social history
- Encourage Non-Opioid/Alternative Approaches
- Rx short-acting opioids ONLY enough for acute pain (3 days)
- Pt Ed side effects, risk of dependence/addiction, safe use, proper disposal

Side Effects of Opiates

- Respiration: sleep apnea/COPD
- Urinary tract: enlarge prostate
 - Can be used to treat incontinence
- GI tract: Slows motility
 - Lomotil
 - Diphenoxylate + atropine
 - Subtherapeutic for pain relief

TOLERANCE

- Tolerance
 - Reduced response to drug's action
 - Decreased effect from a constant dose
 - Increase in minimum dose to yield effect
 - Physiological
 - Changes in binding of a drug to receptors
 - Changes in receptor transduction process

DEPENDENCE

- Dependence
 - Drug necessary for normal physiological functions

Withdrawal reactions

- Opposite of the physiological effects of the drug)
 - Pain and irritability
 - Hyperventilation
 - Dysphoria and depression
 - Restlessness and insomnia
 - Increase bp
 - Diarrhea
 - Pupillary dilation
 - Hyperthermia
 - Tearing/Runny nose
 - Chills/goosebumps

Combination Opiate Analgesics

- | | |
|---------------|--------------------|
| • Tylenol 1-4 | APAP + Codeine |
| • Vicodin | APAP + Hydrocodone |
| • Percodan | ASA + Oxycodone |
| • Percocet | APAP + Oxycodone |
| • Ultracet | APAP + Tramadol |

Pain Control Without Opioids

- 500-100mg Tylenol + 400-600 mg Ibuprofen
 - ~equivalent analgesia to opioids
- Contraindications/Caution for each drug
 - Ibuprofen
 - Pregnancy
 - Bleeding/GI
 - Renal disease
 - Acetaminophen
 - Liver disease