Financial Disclosures

- No disclosures

Importance

- Know drugs you’re administering to patient
- Patient education
- Reactions
- Triage

Outline

- Importance
- Instillation
- Identification
- Autonomic Nervous System
  - Adrenergic and Cholinergic Agents
  - Mydriatics, Miotics, and Cycloplegics
  - Glaucoma Medications
- Corticosteroids
- NSAIDs (non-steroidal anti-inflammatory)
- Anti-Allergy
- Anti-infective (bacterial, viral, fungal)
- Systemic Effects of Ocular Medications
- Ocular Effects of Systemic Medications
- Self-Test Questions

Importance

- For the COA/COT/COMT
- Old (pre-2013):

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New (post-2013)

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COA/COT/COMT

Old

COA/COT/COMT

New

Instillation

- Essential Steps:
  - Wash Hands with Soap and Water or hand sanitizer
  - Check dropper tip for imperfections
  - Avoid touching dropper tip to any surface
  - Tilt head back, pull down lower eyelid with one hand
  - With other, hold dropper close to eye without touching it, brace hand on face if necessary
  - While looking up squeeze bottle so a single drop dispenses
  - Drop is successfully instilled if it lands anywhere on eye or in pocket created with lower lid
  - Close eye gently, and apply pressure with hand to tear duct
  - Dab eye (closed) with tissue
  - Wash hands
  - If instilling more than one drop wait at least 5 minutes between drops

Identification

- ALWAYS read label
- Coloured top for different drops
  - Red - cycloplegic/mydriatic
  - Green - miotics
  - Tan - antibiotics
  - Pink/white - steroids
  - Gray - NSAIDs
  - Yellow - beta blockers
  - Purple - alpha agonist
  - Teal - prostaglandin analogues
  - Orange - CAIs
  - Blue - Combo glaucoma
- Colours do NOT show concentration

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Nervous System

**Autonomic Nervous System**
- Regulates involuntary actions of body
- Consists of two parts:
  - Sympathetic – primarily excited state of body
    - “Flight of fight”
  - Parasympathetic – primarily rest and relaxation
- Two systems oppose and work together for dynamic homeostasis
- Sends messages by way of nerve impulse (action potential) using neurons and neurotransmitters

**Autonomic Nervous System**
- Drugs can either enhance or depress a given system
- Mimetic – “mimics” system, increases activity
- Lytics – decrease activity
- Sympathomimetic – increase sympathetic activity
- Sympatholytic – decrease sympathetic activity
- Parasympathomimetic – increase parasympathetic activity
- Parasympatholytic – decrease parasympathetic activity

**Autonomic Nervous System**
- Sympathetic:
  - Pre-ganglionic: Nicotinic
  - Post-ganglionic: Adrenergic ($\alpha_1, \alpha_2, \beta_1, \beta_2$)
  - Effector: Organ
- Parasympathetic:
  - Pre-ganglionic: Nicotinic, Muscarinic
  - Post-ganglionic: Nicotinic (Muscle, Neuronal)
  - Effector: Organ

**Autonomic Nervous System**
- Sympathetic Nervous System
  - Tends to have excitatory end physiologic effect
  - But excitatory and inhibitory signals to an excitatory system
  - Fight or flight response
  - Pupils dilate
  - Breathing increases, bronchioles dilate
  - Heart rate increases, increase contraction, vasoconstriction to skin and digestive organs
Autonomic Nervous System

- Sympathetic:
  - Pre-ganglionic Nucleus → Ganglion → Post-ganglionic Effector Organ (Adrenergic $\alpha_1, \alpha_2, \beta_1, \beta_2$)
  - Neurotransmitter: Ach
  - Receptor Type: Nicotinic

- Parasympathetic:
  - Pre-ganglionic Nucleus → Ganglion → Post-ganglionic Effector Organ (Muscarinic $M_1, M_2, M_3$, Nicotinic (Muscle, Neuronal))
  - Neurotransmitter: Ach
  - Receptor Type: Muscarinic $M_1, M_2, M_3$

Sympathetic Nervous System

- Neurotransmitters: Epinephrine, Norepinephrine
- Receptors: Adrenergic ($\alpha_1, \alpha_2, \beta_1, \beta_2$)
- Sympathomimetic: Adrenergic Agonists
- Sympatholytic: Beta blockers

Parasympathetic Nervous System

- Neurotransmitters: Acetylcholine
- Receptors: Muscarinic ($M_1, M_2$), Nicotinic (muscular, neuronal)
- Parasympathomimetic: Cholinergic Agonists
  - Pilocarpine
- Parasympatholytic: Most cycloplegics and mydriatics

Autonomic Nervous System

- Parasympathetic Nervous System
  - Tends to have resting effects “rest and digest”
    - But excitatory and inhibitory signals
  - Conserve Energy
  - SLUD
    - Salivation
    - Lacrimation
    - Urination
    - Defecation
    - Pupil constrict
    - Digestion
    - Flushed Skin

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Adrenergic Agents

- **Mydriatics**
  - Phenylephrine – vasoconstrictor
  - Other vasoconstrictor: Naphazoline
  - Cocaine

- **IOP lowering medications (decrease aqueous production)**
  - Beta blockers (timolol)
  - Alpha agonists (trimonidine)
  - Discussed more in glaucoma medications

- **Cocaine**

Miotics, Mydriatics and Cycloplegics

- **Miotics**
  - Dilate pupil as primary action
  - Nearly always have weaker cycloplegic effect
  - Phenylephrine – no cycloplegic effect
  - Also have α receptors on blood vessels
  - Has effect on skeletal muscle

- **Cocaine**

- **Phenylephrine**
  - Also have receptors on blood vessels
  - Has effect on skeletal muscle
  - Raise eyelid

- **Atropine**
  - Strongest of cycloplegics
  - Can have systemic toxicity
  - Nearly always on tests – in reality all systemic toxicity and deaths were on very young or mentally challenged patients
  - Look for redness, hot and dry skin, dry mouth, irregular pulse, hallucinations
  - Be cautious when administering to young children or with mentally challenged patients

Cholinergic Agents

- **Miotics**
  - Pilocarpine
  - Carbachol (Miostat) – muscarinic and nicotinic

- **Cycloplegic**
  - Atropine
  - Cyclopentolate
  - Tropicamide

- **Botox (blocks Ach)**

Miotics, Mydriatics and Cycloplegics

- **Mydriatics**
  - Phentolamine – α receptor blocker

- **Cycloplegic**
  - Atropine
  - Cyclopentolate – antimuscarinic

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Glaucoma

- IOP lowering medication
- Two ways to lower IOP
  - Increase outflow of aqueous
  - Decrease production of aqueous
- Classified by mechanism of action
  - Beta blockers (yellow)
  - Alpha Agonists (purple)
  - Prostaglandin Analogues (teal)
  - Carbonic Anhydrase Inhibitors (Orange)
  - Combination (blue)

IOP Lowering Medications

- Beta blockers
  - Non-selective for beta receptors
    - Beta 1 on ciliary body
    - Beta 2 on heart, lungs
    - Contraindicated in lung problems (asthma) or heart (low pulse or blood pressure)
  - Timolol 0.25%, 0.5% (Timoptic, Timoptic XE, Betimol, Istaol)
  - Levobunalol (Betagan)
  - Carteolol (Ocupress)
  - Betoptic S – Beta 1 selective

IOP Lowering Medications

- Adrenergic Receptors
  - Stimulation of beta receptors increases production
  - Stimulation of alpha receptors decrease production
  - Uses Carbonic Anhydrase to actively form aqueous (80%)

IOP Lowering Medications

- Cholinergic Agonists
  - Pilocarpine
    - Stimulates muscarinic receptors, stimulating accommodation, mechanically pulling open trabecular meshwork
    - Many side effects – accommodation, brow ache
    - Carbachol (Miostat) – intraocular, longer lasting

IOP Lowering Medications

- Adrenergic Agents – affect alpha or beta receptors
- Alpha agonists
  - Affect alpha 2 receptors
  - Decrease production and increase outflow
  - Brimonidine 0.2%, 0.15% (Alphagan 0.15%, 0.1%)
    - High allergic reaction rate in higher % concentrations
  - Iopidine

IOP Lowering Medications

- Carbonic Anhydrase Inhibitors
  - Oral and Topical
  - Inhibit carbonic anhydrase, reducing production
    - 80% of aqueous production is actively produced and requires anhydrase
  - Topical
    - Brinzolamide (Azopt)
    - Dorzolamide (Trusopt)
  - Oral
    - Acetazolamide (Diamox), Methazolamide (Neptazane)
  - Contraindicated with sulfa allergies
  - Oral side effects (tingling, fatigue, metallic taste, kidney stones)
IOP Lowering Medications

- Prostaglandin analogues
  - Latanoprost (Xalatan)
  - Lumigan
  - Travatan
  - Mimic Prostaglandins
  - Increase uveoscleral outflow
  - Prostaglandins are naturally occurring inflammatory markers, however concentration is low so there is no evidence to support causing inflammation in eye
  - Known side effects of skin pigmentation, increase iris pigmentation, lash growth (Latisse)

Inflammatory Process

- When there is an insult to the body it responds with inflammation
  - Beneficial to prevent infection and start healing
  - Some effects need to be tempered or eliminated
- Acute and chronic inflammation
- Main signs of inflammation:
  - Heat - vasodilation
  - Redness - vasodilation
  - Pain – chemicals stimulate nerve endings
  - Swelling – increased vascular permeability
  - Loss of Function – many reasons

IOP Lowering Medications

- Combo
  - Combigan (brimonidine and timolol)
  - Cosopt (timolol and dorzolamide)
  - Simbrinza (brinzolamide and brimonidine)

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Inflammatory Process

- Steroids inhibit phospholipase A2, shuts down all of lower pathway
- NSAIDs inhibit cyclooxygenase, inhibiting pathway below
Corticosteroids

- Control inflammation, in various parts of body and eye
- Systemic and topical steroids
- Commonly in eye these are
  - Conjunctiva – scleritis, episcleritis
  - Cornea – edema, burns, haze, rejection (grafts)
  - Uveitis
  - Optic Nerve – any inflammation (neuritis)
  - Retina – edema, inflammatory syndromes
- Reduce redness, pain, swelling
  - Also decrease allergic response (histamines, mast cells)
- Very non-specific and acts high up in pathway

Topical Steroids

- Diffuprednate 0.05% (Durezol)
  - Emulsification greatest physiologic effect
- Prednisolone Acetate 1% (Pred Forte, Omnipred)
  - Acetate, good penetration, what most others are compared to
- Prednisolone Acetate 0.12% (Pred Mild)
- Dexamethasone 0.1%
  - Sodium phosphate (Decadron) and suspension (Maxidex)
- Loteprednol 0.5% (Lotemax)
- Loteprednol 0.2% (Alrex)
- Fluoromethalone 0.1% (FML)
- Also many combination Antibiotic/Steroids – will be covered in Antibiotic Section

Injectable Steroids

- Multiple advantages
  - Can be put nearer to location
  - Depot injected (longer lasting)
  - Can have greater penetration (intravitreal)
- Side effects correlate with some of those advantages
- Commonly include
  - Triamcinolone (Kenalog)
  - Decadron
  - Ozurdex*
- Multiple areas
  - Subconjunctival
  - Sub-tenon’s
  - Intravitreal
  - Translesional/Subdermal

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NSAIDs
- Non-Steroidal Anti-Inflammatory Drugs
  - Work lower down inflammatory pathway
  - Less effective in reducing inflammation, but fewer side effects
  - Decrease inflammation and fever, as well as pain (analgesic)

NSAIDs
- Ocular and systemic side effects of NSAIDs – ocular from drops, systemic from oral
  - Ocular
    - Corneal melt
    - Corneal toxicity
  - Systemic
    - GI upset and ulcers
    - Renal dysfunction
    - Photophobia

NSAIDs
- Include oral and topical
  - Non-Reversible (Aspirin) and Reversible (Others)
    - Oral
      - Ibuprofen (Advil, Motrin) – reversible
      - Naproxen (Aleve) – reversible
      - Aspirin/Acetylsalicylic Acid – non-reversible
      - Acetaminophen (Tylenol) – classified as NSAID but works differently, no anti-inflammatory properties but good analgesic (anti-pain) properties
    - Topical
      - Diclofenac (Voltaren)
      - Bromfenac (Prolensa, Bromday, Xibrom)
      - Ketorolac (Acular, Toradal)
      - Nepafenac (Ilevro, Nevanac)
      - Flurbiprofen (Ocuflun)

NSAIDs
- Ocular use approved for:
  - Reducing post-operative inflammation
  - Reducing risk of post-operative CME
  - Can treat CME (if mild, often started first due to being non-invasive)
  - Allergic conjunctivitis

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Allergic Cascade

- Cascade of events that causes allergic response
- Allergic response wide range of symptoms from mild to severe, usually includes itching, redness, swelling, or anaphylactic
- Allergen (environmental stimulus) binds to IgE that is attached to a mast cell, which then releases histamine
- Histamine interacts with histamine receptors, majority of symptoms from binding H1 receptor

Anti-Allergy Medications

- Oral antihistamine
  - Benadryl (first generation)
  - Claritin, Allegra, Zyrtec
- All anticholinergic (parasympathetic system)
  - Increase dry eye
- Topical
  - Bepotastine besilate (Bepreve)
  - Alcaftadine (Lastacaft)
  - Olapatadine (Pataday, Patanol)
  - Ketotifen fumarate (Zaditor) – OTC

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Infections

- Infection occurs when a microorganism invades the body, and the body can’t repel it
- Can be bacterial, fungal, viral, or parasitic
- Immune system divided into two systems
  - Innate – mechanical barriers and non-specific cells
  - Adaptive – responds following exposure
- Immune compromised (HIV/AIDS, on steroids etc) are more susceptible
- Nearly always has associated inflammation, but inflammation and infection are NOT the same
Anti-Infective Agents

- Each type of anti-infective is designed to combat a certain type of infection
  - Antibacterial (bacteriostatic and bacteriocida) – bacteria
  - Antiviral – virus
  - Antifungal – fungal
  - Antiparasitic – parasite
- “Spectrums of action” for each drug – the range of microbes the drug is effective against

Antibacterial Agents

- Combat bacterial infections
- Classified into two categories
  - Bacteriostatic – Prevent further bacterial growth
  - Bacteriocidal – Kills bacteria
- Large spectrum of bacteria, no one drug that kills all
- Biggest difference in range is based on cell wall of bacteria
  - Gram Positive – Staphylococcus and Streptococcus
    - Has thick cell wall
  - Gram Negative – pseudomonas, haemophilis
- Resistance – as antibiotics are used, bacteria can develop resistance to them, making that antibiotic less useful

Antiviral Agents

- Effective against viruses
  - Mostly used to treat Herpes Simplex and Varicella Zoster, as well as cytomegalovirus
  - Herpes Simplex
    - Type I and Type II – usually Type I (cold sore)
  - Varicella Zoster – chicken pox, follows trigeminal nerve
    - Hutchinson’s Sign
    - Zoster vaccine
Antiviral Agents

- Oral and Topical
- Topical
  - Gangiclovir gel (Zirgan)
  - Trifluridine (Viroptic)
- Oral
  - Valacyclovir (Valtrex)
  - Acyclovir
- Often injected:
  - Foscarnet
  - Ganciclovir
- Usually for CMV in patients with AIDS/HIV

Antifungal Agents

- Fungal infections tend to be slow growing but can be very damaging with often poor prognosis
- Two main types of fungal infections
  - Filamentary – Most commonly Aspergillus, sometimes Fusarium
  - Yeast – Most commonly Candida
- Only one drug (natamycin) designed for topical available in US, others adapted for ocular treatment:
  - Natamycin – best for filamentary
  - Fluconazole – best for yeast
  - Amphotericin B – very toxic to cornea, but often needed

Combination Anti-Bacterial/Steroid

- Combination drops that include anti-bacterial and steroids
  - Tobradex – tobramycin and dexamethasone
    - This is NOT Tobrex
  - Maxitrol – neomycin, polymixin B, dexamethasone
    - Higher allergy rate (neomycin)
  - Zylet – loteprednol and tobramycin
- Extremely common prescribed
- Difference in stopping steroid vs antibacterial

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Systemic Effects of Ocular Medications

- Effects of ocular medications all can have systemic effects, though often much reduced
- Can reduce side effects by punctual occlusion when instilling
- Some common things to watch for:
  - Beta blockers – can affect vasoconstriction and pulse, watch for breathing or cardiac problems
  - CAIs – metallic taste
  - Phenylephrine – could increase heart rate, contraindicated in pregnant patients
  - Atropine – anticholinergic - possible parasympathomimetic crisis
  - Any drug (often sulfa or antibiotics) – SJS

Ocular Effects of Systemic Medications

- Prednisone – PSC, increase IOP
- Alpha blockers (Flomax) – IFIS and poor iris dilation
- Antihistamines – Dry Eye
- Amiodarone – vortex keratopathy
- Chloroquine, Hydroxychloroquine (Plaquenil) – maculopathy, rare vortex keratopathy
- Oral contraceptives and tetracyclines – papilledema
- Ethambutol – optic neuritis
- Barbituates – optic atrophy
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Self-Test Questions

Which of the following situations should cause you concern?
- A) Instilling tropicamide in a pregnant patient
- B) Instilling a steroid in a patient who just finished a course of Zirgan and Valtrex for herpes simplex
- C) Instilling Atropine in a child with Down’s Syndrome
- D) Instilling a prostaglandin in a patient with sulfa allergies

The primary neurotransmitter of the parasympathetic nervous system is:
- A) Acetylcholine (Ach)
- B) Epinephrine/Norepinephrine (Epi/Norepi)
- C) Dopamine
- D) GABA

Phenylephrine works as a ____________ system, while most cycloplegics work as ____________

- A) sympatholytic, sympathomimetic
- B) sympathomimetic, parasympatholytic
- C) sympathomimetic, parasympathomimetic
- D) parasympatholytic, sympathomimetic

The _________ and _________ of the autonomic nervous system work together to balance each other

- A) Parasympathetic, Antiparasymathetic
- B) Sympathetic, antisymathetic
- C) Sympathomimetic, Parasympathomimetic
- D) Parasympathetic, Sympathetic

Match the cap colour with the drug class
- Dilating agents
- Miotics
- Antibiotics
- NSAIDs
- Steroids
- Beta blockers
- Alpha agonists
- CAIs
- Prostaglandins

- Pink/White
- Tan
- Orange
- Grey
- Red
- Purple
- Green
- Yellow
- Teal
Punctal occlusion does when instilling drops?
- A) Reduces risk of contamination
- B) Reduces risk of systemic adverse events
- C) Increases potency of drop
- D) Increases effective concentration of drop

Which of the following IOP lowering medications work on the adrenergic receptors or the sympathetic nervous system – choose all that apply?
- A) CAIs
- B) Beta blockers
- C) Prostaglandin analogues
- D) Alpha agonists

Steroids should be used in which of the following situations?
- A) Fungal infection
- B) Viral infection
- C) Inflammation
- D) Allergic reactions
- E) A and B
- F) C and D

Which of the following could be contraindications for Cosopt (Timolol-Dorzolamide)?
- A) Breathing problems
- B) Low pulse
- C) Sulfa allergy
- D) All of the above

Systemic steroids can cause which of the following?
- A) Cataracts
- B) IOP increase
- C) Blood sugar dysfunction
- D) All of the above

Which is broader acting in its effects on the body?
- A) Corticosteroids
- B) Reversible NSAIDs
- C) Irreversible NSAIDs
- D) Antihistamines
What two medications could be combined without increasing the risk of overdosing?

A) Aspirin and Ibuprofen
B) Ibuprofen and Naproxen
C) Naproxen and Aspirin
D) Ibuprofen and Acetaminophen

A topical antiviral is:

A) Zirgan (ganciclovir)
B) Natamycin
C) Tobradex
D) Prednisolone

Steroids work to inhibit ______ which is relatively ______ while NSAIDs inhibit ______ which is relatively ______

A) COX (cyclooxygenase), upstream, Phospholipase, downstream
B) COX (cyclooxygenase), downstream, Phospholipase, upstream
C) Phospholipase, upstream, COX (cyclooxygenase), downstream
D) Phospholipase, downstream, COX (cyclooxygenase), upstream
E) I stopped reading already

The drop with the largest spectrum of action (coverage) is:

A) 1st generation fluoroquinolone
B) Tobramycin
C) 3rd generation fluoroquinolone
D) Erythromycin

If you have seasonal ocular allergies the best choice to minimize symptoms would be:

A) Start antihistamine 2 weeks before the onset
B) Start mast cell stabilizers/antihistamine combo 2 weeks before onset
C) Take an antihistamine/mast cell stabilizer at first symptoms
D) Start antihistamine at first symptoms

The most severe adverse reaction listed is:

A) Conjunctival injection
B) Epiphora
C) Swelling of mucosal membranes
D) Blurriness instantly upon instillation
Which of the following has a black box warning for tendonitis?

- A) Cephalosporins
- B) Macrolides
- C) Aminoglycosides
- D) Fluoroquinolones

If a patient is allergic to penicillin, what are they immediately also considered allergic to?

- A) Cephalosporins
- B) Fluoroquinolones
- C) Macrolides
- D) Aminoglycosides

THANK YOU!