

Pharmacology Update

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Why the growth?

- We diagnose and intervene earlier
- We treat more aggressively
- Patients live longer

When Do We Use Antibiotics?

My Disclosures

Dr. Gupta is not a member of any speakers bureau nor does he get paid by any pharmaceutical or ophthalmic instrument company mentioned in the lecture.

Before Prescribing Anything...



- Take a thorough medical history
- HPI and ROS
- Current Medications
- Allergies
- Pregnancy/Nursing

Prophylaxis in Cataract Surgery

When Do We Use Antibiotics?

- To treat ocular trauma - abrasions, ulcers, after FB removal

When Do We Use Antibiotics?

- To manage patients who have a red eye emergency after ruling out causes other than conjunctivitis

Things to quickly rule out

- Iritis
- Acute angle closure glaucoma
- Corneal ulcer
- Herpetic infection
- Fungal infection
- Corneal FB/Penetrating injury

ACG

- Pt complaint of dull ache
- Steamy Cornea
- Mid fixed dilated pupil
- Elevated IOP

Treatment of ACG

PACG : Treatment of the acute attack

- Pilocarpine eye drop 1-2% in the affected and the fellow eye
- Topical beta-adrenergic blocker
- Carbonic anhydrase inhibitor
- Hyperosmotic agent: Mannitol 20% I.V., Oral glycerol
- Globe compression

How to rule out penetration

- History
- Dilation
- Bscan if not sure

What is the most important risk factor for eye infections?

Wearing contact lenses

Types of culture

- Blood agar
- Chocolate agar
- Sabouraud's medium
- Thioglycolate broth
- Gram stain
- Giemsa stain

When to Culture

- Infiltrate >2mm with epi defect
- Central or paracentral ulcer
- Significant tissue loss
- Hypopyon
- Poor response to initial therapy
- If infection occurs after any surgical procedure
- If history suggests unusual organisms

When to Culture

- When something in history or exam seems out of the ordinary
- When patient fails to get better

Antibacterial agents

- Sulfa Preparations
- Erythromycin
- Bacitracin
- Bacitracin / Polymyxin B
- Bacitracin / Polymyxin B / Neomycin
- Tetracycline
- Gentamycin
- Tobramycin
- Trimethoprim / Polymyxin B

Common Indications for Oral Antibiotics

- Internal hordeola
- Blepharitis
- Ocular Rosacea
- Preseptal cellulitis
- Dacryocystitis
- Dacryoadenitis

Zithromax (azithromycin)

- Macrolide antibiotic (erythromycin)
- Drug of choice in PCN sensitive patients
- Adult:
 - 250 mg bid(day 1), 250mg qd (day 2-5)
 - 500 mg qd x 3 days, tri-pack
- Covers Staph, Strept, and Haemophilus

Zithromax (azithromycin)

- “The Vegas Drug”
 - If what happens in Vegas follows your patient home
 - DOC for Chlamydia... 1 g qd

Doxycycline

- Effective member of tetracycline family
- Typical dosing 50 mg BID

Doxycycline

- Warn female patients that BCP may not work
- Suggest patient take with food to minimize GI upset
- Warn of photosensitivity, teeth discoloration
- Can enhance Coumadin and action of digoxin

Augmentin

- Amoxicillin and potassium clavulanate
- Watch for PCN allergies
- Adults: 250, 500, and 875 mg
- Children < 100 pounds: oral suspension 25-45 mg/kg divided into 2 doses
- Covers Staph, Strept, and Haemophilus

Keflex (cephalexin)

- Some cross over reaction to PCN sensitive patients
- Good for Gram +, not Haemophilus (G-)
- Adult: typically 500 mg bid x 1 week
 - Max 4g in 24 hours
- DOC for blow out fractures

The Allergic Cascade

- Allergy is a Type I hypersensitivity reaction
 - Mediated by IgE
- Four phases – complex process:
 - Sensitization
 - Mast cell degranulation
 - Activation or Early phase response
 - Late phase response

OTC Products

- Naphcon
- Visine
- Opcon A

OTC Products

- Pazeo
- Zaditor

The Ones Which Still Need a Rx

- Lastacaft (Alcaftadine)
- Bepreve (Bepotastine)
- Elestat (Epinastine)

The Newest Stuff

- Zerviate
 - Basically ocular form of Zyrtec (.24% Ceftrizine)
 - Approved in 2017 but just being launched now in US by Nicox
 - BID dosing

What if the combination products are not enough?

- Soft steroids such as Alrex or Lotemax work well

**Rx: Alrex and combination product together
D/C Alrex after 1-2 weeks and keep
combination for LT therapy**

What if the combination products are not enough?

- Oral Allergy products
 - Vast majority of oral products are now OTC

When do I use oral anti-allergy meds?

- Any patient with systemic symptoms in addition to ocular symptoms
- Moderate to severe AC
- Watch out for drying effect

DES: Tests to Confirm Your Diagnosis

Artificial tears are the mainstay of initial topical therapy



- Preservative free vs preserved
- Low viscosity vs high viscosity
- Ointments

What if tears aren't enough?

- Restasis (Cyclosporin) or Xiidra (Lifitegrast)
- Punctal Plugs
- Topical Steroids
- Biologics?

Billing Essentials

- Document that patient is still experiencing problems after using artificial tears
- Reimbursement is roughly \$260 for occluding RLL and LLL
- Do on separate visit than comprehensive exam
- Write Interpretation Report

Restasis(Cyclosporin)

Mechanism of Action

- Activated T cells produce cytokines that result in
- Increased cytokine production
- Neural signal to lacrimal gland that disrupts production of natural tears

Xiidra (Lifitegrast)

- BID dosing
- Approved for 17 years and older
- Comes in single use plastic vials

Xiidra (Lifitegrast)

- Works by interfering with T-cells so decreases their impact on the lacrimal gland trying to restore their normal function
- Patients demonstrate improvement as early as 4-6 weeks

Also... Cequa

- Basically another version of Restasis
- = .09% cyclosporine A
- BID dosing
- By Sun pharmaceuticals

Going Forward

- Patient Education about Dosing:
 - 1 drop in each eye every 12 hours
 - Do not use "as needed" like traditional drops
 - Use 1 vial more than once
- Contact Lenses
 - Wait 15 minutes to insert CL after Restasis

Better way to fix this

Once you put a patient on either medication, you **MUST** see them more than once a year.

You should see them every 6 months or even every 4 months

More Options

- Omega 3's
- Humidifiers
- Warm Compresses

What's new for Dry Eyes?

- Biologics such as Regener-Eyes – sterile biologic eyedrop made of anti-inflammatory cytokines and growth factors

Adenoviral Conjunctivitis

- Pharyngoconjunctival fever
 - Commonly type 3 adenovirus
 - Severe pharyngitis and fever
 - Minimal corneal involvement
- Epidemic keratoconjunctivitis
 - Types 8, 19, and 37 adenovirus
 - Subepithelial corneal infiltrates common

Management of Viral Conjunctivitis

- Usually self-limiting
- Warn patient about infectious nature
- OTC lubricants and cool compresses

Management of Viral Conjunctivitis

- Rx: Zylet or Tobradex QID
- See patient for follow-up in 7-10 days and then discontinue medication if totally resolved

Management of Viral Conjunctivitis

Topical Betadine

Protocol

- Must be done within first 48 hours of onset of symptoms
- Dilute betadine by 50%
- Instill topical anesthetic
- Instill drops and use Qtip to apply to lid margins
- Rx: Zylet or Tobradex

Trifluridine (Viroptic)

- Approved in 1980
- Mechanism of action is non-selective
- Toxicity contributes to superficial punctate keratitis or filamentous keratitis, blepharitis, and canicular punctal occlusion
- Prolonged use beyond 21 days can lead to corneal epithelial dysplasia, conjunctival scarring, anterior ocular ischemia, and contact dermatitis
- Instilled 9 times a day

The newest antivirals

- Avaclyr 3% acyclovir ophthalmic ointment
- FDA approval Spring 2019
- FERA pharmaceuticals
- 5x/day until defect heals, then 3 x day for 3-4 days
- Not readily available

Herpes Simplex

- Lid vesicles with edema
- Conjunctivitis
- Epithelial lesions (dendritic, punctate, geographic)
- Stromal infiltrative disease (disciform)

Zirgan (Ganciclovir)



- Formulated as gel, not solution
- Targets only infected cells
- Recommended dosing 5x/day
- Being used off-label for adenoviruses

Herpes Zoster

- Caused by the reactivation of the varicella virus
- Signs and symptoms
 - Fever, chills, malaise, flu like symptoms
 - Acute vesicular rash that follows CN V distribution
 - Does not cross the mid-line

Oral AntiVirals

■ Zovirax (Acyclovir)

- Analog of guanosine
- Specifically targets virally-infected cells
- Tx: 800 mg by mouth 5 x D for 7 days for HZO;
400 mg 5 x D for 7 days for HSK

Oral AntiVirals

■ Valtrex (Valacyclovir)



- Prodrug of acyclovir - greater bioavailability
- Can be taken without regard to meals
- 1,000 mg caplet tid x 7 days for HZO; 500 mg tid x 7 days for HSK

Zoster Vaccine

- Zosatavox
- 1 in 3 persons in US will develop zoster
- FDA approved for patients 50 and up
- CDC recommends for everyone 60 years and older

Zoster Vaccine

- Cannot use if history of severe allergic response to Neomycin or gelatin
- Must be off oral antivirals for one day before and two weeks after the vaccine
- Reports of reactivation of the ocular HZ disease after the vaccination

Zoster Vaccine

- Effect declines after roughly 8 years
- Only 24% of US adults over 60 have received it so far

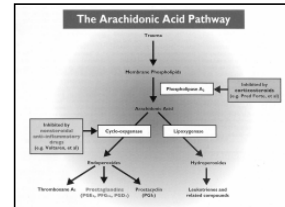
Zoster Vaccine

- Newest approved is Shingrix
- One shot, followed by a second shot 2-6 months later

When Do We Use Them?

- Decrease Inflammation
- Prevent Scarring
- Increase patient comfort

How Do They Work?



Topical Steroids

- Fluoromethalone - FML
- Prednisilone Acetate - Omnipred
- Dexamethasone - Maxidex
- Loteprednol – Alrex and Lotemax

Prednisolone

- 5 times more potent than hydrocortisone
- Previous gold standard of topical steroids
- The acetate suspension facilitates corneal penetration to provide increased concentrations in the anterior chamber

Difluprednate (Durezol)

- Indicated for the management of inflammation postoperatively
- Already being used off label for uveitis
- ? Use in CME

Difluprednate (Durezol)

- First emulsion formulation of a steroid
- Ketone based product of Prednisilone
- Equal efficacy of Pred with half of the dosing

Lotemax gel

- Loteprednol 0.5%
- Same active ingredients as drops but now you don't need to shake bottle since its' not a suspension

What do you do if patient demonstrates an IOP spike?

- Do nothing
- Discontinue the steroid
- Switch to a different steroid
- Add IOP lowering agent

Oral Steroids

Side effects of Corticosteroids

- Increased IOP
- Cataracts
- Decreased healing
- Re-emergence of certain viral and fungal infections

DG Rules for Steroids

- Steroids can be an optometrist's best friend

Don't be afraid to use them

Clinical Uses

- Contact dermatitis
- Reaction to insect bites
- Recalcitrant CME
- Recalcitrant uveitis
- Severe retinitis or scleritis

Other Clinical Uses

- Myasthenia Gravis
- Inflammatory orbital pseudotumor
- Thyroid Eye Disease
- Optic neuritis
- GCA

Dosing

- Beware of body weight when prescribing
- Most common Rx
 - Medrol Dose Packs – automatically tapers
 - Prednisone 10 mg tablets

Things to watch out for...

- Side effects (IOP , cataracts)
- Elevated bp and blood sugars
- Stomach pain and ulcers
- General “mental haze”

Topical Analgesics: NSAIDs

Ketorolac Tromethamine 0.4%

Marketed as Acular (Allergan)

Bromfenac Ophthalmic Solution 0.09%

Marketed as Xibrom (ISTA)

Nepafenac Ophthalmic Solution 0.1%

Marketed as Nevanac (Alcon)

Oral Analgesics

OTC's	Dosage
■ Acetylsalicylic acid (ASA - aspirin)	325-500 mg
■ Acetyl-para-aminophenol (APAP-Tylenol)	325-500 mg
■ Ibuprofen (Advil, Nuprin)	200 mg
■ Naproxen (Aleve)	220 mg

Know Your Maximum Daily Allowances

■ Acetaminophen	400 mg
■ Aspirin	6000 mg
■ Ibuprofen	3200 mg
■ Naproxen	1000 mg
■ Propoxyphene	600 mg
■ Codeine	240 mg
■ Hydrocodone	60 mg

Controlled Substances

- Schedule I: High abuse potential (heroin, marijuana, LSD)
- Schedule II: High abuse potential with severe dependence liability (narcotics, amphetamines)

Controlled Substances

- Schedule III: Moderate dependence liability (certain narcotics, nonbarbiturate sedatives, etc)
- Schedule IV: Less abuse potential than S3; limited dependence liability (nonnarcotic analgesics, antianxiety agents, etc)
- Schedule V: Limited abuse potential (small amounts of narcotics in antitussives or antidiarrheals)

Concerns About Addiction

“Clinically significant dependence develops only after several weeks of chronic treatment with relatively large doses of morphine-like opioids.”

The Medical Letter
August 21, 2000

DG Rules for Painkillers

Prescribe conservatively

- Patient's perception of pain is always worse at the time of the incident
- The vast majority of cases can be handled with OTC products

Top 10 Systemic Medications

- | | |
|-----------------|---------------|
| ■ Levothyroxine | ■ Metoprolol |
| ■ Lisinopril | ■ Omeprazole |
| ■ Atorvastatin | ■ Simvastatin |
| ■ Metformin | ■ Losartan |
| ■ Amlodipine | ■ Albuterol |

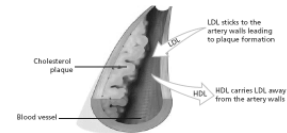
Why is the # of people with these conditions growing?

- We live longer than we used to
- We weigh more than we used to
- We don't move around the way we used to

Elevated Cholesterol

Low density lipoprotein

Bad cholesterol – bind to arteries and increase risk for disease



Low density lipoprotein

- Optimal: <100
- Borderline high: 130-159
- High: > 160

High-density lipoprotein

- Good cholesterol – helps remove cholesterol from the arteries

HDL: Normal Values

- Low: <40
- High: > 60

Triglycerides

- Generally get higher with physical inactivity, smoking, and obesity
- Optimal: <150
- Borderline: 200-499
- High: >500

Total cholesterol

- Overall measure of hypercholestermia
- Desirable: <200
- Borderline: 200-239
- High: >240

Treatment

- Lifestyle changes – diet and exercise
- Medications

Diet changes

- The National Cholesterol Education Program recommends the following diet:
- Saturated fat—less than 7% of calories
- Monounsaturated fat—about 20% of calories
- Polyunsaturated fat—about 10% of calories
- Protein—about 15% of calories
- Carbohydrates—about 50% of calories
- Fiber— about 25 grams of soluble fiber per day
- Cholesterol—less than 200 milligrams per day



1st Line Medications

- Statins are also called HMG-CoA reductase inhibitors. They include lovastatin (Mevacor), simvastatin (Zocor), pravastatin (Pravachol), fluvastatin (Lescol), atorvastatin (Lipitor), and rosuvastatin (Crestor).
- Statins block an enzyme called HMG-CoA reductase, which is necessary for the production of cholesterol.
- Statins lower LDL cholesterol number and they lower your risk of developing hardening of the arteries (atherosclerosis)

Treatment

- On average, diet and exercise can lower LDL cholesterol by about 10%.
- Medications can lower LDL cholesterol by another 25% to 50%.

Lipids & the Eye

- Amarois Fugax/Hollenhorst plaques
- Retinal vein occlusions
- Xanthelasma
- Corneal arcus

What is normal BP?

- Systolic = 120 mm Hg
- Diastolic = 80 mm Hg

Diagnosis of Hypertension

- Repeated abnormal elevation of BP on 3 separate occasions over at least 6 weeks
- A single blood pressure > 200/120



Treatment

- Exercise
- Low Sodium Diet
- Medications

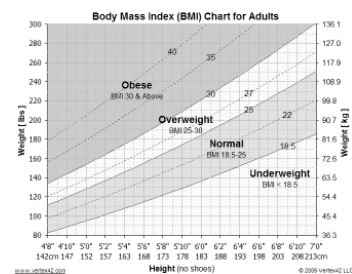
Calculate Body Mass Index

$$BMI = \frac{\text{weightInPounds} \times 703}{\text{heightInInches} \times \text{heightInInches}}$$

Or

$$BMI = \frac{\text{weightInKilograms}}{\text{heightInMeters} \times \text{heightInMeters}}$$

Lose Weight: How much?



Drug Classes

- Thiazide diuretics
- Beta blockers
- Angiotensin-converting enzyme (ACE) inhibitors
- Angiotensin II receptor blockers (ARBs)
- Calcium channel blockers
- Renin inhibitors

2 things you can do when your patient has hypertensive retinopathy

- Emphasize need for yearly ocular health exams
- Perform fundus photography

Definition:

- “A metabolic disease in which the body’s inability to produce any or enough insulin causes elevated levels of glucose in the blood.”

Grades of HTN Retinopathy

- Grade 1
 - Vascular Attenuation
- Grade 2
 - As grade 1 + Irregularly located, tight constrictions - Known as 'AV nicking' or 'AV nipping' - Salu's Sign
- Grade 3
 - As grade 2 + Retinal edema, cotton wool spots and flame-hemorrhages 'Copper Wiring' + Bonnet's Sign + Gunn's Sign
- Grade 4
 - As grade 3 + optic disc edema + macular star 'Silver Wiring'

How do you show meaningful use?

“Patient educated to work with PMD on maintaining proper bp”

3 classic symptoms of DM

- Polydipsia
- Polyuria
- Polyphagia

Type 1 Diabetes

- auto immune disorder
- insulin-producing cells destroyed
- daily insulin replacement necessary
- age of onset: usually childhood, young adulthood
- most prevalent type of diabetes in children and adolescents

Type 2 Diabetes

- Insulin resistance – first step
- Age at onset:
 - Most common in adults
 - Increasingly common in children
 - overweight
 - inactivity

Measures of Hyperglycemia

- Random plasma glucose (RPG)
- > 200 is a problem

Measures of Hyperglycemia

- Fasting plasma glucose (FPG)
- Anything over 126 is a problem

Measures of Hyperglycemia

- Oral glucose tolerance test (OGTT)
- Anything over 200 is a problem

Glycosylated Hemoglobin

- Reflects the percentage of free glucose bound to hemoglobin in RBC

Glycosylated Hemoglobin

- Normal: 5.7%
- Pre-Diabetes: 5.7 to 6.4%
- Diabetes > 6.5 %

Oral Meds for Diabetes

Agent Class	Representative	Mechanism of Action	Fasting Plasma Glucose (mg/dL)	HbA _{1c} (%)
Sulfonylureas	Glibenclamide, Glipizide, Glimepiride	Stimulates pancreatic insulin release	65-70	1.0-2.0
Meglitinides	Repaglinide, Nateglinide	Stimulates insulin release	60-70	1.0-2.0
Biguanides	Metformin (Glucophage)	Decreases hepatic glucose production, increases peripheral absorption of glucose	55-70	1.0-2.0
Thiazolidinediones	Avoglanone (Avandia), Rosiglitazone (Actos)	Increases insulin sensitivity	60-80	0.5-1.0
DPP-4 inhibitors	Sitagliptin (Januvia), Saxagliptin (Onglyze)	Inhibits DPP-4, increases insulin sensitivity	62-68	0.5-0.8
SGLT inhibitors	Cangliflozin (Invokana), Dapagliflozin (Farxiga), Ertugliflozin (Jardiance)	Decreases glucose reabsorption in the kidneys	70-80	0.5-1.0
Alpha-Glucosidase inhibitors	Acarbose (Precose), Miglitol (Glyset)	Delays carbohydrate absorption	65-70	0.5-1.0
Insulin Secretagogues	Glucagon-like peptide-1 (GLP-1) agonists	May reduce endogenous insulin production	65	0.5

Ocular Manifestations of Diabetes

- Cataracts
- Glaucoma
- Ocular Surface Disease
- Diabetic Retinopathy
- CN Palsies

A. Diet

- Diet is a basic part of management in every case. Treatment cannot be effective unless adequate attention is given to ensuring appropriate nutrition.
- **Dietary treatment should aim at:**
 - ensuring weight control
 - providing nutritional requirements
 - allowing good glycaemic control with blood glucose levels as close to normal as possible
 - correcting any associated blood lipid abnormalities

Insulin

Main types of insulin preparations				
Type	Onset	Peak	Duration	Comments
Rapid-acting insulin analogue	5-15 min	30-60 min	2-5 hr	Can be injected at the start of a meal
Short-acting (soluble/regular insulin)	30 min	1-3 hr	4-8 hr	Usually injected 15-30 minutes before a meal. Clear solution
Intermediate or long-acting insulin (NPH, lente) (isophane or zinc insulin)	1-2 hr (NPH, lente)	4-8 hr	8-12 hr (NPH)	Used to control glucose levels between meals. May be combined with short-acting insulin
	2-3 hr (Ultra lente)	4-8 hr	8-24 hr (Ultra lente)	
Long-acting insulin analogue	30-60 min	No peak	16-24 hr	Usually taken once daily

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Pediatric Use of Ocular Medication

Medication	Approved for use	Medication	Approved for use
<i>Allergy Medications</i>			
Acular	≥ 3 yrs	<i>Antibiotics</i>	
Alamast	≥ 3 yrs	Polytrim	≥ 2 yrs
Alocril	≥ 3 yrs	10% Sulfacetamide	≥ 2 mos
Emadine	≥ 3 yrs	Erythromycin	≥ 2 mos
Optivar	≥ 3 yrs	Tobrex	≥ 2 mos
Zaditor	≥ 3 yrs	Ciloxan oint	≥ 2 yrs
Patanol	≥ 3 yrs	Ocuflax	≥ 1 yr
Opticrom	≥ 4 yrs	Zymar	≥ 1 yr
Alomide	≥ 2 yrs	Vigamox	≥ 1 yr
Colom	≥ 4 yrs	Quixin	≥ 1 yr
<i>Antiviral</i>			
Viroptic	≥ 6 yrs	<i>Anti-inflammatory</i>	
<i>Combination</i>		Fluorometholone	≥ 2 yrs
Tobradex	≥ 2 yrs		

Pregnancy Categories

- Always prescribe with caution in women who are pregnant, nursing, or women who may become pregnant
- If in doubt, consult their Ob/Gyn

FDA Pregnancy Categories

- A - Controlled studies demonstrate no risk
- B - No evidence in risk in humans. Either animal studies show risk and humans do not OR if no human studies, animal studies negative
- C - Risk cannot be ruled out. Human studies lacking but animal studies are positive for fetal risk or lacking
- D - Positive Evidence of risk
Investigational or post-marketing data show risk to fetus. If needed in life-threatening situation or serious situation or serious disease, drug may be acceptable
- X - Contraindicated in pregnancy
Fetal risk clearly outweighs any benefit to patient

Commonly Prescribed Drugs

- Zymar – C
- Zylet – C
- Alrex – C
- Lotemax – C
- Tobradex -C
- Restasis – C
- Patanol – C
- Elestat – C
- Vigamox - C
- Erythromycin – B
- Tobramycin – B
- Doxycycline – D
- Tetracycline – D
- Neomycin -- D

Generic vs Label

- There are many generics
- The same active ingredient does not always mean the same efficacy

Where it makes a difference

- Glaucoma
- Iritis – name brand steroids better than generic