Systemic Management of Ocular Disorders

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Initiating Systemic Treatment

- Patient history
  - Ocular history
  - Medical history
  - Medication history
  - Social history
- Clinical examination
- Additional testing
  - Blood work
  - Cultures
  - Imaging

Choosing a Treatment Plan

- Considerations when selecting therapeutic agents:
  - Identity of organism or inciting agent
  - Site of the infection or inflammation
  - Safety of the drug
  - Individual patient factors
  - Cost of therapy
- Empiric therapy
  - Initiate broad spectrum treatment prior to organism identification
  - Tailor treatment once organism identified

Patient Factors

- Contra-indications?
  - Patient health
  - Allergies
  - Drug-drug interactions
- Special consideration
  - Pediatrics
  - Geriatrics
  - Pregnancy
  - Lactating mothers

Pregnancy Category A	Adequate and well-controlled human studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).
Pregnancy Category B	Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women
Pregnancy Category C	Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
Pregnancy Category D	There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
Pregnancy Category X	Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

Bacterial Infections

Normal Bacterial Flora

- Normal Host-Organism Relationships
  - Skin
  - External ocular surface
  - Nasal mucosal tissue
  - Oral cavity
  - Gastrointestinal pathway
  - Colon, rectal pathway
  - Vaginal tissue
- Abnormal Host-Organism Relationship
  - Infection

Principles of Antimicrobial Treatment

- Bactericidal agent: cells killed
- Bacteriostatic agent: no growth of new cells but existing cells not killed
- Both effective chemotherapeutic agents
- Both rely to some degree on host defenses to eliminate infection
- Same drug may have both properties depending the concentration of drug, organism involved and targeted location for treatment
- Choice of bactericidal vs. bacteriostatic agent may depend on status of host and specific site of infection
  - i.e. must use bactericidal agent for CSF d/t lack of host defenses

Antimicrobial Drug Classes

- **Inhibit bacterial cell wall synthesis**
  - Penicillins
  - Cephalosporins
  - Vancomycin
  - Bacitracin
- **Increase cell membrane permeability**
  - Polymyxin B
  - Gramicidin
- **Inhibit bacterial DNA replication**
  - Fluoroquinolones
- **Inhibit bacterial protein synthesis at the ribosomal level**
  - Aminoglycosides
  - Tetracyclines
  - Chloramphenicol
  - Clindamycin
- **Affect bacterial tetrahydrofolate cofactor system**
  - Sulfonamides
  - Trimethoprim
  - Pyramethamine

Most Useful Antibiotics for Eye Care

- **Amoxicillin with clavulanate potassium (Augmentin)**
  - Typical dosage 1-1.5 gm per day in split doses for 10 days
- **Cephalosporin**
  - Typical dosage 1-1.5 gm per day in split doses for 10 days
    - First generation: Gram positive coverage
      - Cephalexin (Keflex)
    - Second generation: Expanding Gram negative coverage
      - Cefaclor (Ceclor)
    - Third generation: Increased Gram negative, decreased Gram positive
      - Ceftriaxone (Rocephin): injectable only
- **Sulfamethoxazole and Trimethoprim (Bactrim)**
  - Typical dosage 800mg sulfmethoxazole/160mg trimethoprim every 12 hours
- **Fluoroquinolone**
  - Levofloxacin (Levaquin)
  - Typical dosage 500mg to 750mg daily

Key Points

- Any cellulitis must be managed aggressively
- If suspect orbital cellulitis, need CT scan, blood cultures and IV antibiotics STAT
- Ocular signs of orbital cellulitis include pupillary abnormalities, extraocular muscle motility restrictions, conjunctival congestion, optic nerve edema

Orbital Fracture Management

Further treatment based on imaging results

- Medial Orbit: Observe and consider surgical repair if medial rectus entrapment
- Orbital Apex: Difficult to manage & controversial
- Orbital Roof: Neurosurgical consult
- Zygomatic: Observe vs. surgery
- Orbital Floor:
  - Systemic Antibiotics
  - Nasal Decongestants
  - Ice Compresses

Tetracyclines

- Efficacy against Gram positive, Gram negative, aerobic and anaerobic bacteria
- Effective against *Chlamydia*, *Rickettsia*, *Mycoplasma*, spirochetes and some protozoa
- However, broad resistance has limited the clinical usage of these agents
- **Appear to have anti-inflammatory properties**
- **Inhibits collagenase activity**
- **Metalloproteinase-9 inhibitor**

Tetracyclines

- Tetracycline 250 mg qid
  - Duration depends on clinical entity being treated, always take on empty stomach, many foods interfere with absorption, particularly dairy products)
- Doxycycline (Vibramycin) 50-100 mg bid
  - Duration depends on clinical entity being treated, absorption more tolerant of other foods
- Minocycline (Cleeravue-M) 50-100 mg bid
  - Duration depends on clinical entity being treated

Recurrent Corneal Erosion

- Doxycycline 50 mg BID x 2 months
- Topical steroid (FML) TID x 2 months

Viral Infections

Viral Infections

- Small infectious units
  - Nucleic acid genome
  - Protein capsid shell with/without external lipid envelope
- Transmission to eye
  - Transplacental
  - Direct contact
  - Exposure to air-borne particles
  - Viremia
  - Extension from adenxal disease
  - Respiratory tract to nasolacrimal duct

Herpes Simplex Virus

- Most common virus in humans
- 90% of humans are infected by 15 years of age
- HSV-1 and HSV-2 share almost 50% of DNA
  - Both infect mucosal surfaces (usually mouth or genitals)
  - Both establish latency in the central nervous system
  - The primary difference between the HSV-1 and HSV-2 is in where they ***typically*** establish latency
    - HSV-1 usually establishes latency in the trigeminal ganglion
    - HSV-2 usually establishes latency in the sacral ganglion

Antiviral Agents

- Nucleoside analogs → phosphorylated by viral thymidine kinase → nucleoside triphosphate which inhibit HSV DNA polymerase
- Topicals:
  - Trifluridine 1% oph soln (Viroptic)
    - q2h (max 9 times a day) for up to 10 days; then q4h for another 7 days (do not exceed 21 days)
    - Pregnancy category C
  - Vidarabine 3% oph ung (Vira-A)
    - Apply ½ inch ribbon into lower conjunctival sac 5 times a day for 10 days
    - Pregnancy category C
  - Gancyclovir 0.15% oph gel (Zirgan)
    - FDA approved in 2009
    - q3h (approx 5 times per day) until the corneal ulcer heals, then tid for 7 days.
    - Pregnancy category C

Antiviral Agents

- Oral:
  - Acyclovir (Zovirax)
    - Acute disease: 400 mg PO 5 times a day
    - Prophylactic maintenance: 400 mg PO bid
    - Pregnancy category B
  - Valacyclovir (Valtrex) **
    - Acute disease: 1000 mg PO bid for 10 days
    - Prophylactic maintenance: 500 mg or 1000 mg PO qd
    - Pregnancy category B
  - Famciclovir (Famvir)
    - Acute disease: 250 mg PO tid for 10 days
    - Prophylactic maintenance: 250 mg PO bid
    - Pregnancy category B

Herpes Zoster Virus

- Varicella zoster virus establishes latency in central nervous system after chickenpox infection
- Herpes zoster ophthalmicus occurs in approximately 10–25% of cases.
- Direct contact with blisters can transmit VZV to a person who has no immunity to the virus. The newly infected individual may then develop chickenpox.
- Patient is contagious until the rash has developed crusts.

Herpes Zoster-Varicella

- Headache, malaise, fever for 2-3 days
- Occasionally severe pain over involved dermatome
- Pustular vesicle formation along nerve distribution 3-4 days later
- Vesicles crust in 7-10 days
- Ocular manifestations occur 4 to 6 days after skin vessicles erupt, and include conjunctivitis, keratitis, episcleritis, uveitis, cranial nerve palsies, optic neuritits, and retinitis

HZV Treatment

- Optimal to initiate treatment within 72 hours
- Antivirals:
  - Acyclovir (Zovirax)
    - Acute disease: 800 mg PO 5 times a day for 7 to 10 days
    - Chronic suppressive therapy for recurrent disease: 400 mg bid up to 12 months
  - Valacyclovir (Valtrex)
    - Acute disease: 1 gram PO TID for 7 days
  - Famciclovir (Famvir) **
    - Acute disease: 500 mg PO q8h for 7 days

HZV Treatment

- Analgesics – pain control
- Corticosteroids - relieve acute pain and limit the development of post-herptic neuralgia
  - Prednisone 5-60 mg per day PO qd (or divided bid or qid)
    - taper over 2 weeks as symptoms resolve
    - Pregnancy category C

Post-herpetic Neuralgia Treatment

- Tricyclic antidepressants
  - Amitriptyline (Elavil 10, 25, 50, 75, 100, and 150 mg)
    - 0.5-2 mg/kg PO qhs, not to exceed 150 mg/day
    - Pregnancy category D
- Gabapentin (Neurontin)
  - 30-600 mg PO tid
  - Pregnancy category C
- Capsaicin ointment (Zostrix)
  - Apply to affected area qd to QID
- Lidocaine patch (Lidoderm)

Zostavax

- Live vaccine
- Reduces incidence of herpes zoster by 51.3%
- Reduces cases of post-herpetic neuralgia by 66.5%
- The CDC Advisory Committee on Immunization Practices recommend that all adults over 60 years old receive vaccine

"Other" Infections

Chlamydia trachomatis

- Gram negative bacteria
- Obligate intracellular pathogen
- Three strains of C. trachomatis
  - Trachoma (serotypes A, B, Ba or C)
    - Trachoma
  - Urethritis (serotypes D through K)
    - Inclusion conjunctivitis
  - Lymphogranuloma vereneum (serotypes L1, 2 and 3)
    - Conjunctival granulomas
    - Interstitial keratitis

Treatment

- Azithromycin (Zithromax)
  - 1 gram PO in single dose, or 500 mg PO on day 1, followed by 250 mg qd for 2 to 5 days
  - Pregnancy category B
- Tetracycline (Sumycin)
  - 250-500 mg PO qid for 3-6 weeks
  - Pregnancy category D

Toxoplasmosis gondii

- Obligate intracellular parasite that finds host in mammals and birds
- Humans may become infected when they ingest the parasite's eggs or cysts
- Once infected the parasite may be passed across the placenta from a pregnant mother to her fetus resulting in a congenital form of the disease
- The classic clinical finding of ocular toxoplasmosis is a focal chorioretinitis with overlying vitritis

Traditional Treatment

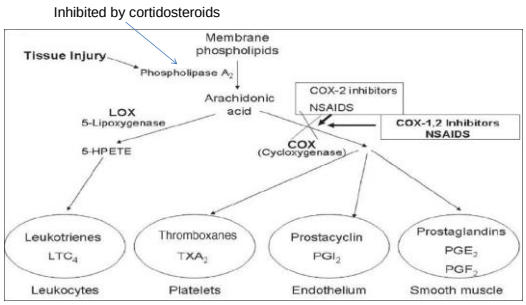
- Pyrimethamine (Daraprim)
  - 75 mg PO qd or 50 mg PO bid loading dose, followed by 25 mg PO bid
  - Pregnancy category C
- Sulfadiazine (Microsulfon)
  - 2-4 g PO single loading dose, followed by 1 g PO qid
  - Pregnancy category C
- Prednisone (Deltasone, Meticorten, Orasone)
  - 60-100 mg per day PO for 1-2 weeks; then, taper over 2-3 weeks
  - Pregnancy category C

Alternative Treatment

- Trimethoprim and sulfamethoxazole (Bactrim DS)
  - 1 DS tab contains 800 mg of sulfamethoxazole and 160 mg of trimethoprim
  - 1 DS tab PO bid for first 2 weeks; then 1 regular tab PO bid for next 3-4 weeks
  - Widely accepted as an effective treatment and has the benefit of less systemic side effects compared to sulfadiazine
  - Consider adding folic acid supplement for long courses
  - Oral corticosteroids may be used in conjunction with Bactrim

INFLAMMATION AND PAIN

Arachidonic Acid Pathway



Nonsteroidal Anti-inflammatory Drugs (NSAIDS)

Pharmacological Effects
- Analgesic
- Anti-inflammatory
- Antipyretic
- Anticoagulant
- Effective for mild to moderate pain
- Higher doses may be necessary depending upon the agent to achieve anti-inflammatory effects
- Most have ceiling effect

Oral NSAIDS

- Acetylsalicylic acid (aspirin, ASA)
  - 325-500 mg q4-6h
- Ibuprofen (Motrin, Advil, Nuprin)
  - 400-600 mg q4-6h
- Naproxen sodium (Aleve, Anaprox)
  - 450-550 mg loading dose, then 225-275 mg q6-8h
- Ketoprofen (Orudis, Oruvail)
  - 25-50 mg q6-8h
- Diclofenac (Voltaren-XR, Cataflam)
  - 75 mg bid
- Indomethacin (Indocin)
  - 25 mg tid
- Tolmetin (Tolectin)
  - 400-600 mg q6h

COX-1 and COX-2

- COX-1: Constitutive (always present)
  - Required for variety of bodily functions (i.e. maintaining stomach lining)
  - Role in inflammatory process in pain perception
- COX-2: Inductive (induced by cell damage)

- Cox 2 Inhibitors:
  - Celecoxib (Celebrex)
    - 100 mg bid CAUTION
  - Vioxx no longer available

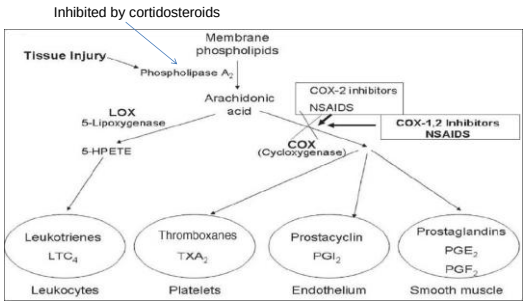
Most Useful Analgesics of Eye Care

- Peripheral Acting Agents: NSAIDS
- Central Nervous System Acting Agents
  - Non-narcotic agents
    - Acetaminophen (Tylenol): 325-500 mg q4-6h
    - Tramadol (Ultram): 50-100 mg q4-6h
  - Narcotic Agents (Controlled Substances)
    - Codeine (Tylenol 3 or 4): 30-40 codeine mg q4-6h
    - Hydrocodone (Lortab, Vicodin): hydrocodone 5-10 mg q4-6h

Important Clinical Points Narcotic Agents

- Narcotic agents actually safer for patients with NSAID contraindications (peptic ulcers, etc.)
- Peak effect 1.5-2.0 hours after oral dose - advise patients who have acute, severe pain
- Additive or synergistic effect possible when combined with NSAIDS
- Increased dose of narcotic agent will increase analgesic effect but will also risk increased side effects

Arachidonic Acid Pathway



Important Considerations Before Prescribing

- Is the patient diabetic?
- Does the patient have any infectious disease such as syphilis or tuberculosis?
- Does the patient have any gastrointestinal problems such as peptic ulcers?
- Is the patient pregnant?

Oral Steroids

- Prednisone
  - widely available and inexpensive
  - Dosage is individualized for the severity and nature of the condition.
    - Most ocular inflammatory conditions respond to an initial dose in the range of 40-60mg and tapering over a one- to three-week period.
    - Example: 40mg for two days, 30mg for two days, 20mg for two days, 10mg for two days and 5mg for two days.
- Methylprednisolone (Dosepak)
  - Composite of 4mg tablets, six tablets (24mg) are taken on day one and reduced by one tablet per day over the next six days.
  - 24mg is suboptimum therapy in most instances where an oral steroid is indicated
  - Dosepaks are expensive compared to generic prednisone.

Ocular Allergies

Review of Allergic Reactions

- **Type I reaction** (immediate hypersensitivity reactions)
  - IgE–mediated release of histamine, tryptase, chymase, heparin, chondroitin sulfate, prostaglandins, thromboxanes, and leukotrienes from mast cells and basophils
  - Leads to increased vascular permeability and migration of eosinophils and neutrophils
  - Ocular examples: allergic conjunctivitis
- **Type II reactions** (cytotoxic hypersensitivity reactions)
  - Autoimmune reactions mediated by IgG or IgM, then complement fixation
  - Ocular examples: Mooren ulcer, cicatricial pemphigoid, *Graves disease and myasthenia gravis.*
- **Type III reactions** (immune-complex reactions)
  - IgG mediated, then complement
  - antigen-antibody immune complexes deposit in tissue leading to inflammation
  - Ocular examples: Stevens-Johnson syndrome , marginal corneal infiltrates, Wesley rings
- **Type IV reactions** (delayed hypersensitivity reactions, cell-mediated immunity)
  - T cell mediated
  - Onset usually after 48 hours
  - Ocular examples: contact dermatitis, drug allergies, phlyctenular keratoconjunctivitis, corneal graft rejection

Allergic Conjunctivitis

- Seasonal allergic conjunctivitis
  - Tree pollen, grass, weeds
- Perennial allergic conjunctivitis
  - Pet dander, dust mites, cockroaches
- Vernal keratoconjunctivitis
- Atopic keratoconjunctivitis
- Giant papillary conjunctivitis

Allergic Conjunctivitis Treatment

- **Artificial tears**
  - Dilute allergens and inflammatory mediators and flushes allergens from ocular surface
- **Topical antihistamines**
  - Superior to systemic treatment as it ensures direct delivery to the tissue
  - Block histamine receptors, but no effect on other mediators
- **Topical mast cell stabilizers**
  - Mechanism of action not fully understood
  - Prevents degranulation of mast cell
- **Topical nonsteroidal anti-inflammatory drugs**
  - Act on the cyclooxygenase metabolic pathway inhibiting production of prostaglandins and thromboxanes.
  - No role in blocking mediators formed by the lipoxygenase pathway (ie leukotrienes)
- **Topical corticosteroids**
  - Prevents formation of arachidonic acid
  - Block both cyclooxygenase and lipoxygenase pathways
- **Topical vasoconstrictors**
  - Short term relief of vascular injection

Topical Antihistamines

- Emedastine difumarate (Emadine)
  - qid dosing
  - Pregnancy category B
- Levocabastine (Livostin)
  - qid dosing
  - Pregnancy category B
- Epinastine (Elestat)
  - bid dosing
  - Pregnancy category C
- Azelastine (Optivar)
  - bid dosing
  - Pregnancy category C
- Bepotastine besilate (Bepreve)
  - bid dosing
  - Pregnancy category C
- Alcaftadine (Lastacaft)
  - qd dosing
  - Pregnancy category B

Mast Cell Stabilizers

- Olopatadine (Patanol, Pataday)
  - Bid (Patanol) or qd (Pataday) dosing
  - Pregnancy category C
- Lodoxamide tromethamine (Alomide)
  - qid dosing
  - Pregnancy category C
- Ketotifen (Zaditor)
  - q8 to 12 hour dosing
  - Pregnancy category C
- Nedocromil (Alocril)
  - bid dosing
  - Pregnancy category B

Corticosteroids and NSAIDs

- Loteprednol etabonate (Lotemax, Alrex)
  - qid dosing
  - Pregnancy category C
- Ketorolac tromethamine (Acular)
  - qid dosing
  - Pregnancy category B

Contact Dermatitis

- Type IV allergic reaction or irritant exposure
- Irritants include acids, bases, and resins found in drugs, dyes, plants, preservatives, cosmetics, and metals.
- Allergen usually encountered within 72 hours of reaction
- Irritant usually encountered within few hours of reaction

Topical Treatment

- Topical corticosteroids
  - Use caution when prescribing
  - Clobetasone butyrate (Eumovate)
    - Apply 0.05% ointment to affected area tid to qid
- Topical immunomodulators
  - Tacrolimus (Protopic)
    - Apply 0.1% ointment to affected area bid
  - Pimecrolimus (Elidel)
    - Apply 1% cream to affected area bid
    - Pregnancy category C

Systemic Antihistamines

- First generation H-1 blockers cross the blood-brain barrier and have significant antimuscarinic activity
  - Diphenhydramine (Benadryl)
    - 25-50 mg PO q 4 to 6 hours
    - Pregnancy category B
  - Chlorpheniramine (Chlor-Trimeton)
    - 4 mg PO q 4 to 6 hours
    - Pregnancy category B
  - Clemastine (Tavist-1)
    - 1 mg q 12 hours
    - Pregnancy category B
  - Hydroxyzine (Atarax, Vistaril, Vistazine)
    - 5-25 mg PO qd to qid
    - Pregnancy category C

Systemic Antihistamines

- Second generation H-1 blockers cross the blood-brain barrier less readily and have less antimuscarinic activity
  - Fexofenadine (Allegra)
    - 60 mg PO bid *or* 180 mg PO daily
    - Pregnancy category C
  - Loratadine (Claritin, Alavert)
    - 10 mg PO daily
    - Pregnancy category B
  - Cetirizine (Zyrtec)
    - 5 to 10 mg PO daily
    - Pregnancy category B
  - Desloratadine (Clarinex)
    - 10 mg PO daily
    - Pregnancy category C

Age Related Macular Degeneration

The Age-Related Eye Disease Study (AREDS) Grading System

- **Category 1:** < 15 small drusen (<65 µm)
  no RPE changes
  same appearance in fellow eye
- **Category 2:** small/medium drusen with total area < 125 µm, or
  intermediate drusen > 63 µm but < 125 µm, or
  no geographic atrophy with / without RPE changes
  Fellow eye Category 1 or 2
- **Category 3:** 20 intermediate soft indistinct drusen, or
  65 intermediate hard drusen, or
  one large drusen (> 125 µm), or
  non-central geographic atrophy
  Fellow eye Category 1, 2, or 3
- **Category 4:** Category 1, 2, or 3
  Fellow eye with advanced AMD:
  choroidal neovascular membrane
  central geographic atrophy
  pigment epithelial detachment
  sub-retinal fibrosis

Treatment of Non-neovascular AMD: AREDS Recommendations

- Patients > 55 years old should receive yearly dilated fundus exams to evaluate risk for AMD
- Patients with extensive intermediate drusen, or at least one large drusen, or non-central geographic atrophy (Category 3), or advanced AMD in one eye (Category 4) should receive daily high dose antioxidants and zinc.
- Therapeutic regimen reduces risk of development of advanced AMD by 25%

AREDS Recommended Supplement

- 500 mg Vitamin C
- 400 International Units Vitamin E
- 15 mg Beta-carotene
- 80 mg Zinc
- 2 mg Copper

- Contraindications:
  - Beta-carotene should be avoided in patients with a history of smoking
  - Drug interactions
    - Fluoroquinolone antibiotics
    - Doxycycline
    - Tetracycline
    - Warfarin

AREDS Report # 22

- Evaluated relationship of dietary carotenoids, vitamin A, alpha-tocopherol and vitamin C with AMD
- Nutrient intake estimated from questionnaire at enrollment
- Dietary lutein / zeaxanthin intake inversely associated with neovascular AMD, geographic atrophy and large or extensive intermediate drusen

The Veterans LAST Study

Lutein Antioxidant Supplementation Trial

- Evaluated relationship of lutein alone or lutein in combination with antioxidants, vitamins and minerals with visual function in AMD
- Both lutein alone and lutein with supplements improved the macula pigment optical density, glare recovery, near visual acuity and contrast sensitivity in patients with AREDS Category 2, 3 and 4 AMD
- Dosage: 10 mg lutein

Zeaxanthin and Visual Function Study

- 60 patients (57 male, 3 female) with mild to moderate AMD
- Randomly assigned to one of three treatment groups:
  - 8 mg Zeaxanthin
  - 8 mg Zeaxanthin + 9 mg Lutein
  - 9 mg Lutein
- Macular pigment optical density increased in all three groups (no between group differences)
- Zeaxanthin group demonstrated:
  - 1.5 line improvement in detailed high contrast visual acuity
  - Increased clearing of kinetic visual field central scotoma
- Lutein group demonstrated:
  - Improved low contrast sensitivity
  - Contrast sensitivity function
  - Glare recovery

Richer SP, Stiles W, Graham-Hoffman K, Levin M, Ruskin D, Wrobel J, Park DW, Thomas C. Randomized, double-blind, placebo-controlled study of zeaxanthin and visual function in patients with atrophic age-related macular degeneration. The Zeaxanthin and Visual Function Study (ZVF) FDA IND #78, 937. Optometry. 2011 Nov;82(11):667-680.e6.

Zeaxanthin and Visual Function Study

- Take home message:
  - Zeaxanthin-induced foveal macular pigment optical density elevation mirrored that of lutein
  - Zeaxanthin provided complementary distinct visual benefits by improving foveal cone-based visual parameters
  - Lutein enhanced those parameters associated with gross detailed rod-based vision
  - There is considerable overlap between the two carotenoids.
  - Equally dosed Zeaxanthin + Lutein fared worse in terms of raising macular pigment optical density
    - Equal dosing is not found in diet
    - Likely due to duodenal, hepatic-lipoprotein or retinal carotenoid competition.
    - Findings consistent with retinal distribution and zeaxanthin foveal predominance

AREDS 2

- Effects of high supplemental doses of dietary xanthophylls (lutein / zeaxanthin (10mg/2mg)) and omega -3 fatty acids (DHA / EPA (350mg/650mg)) on the development of advanced AMD, cataract and moderate vision loss
- Effects of eliminating beta-carotene and reducing zinc in the original AREDS formulation
- Inclusion criteria:
  - Men and women aged 50 to 85 years
  - Large drusen in both eyes or large drusen in one eye and advanced AMD (neovascular AMD or geographic atrophy) in the fellow eye
- Enrollment concluded June 2008 and participants will be followed for a minimum of five years

Omega-3-Rich Fish and Shellfish

- Cross-sectional study to determine the relationship between fish and shellfish consumption and AMD in Salisbury Eye Evaluation (SEE) study participants.
- 2,391 people aged 65 to 84 years who reported fish and shellfish were a normal part of the diet.
- The distribution of total weekly fish and shellfish consumption was not different between specific AMD categories compared with controls.
- Participants with advanced AMD (exhibiting either CNV or GA) were significantly less likely to consume fish and shellfish high in omega-3 fatty acids.
- No significant difference from dietary zinc from crab and oyster
  - Levels of zinc obtained from seafood are low compared with supplement levels

Swenor BK, West SK, Bressler S, Caulfield L. The impact of fish and shellfish consumption on age related macular degeneration. Ophthalmology. 2010;117(12):2395-2401.

Peer-reviewed Analysis of AREDS

- Higher intake of omega-3 fatty acids (DHA and EPA in same composition as in fish) associated with lower risk of progression to advanced AMD
- AREDS supplement + increased dietary beta-carotene had 50% INCREASED risk for advanced AMD.
- Participants with early AMD who had sufficient amounts of AREDS vitamins in diet and took AREDS supplement had acceleration of disease.

Chiu C-J, Klein R, Milton RC, et al. Does eating particular diets alter risk of age-related macular degeneration in users of the age-related eye disease study supplement? Br J Ophthalmol. 2009;93(9):1241-1246.

GLAUCOMA

Carbonic Anhydrase Inhibitors

- Acetazolamide (Diamox)
  - 250 mg tabs qid acetazolamide
  - 500 mg sequels acetazolamide
- Methazolamide (Neptazane)
  - 25-50 mg tid methazolamide

Glaucoma

- Marijuana
  - 400 different chemicals in marijuana
    - Tetrahydrocannabinol (THC) most active component
  - Short term 20% decrease in IOP with high doses
    - Mechanism of action unknown
    - Dose: cigarrettes with 4 mg TCH or oral doses of 20 mg TCH
  - Would require multiple daily doses (q 3 hours) to be effective leading to well known side effects
  - Topically has not been proven to be effective to date
    - Cannibus derivatives currently being studied

Glaucoma

- Herbals:
  - Bilberry reported to promote optic nerve health, but no scientific evidence to support its use
  - Ginko biloba:
    - Derived from the dried ginko leaf
    - NMDA blocker (N-methyl-D-aspartate) - neuroprotective activity
    - Most popular standardized extract is Egb 761
      - 35:1 to 67:1 ratio of dried leaves to final extract
        - 24% ginko flavone glycosides
        - 6% terpene lactonesand proanthocyanodines
  - Potential mechanisms of action:
    - Increased blood flow
    - Inhibit platelet-activating factor
    - Protects against damage from free radicals and lipid peroxidation
    - Nitric oxide inhibition

Glaucoma

- Ginkgo Biloba
  - One study indicated increased end diastolic velocity within optic nerve with no effects on arterial blood pressure, heart rate, or IOP

Chung HS, Harris A, Kristinsson JK, Ciulla TA, Kagemann C, Ritch R. Ginko biloba extract increases ocular blood flow velocity. J Ocul Pharmacol Ther. 1999 Jun;15(3):233-40.

  - Another study found improvement of pre-existing visual field defects in some normal tension glaucoma patients

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  - Dosage in both studies was 40mg PO TID

Thank You

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