What’s Hot: Innovations in Ophthalmic Medications, Vitamins, and Nutraceuticals
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How Granny Townsend Saved My Father’s Life
Colostrum
- lymphocytes
- IgA, IgG, IgM.
- lactoferrin,
- lysozyme
- lactoperoxidase
- complement
- proline-rich polypeptides

How Italian Beauties Wooed & Killed Their Lovers with the same Plant

The Take Home…
Today’s nutraceutical is tomorrow’s medication.....
Definitions

Medication: a drug or other substance used to treat disease or injury; a medicine
Vitamin: organic food component needed in very small amounts for growth and maintaining good health
Nutraceutical:* a functional food that aids in the prevention and/or treatment of disease(s) and/or disorder(s) other than anemia

*(a blending of “nutrition” & “pharmaceutical”)

What’s Hot? Medications!

Glaucoma what we have...
- Alpha agonists
- Beta blockers
- Carbonic anhydrase inhibitors
- Cholinergic antagonists
- Combination medications
- Prostaglandin analogs

What’s Hot? Medications!

Glaucoma in the Pipeline
Latanoprostene bunod 0.24% (Vesneo; B&L)
- A nitric oxide-donating prostaglandin F2-a analogue
- Rapidly metabolized by esterases to:
  - Latanoprost acid- active molecule in Xalatan
  - Decreases IOP by extracellular matrix remodeling
  - Increases uveoscleral aqueous humor outflow
  + Butanediol mononitrate- releases nitric oxide
  - Nitrouric oxide- lowers IOP
  - Increases conventional (trabecular meshwork & Schlemm’s canal) aqueous outflow

Latanoprostene Bunod & IOP

What’s Hot? Medications!
Glaucoma in the Pipeline
- Rhopressa (Aerie Pharmaceuticals) 1 gtt/day OU
  - Rho kinase inhibitor
  - Kinases: enzymes that catalyze the transfer of phosphate groups from high-energy molecules to low energy substrate (protein)
  - Function: to transmit signals and regulate complex processes in cells

What’s Hot? Medications!
Glaucoma in the Pipeline
- Rhopressa (Aerie Pharmaceuticals) 1 gtt/day OU
  - MOA: inhibits actions of ROCK
    - Increases outflow through trabecular meshwork
    - Reduces episcleral venous pressure, or EVP
    - Norepinephrine transporter (NET)
      - Reduces the production of aqueous
    - IOP reduction phase 2 clinical trial
      - Day 14 = 6.2 mmHg Day 28= 5.7 mmHg

What’s Hot? Medications!
Glaucoma in the Pipeline
- Roclatan (Aerie Pharmaceuticals)
- Fixed-dose combination of Rhopressa™ + latanoprost
- Lowers IOP through the same three MOAs as Rhopressa
  - Rho Kinase (ROCK) inhibition
    - Increases outflow via trabecular meshwork
    - Reduces episcleral venous pressure
    - Norepinephrine transporter (NET)
      - Reduces the production of aqueous
  - Latanoprost increases outflow via uveoscleral pathway
- Phase 2b clinical trial: on day 29
  - Reduced mean diurnal IOP from baseline 25.1 mmHg to 16.5 mmHg
  - 34% decrease in IOP
  - ISSUE! Chronic injection is an issue with these meds!

Nutrition – targets for Glaucoma
- Growing recognition of glaucoma as neuro-degenerative disease, rather than just of high IOP (esp. since normal tension glaucoma can still lead to damage)
- Researchers focusing more on neuro-protection
- Oxidative Stress (free radical damage)
- Decreased blood flow
- Other factors:
  - Damaging compounds (e.g. excess glutamate), impaired mitochondrial function
- ONF provides components to address all these issues
Nutrition Support for Glaucoma

- Targeted support for glaucoma / optic nerve health.
- Delivers eye-healthy omega-3 fatty acids and key antioxidants including alpha-lipoic acid, vitamins C and E, and n-acetyl cysteine.
- Provides Ginkgo biloba and flavonoids to support ocular blood flow, as well as select B vitamins, magnesium, taurine, to promote normal vascular function.
- CoQ10 protects mitochondrial function

Retail: $39.95
Wholesale: $26.50
Staff: $16.00

Optic Nerve Formula®
Nutrition Support for Glaucoma

Growing recognition of glaucoma as neuro-degenerative disease, rather than just of high IOP (esp. since normal tension glaucoma can still lead to damage)

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ONF provides components to address all these issues

Optic Nerve Formula (ONF) Focus: Neuroprotection

- Despite lowering eye pressure (IOP), some glaucoma patients will suffer increasing damage
- Researchers therefore now looking beyond just IOP
- Neuroprotection aims to protect neurons along the entire visual pathway, chiefly retinal nerve cells (retinal ganglion cells)

Glaucoma: the cycle of damage

High IOP
Mitochondria Dysfunction
Oxidative Stress
Damage to eye’s drainage system (trabecular mesh)
Release of damaging compounds (nitric oxide, glutamate)
Nerve Cell Death
Impaired Blood Flow
Terminology: “RGC”

Retinal Ganglion Cell (RGC)

ONF Actions

- Protecting nerve cells
  - Supporting blood flow
  - Countering toxic compounds
  - Protecting against oxidative stress
    - Protecting mitochondria

Examples of ONF Ingredient targets:

**Improving Blood flow**—Low blood flow to optic nerve damages nerve cells (RGCs)

Blood Flow Support Nutrients: *ginkgo biloba, bilberry & grape seed extracts, vitamin C, magnesium & B-vitamins (lower Homocysteine)*

**Anthocyanin & Procyanidins**

*proprietary blend: “Mirtogenol” in asymptomatic intraocular hypertension*

1. 2008 Study: Pro- / Antho- combo found to lower IOP* & improve ocular blood flow
2. 2010 Study: combo, alone or with Latanoprost increased ocular blood flow, lowered IOP*, potentiating IOP-lowering action of Latanoprost

- *NOTE: ONF ingredients/levels, are designed to not affect IOP (to avoid conflicts with patients’ IOP meds). Above study used much higher dose.

ONF procyanidin source = grapeseed extract, above studies used French maritime pine bark extract (Pycnogenol) as anthocyanin source. Both Mirtogenol & ONF use Bilberry as source of anthocyanidins

Oxidative Stress is Underlying Factor in multiple factors in glaucoma:

- Cellular level: Mitochondrial Dysfunction – when mitochondria are sick, this causes oxidative stress, beginning cascade of damage at the tissue level:
  - Damage to trabecular meshwork (contributing to IOP)
  - Vascular dysfunction, leading to Impaired blood flow
  - Release of damaging compounds (glutamate / nitric oxide)
  - Retinal ganglion cell death

What’s Hot? Medications!
Dry Eye in the Pipeline

- October 10, 2003: the FDA approved Restasis!
- Targets for dry eye therapy
  - Inflammatory cells
  - Inflammatory mediators
  - Enhanced contact time w/ target cells
- Is this really important
  - Dry eye- the #1 presentation to eye care
  - Optometry owns it…... If we will!

What’s Hot? Medications!
Dry Eye in the Pipeline

Issues
- Symptoms and signs often correlate poorly or not at all!
- Since 2003 huge shift
- Aqueous tear deficiency to evaporative dry eye
- Inflammation: significant role of immunologic cells and mediators
- Palliative to restorative treatment modalities

Cyclosporine

- Restasis (cyclosporine A 0.05%- Allergan)
  - A very successful front line therapy for DED
  - Target $250 million  Reality $1 billion
- Ikervis (0.1% cyclosporine-Santen)
  - March 2015 received approval in the EU
  - Once per day dosing
  - Higher concentration
  - Suspended in a cationic nanomolecular carrier
  - Four-fold tissue concentration of the drug
Cyclosporine

- CyclASol (cyclosporine A 0.05%-Novalique)
  - Carrier-a preservative free solution of semifluorinated alkanes (SFA)
  - SFA penetrate physiological barriers more easily than water-based preparations
  - Novaliq is enrolling subjects in FDA phase II clinical trials

Lifitegrast

- Lifitegrast (Shire Pharmaceuticals) is an integrin (WTH is an integrin?)
  - Integrins facilitate binding of leukocytes via intercellular adhesion molecules (ICAMs)
  - Lifitegrast- blocks the actions of ICAM-1
  - OPUS 1 and 2
    - Reduced corneal (fluorescein) and conjunctival (lissamine green) staining,
    - Improved ocular discomfort and eye dryness

Systemic Nutrients for Dry Eye?

- Science?
- OD’s role
- Scientific basis
- Ethics
- Financial considerations

Landmark Studies in Dry Eye

INTERNATIONAL WORKSHOP ON MEIBOMIAN GLAND DYSFUNCTION
NICHOLS

- Produced a new definition differentiating MGD from other MG pathologies.
- “MGD is “a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion. It may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease”.

Think inflammation!
Meibum is critical to ocular surface health and vision.

Retards aqueous layer evaporation.

Reported prevalence varies from 3.5% to 70%.

Chronic inflammation of MG may ultimately lead to loss of structures.

Anti-inflammatory Fatty Acids

ALÀ & LA:
Most abundant omega 3/6s in diet. Both must convert to other omegas to effect inflammation, but are inefficiently / inconsistently converted (due to rate-limiting enzyme), reducing their effectiveness (example: only 15-20% of ALÀ converted)

Flaxseed oil provides ... mostly ALÀ (plus small amount of LA)
Both inefficiently used
Anti-inflammatory Fatty Acids

Fish oil provides EPA and DHA
Efficiently used, good health benefits overall

Anti-inflammatory Fatty Acids

Black currant seed oil provides GLA (plus ALA & LA). GLA efficiently reduces inflammation through a unique pathway – and with dry eye specific effects. GLA is not obtainable through diet, fish or flax.

Anti-inflammatory Fatty Acids

EPA & GLA are the powerhouses of the omegas – they are effective precursors of anti-inflammatory compounds

Anti-inflammatory Fatty Acids

What about the pro-inflammatory aspects of the omega-6s?
**Anti-inflammatory Fatty Acids**

1) GLA heavily favors the anti-inflammatory pathway

2) As back up, adding EPA to GLA in proper balance, blocks production of pro-inflammatory pathway

**Omega-3 (Parent)**

- **18:3w6** GLA
- **20:5w3** EPA
- **20:3w6** DGLA

**Omega-6**

- **18:2w6** Linoleic Acid (LA)
- **20:4w6** Arachidonic Acid

**Prostaglandins**

- **Series 1 (‘good’) Prostaglandins**
- **Series 2 (‘bad’) Prostaglandins**
- **Series 3 (‘good’) Prostaglandins**

**Rate-Limiting**

- **Delta-4 Desaturase**

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**The HydroEye Clinical Trial**


Learn more, watch video: SHH.com/HydroEyeTrial

HydroEye users showed:

- Significant improvement in irritation symptoms & significantly better symptom scores vs. placebo
- Significantly better corneal smoothness vs. placebo
- Significantly lower levels of inflammatory markers vs. placebo.

**SUMMARY OF FINDINGS:**
What's Hot? Medications!  
Macular Degeneration

- Studies we should know
  - AREDS
  - AREDS-2
  - SELECT


- 3640 participants, 11 clinical centers between
- Formula
  - 15 mg betacarotene (25,000 IU of Vitamin A)
  - 500 mg vitamin C
  - 400 IU vitamin E
  - 80 mg zinc oxide
  - 2 mg copper oxide (prevent copper deficiency)

AREDS

- Subject randomized to one of four groups
  1. High-dose antioxidant vitamin combination (vitamins C and E and beta-carotene)
  2. High dose antioxidant vitamin combination plus zinc*
  3. Zinc supplementation alone*
  4. Placebo
- * Subjects receiving zinc also received copper to prevent copper deficiency


- Media: allowed quality stereoscopic fundus photos
- Severity of AMD: graded severity at study entry
  - Category 1: mild not included in study
  - Category 2: extensive intermediate drusen or large drusen
  - Category 3: noncentral geographic atrophy in at least 1 eye
  - Category 4: advanced AMD or vision loss due to AMD in 1 eye only
AREDS: 1992–1998: Results

- Elevated zinc levels associated with:
  - Increased UTI and prostatic hyperplasia in men
  - Increased stress incontinence in females
- After 5 years:
  - 15 category 2 participants progressed to advanced AMD
  - Treatment did not slow progression from category 2 to category 3 or 4.


- Intermediate-sized drusen or multiple small drusen = low risk AMD: TX not warranted
- AREDS- moderate beneficial effect in persons at high risk of advanced AMD
- AREDS- 300,000 of the 1 million persons expected to develop advanced AMD in US would not do so.
- Not for smokers: risk for lung CA

AREDS-2 Purpose

- 4203 subjects aged 50–85 years of age
- Determine effect of adding
  - Leutein + zeaxanthin
  - Omega-3 EFA
  - Leutein + zeaxanthin + omega-3 EFA
  - Removing beta carotene
  - Reducing level of zinc
  - Removing beta carotene and reducing zinc

AREDS-2 Results May 2013

- Lutein & zeaxanthin OK substitutes for beta carotene: no ↑ in risk for lung cancer
- Addition of lutein & zeaxanthin ⇒ 20% reduction in severe AMD
- Adding omega-3 did not reduce the risk of progression to severe AMD
Dietary Antioxidants & Primary Prevention of Age Related Macular Degeneration
- Purpose: evaluate the effectiveness of dietary antioxidants primary prevention of ARMD
- Evaluated 9 cohort studies: 149,203 people, with 1878 cases of early AMD
- Results: vitamin A, vitamin C, vitamin E, zinc, lutein, zeaxanthin, α carotene, β carotene, β cryptoxanthin, and lycopene have little or no effect in the primary prevention of early AMD

Nutrition, Macular Degeneration and Reality
- The ideal: people get their ideal dietary nutrients via the food they eat
- The reality: supplementation is not ideal, but beats the alternative
- Optometry’s role: provide
  - Education
  - Access for patients to get what they need

Chong EW et al Dietary antioxidants and primary prevention of age related macular degeneration: systematic review and meta-analysis. BMJ 2007;335:755