CURRENT CONCEPTS OF MYOPIA CONTROL

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I have no Financial Interest


Myopia Statistics
- US population 25% from 1975-1995, 40% in 2010
  - 84% of young Asians develop myopia
- Women > Men
- Caucasian > Blacks
- 7 – 16 years – initial development and greatest progression
- Mean rate of myopia progression in 0.35 – 0.60D for children aged 6 to 15 years
- Early myopia = faster progression and more myopia

Is There A Reason To Reduce the Prevalence or Progression of Myopia?
- Choroidal neovascularization (leading cause of vision impairment in patients younger than 50 years CNV) secondary to pathological myopia
- Myopic degeneration is the 6th leading cause of vision loss
- Leading cause of retinal detachment
- Associated with increased incidence of glaucoma and cataract

Data Make Tx of Myopia A Public Health Issue
- Consider the increase in urban, educated people
  - Population is increasing with more people living in urban environments
- Consider the increase incidence of myopia
  - USA approaching 40%, Asia 80%
- Consider the increased degree of myopia
  - Larger proportion becoming 4-5 D of myopia

Prevalence of Myopia

Available on Coopereyecare.com/Publications
Or AOA website Optometry Journal

From Earl Smith III OD, PhD
Increase In Incidence of Maculopathy & RD w Severity of Myopia

Longitudinal Studies of Untreated Childhood Myopia-Rate of Progression

<table>
<thead>
<tr>
<th>Study</th>
<th>Age (years)</th>
<th>Mean progression rate (degree/year)</th>
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<tbody>
<tr>
<td>Kennedy (1995)</td>
<td>6 – 15</td>
<td>0.16</td>
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<tr>
<td>Jonce (1991)</td>
<td>7 – 13</td>
<td>0.65</td>
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<td>Yan (1989)</td>
<td>6 – 14</td>
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<td>Gavenius (1987)</td>
<td>6 – 15</td>
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<td>Genn (1987)</td>
<td>6 – 15</td>
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<td>Bové (1984)</td>
<td>8 – 12</td>
<td>0.62</td>
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<tr>
<td>Oakley (1973)</td>
<td>6 – 21</td>
<td>0.34</td>
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<tr>
<td>Stoger (1959)</td>
<td>8 – 15</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Occupational Myopia

- Professionals, writers etc have more myopia than farm construction workers or seamen
  - Tscherning (1882), Seggel (1884), Duke Elder (1930), Goldschmidt (1968)
- Increase in myopia after VDT use Tokoro (1988)
- Adams McBrien (1992) showed that 66% of microscopist become myopic

At What Age Does Myopia Progression Stop?

- Use to be thought to stop at age 20
- Change in environment
  - Increase in number of college graduates
  - Increase in the number of graduate school students
  - Increase of near work with computers etc
  - Increase use of mobile phones, i-pads, etc
  - Studies show that 10% of the work force after graduate school continue their progression of myopia well into their 30s

Lack of Outside Exposure is a Risk Factor For the Development of Myopia

- Not the inverse of reading or near work
- Not necessary related to sports involvement
- May be related to amount of light
- Animal studies show that amount of light exposure is related to myopia development
Clinical Dictum-Outdoors

Emmetropic children with two myopic parents (the largest genetic risk) who spent the lowest amount of time outside (5 hours or less per week) have a 60% chance of becoming myopic. Emmetropic children with two myopic parents who spent 14 hours per week or more outside, the probability of becoming myopic was reduced to 20%.

Donald O. Mutti, OD, PhD

Outdoor Time is A Factor But

- Can not explain the increase in myopia noted in office workers on computers
- Can not explain the high percentage of myopia in professionals, microscopists, Orthodox religious vs secular Jews
- Relationship with intelligence

Animals Become Myopic

- Barrett (1932) differences in refractive error between domestic and wild animals
  - Caged cats 75% myopic, wild 85% hyperopic (Belkin et al 1977)
- Young (1964) laboratory, hooded monkeys became more myopic than there counterparts.

Experimentally Induced Myopia

- Neonatal form deprivation and defocused light induces significant myopic changes Wallman et al (1978), Raviola and Wiesel (1985)
  - Monkeys, chicken or tree shrews are monocularly lid sutured, or translucent occluded
  - Local axial change occurring in the sclera at the specific site (VF) where deprivation takes place. Occurs in the presence of a severed optic nerve

Blur Induced RE

- Schaeffel et al (1988) used both plus and minus lenses to induce refractive changes in the chick (one eye +, other -, or control)
  - Eye with plus becomes pseudo myopic and develops hyperopia
  - Eyes with minus become pseudo hyperopic and develop myopia
  - Measurements are cycloplegic

Blur Induced RE

- Fairly linear changes in refractive power from -10 to +20 D
  - Choroid thickens to reduce blur in with plus
  - CNS is not necessary for the response
    - Happens with optic N severed
    - Brain removed
    - Happens if ganglionic cell activity is blocked (tetrodotoxin)
    - Regulated by retinal signals
Blur by Occluder, Translucent, or Minus Lens Causes Elongation

MRI Images of Elongation Due to Defocused Light

Smith Demonstrates that the Periphery is More Important in Emmetropization

Blur Induced RE

- These results suggest that the ocular system can determine the direction of defocused light
- Thus growth regulating systems mechanism changes the size of the vitreous cavity
- Change occurs in the sclera

Happens Even If You Cut the Optic Nerve Regional Retinal Signals

- Doesn’t occur if you use atropine
- Atropine works by non-accommodative mechanism
  - When the optic N is cut
  - Segmental occluders or lenses
  - Animals that use non-muscarinic mechanisms to accommodate

Peripheral blur drives the system towards “emmetropization”
Ablate the macula, peripheral blur results in change in length of the eyeball

Smith, E. Charles F. Prentice Award Lecture 2010: A Case for Peripheral Optical Treatment
Strategies for Myopia OPTOMETRY AND VISUAL SCIENCE, 88(9): 2011
Peripheral Blur Causes Elongation of the Eye Even When Central Vision is Clear

Peripheral Defocus Dominates
- In Monkeys if the fovea is ablated
- Either Peripheral form deprivation and hyperopic defocus produces changes in refractive error
- If there is a conflict between peripheral and retina signals, peripheral dominate
- Repeated with contact lenses with center plano and peripheral -5D or +5D (Troilo 2014) and the effect is larger with smaller pupil plano lenses in adolescent monkeys

Smith’s Conclusions
- Ocular Growth and Refractive Development Are Controlled by Visual Feedback
- The Mechanisms That Regulate Refractive Development are Regional or Local
- Visual Signals From the Fovea Are Not Essential for Visual Dependent Growth and When in Conflict with Peripheral Signals, Peripheral Signals Dominate
- Refractive Errors Usually Vary with Eccentricity and Can Alter Central Refractive Development

Image Shells
- Uncorrected Myope
- Traditional Correction
- Optimal Correction?

Greater Peripheral Accommodative Differences Occur During Near Viewing
- When viewing outside both central and peripheral stimuli are in focus, minimal dioptric difference
- When viewing at near, central targets are accurately accommodated for and are clear but peripheral targets at near are out of focus due to the dioptric difference

Myopic Gene is Turned On by a Near World Environment
- Some mice have the APLP2 gene and if those mice were exposed to a near vision environment they became myopic. If they were not exposed to a near vision demand they did not develop myopia
- The same gene has been found in humans. "These variants showed evidence of differential effect on childhood longitudinal refractive error trajectories depending on time spent reading (gene x time spent reading x age interaction"
How Do We Change the Process

• Can either change the stimulus (glasses, contact lenses, prisms, vision therapy, sunlight) which contributes to myopic elongation.
• OR block or interfere with biochemical process

Atropine and Animals

• Atropine, a non-selective muscarinic stopped the progression of myopia in stump tailed monkeys but not rhesus monkeys
  • Thus accommodation per se was not the mechanism
• Chicks demonstrated regional myopia depending on the area of the retina deprived – thus, not accommodative nor central
  • Chicks have striated muscle in the ciliary body, thus, accommodation occurs by nicotinic action, not muscarinic

Treatment - Myopia Control

• Bifocal lenses
• Multifocal lenses
• Contact lenses
• Orthokeratology
• Atropine
• VT
• Surgery

Treatment with Bifocals

• Oakley Young (1975), Daubs and Shotwell (1983), and Goss (1986) show positive effects of bifocals
  • It seems that patients with esophoria did better than others

Oakley and Young (1975)

• N= 43 Native American (NA) and 226 Caucasian (C), ages 6 -15
• All subjects were under corrected by 0.50D
• Bifocal Add +1.50 or +2.00, regardless of phoria
• Under correction effect? Increase -0.50 D/yr
  • Native Americans: bifocal: -0.11 D/yr control: -0.37 D/yr
  • Caucasians: bifocal: -0.03 D/yr control: -0.53 D/yr

Fulk and Cyert (1996)

• Prospective study
• N = 32 children with esophoria at near
• Randomly divided into single-vision or +1.25 D bifocal.
• Last 6 months: SV: 0.80D/yr BF: 0.57D/yr
• Conclusion: bifocals help in esophores
Houston Myopia Study (1987)

- N=207 Multicultural patients
- 3 year randomized clinical trial
- 3 groups: single vision, +1.00, +2.00 add
- Progression: -0.34, -0.36, -0.34 D/year
- No statistically significant difference between groups
- Highly criticized for not taking phoria measurements into account.

Hong Kong Bifocal Study

- 2 year study of myopic children 9-12 (initial myopia -3.70)
- 32 SV; 22 +1.50; 14 +2.00 add
- Mean progression after 2 yrs. SV - 1.23; +1.50 - .76;
- +2.00 - .66
- Progressive lenses slow myopia
- Progression of Myopia in Hong Kong Chinese Schoolchildren is slowed by wearing progressive lenses
  (Leung JT, Brown B)  Optom Vis Sci 1999

Correction Of Myopia Evaluation Trial Study

- N=469, 4 Optom schools; 6-11 yrs myopia 1.25-4.50
- SV or +2.00 PALs, evaluated yearly for 3 yrs.
- Mean progression SV - 1.48 D; PAL 1.28 D a diff of .20 D which was significant @ p=.004
- Change was due to an increase in axial length
- Most of the change occurred in the first yr
- A Randomized Clinical Trial Of Progressive Addition Lenses Versus Single Vision Lenses On The Progression Of Myopia In Children (Gwiazda, Hyman et al) Investigative Opthal 2003; 44 1492

Bifocal with BI prism

- Rapidly progressing Chinese/Canadian children
- Cheng, D., K. L. Schmid, et al. in OVS
- In this unmasked study myopic progression averaged .77D/year in the single-vision lenses group; .48 D/year in the +1.50 executive bifocal group, and .35 D/year for prismatic bifocal group (+1.50 Add with 3Δ BI in each eye
- Best result of any bifocal or multi-focal lens
- High fitting

**Why did this work?**
Under-Correcting Myopia

- The under-corrected eyes elongated faster (became more myopic) than fully corrected eyes.
- Thus, under-correcting may actually stimulate more myopia. Studies were stopped.


Regular Soft and Gas Permable Lenses Have No Effect in Slowing Myopia

- CLAMP study by Walline 2004
- No change in axial length with rigid contact lenses.

Orthokeratology

- Reim 2003 performed a retrospective study on 253 children age 6-18, -50 to -5.25 for 3 yrs. Mean increase .13D/yr.
- Walline COOK study 29 children between 8-11 with ortho K fitting was safe.
- Cho et al LORIC age 7-12, -25 to -4.50, SV control from another study demonstrated reduction in axial length growth. Large variation in effect.

Walline Study

- CRAYON Study ~ 40 children age 8-11yr
  - -.75 to -4.00 fit w CRT
  - 70% completed the study
  - A scan of children fitted with Ortho-K lenses demonstrated less change than a matched control group soft contact lenses

Swathbick et al

- 26 Myopic children wore a RGP lens in one eye during the day and a reverse geometry Ortho-K in the other eye
- 6 mos later A scan measurements were taken and the eyes were crossed over (A-B reversal design)
- 40% reduction in myopic elongations
- Axial length increased more in the RGP eyes
- Small N, no long term data


Corneal Refractive Therapy

- Pretreatment: 20/400
- CRT: 20/20
- Post Treatment: 20/20
Achieved vs. Attempted (109 Patients)

Achieved

Attempted

5 Yr Orthokeratology Results

Long-term effect of overnight orthokeratology on axial length elongation in childhood myopia: a 5-year follow-up study.

Seven Year Ortho-K Retrospective Study

- Kwok-Hei Mok, and Sin-Ting Chung (Clinical Optometry 2011) measured refractive and central corneal curvature after a washout period
- Myopic progression was calculated as a change of myopia from the baseline to the final visit.
- Average myopic progression of Ortho-K contact lens was \(-0.37 \pm 0.49\) D (0.05 D/yr)
- Average myopic progression of the single-vision spectacle group was \(-0.06 \pm 0.08\) D (0.02 D/yr)

SMART STUDY

- Eiden et al. evaluated the long-term ability of OK lenses to slow the progression of myopia (in progress results not published yet)
- Washed out Ortho-K wearing
- A-scan measurements
- NC in A-scan, but slowing of myopia progression by about 50% over 3 year period of time

Orthokeratology Meta-Analysis

- 7 studies, 435 subjects, 218 OK and 217 Control, 2 year follow up.
- Axial Length was the outcome measure
- "At 2 years follow-up, the AL elongation of the orthokeratology group was significantly slower than that of the control group (WMD, −0.26 mm; 95% CI, −0.31 to −0.21; p < 0.001)"

Low Risk of Microbial Infection

1. 2/10,000 for DW GP contact lenses
2. 8/10,000 for CRT
3. 2-12/10,000 for DW soft contact lenses
4. 18-25/10,000 for EW soft contact lenses

Bullimore et al. Optom Vis Sci 2013;90:937-944
Who Does The Best w Ortho K

- The larger the refractive error the better the response or stated another way – the lower the prescription the less effective Ortho-K is
- The smaller the treatment zone the more effective Ortho K is. Stated another way ortho K lenses designed to slow myopia use smaller OZ
- The larger the pupil the more effective Ortho K is (get more surface area with corrected hyperopic defocus)

Summary

- Ortho-K results in a 30-50% reduction in the progression of myopia
- Ortho-K and LASIK/PRK are different
  - Ortho
  - Can be used in young children
  - High drop out rate – about 20%
  - Concern for corneal infection
  - WOW factor – happy kids

Soft Lenses to Correct Peripheral Defocus

- Phillips and Antstoe demonstrate that dual-focus multifocal lenses can slow the progression of myopia
- One group wore the multifocal while a second group wore multifocal lenses with 2D of defocused light for 10 months
- .44 D/yr for dual focus compared to .69 D/yr for the control

Holden Study on Multifocal Contact Lenses (2011)

- 6 mos of wear
  - .26 D/year vs .60 D/yr
  - No long term data
  - Remember bifocals/progressives were effective in the first year, but the effect dissipated

Multifocal Contact Lens Myopia Control

- Walline, J; Greiner, Katie L McVey, E; Jones-Jordan Optom Vis Sci. 2013 Nov;90(11):1207-14
- Determine the progression with Cooper “D” lens over time compared to Historical controls
  - Adjusted mean standard error sph eq progression of myopia at 2 years was -1.03 D for SV CL and -0.51 for Cooper “D”
  - Axial length changes were 0.41 for SV and 0.29 Cooper
  - Cooper “D” reduced the progression of myopia by 50% and reduced axial elongation by 29%

Soft Bifocals

- Slows axial length growth
  - 29%
  - 33% Dropout
  - Walline et al. Optom Vis Sci 2013:90:1207-1214

- Slows axial length growth
  - 31%
  - 42% Dropout
The VTI Multifocal Center Distance CL

- Center-distance design. As one moves radially outward from the center of the lens, power rises dramatically and creates an annular blur zone.

<table>
<thead>
<tr>
<th>Suppressed Blur</th>
<th>Clear Vision</th>
<th>Suppressed Blur</th>
</tr>
</thead>
</table>

Myopia Progression Control

- Looking for FDA Indication for the Correction of Myopia
- Animal (chick) model study for MPC – Demonstrated no myopic progression up to 10D
  - Woods et al., IOVS, 2011
  - Recent data indicated halting AND reversal
    - Irving et al., AAO 2014
- Human proof of concept trials on 3 known risk factors for MPC – COMPLETED
  - Correction of Peripheral hyperopia
    - Miller et al., 2011
- Human trial for wearability in children – COMPLETED
  - Rated as highly on the PREP QOL Scale as Single Vision Acuvue Advance
    - Woods et al., 2011

What is Wrong With These Studies

- No long term studies
  - Remember both atropine and bifocal studies did much better in year one
  - No studies that looked at what happened when the lenses were discontinued
  - No real controls

What Can I Prescribe Now Using Soft Lenses

- Cooper multifocal D +2.00 add and Acuvue Oasys for Presbyopia lenses are as similar as you can get for now
- VTI releasing the first soft CL that is designed to slow the progression of myopia
- Might add low dosages of atropine with it
- Tom Adler has found that any multifocal works, not much different (His studies were started before peripheral defocus theories got hot)
- VTI might have the lens (based upon Monkey studies)

Holden Study on Glasses (2010)

- Three experimental designs
- Peripherally correcting lenses
- Minimal effect on slowing myopia
- Not a surprise, can control where someone is looking
### Vision Therapy

- No controlled study
- Tractman – Accommodrac™ – not repeatable

### Atropine

- Gimbel (1977), Bedrossian (1979), Kennedy (1995), Syniuta & Isenberg (2000) show that myopia progression drops from .35-.85 diopters to .05-.12 diopters
- 22 studies support the use of atropine
- Problems with light sensitivity, flush, allergies are minimal

### Bedrossian - Monocular Treatment (1971)

- N = 62, Ages 8 – 13
- Monocular trial, fellow eye used as control
- 1% Atropine sulfate, 1gtt, QD (morning)
- Patients were not given a bifocal
- Increases in myopia:
  - Treated eye: +0.20D/year
  - Control eye: -0.85D/year

### Chiang (2001) – Atropine and Bifocal Spectacles

- N = 706, Ages 6 – 16
- 1% atropine solution 1X/week.
- Median treatment was 3.62 years.
- Study involved a homogeneous population of Caucasian patients.
- Mean rate of progression was 0.08 D/year

### Chou (1997) - Atropine to Control Progression in High Myopia

- N = 20, Ages = 7 - 14
- Refraction: -6.0D
- Time = 5 years
- Treatment = 0.5% atropine QHS
- High compliance/Low drop out rate
- Follow up exams = every 4 months
- Myopic progression: -0.08D/year

### Reduction in Elongation of the Eye w Atropine

- Chew (1999) study mean progression of -2.00 in control group and +1.7 in the atropine group
- Control group increased axial length by 1.88mm while atropine group decreased length by 0.17
- Not accommodatively induced, atropine blocks the retinal/choroid signal for elongation
Chua et al - ATOM 1 Study (2006)

- 400 children between 6 and 12 years of age
- Refractive error of spherical equivalent: -1.00D to -6.00D
- Astigmatism: -1.50D or less
- Only 1 eye was chosen for treatment
  - 1 get 1% atropine or placebo eye drops qhs x 2 years
  - All children Rx photo-chromatic, progressive lenses

Results at 2 years

<table>
<thead>
<tr>
<th></th>
<th>PLACEBO</th>
<th>ATROPINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in Refractive Error</td>
<td>-1.20±0.69D</td>
<td>-0.28±0.92D</td>
</tr>
<tr>
<td>Change in Axial Length</td>
<td>+0.38±0.38mm</td>
<td>-0.02±0.35mm</td>
</tr>
</tbody>
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Myopia Progression over 2 years

Adverse Effects Reported in ATOM Study

- Allergic or hypersensitivity reactions or discomfort (4.5%)
- Glare (1.5%)
- Blurred near vision (1%)
- Logistical difficulties (3.5%)
- Others (0.5%)

Results

- Over a 2-year period, atropine treatment achieved approximately a 77% reduction in mean progression of myopia compared with placebo treatment.

Yearly Progression of Myopia is Stopped by Atropine
Patient is Now 19

- -3.75 Myope
- Was recently fitted with Ortho-K lenses and happy (1 year w/o progression)
- If myopia progresses atropine .025% will be added

VARIABLES

CONCENTRATIONS OF ATROPINE

Myopia Progression (D/Y)

<table>
<thead>
<tr>
<th></th>
<th>CONTROL</th>
<th>0.1% ATROPINE</th>
<th>0.25% ATROPINE</th>
<th>0.5% ATROPINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEAN RATE OF MYOPIA PROGRESSION (D/Y)</td>
<td>-0.06+/-.06</td>
<td>-0.47+/-.30</td>
<td>-0.45+/-.55</td>
<td>-0.04+/-.03</td>
</tr>
</tbody>
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Shin et al – Progression Less than 1D in a Year

- Atropine .5%
  - 68% did not progress
- Atropine .25%
  - 49% did not progress
- Atropine .1%
  - 42% did not progress
- Control
  - 8% did not progress

Lee et al - Atropine .05%

- Mean myopia progression for the patients treated with atropine .05% was 0.28 D/year, compared to that of the control group of 0.75 D/year
- There was a lower ratio of myopia that progressed greater than 0.50 D in 1 year as compared to controls (66.7% versus 77.8%; P = 0.001).
Atropine .025% Slows the Progression of Early Myopes

- Early myopes less than a diopeter
- No accommodative changes
- No pupillary dilation

Seasonal Prescription

- Atropine .1% for the summer
- Atropine .25% for spring and fall
- Atropine .5% for the winter
- UV protecting glasses were used in all glasses
- Progressives in children with near vision blur
- 93% no blur and/or photophobia

Low Concentration of Atropine ATOM 2

- 400 children aged 6-12 years with myopia of at least -2.0 diopters

ATOM 2 – Low Concentration

- mean myopia progression at 2 years
- Atropine .5% -0.30 +/-0.60 (AL=0.27)
- Atropine .1% -0.38 +/-0.60 (AL=0.28)
- Atropine .01% -0.49 +/-0.63 (AL=0.41)

- ATOMs-1.20 +/-0.69 D in the placebo
- Atropine 1% -0.28 +/-0.92 D

Lower Concentration

- Less effect on accommodation and pupil size

Atropine Studies w Various Percentage of Atropine

- Atropine .1% is the gold standard
- Atropine .5% is as effective
- Atropine .1%
- Atropine .025%
- Atropine .01%
- Seasonal prescription
Effect on Myopia Progression after Cessation of Atropine

• 400 children 6 to 12 years old
• Refractive error of SE: -1.00D to -6.00D
• Astigmatism: ±1.50D or less
• 12 months after stopping treatment of 1% atropine or vehicle eye drops once nightly for 2 years

Results

• The average rate of myopia progression of the atropine-treated eyes over the entire 3-year period was still less than the rate in placebo treated eyes and axial length measurement differences were greater

Cessation of Low Concentration

• Chia A, Chua WH, Wen L, Fong A, Goon YY, Tan D. Atropine for the treatment of childhood myopia: changes after stopping atropine 0.01%, 0.1% and 0.5%. Am J Ophthalmol. 2014

• 400 patients who used low dosage atropine for 24 mos
• Over the following 12 mos, myopic progression was greater in the 0.5% eyes (-0.87 +/- 0.52 D), compared to the 0.1% (-0.68 +/- 0.45 D) and 0.01% eyes (-0.28 +/- 0.33 D, P < 0.001).
• AL growth was also greater in the 0.5% (0.35 +/- 0.20 mm) and 0.1% (0.33 +/- 0.18 mm) eyes, compared to the 0.01% eyes (0.19 +/- 0.13 mm, P < 0.001).

Summary of ATOM 1 & 2

• Less Rebound w Axial Length Measurements
• Using axial length Atropine 1% is clearly the winner
• 1% is the best
5 Yr. Out Come From Chia et al
Atropine .5%, .1% and .01%

- Phase 1 - 2 yrs of treatment with various concentrations of atropine
- Phase 2 – 1 year of washout – No treatment
- Phase 3 – Treatment of those that progressed during Phase 2

Phase 2

- Rebound discussed
- Interesting finding approximately 50% of the kids on atropine did not progress during the 1 yr washout period suggesting that atropine might create a stop signal

Percentage That Needed Retreatment

<table>
<thead>
<tr>
<th>Concentration</th>
<th>0.5</th>
<th>0.1</th>
<th>0.01</th>
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<tbody>
<tr>
<td>6.0-8.0</td>
<td>100</td>
<td>90</td>
<td>63</td>
</tr>
<tr>
<td>8.1-10</td>
<td>87</td>
<td>80</td>
<td>27</td>
</tr>
<tr>
<td>10.1-13</td>
<td>41</td>
<td>27</td>
<td>8</td>
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Take Away

- Might be able to titrate or stop the use of atropine
- Data also suggest that one needs to titrate concentration like we do in steroids to stop a rebound effect
- In any case the progression of myopia and the need to continue treatment decreases with age.

Chia Implies

- That atropine .01% is more effective than Atropine 1%
- Just not true because you don’t go cold turkey
- BUT agree that older children (after age 8) and more moderately progressive children can be started on Atropine .01 or .02
- BUT very progressive kids still need Atropine 1%

Must Keep Children on Atropine for 2 Years

- Get more of an effect in year 2 than 1
What Is Wrong With Rebound Studies

- All atropine 1% patients stay on treatment usually
  - 4 to 10 on atropine 1%
  - Atropine .02% or otho K
- It is not how the medication is used, ie.
  - 2 years use
  - Washout
  - 1 year w/o treatment

Summary

- Although the effect of the drug on myopia was relatively reduced after cessation for 1 year, the change in the axial length was significantly less than in eyes not treated with atropine.
- Future studies needed:
  - Is 2 years of Atropine enough?
  - What happens after a longer period of drug-free treatment?

Atropine 1% vs Lower Concentrations

- By combining the 2 studies, they found that in the initial 8 months, there was a hyperopic shift in the 1.0% group and continued myopic progression in the other groups, which was greater in the lower doses, before growth slowed between the 8- and 24- month periods.

Mechanism of Atropine

- It is believed that atropine acts directly or indirectly on the retina or scleral, inhibiting thinning or stretching of the scleral, and thereby eye growth.2
- However, the rate of growth seemed to continue at a steady pace over the washout year in children previously receiving the higher 0.1% and 0.5% doses of atropine, slowing only when atropine 0.01% was restarted.

Conclusions

- From clinical experience, we also note that by slowly tapering the frequency of atropine, we can dampen the change in myopia and retain the beneficial effect on myopia progression.
- On the basis of these results, we conclude that low-dose (0.01%) atropine for periods up to 5 years is a clinical viable treatment of myopia.

Case Example

- A -6.50 myope has been put on Atropine 1%
- Developed symptoms was switched to Atropine .02%
  - 6 mos follow up and had increased to -7.25
  - Put back on Atropine 1%
  - Refraction -6.50
  - Conclusion: false rebound
What to do if Atropine .01% Does Not Work

- Increase dosage
- Add multifocal or ortho K lenses
- Stop all treatment, in some cases nothing will work

Summary

- Although the effect of the drug on myopia was relatively reduced after cessation for 1 year, the change in the axial length was significantly less than in eyes not treated with atropine.
- Future studies needed:
  - Is 2 years of Atropine enough?
  - What happens after a longer period of drug-free treatment?

Atropine Tx Has Increased

- Five different concentrations of atropine eye drops are available under the NHI program. Atropine 0.5 and 1% since 1995, 0.3% since 2001, and 0.1% since 2004.
- Other treatments such as ortho-K, contact lenses, bifocals are not reimbursed and thus not prescribed very often
Percentage of Children on Atropine

What Is The Strongest Concentration That Will Not Cause Clinically Significant Mydriasis Or Blur Secondary To Cycloplegia?

- Concentration of atropine was varied and measured mydriasis and cycloplegia
- measurement of pupil size, AA, and symptom survey the highest dosage of atropine that would not induce clinical symptoms
- Atropine .02% was the highest percentage that did not caused clinically significant symptoms associated with atropine administration

Guidelines

- Atropine 1% qhs for young progressive myopes with strong family history
- Atropine .5% may be used as a substitute
- Atropine .02% or .01% early myopes or additive if Ortho-K is not working
- Choose of atropine vs ortho-K –I let the child make the decision
- Seasonal Atropine for those that want an option in between

Atropine Slows Myopia Progression More in Asian than White Children by Meta-analysis

- Meta analysis of retrospective and prospective studies were the same
- Myopia progresses faster in Asian than white children .55 D/yr vs .35 D/yr
- Atropine slows myopic progression more in Asian (.50 D/yr) children than white children D/yr

Shu-Mei Li, Shan-Shan Wu, Meng-Tian Kang, Ying Liu, Shu-Mei Jia, Si-Yuan Li, Si-Yan Zhen, Luo-Ru Liu, He Li, Wei Chen, Zhao Yang, Yan-Yun Sun, Ningli Wang, and Michel Millodot VOL. 91, NO. 3, PP. 342-350 OPTOMETRY AND VISION SCIENCE
Pirenzipine

- Selective M1 Muscarinic antagonist
- Used in Japan for peptic ulcers
- Prevents myopia in animals without accommodative or pupillary changes
- Has undergone initial trials in humans
- Clinical trials using 1 or 2% BID
- 50% reduction in Singapore and American kids (N=178 8-12)

Valley Forge Sells Rights of Distribution to Novartis

- Phase III clinical trials
- Phase II showed 50% reduction in myopia
- Three years until it will be released
- High number of local effects – burning and redness
- FDA kills it

Who Should We Treat?

- Anyone who demonstrates myopia at a young age
  - Loss of plus lens with cycloplegic refraction
  - 87% sensitivity
  - 73% specificity

Treatment Options

- Bifocal vs progressive
  - +2.50
- Early myopia – trial of vision therapy
- Atropine with bifocal
- Ortho K
- Multifocal progressive with low dosage atropine
- LASIK
- Future Pirenzipine (Valley Forge sells rights to Novartis)

Should We Mix And Match Them?

- Atropine 1% is not tolerated what next
- Ortho K
- Lower dosage – What dose?
- Ortho K and atropine .025% or .01%
- Bifocal contact lenses w and w/o atropine

TREATMENT RESULTS OVER TIME
<table>
<thead>
<tr>
<th>Case 1</th>
<th>Case 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>* 6 year old boy</td>
<td>* 8 year old Asian child with both parents being myopic</td>
</tr>
<tr>
<td>* -4.50 OU</td>
<td>* Presents with -1.50 OU</td>
</tr>
<tr>
<td>* Retinal detachment OD</td>
<td>* What do you recommend</td>
</tr>
<tr>
<td>* What should we do</td>
<td>* Athletic vs A real reader</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Case 3</th>
<th>Case 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>* 8 year old with -0.50 OU, one parent is myopic</td>
<td>* 25 year old female who is on computers all day comes in wearing -3.00 OU and now demonstrates -3.75 what can you do</td>
</tr>
<tr>
<td>* Parent asks can we do anything to stop the progression of myopia</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Case 5</th>
<th>Case 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>* At age 3 RE= +1.00</td>
<td>* 43 year old female keeps increasing, she has increased from a -8.50 to a -9.25. Her sister had a RD. She needs a 1.25 Add</td>
</tr>
<tr>
<td>* At age 4 RE = +.25</td>
<td>* What would you do?</td>
</tr>
<tr>
<td>* At age 5 RE= -.25</td>
<td>* Would you prescribe it</td>
</tr>
<tr>
<td>* What would you do</td>
<td>* What would you think the effect of accommodation would be.</td>
</tr>
</tbody>
</table>
Arthur Schopenhauer in the 1800s described three stages of truth: "All truth passes through three stages. First, it is ridiculed. Second, it is violently opposed. Third, it is accepted as being self-evident."

I suspect that after hearing what I have said today, most of you will be at the first stage, disbelief and ridicule, some will be in the second stage, and a few will have known this all along.