2019 AZOA Fall Congress Curriculum
Handouts for all courses were not made available to the AZOA
How is changing eye care

Bryan M. Rogoff, OD, MBA, CPHM, FAAO

COPE: 63471-PD

COFFEE: 63471-PD

Financial Disclosures

<table>
<thead>
<tr>
<th>Commercial Interest</th>
<th>Example: Company</th>
<th>What was Received</th>
<th>For What Role</th>
<th>Nature of Relevant Financial Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td>UnitedHealth Care</td>
<td>AVMs</td>
<td>Honorarium</td>
<td>Speaker</td>
<td>What was Received</td>
</tr>
<tr>
<td>Sight Sciences</td>
<td>Consulting Fee</td>
<td>Consulting Fee</td>
<td>Consultant</td>
<td>Advisory Board</td>
</tr>
<tr>
<td>Avensys/CBD</td>
<td>Consulting Fee</td>
<td>Consulting Fee</td>
<td>Consultant</td>
<td></td>
</tr>
<tr>
<td>USP scientists</td>
<td>Honoraria</td>
<td>Honoraria</td>
<td>Speaker</td>
<td></td>
</tr>
</tbody>
</table>

Current & Popular Uses

<table>
<thead>
<tr>
<th>Logic &amp; Rules</th>
<th>Example: TurboTax</th>
</tr>
</thead>
<tbody>
<tr>
<td>TurboTax</td>
<td>Rules engine</td>
</tr>
<tr>
<td>Tax laws</td>
<td>Define the paths or processes</td>
</tr>
<tr>
<td>Retinal photography</td>
<td>Screening diabetic retinopathy</td>
</tr>
</tbody>
</table>

Course Objectives

Briefly review the foundation and concepts of artificial intelligence.
A conceptual model of how AI is currently positioned in eye care.
The staged (step-wise) process of AI-enabled retinal photography within the telemedicine model.
The limits of AI in eye care.
Proposed model of optometry-centered model of AI and retinal photography: screening diabetic retinopathy.
CURRENT & POPULAR USES
Machine Learning Examples:
- Image Recognition
- Virtual Personal Assistant
- Traffic Predictions
- Social Media Services
- Fraud Detection
- Email Spam
- Malware Filtering
- Online Customer Support
- Search Engine Results
- Product Recommendations
- Financial Trading
- Healthcare
- Marketing
- Etc.

WHAT IS ARTIFICIAL INTELLIGENCE?
"The theory & development of computer systems able to perform tasks normally requiring human intelligence, such as visual perception, speech recognition, decision-making, and translation between languages."

WHAT IS ARTIFICIAL INTELLIGENCE?
"A branch of computer science dealing with the simulation of intelligent behavior in computers."
"The capability of a machine to imitate intelligent human behavior."

WHAT IS ARTIFICIAL INTELLIGENCE?
"Artificial intelligence is a branch of computer science, the study of the relation between computation and cognition."
Dartmouth College 1956

Summer Research Project on Artificial Intelligence

Invited a group of researchers from a variety of disciplines including language simulation, neuron nets, complexity theory, and more.

John McCarthy

Together they discussed clarification and development of the concepts of "thinking machines," which had been quite divergent for that time period.

McCarthy is said to have picked the name artificial intelligence for its neutrality, to avoid highlighting one of the tracks being pursued at the time for the field of "thinking machines" that included cybernetics, automata theory and complex information processing.

The proposal:

• "The study is to proceed on the basis of the conjecture that every aspect of learning or any other feature of intelligence can in principle be so precisely described that a machine can be made to simulate it."

What is Machine Learning?

Machine Learning is a subset of artificial intelligence.

"...Machine Learning is a system of artificial computer intelligence that provides computers with the ability to automatically learn without being programmed..."

Sergio A., 2018

What is Deep Learning?

"Input data is filtered or processed through layers of networks, with each layer refining the results for better decisions. Simulates the human brain."

Miootto, Wang, Wang, Jiang, & Dudley, 2018

Deep learning for healthcare: review, opportunities and challenges
What is Artificial Neural Networks?

"...computational paradigms based on mathematical models that shape the functional characteristics and computational properties of the brain..." It adds cognitive functions to an AI system.

Artificial Intelligence

A technique for incorporating human intelligence to a machine. It is the superset of Machine Learning & Deep Learning.

Machine Learning

It is a sub-field of AI that comprises of algorithms & statistical models used by machines to perform a specific task & improve with experience by learning on its own.

Deep Learning

It is the sub-field of Machine Learning that uses Artificial Neural Networks for computation for giving accurate results.

Artificial Intelligence

Weak

- The machine programs act according to well-defined responses.
- They are confined to a set of rules that we provide, and they give the responses within the limits of those rules.
- It does not have the ability to make decisions and make any changes by itself.
- Example: Oven Timer

Strong

- Innovate designing of algorithms for machines that try to learn by themselves using the input data and improve the accuracy in giving outputs.
- ML & DL comes under this category.
- Example: Speech recognition, Visual perception, & Language translation.

Machine Learning

ML is the subset of AI where ML algorithms are designed in such a way that the machine tries to learn by itself rather than being explicitly programmed on each and every instruction.

With the addition of more and more data, it tries to internally modify itself and then according to the data which it is exposed so that it will not rely on human experts to program them.

There are different types of Machine Learning:
- Supervised Learning
- Unsupervised Learning
- Reinforcement Learning
Machine Learning

Supervised Learning

The machine is provided with a labeled dataset that contains examples. It learns from both input and output parameters.

When the machine is given a new dataset, the supervised learning algorithm examines the data and produces the correct output according to the labeled data.

Predicts the output.

Supervised learning is best for classification & regression problems.

Example: Detecting Cancer Patients

Unsupervised Learning

The machine would not have any labeled dataset. The algorithm is designed in a way that it tries to learn by analyzing any input of data.

Tries to find patterns, structures & make clusters of similar data types.

Does not predict any specific output.

Example: Netflix recommendations

Reinforcement Learning

Reinforcement algorithms are designed in such a way that they learn from feedback to find the optimal solution.

Adopts the principle of reward & punishment, and tries to move to the correct result.

Decides to take action in certain situations.

The main challenge is preparing the simulation environment, which is highly dependent on the task to be performed.

Example: Training models that control autonomous cars

Deep Learning

Deep learning is a subset of machine learning where artificial neural networks, algorithms inspired by the human brain, learn from large amounts of data.

Algorithms perform tasks repeatedly & each time making minor tweaks to improve the solution.

Artificial Neural Networks (ANN) have various layers that enable learning, thus called “Deep” Learning.

ANNs have been around for at least 50 years.

The fundamental unit of a neural network is a node, which is loosely based on the biological neuron in the mammalian brain.
Deep Learning

Types of Neural Networks
1. Unsupervised Pre-trained Networks
2. Convolutional Neural Networks
   A NN that has been extended across space using shared weights.
3. Recurrent Neural Networks
   A NN that has been extended across time by having cycles which feed into the next layer instead of into the next layer in the same time step. RNN is designed to recognize sequences. It has cycles inside that implies the presence of short memory in the net.
4. Recursive Neural Networks
   A hierarchical network where there is really no time aspect to the input sequence but the input has to be processed hierarchically in a tree fashion.

Artificial Intelligence in Eye Care

Glaucoma
- Not many Deep Learning methods.
- Fundus Photos, Wide-Field OCT, & VFs are used to construct detection algorithms.
- Best for Open-Angle Glaucoma.
- Local biomarkers of the optic disc are used for detection.
- Clinical testing demonstrated AUC of 0.8384, similar to human detection.
- High sensitivity and specificity.

A study to explore this question, employing a data-driven approach using deep learning techniques.
Visual Field Index (VFI) is a global metric that represents the entire visual field.
Study estimates the visual field index (VFI) from a single 3D raw optical coherence tomography (OCT) image of the optic nerve with Pearson correlation of 0.88 (VERY ACCURATE!) Can give ECPs precise information without the need for multiple and time-intensive tests when gathering data for a glaucoma diagnosis.

Summary:
Artificial intelligence has the potential to revolutionize the screening, diagnosis, & classification of glaucoma, both through the automated processing of large data sets, & by earlier detection of new disease patterns. In addition, artificial intelligence holds promise for fundamentally changing research aimed at understanding the development, progression, & treatment of glaucoma, by identifying novel risk factors & by evaluating the importance of existing ones.
**Artificial Intelligence in Eye Care**

### Glaucoma

**Challenges:**
- No defined rules of glaucoma like Diabetic Retinopathy
- Rate of Progression

### Uveitis

**Dataset:**
- Initiated in the UK by the Royal College of Ophthalmologists.
- In the US, AAO IRIS (Intelligent Research in Sight) contains data samples over 24.19 million unique patients & 86.02 million visits.
- ICD Classification will enhance big data analysis by providing granularity of diagnostic reporting.

**Designed & built a rule-based expert system to diagnose uveitis.**

**Goal:**
- To mitigate the lack of human experts by helping general ophthalmologists achieve a correct diagnosis with minimal time and effort.
- Educational tool for newly graduated doctors to support their diagnostic decisions.

### ARMD

**Machine Learning of OCT images are used to predict low & high anti-VEGF requirements.**

**Algorithms:**
- Fed into Random Forests (RF) to find a predictive model.
- 70%-80% AUC prediction is obtained using a Deep Convolutional Neural Network (DCNN)

**Used in image-guided predictions for interval treatments for neovascularization in ARMD & DR.**
Artificial Intelligence in Eye Care

**ARMD**
Practical implementation of AI-based software as a cloud-based tool aimed for telemedicine.

Dataset of labeled 55,000 OCT images obtained from ARMD patients and trained three types of CNNs to perform AMD diagnosis.

AI-based system achieved the same image discrimination rate as that of retinal specialists.

Detection accuracy was generally higher than 90%

Retinal specialists accuracy 92.73%

**Diabetic Retinopathy**
Most studies focus on the analysis of fundus photographs.

Retinal camera sensors play an important role of the confusion matrix as individual pixels play an important role of image-level predictions in models.

Deep Learning models highlight important abnormal regions for physician predictions.

DL algorithms identify specific patterns.

**Diabetic Retinopathy**
Verily built an AI tool that’s enabling wider access to care & screening for diabetic retinopathy & diabetic macular edema in India.

“This dataset was used to train a deep neural network to detect referable diabetic retinopathy. We then tested the algorithm’s performance on two separate clinical validation sets totalling ~12,000 images, with the majority decision of a panel seven or eight U.S. board-certified ophthalmologists serving as the reference standard...”

The algorithm has since been refined and is now in clinical use at the Aravind Eye Hospital where it’s helping ease the burden on both physicians & improving the patient experience.

Verily has received EU clearance for medical devices.
IDx is the only one the FDA approved Class 2 device due to its 87.2% sensitivity and 90.9% specificity, which does not require an interpretation by a physician.

EyeArt received a Medical Device License from Health Canada for its AI-enabled cloud-based diabetic retinopathy (DR) automated screening software system.

Results:
In the 101,710 encounters, prevalence of encounters with moderate non-proliferative DR (NPDR) or higher or with surrogate markers for CSME was 19.3% and prevalence of encounters with potentially treatable DR (severe NPDR or PDR) was 5.1%.

EyeArt’s screening sensitivity was 91.3% and specificity was 91.1% with area under the receiver operating characteristic curve (AUROC) of 0.965. EyeArt’s sensitivity for detecting potentially treatable DR was 98.5%.
Artificial Intelligence in Eye Care

Diabetic Retinopathy

Conclusion:
EyeArt automated system has high screening sensitivity and specificity on both mydriatic and non-mydriatic retinal images as demonstrated on a large real world dataset making it safe and effective for DR screening.

Validation of EyeArt Automated Diabetic Retinopathy Screening System on Large Cohort of Mydriatic and Non-Mydriatic Telemedicine Data from EyePACS

June 2017

Artificial Intelligence in Eye Care

Cataract

Deep Learning models to diagnose senile cataracts.

CNN-based computer-aided diagnosis (CAD) framework to classify and grade pediatric cataracts for improving clinical workflow of cataract's diagnosis in the background of large-

Study wanted demonstrate the performance & effectiveness of the deep features extracted in the CNN, the study investigated the features combined with support vector machine (SVM) & softmax classifier & compare with traditional representative methods.

Localization and diagnosis framework for pediatric cataracts based on slit-lamp images using deep features of a convolutional neural network

March 2017

Artificial Intelligence in Eye Care

Keratoconus

Conclusion:
The main advantage of the proposed algorithm is that it can be used as an integrated part of the diagnostic process.

From the obtained results, we can conclude that the proposed KeratoDetect algorithm ensures a high level of performance.

The main contribution of this work is the development and integration in the diagnostic process of an assistant software to help the ophthalmologist.

KeratoDetect: Keratoconus Detection Algorithm Using Convolutional Neural Networks

January 2019
Artificial Intelligence in Eye Care

Keratoconus

Machine learning algorithms have the potential to interrupt classical medical screening programs, being able to provide diagnostics in a very short time as well as helping to increase patient care and comfort.

The contribution of this paper consists in applying a machine learning mechanism to keratoconus disease detection.

The high level of performance can come to help the medical staff in correctly diagnosing keratoconus.

In conclusion, this paper presents the development of a screening tool based on a learning algorithm that automatically detects the keratoconus disease based on corneal topographies.

The algorithm can be implemented in the device that performs the topography as an add-on in order to assist the ophthalmologist in rapid screening of its patients.

Objectives:
1. Improve the quality of life of individuals who have diabetes by detecting referable disease in a timely manner.
2. The cost of DR photographic screening is balanced by the need for referring only those who need treatment within a specified time (~30-60 days).
3. An automated method for grading photographs for referable conditions is preferred over manual reading.

Deep Learning for Detection of Diabetic Eye Disease - 2016

"AI has proven to be better than human readers in sensitivity & specificity for referable diabetic eye disease."

"The results show that our algorithm's performance is on par with that of ophthalmologists.

The algorithm has a F-score (combined sensitivity and specificity metric, with max=1) of 0.95, which is slightly better than the median F-score of the 8 ophthalmologists we consulted (measured at 0.91)."
Studies have shown that digital photography is as effective as a dilated eye exam, & patients with vision-threatening disease can be rapidly identified and promptly referred for examination & management.

The broad range of telemedicine technologies & protocols for diabetic retinopathy reflects progressive improvement in diagnostic sensitivity & specificity, with enhanced cost-effectiveness.

**Artificial Intelligence & DR Photographic Screening Program**

1. Retinal Photo
2. Optical Coherence Tomography (OCT)
3. Refractive & Cornea
4. Artificial Neural Networks - Repeat procedure & teach, can teach many more.
5. Swarm Intelligence - Reduce the variations in human decision making by analyzing much larger datasets, can fill in gaps of other sources.
6. "Subject-Matter-Expert-Turning-Test"

**Components**

- Sensor System
- Response
- Output

1. Simulate human thinking by narrowing search possibilities
2. Feigenbaum Test
3. "Subject-Matter-Expert-Turning-Test"
Artificial Intelligence & DR Photographic Screening Program

1. The most common use of Artificial Intelligence in eye care is...
2. The process of detection is called...
3. The images must be as clear as possible & have as much of the retina as possible.

Image Processing

1. Import the image from a camera in digital form
2. Manipulate / analyze or pre-process the image or enhancement or data compression.
3. Sharpen the image to increase the contrast between dark & light areas.
4. Use Pattern Recognition:
   a. Extract vascular tree of the posterior pole.
   b. Localize the optic disc
   c. Segment the optic disc
   d. Detection of exudates, CWS, & drusen: provide the best biomarkers for chromaticity.
   e. Calculate the Mahalanobis distance to measure the distances or differences between chromaticity values.
   f. Repeat the process for detection & localization of exudates / drusen.
   g. Remove the optic disc properties from the image & thus leave the exudates / drusen.

Differentiation between retinal features like the optic nerve head & exudates / drusen are difficult but not as difficult as retinal hemorrhages from the background retina.

Output to the clinical as a probability of having a referable condition.

Lowers the burden of clinical decision making.
What are the Limits of AI?

Unlimited
- Machine Learning is vastly superior to the physical learning of the human brain.
- As more and more powerful computers can perform more and more operations in tiny fractions of a second.
- Machine thinking provides people with patterns that they can never recognize or only recognize in an unacceptably long time.

Limited
- Only detects patterns.
- Machine Learning gains knowledge through statistical correlations instead of logical conclusions.
- AI lacks common sense.
- AI lacks intuition.
- AI can't explain itself.
- AI lacks empathy.
- AI lacks responsibility.
- AI is data-hungry & brittle.

Machine Learning gains knowledge through statistical correlations instead of logical conclusions.

Implications for Eye Care

Implications for Eye Care: The Neural Basis of Economic Decision-Making in the Ultimatum Game
Sanfey AG., Rilling JK., Aronson JA., Nystrom LE., Cohen JD.

1. In the Ultimatum Game, two players are given the opportunity to split a sum of money.
2. One player is deemed the proposer and the other, the responder.
3. The proposer makes an offer as to how this money should be split between the two.
4. The second player (the responder) can either accept or reject this offer.
5. If it is accepted, the money is split as proposed, but if the responder rejects the offer, then neither player receives anything.

Implications for Eye Care

Implications for Eye Care: Applications of Artificial Neural Networks in Health Care Organizational Decision-Making: A Scoping Review
Shahid N., Rappon T., Berta W.

1. With the digitization of health care, hospitals are increasingly able to collect large amounts of data managed across large information systems.
2. With its ability to process large datasets, machine learning technology is well-suited for analyzing medical data and providing effective algorithms.
3. Considering the prevalent use of medical information systems & medical databases, ANN have substantial applications in biomedical research, diagnosis & disease monitoring.
Implications for Eye Care

Applications of Artificial Neural Networks in Health Care Organizational Decision-Making: A Scoping Review
Shahid N., Rappon T., Berta W.

Implications
1. The most successful applications of ANN are found in extremely complex medical situations.
2. It was found ANN to be mainly used for classification, prediction and clinical diagnosis across cardiovascular, telemedical and organizational behavior.
3. Neural networks have been used effectively as a tool in complex decision-making in strategic management, specifically in strategic planning, performance, assessing decision-making.

Proposed Model of an Optometric-Centric AI Diabetic Retinopathy Program

Objectives:
1. "to identify disease in its pre-clinical, and therefore hopefully still curable, phase" (Morabia & Zhang, 2004)
2. "...facilitate intervention and to improve outcomes.
3. The clinical validity of a screening test refers to its ability to detect or predict the clinical disorder of interest.
4. That is, for clinicians, the utility of a screening test is determined by its ability to predict the disorder, i.e., the probability that a subject has the disorder given the screening test result (positive predictive value, PPV)..." (Yuan, Xu, et al., 2016)

The Practical Aspects of the AI System:
1. Process many more events than can any human
2. Photographic screening can be as sensitive and specific as face-to-face visits. (Ting et al., 2017)
3. Artificial intelligence meets or exceeds the specificity and sensitivity of human clinical visits. (Ting et al., 2017; Chang, 2018; Ting et al., 2017)
Proposed Model of an Optometric-Centric AI Diabetic Retinopathy Program

Stages:
1. Establish goals and objectives of the program
   b. Identify individuals who need timely care, optimizing schedules.
   c. Utilize optometrists & ophthalmologists in their optimal roles.
   d. Establish criteria for referral or monitor.
   e. Calculate performance metrics.

2. Contract or assign optometric readers & network of referral optometrists for surveillance & ophthalmologists for medical/surgical intervention.
3. Acquire or assign appropriate personnel & equipment.
4. Modify workflow processes for the distribution of HIPAA-protected digital medical images to the AI servers.
5. Evaluate current patient data set & create inclusion criteria for image acquisition.
6. Distribute images to AI servers.
8. Return conclusion to primary care providers.

I Can Outperform Doctors. So Why Don’t Patients Trust It?

In the Journal of Consumer Research, it showed a strong reluctance across procedures ranging from a skin cancer screening to pacemaker implant surgery. It found that when health care was provided by AI rather than by a human care provider, patients were less likely to utilize the service and wanted to pay less for it.

They also preferred having a human provider perform the service even if that meant there would be a greater risk of an inaccurate diagnosis or a surgical complication.
The reason was found that is not the belief that AI provides inferior care. Nor is it that patients think that AI is more costly, less convenient, or less informative. Rather, resistance to medical AI seems to stem from a belief that AI does not take into account one’s idiosyncratic characteristics and circumstances. People view themselves as unique, and we find that this belief includes their health.

**Study 2:** Offered more than 200 business school students at Boston University & at New York University the opportunity to take a free assessment that would provide them with a diagnosis of their stress level and a recommended course of action to help manage it.

The results: 40% signed up when they were told that a doctor was to perform the diagnosis, but only 26% signed up when a computer was to perform the diagnosis.

**Study 3:** Surveyed over 700 Americans from an online panel to test whether patients would choose AI providers when AI’s performance was clearly superior to that of human providers.

Research participants to review information about the performance of two health care providers in terms of their accuracy in diagnosing skin cancer or making triage decisions for medical emergencies, or the rate of complications associated with pacemaker implant surgeries that these providers had performed in the past.

When participants chose between two human doctors varying in their performance, all participants preferred the human doctor with the higher performance. But when choosing between a human doctor and an AI provider (e.g., an algorithm, chatbot, or a robotic arm directed remotely through a computer program), participants’ preference for the higher-performing AI provider was significantly weaker.

In other words, participants were willing to forego better health care to have a human, rather than an AI, care provider.
Resistance to medical AI also showed up in willingness to pay for the same diagnostic procedure. 103 Americans from an online panel a reference price of $50 for a diagnostic stress test that could be performed by either an AI or human provider, both had an accuracy rate of 89%. Participants in the AI default condition were told that the diagnosis cost $50 when administered by an AI. They then indicated what they would be willing to pay to switch to a human provider instead.

Participants were willing to pay more to switch to a human provider when the default provider was AI than they were willing to pay to switch to an AI provider when the default provider was a human. Having a physician confirm the recommendation of an AI provider should make people more receptive to AI-based care.

We found that people are comfortable utilizing medical AI if a physician remains in charge of the ultimate decision.

Thank You!

Bryan M. Rogoff, OD, MBA, CPHM, FAAO
E-Mail: bryanrogoff@eye-exec.com
Strategies for Telemedicine for Anterior Segment

FINANCIAL DISCLOSURES

<table>
<thead>
<tr>
<th>Commercial Interest</th>
<th>Nature of Relevant Financial Relationship</th>
<th>What was Received</th>
<th>For What Role?</th>
</tr>
</thead>
<tbody>
<tr>
<td>UnitedHealth Care</td>
<td>Example: Company X</td>
<td>Honorarium</td>
<td>Speaker</td>
</tr>
<tr>
<td>Avesis</td>
<td></td>
<td>Honoraria</td>
<td>Advisory Board</td>
</tr>
<tr>
<td>Sight Sciences</td>
<td></td>
<td>Consulting Fee</td>
<td>Consultant</td>
</tr>
<tr>
<td>Anthem BCBS</td>
<td></td>
<td>Consulting Fee</td>
<td>Speaker</td>
</tr>
<tr>
<td>VSP</td>
<td></td>
<td>Honoraria</td>
<td></td>
</tr>
<tr>
<td>Sight Sciences</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Anthem BCBS</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>VSP</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>UnitedHealth Care</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Avesis</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Sight Sciences</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Anthem BCBS</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>VSP</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>UnitedHealth Care</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Avesis</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Sight Sciences</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Anthem BCBS</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>VSP</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>UnitedHealth Care</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Avesis</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Sight Sciences</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Anthem BCBS</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>VSP</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>UnitedHealth Care</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Avesis</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Sight Sciences</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Anthem BCBS</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>VSP</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>UnitedHealth Care</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Avesis</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Sight Sciences</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Anthem BCBS</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>VSP</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>UnitedHealth Care</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Avesis</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Sight Sciences</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Anthem BCBS</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>VSP</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>UnitedHealth Care</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Avesis</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Sight Sciences</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>Anthem BCBS</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
<tr>
<td>VSP</td>
<td></td>
<td>Consulting Fee</td>
<td></td>
</tr>
</tbody>
</table>

What is Telemedicine?

History of Telemedicine

1844
The electric telegraph is invented by Samuel Morse

1861 - 1865
The telegraph is used for ordering medical supplies and communicating deaths and injuries on the battlefield during the U.S. Civil War.

What is Telemedicine?

Telemedicine has many definitions.

- It is the remote treatment of patients by medical professionals through the use of telecommunications tools such as telephones, smartphones, and computers.

World Health Organization (WHO):

“The delivery of health care service, where distance is a critical factor, by all health care professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and education, and for the continuing education of health care providers, all in the interests of advancing the health of individuals and their communities.”
What is Telemedicine?

Telemedicine has become one of the fastest growing investments with private equity and venture capitalists. It is predicted to have an approximate worth of $34 billion globally towards the end of 2020. The United States would account for more than 40% of the market. Not only as it is seen as being profitable for investors, but it is a way of lowering the cost of care which has been a demon for healthcare systems around the world.

The smartphone has become the ultimate tool and has been the catalyst for telemedicine to be effective. About 75% of Americans own a smartphone. Smartphone adoption has doubled since a Pew Research Center started conducting a survey in 2011. 92% of 18-29 year-olds own one, 74% of Americans older than 50 years old and an astonishing 42% of Americans 65 years old own a smartphone. This created the demand from patients for their healthcare.

Telehealth Telemedicine

- Much broader in spectrum, more universal term.
- Non-clinical services.
- Surveillance, health promotion and public health functions.
- Clinical application of technology.
- Remote clinical services.
- To improve a patient’s clinical health status.
- Follow-up visits, management of chronic conditions, medication management, specialist consultation.

Modalities:

Mobile Health (mHealth)

- Evolving provision of health care services.
- Data from personal mobile devices.
- Applications can range from targeted text messages that promote healthy behavior to wide-scale alerts about disease outbreaks.
- Food and Drug Administration (FDA), the Federal Trade Commission (FTC) and the Department of Health and Human Services (HHS).
What is Telemedicine?

**Modalities:**

**Mobile Health (mHealth)**
- FDA has listed regulated mHealth devices and placed them in different classes:
- "Healthcare products intended for, or claimed to be used for the diagnosis, cure, mitigation, treatment, or prevention of a disease or medical condition intended to affect the structure or function of any part of the body."
- Class I devices are low risk and subject to less regulatory control.
- Class II requires greater regulatory control to provide reasonable assurance of safety and effectiveness.
- Class III is the highest risk and subject to highest regulatory control.

**Mobile Apps**
- Subject to FDA regulation if they are:
  - Extensions of a medical device for the purposes of controlling the device or displaying, storing, analyzing or transmitting patient-specific medical device data.
  - Transforms mobile platform into a regulated device by using attachments, display screens or sensors or by including functionalities similar to those of current medical devices.
  - Uses patient-specific information to analyze, diagnose and/or treat a patient; or Involve in active patient monitoring.

**Remote Patient Monitoring (RPM)**
- Also referred to as tele-monitoring:
- Patients with chronic diseases are monitored outside clinical settings, usually in their homes, through the use of mobile medical devices.
- Blood pressure, blood sugar, weight, heart rate, electrocardiograms, blood oxygen levels and other biometric vitals.
- RPM is real-time and allows health professionals to act on the information received to focus on treatment plans.
- It serves to reduce hospitalizations, readmissions and shorten the lengths of stay in hospitals.

**Store-and-Forward**
- The acquisition of asynchronous data.
- Imaging, documents and lab results are sent to be forwarded to health care providers off-site for clinical evaluation to aid in diagnosis.
- Patients can receive timely specialty care without the need to travel beyond their primary care providers’ offices and reduce the wait time of diagnosis.
- It is most commonly used in medical disciplines of radiology, pathology, dermatology and ophthalmology.
What is Telemedicine?

**Modalities:**

- **Live Video (Synchronous):**
  - The interaction of physicians to patients where they communicate in real-time.
  - This offers an affordable and easily accessible solutions to connect patients to doctors anywhere and have a virtual doctor visit.
  - Interactive sessions can be conducted at a patient's home, or medical facility using audio and/or video conferencing communication.
  - All software must be compliant with the Health Insurance Portability and Accounting Act (HIPAA) regulations.

State & Federal Regulations

**THE BALANCED BUDGET ACT OF 1997**
- Telemedicine was first introduced
- Authorized partial Medicare reimbursements to providers where there were shortages ONLY in rural areas
- Limited scope - Synchronous Only! Providers were required to be with the patient at the time of the consultation.
- Prohibited Asynchronous communications
- Reimbursements:
  - 25% for referring; 75% for specialist
  - No Facility Fees; No Communication Fees

**Benefits Improvement and Protection Act of 2000 (BIPA)**
- Expanded the BBA coverage and definitions of telemedicine
- Defined as occurring between an originating site and distant site.
- Extended funding for more federal demonstration projects to include non-metropolitan.
- Physicians, nurse practitioners, physician assistant, nurse midwife, clinical nurse specialist, clinical psychologist, and clinical social worker.
- Removed the sharing of reimbursements requirement
- Originating provider to now receive a Facility Fee

**2008 Medicare Improvements for Patients and Providers Act (MIPPA)**
- Added additional eligible facilities for telemedicine reimbursements:
  - Skilled Nursing Facilities
  - Community Mental Health Centers
  - Hospital-Based or Critical Access Hospital-Based renal dialysis centers.
Strategies for Telemedicine for Anterior Segment

State & Federal Regulations

Medicare Telehealth Parity Act of 2017

• Phase 1:
  • Expanded the definition of "originating sites" to include all federally qualified health centers and rural clinics in areas with less than 50,000 people
  • Expanded the list of eligible providers to include:
    • Certified diabetes educators, respiratory therapists, physical therapists, occupational therapists, speech language pathologists & audiologists

Medicare Telehealth Parity Act of 2017

• Phase 2:
  • Expanded the definition of originating sites to include a home telehealth site
  • Increased the population threshold of eligible areas to those with up to 100,000 people

Medicare Telehealth Parity Act of 2017

• Phase 3:
  • Expanded the eligible areas to those with populations over 100,000
  • Reimbursed remote patient monitoring (RPM) for the following:
    • Heart failure
    • Chronic obstructive pulmonary disease (COPD)
    • Related comorbidities.

• Included CHRONIC Care Act of 2017
  • Starting January 1, 2019, Medicare patients with end-stage renal disease (ESRD) on home dialysis may receive their monthly clinical assessments at home using telehealth.
  • Tele-Stroke: Patients arriving at a hospital with acute stroke symptoms may receive a telehealth consultation to determine the best course of treatment, without regard to their geographic location.
  • Medicare Advantage (MA) plans may offer additional, clinically appropriate telehealth benefits in their annual bid amount beyond the services that receive payment under traditional Medicare.

Bipartisan Budget Act of 2018
Strategies for Telemedicine for Anterior Segment

State & Federal Regulations

Bipartisan Budget Act of 2018

- Accountable Care Organizations (ACOs) to expand the use of telehealth by allowing other ACOs to take advantage of the existing Next Generation ACO telehealth waiver
- It waives the geographic location criteria
- Allows the patient’s home to serve as the originating site
- Allows for the use of teledermatology & teleophthalmology.

State Regulation

- Managed care and Medicaid, there has been expansion allowing store-and-forward and RPM
- Some states restrict specific practitioners and specialties while some states have various definitions of telehealth services.
- 48 states, including the District of Columbia (excluding MA and RI) have a variation of Medicaid reimbursement for interactive / live video telemedicine
- 15 states (AL, AZ, CT, CA, IL, MD, MN, MI, MO, NM, NE, OK, VA and WA) include store-and-forward reimbursement for Medicaid with some having limitations to specific specialties
- 21 states (AL, AK, AZ, CO, IL, IN, KS, IA, MA, MN, MI, MO, NE, NY, OK, SC, TX, UT, VT, VA and WA) have remote patient monitoring for Medicaid services

Regarding telemedicine, two rules apply:

Privacy and Security Rules

Apply to “covered entities”:

- Providers, Medical Clearinghouses & Insurers

Privacy Rule

Focuses on the use & disclosure of PHI

Must have protocols and procedures in place that protect & secure PHI when it is received, handled, transferred, or shared, regardless of how the PHI is obtained (via paper, orally, or electronically)

Minimum PHI is necessary to care for a patient & sets limits and conditions on the uses & disclosures that may be made of such information without patient authorization.
Establishes **standards of protection** for patient’s electronic personal health information (ePHI)

3 areas of protection to be in compliance:
- Administrative
- Physical
- Technical

This ensures confidentiality, integrity, and security of ePHI regardless if the entity creates, uses, or maintains the information.

Both the Privacy and Security Rules apply to both in-person and telehealth visits.

Only authorized users should have access to ePHI

A system of secure communication should be implemented to protect the integrity of ePHI

A system of monitoring communications containing ePHI should be implemented to prevent accidental or malicious breaches.

SMS messaging, Skype, FaceTime or e-mail SHOULD NEVER be used as methods for communications with a patient

Service providers such as Verizon, Google, Skype, Comcast etc. keeps copies of communications on their servers

They are required to enter a **Business Associate Agreement (BAA)** with a medical professionals to be HIPAA compliant.

“**That it is a criminal offense to knowingly & willfully offer, pay, solicit, or receive, directly or indirectly any remuneration in return for referring, furnishing, arranging or recommending items or services reimbursable by any federal health care program.**”

Common safe harbors for telehealth: space rental, personal services & management contracts, bona fide employment, electronic health records items and services, & managed care organizations.
Strategies for Telemedicine for Anterior Segment

**Stark Law**
Prohibits “Physicians (or an immediate family members of that physician) who has a financial relationship with an entity from referring patients to that entity for certain designated health services payable by Medicare.”

- Referrals and claims that are violated are each punishable by a $15,000 civil penalty. Circumventing schemes can be punishable by $100,000.

**Civil Money Penalty Law**
Imposition of civil money penalties against an entity that offers or gives remuneration to any beneficiary of an FQHC likely to influence the receipt of reimbursable items or services or choice of provider.

- Telehealth exceptions: Preventive Care, Financial Need Exception & Promoting Access to Care

However, with the Bipartisan Budget Act of 2018, providers can now give free telehealth technology and equipment to patients for at-home dialysis and would NOT constitute remunerations.

**Anterior Segment & Telemedicine**
Telemedicine has been proven to improve patient care, increase access in under-served areas and reduce costs while having better outcomes.

- Developing technologies with HIPAA compliant software and imaging devices, applications regarding eye care are increasing.
  - Screening and diagnosing diabetic retinopathy
  - Anterior segment imaging
  - Glaucoma screening
  - Low vision consultation

**Anterior Segment & Telemedicine**
**Ocular Emergencies**
- Patients routinely go to the ER for their urgent eye needs
- Many hospitalized patients require eye care
- ECPs typically practice outside of hospitals & often cannot evaluate patients with eye complaints urgently.
Anterior Segment & Telemedicine

OCULAR EMERGENCIES

STUDY: Telemedicine for ophthalmic consultation services: Use of a portable device and layering information for graders

Maria A Woodward, J Clay Bavinger, Sejal Amin, Taylor S Blachley, David C Musch, Paul P Lee, & Paula Anne Newman-Casey

Published March 1, 2016
Journal of Telemedicine & Telecare

Compared remote, image-based patient consultations to in-person consultations at emergency department and inpatient hospital settings.

Methods

- Patients evaluated by the ophthalmic consultation services (gold standard) were imaged over a two-week period.
- A trained study coordinator took anterior segment photographs (AS) and posterior segment photographs (PS) with a portable camera (PictorPlus, Volk Optical, Cleveland, OH).
- Ophthalmologists (graders) determined photograph quality, presence of pathology, and their confidence in disease detection. At a separate session, graders reassessed photographs accompanied by a one-sentence summary of demographics and chief complaint (CHx).
- Computed accuracy and reliability statistics.

Results

- They took AS photographs of 24 eyes of 15 patients and PS photographs of 39 eyes of 20 patients.
- The majority of images were rated as acceptable or excellent in quality (AS: 89–96%; PS: 70–75%).
- Graders detected AS pathology with 62–81% sensitivity based on photographs, increasing to 87–88% sensitivity with photographs plus CHx.
- Graders detected PS pathology with 79–86% sensitivity based on a photograph only, increasing to 100% sensitivity with photographs plus CHx.

Discussion

- There is evidence that portable ophthalmic imaging technologies could enable ophthalmologists to remotely evaluate anterior and posterior segment eye diseases with good sensitivity.
- The ophthalmologist could detect ocular pathology on photographs more accurately if they were provided brief clinical information.
Strategies for Telemedicine for Anterior Segment

Ocular Emergencies

STUDY: Characteristics of Patients Presenting to the Emergency Department with Sight-Threatening Ocular Conditions
Dolly A. Padovani-Claudio; Nidhi Talwar; Paul P. Lee; Joshua D. Stein

- Published March 2012
- Investigative Ophthalmology & Vision Science
- To determine patient characteristics associated with emergency department (ED) use for sight-threatening ocular conditions.

Anterior Segment & Telemedicine

Ocular Emergencies

STUDY:

Methods
- Using claims data from a managed care network, all adults aged ≥21 with an eye-related ER visit in 2001-2009 were identified.
- Using ICD-9-CM billing codes, we identified patients who received a sight-threatening ocular diagnosis (e.g., endophthalmitis, orbital cellulitis/hemorrhage, giant cell arteritis, ruptured globe, acute angle closure glaucoma), but no nonocular diagnoses, during an ER visit.
- Multivariable Cox regression was performed to assess the patient characteristics associated with seeking ER care for a sight-threatening ocular condition.

Results
- Among the 107,568 enrollees with an ER visit for any ocular condition, 9237 (8.6%) received a diagnosis of a potentially sight-threatening condition.
- Women had a 22%-decreased hazard of urgent ER eye care (HR=0.78 [CI 0.68-0.89]).
- Compared to urban residents, rural residents had a 45% decreased hazard of presenting to the ER for an urgent eye problem (HR=0.55 [CI=0.33-0.92]).
- Individuals with household net worth levels of $150-500K had a 27% decreased (HR=0.73 [CI=0.58-0.91]) hazard of presenting to the ER with an urgent ocular problem when compared to persons with net worth levels <$25K.
- For every additional year of age, the hazard of presenting to the ER for an urgent eye problem decreased by 1% (HR=0.99 [CI=0.98-0.99]).

Conclusions
- Younger age, male sex, Latino ethnicity, lower income level, and urban residence were associated with presentation to the ER with sight-threatening ocular conditions.
- Efforts focused on preventing ocular injuries among individuals with these sociodemographic characteristics and persons residing in these communities may reduce both ER use and vision loss.
Anterior Segment & Telemedicine

**Ocular Emergencies**

**STUDY:** Reliability of telemedicine for diagnosing and managing eye problems in accident and emergency departments

R J C Bowman, C Kennedy, J F Kirwan, P Sze & I E Murdoch

- Published August 20, 2003
- Eye Volume 17, Pages 743-746
- To assess the accuracy and efficiency of telemedicine in diagnosing and managing eye problems presenting to accident and emergency departments.

**Methods**

- A controlled trial with a face-to-face and telemedicine phases, each involving 40 patients undergoing two consecutive consultations.
- In the face-to-face phase, both consultations were in person; in the telemedicine phase, observer 1 used videoconferencing technology at 384 kbit/s (separate nonslit lamp–torchlight and slit lamp examinations) and observer 2 saw the patient face to face.
- The accident and emergency department at Moorfields Eye Hospital.
- In total, 80 consenting new patients presenting to the department.

**Results**

- Telemedicine consultations erred on the side of clinical caution and were no slower than face-to-face consultations (mean 6 min for observer 1 in both phases).
- Recalls were more likely ($\chi^2 = 5.16, P = 0.02$) after telemedicine consultations with torchlight only (9/40) compared with face-to-face consultations (2/40).
- Although there were more significant disagreements using the telemedicine, in each case the telemedicine diagnosis and management erred on the side of safety.
- No patient would have suffered by wrong management because of the consultation using telemedicine.

**Conclusions**

- Telemedicine was found to be an accurate, safe, and efficient method of diagnosing and managing these patients, especially if slit lamp images were used.
- Advice using telemedicine erred on the side of caution, which resulted in more recalls.
CASE 1

**Anterior Segment & Telemedicine**

**Patient Calls Your Office with Complaints of:**
- Foreign Body Sensation
- Bilateral Red Eyes
- Burning
- Light Sensitivity
- No Change in Vision
- Watery Discharge
- No Hx of Trauma
- Has Upper Respiratory Tract Infection

*What is your differential diagnosis?*

**COPE: 63861-AS**

CASE 1

“Red Eyes” - Conjunctivitis

- Patients with viral conjunctivitis present with foreign body sensation, red eyes, itching, light sensitivity, burning, and watery discharge.
- Whereas with bacterial conjunctivitis, patients present with all the above symptoms, but with mucopurulent discharge and mattering of the eyelids upon waking.
- Viral conjunctivitis usually have a recent history of an upper respiratory tract infection or recent contact with a sick individual.
- Visual acuity is usually at or near their baseline vision.
- The cornea can have subepithelial infiltrates that can decrease the vision and cause light sensitivity.

**COPE: 63861-AS**

CASE 1

“Red Eyes” - Conjunctivitis

- The conjunctiva is injected (red) and can also be edematous.
- In some cases, a membrane or pseudomembrane can be appreciated in the fornix.
- Follicles, small, dome-shaped nodules without a prominent central vessel, can be seen on the palpebral conjunctiva.
- Palpation of the preauricular lymph nodes may reveal a reactive lymph node that is tender to the touch and will help differentiate viral conjunctivitis versus bacterial.

**COPE: 63861-AS**

CASE 1

Diagnosis, Monitoring and Treatment with Telemedicine

**Interactive Telemedicine & Store-and-Forward**

- During a video consult, ODs should ask you a series of targeted questions to determine what type of conjunctivitis patients have.
- Patients should use phone, tablet or desktop using HIPAA compliant app or software with video capabilities to view eye infected to get an accurate diagnosis.
- Eyecare providers can easily see an eye on video to assess for injection, icterus and symmetry; visual acuity with help of eye chart applications which can be downloaded while on the phone; instruct patients to move eyes to evaluate extraocular movements.
- Have the patient use a flashlight to evaluate for reactivity.
- If an accurate diagnosis cannot be made, instruct the patient for an office visit.
**Case 1**

**Treatment for Viral Conjunctivitis**
- Treatment for viral conjunctivitis is aimed at symptomatic relief and not to eradicate the self-limiting viral infection.
- Treatment includes using artificial tears for lubrication four times a day or up to ten times a day with preservative-free tears.
- Cool compresses with a wet washcloth to the perilocular area may provide symptomatic relief, preventing the spread of infection to the other eye or other people.
- Topical steroids can help with the resolution of symptoms.

**Case 1**

**Treatment for Bacterial Conjunctivitis**
- Almost all cases of acute bacterial conjunctivitis are self-limited and will clear within 10 days without treatment.
- Bacterial conjunctivitis is a contagious condition, so patients are instructed in proper hygiene and hand washing.
- The most common antibiotics used for acute bacterial conjunctivitis are as follows:
  - Fluoroquinolones: 2nd generation: Ciprofloxacin 0.3% drops or ointment, or Ofloxacin 0.3% drops; 3rd generation: Levofloxacin 0.5% drops; 4th generation: Moxifloxacin 0.5% drops, Gatifloxacin 0.5% drops, or Besifloxacin 0.6% drops
  - Aminoglycosides: Tobramycin 0.3% drops; Gentamicin 0.3% drops; Macrolides: Erythromycin 0.5% ointment; Azithromycin 1% solution

**Case 2**

**Patient Calls Your Office with Complaints of:**
- Bilateral Red Eyes
- Burning & Irritated
- Light Sensitivity
- Blurred Vision
- Excessive Tearing, especially after using the computer
- No Hx of Trauma
- Contact Lens wearer
- Has Vitamin A deficiency

**What is your differential diagnosis?**

**Case 2**

**Ocular Surface Disorder**
- One of the most common reasons people present to an ECP.
- The symptoms of dry eye can be numerous, including: red eyes, burning, irritation, gritty sensation, blurred vision, and excessive tearing.
- Risk factors include: age, female gender, systemic disease, contact lens wear, medications, and specific nutritional deficiencies (e.g. vitamin A).
- Its putative pathogenetic mechanisms include hyperosmolarity of the tear film and inflammation of the ocular surface and lacrimal gland.
- OSD is clinically subdivided into 4 subtypes: Obstruction, Bacterial Biofilm, Inflammatory & Tear Film Deficiency
**Anterior Segment & Telemedicine**

**CASE 2**

Diagnosis, Monitoring and Treatment with Telemedicine

Interactive Telemedicine, Store-and-Forward, RPM

- Patients use phone, tablet or desktop using HIPAA compliant apps or software with video capabilities to discuss eye discomfort.
- Optometrists can easily see an eye on video to assess for injection, icterus and asymmetry.
- Visual acuity can be assessed with eye chart applications which can be downloaded while on the phone.
- Instruct patients to move eyes to evaluate extra ocular movements.
- Have the patient use a flashlight to evaluate for reactivity.
- If an accurate diagnosis cannot be made, instruct the patient for an office visit.

**CASE 2**

Diagnosis, Monitoring and Treatment with Telemedicine

Interactive Telemedicine, Store-and-Forward, RPM

- The initial diagnosis mostly likely will come from an in-office visit to determine the type of OSD the patient has: obstructive, inflammatory, bacterial biofilm or tear film deficiency.
- Once treatment is determined, telemedicine applications that can conduct SPEED tests and RPM techniques to monitor symptoms.

**CASE 2**

Treatment for OSD

- Depending on the causes, there are numerous treatments for ocular surface disease / tear film dysfunction.
- Common treatment modalities include: Artificial tears, Longer acting agents such as artificial tear gel and ointments and lacrimal system.
- Tear conserving interventions such as punctal plugs.
- Warm compresses & eyelid scrubs.
- Prescription medicines to encourage tear production such as Cyclosporine or Lifitegrast.
- Topical ophthalmic steroids are helpful in controlling the inflammatory aspect of the disease.
- Oral flaxseed oil or fish oil supplements 2000mg/day has also been found to be useful in alleviating symptoms and decreasing the frequency of topical agents.

**CASE 3**

Your Mother Calls You with Complaints of:

- Bump on the right upper eyelid Irritated
- No change in Vision
- No Hx of Trauma
- No pain
- Dad is no help!

What is your differential diagnosis?
Chalazion
- Chalazion is a chronic sterile granuloma residing within eyelid that originates from an obstructed meibomian gland of the tarsal plates.
- If acute secondary infection (e.g., Staphylococcus aureus) takes place, the lesion is known as hordeolum.

Diagnosis, Monitoring and Treatment with Telemedicine
Interactive Telemedicine & Store-and-Forward
- Patients use phone, tablet or desktop using HIPAA compliant apps or software with video capabilities to discuss eye discomfort.
- Ophthalmologists can easily see an eye on video to assess for lid, lacrimal and symptom.
- Visual acuity can be assessed with eye chart applications which can be downloaded while on the phone.
- Instruct patients to move eyes to evaluate extra ocular movements.
- Have the patient use a flashlight to evaluate for reactivity.
- If an accurate diagnosis cannot be made, instruct the patient for an office visit.

Treatment for Chalazion
- Small, asymptomatic chalazion can be left untreated.
- Conservative treatment including lid massage, warm compression and steroid eyedrops can also be used.
- However, with administration of topical or local steroid agents, the intraocular pressure should be monitored.
- Topical antibiotics eyedrops is useful if lesion is associated with inflammatory conditions such as blepharitis.
- Direct injection of steroid (triamcinolone, kenalog) with lidocaine into the lesion may be preferable for lesions in close proximity to the vulnerable lacrimal apparatus where surgical drainage is difficult.
- Steroid injection leads to resolution in most cases.
- Repeated injection can be given 1-2 weeks later if lesion persists.

Hordeolum
- A hordeolum is an inflamed oil gland on the margin of the eyelid at the level of the eyelashes.
- It appears as a red, swollen bump that resembles a pimple in appearance. It is sometimes tender in its acute presentation, especially to the touch.
- They commonly develop over a few days and may drain and heal without treatment.
- Staphylococcal bacteria are the most common causes of eyelid infections, but other organisms normally found on the skin may be precipitating factors.
- Hordeola are found more frequently in patients with dry eyes and chronic blepharitis (eyelid inflammation).
Case 3: Anterior Segment & Telemedicine

Diagnosis, Monitoring and Treatment with Telemedicine

Interactive Telemedicine & Store-and-Forward

- Patients use phone, tablet or desktop using HIPAA compliant apps or software with video capabilities to discuss eye discomfort.
- Optometrists can easily see an eye on video to assess for lids, icterus and symmetry
- Visual acuity can be assessed with eye chart applications which can be downloaded while on the phone.
- Instruct patients to move eyes to evaluate extra ocular movements
- Have the patient use a flashlight to evaluate for reactivity
- If an accurate diagnosis cannot be made, instruct the patient for an office visit.

Case 3: Anterior Segment & Telemedicine

Treatment for Hordeolum

- Hordeola can spontaneously drain without any treatment.
- Warm compresses are aimed at softening the granulomatous tissue and facilitating drainage.
- Lid massage is intended to help express the purulent drainage from the infected gland.
- Lid scrubs with saline or mild shampoo (e.g., baby shampoo) that is tear-free and pH-balanced, may promote drainage by clearing debris from the clogged duct.
- Persistent lesions or larger lesions may require antibiotic therapy; ketlex, doxycycline, erythromycin, or amoxicillin.
- If the infection spreads and progresses to a periorbital or orbital cellulitis, systemic antibiotics are required. Incision and drainage of a persistent abscess may be necessary.

Case 4: Anterior Segment & Telemedicine

Your Boyfriend Calls You with Complaints of:

- Red spot on the white part of the eye
- Just noticed 2 days ago and not resolving
- No change in Vision
- No Hx of Trauma
- No pain
- Was hungover after drinking a case of beer 4 days ago
- OMD is booked 3 weeks out!

What is your differential diagnosis?

Case 3: Anterior Segment & Telemedicine

Subconjunctival Hemorrhage

- Subconjunctival hemorrhage is a benign disorder that is a common cause of acute ocular redness.
- The following actions may cause a small blood vessel to rupture in your eye: violent coughing, powerful sneezing, straining, vomiting.
- The major risk factors include trauma and contact lens usage in younger patients.
- Among the elderly, systemic vascular diseases such as hypertension, diabetes, arteriosclerosis, certain blood-thinning medications, such as warfarin and aspirin & blood clotting disorders are more common.
- Subconjunctival hemorrhage is recurrent or persistent, further evaluation, including workup for systemic hypertension, bleeding disorders, systemic and ocular malignancies, and drug side effects, is warranted.
Telemedicine

Diagnosis, Monitoring and Treatment with Telemedicine

Interactive Telemedicine & Store-and-Foreward

- Patients use phone, tablet or desktop using HIPAA compliant apps or software with video capabilities to discuss eye discomfort.
- Optometrists can easily see an eye on video to assess for lid, iritis and symmetry?
- Visual acuity can be assessed with eye chart applications which can be downloaded while on the phone
- Instruct patients to move eyes to evaluate extra ocular movements
- Have the patient use a flashlight to evaluate for reactivity
- If an accurate diagnosis cannot be made, instruct the patient for an office visit.

Anterior Segment & Telemedicine

Case 3

Treatment for Subconjunctival Hemorrhage

- There is not any approved treatment to accelerate the resolution and absorption of SCH.
- Failure to resolve hemorrhage in persistent or recurrent cases suggests a serious underlying cause.
- A careful history is the most important step in identifying whether there is a serious underlying condition that may require more detailed examination and treatment.
- A detailed history may provide clues to the underlying conditions. It is important to obtain a thorough medication, medical, and ocular history from patients presenting with SCH, including any possible trauma, ocular surgery, contact lens wear, drugs, and heritable conditions.

Anterior Segment & Telemedicine

Other Uses of Telemedicine in Eye Care

Teleophthalmology in Practice: Lessons Learned from a Pilot Project

Haleh Ayatollahi, Aynaz Nourani, Taleb Khodaveisi, Hossein Aghaei, Mehrdad Mohammadpour

Introduction: Ophthalmology is a medical specialty which may benefit from using telemedicine and teleophthalmology services. Both services are significantly important in the rural, remote, and impassable geographical areas, where there is no access to the ophthalmology services and ophthalmologists. The study aimed to design and implement teleophthalmology system using the method of store-and-forward.

Methods: The study was conducted in 10 phases. The first phase was focused on the study design and collecting data. The second phase was based on the requirements analysis. Thereafter, we designed the teleophthalmology system using the method of store-and-forward.

Result: A total of 100,000 teleophthalmology cases were collected, and the collected data was analyzed. The analyzed data was used to study the system's feasibility.

Conclusion: According to the results, it can be concluded that the teleophthalmology technology can be used in eye care by optometrists and ophthalmologists to improve eye care services and to prevent the prevalence of curable eye diseases.

Other Uses of Telemedicine in Eye Care

Smartphones, Tele-ophthalmology, and VISION 2020

Other Uses of Telemedicine in Eye Care

Other Uses of Telemedicine in Eye Care
Conclusion:
Tele-based services can be used for screening common ophthalmic diseases especially in developing countries where easy access to the experts is not available for all people, especially in rural areas. We are facing with an increased number of patients with cardiovascular and metabolic diseases, and tele-screening has an important role in early diagnosis, treatment, and providing better communications between patients and specialists. Thanks to this evolution like the media regarding ophthalmology, initial examination and related images can be obtained by medical staff and then be transferred instantly by social networks to the right persons to screen common preventable causes of blindness. Smartphones that are distributed increasingly even in the most deprived areas have increased the availability of social networks and healthcare system. With future advances in technology, patients might be able to manage themselves with new smartphones. Governments should think about establishing trials and programs to provide various packages for screening the prevalent diseases, and to have a suitable collaboration with health and vision-related organizations and help WHO in reaching the aims of VISION 2020 to accomplish the real sense of "The Right to Sight".

Published: December 18, 2017 International Journal of Ophthalmology

COPE: 63861-AS

Thank You!

Bryan M. Rogoff, OD, MBA, CPHM, FAAO
bmrogoff@eye-exec.com
Anterior and Posterior Segment Case Presentations

“Enough Pearls to Make a Necklace”

Greg Caldwell OD, FAAO
Arizona Optometric Association
November 16, 2019

Disclosure Statement (next slide)

Disclosures- Greg Caldwell, OD, FAAO
- Will mention many products, instruments and companies during our discussion
  - I do not have any financial interest in any of these products, instruments or companies
- Pennsylvania Optometric Association - President 2010
- POA Board of Directors 2006-2011
- American Optometric Association, Trustees 2013-2016
- I never used or will use my volunteer positions to further my lecturing career
- Lectured for: Aerie, Alcon, Allergan, BioTissue, OptoVue
- Advisory Board: Allergan, Sight Sciences, Sun, Takeda
- Evolve: PA Medical Director, Credential Committee
- Optometric Education Consultants - Scottsdale, St. Paul, Quebec City, and Nashville, Owner

Learning Objectives
- Emphasize clinical diagnosis of anterior and posterior segment disease.
- Strengthen clinical treatment of anterior and posterior segment disease.
- Heighten the clinician’s comfort level when treating disease with topical and/or oral medications.
- Gain confidence in ordering and interpreting diagnostic and laboratory tests.
- Gain confidence in making a sub specialty referral.

Optometric Public Service Announcement
Pay Very Close Attention

80 year old man
- Reports a sudden loss of vision OD
- Vision is count fingers at 2 feet OD and 20/25 OS
- APD OD grade 4
- Fundus photos OU
CRAO Treatment/Work-Up/Follow-Up?

- Anterior chamber paracentesis (less than 24 hours)
- STAT blood work
- Sed-rate
- C-reactive protein
  - Qualitative or quantitative?
- CBC with diff
- Monitor for neovascularization, every 3-6 weeks

CRAO, BRAO, TIA (amaurosis fugax)

- Acute Stroke Ready Hospital
  - Hospitals are medical facilities that meet the Joint Commission’s standards to support better outcomes for stroke and support stroke assessment, diagnosis, and treatment of acute stroke
  - Service begins with the ability to immediately activate the hospital’s stroke team, if needed
  - Further initiation of inpatient management of the patient, including potential for IV t PA

25 year old man

- Patient has been to 3 ophthalmologists and 1 optometrist in the past year
- Patient complains of a “ghost image” OS
- Has had 4 dilated exams in the past year, and no diagnosis yet
- He is very passionate that his vision is clear OD and “ghosty” OS. He wants to know why.

“Ghost Image” OS

- Va 20/20
- Current Correction
  - R: -2.50-1.00 x 180
  - L: -3.25-1.00 x 180
- EOMS: full, unrestricted
- CE: ortho D/N
- PERRL (-)APD
- CF: full by FC OU
- SLE-unremarkable
- Fundus-unremarkable

Previous unremarkable tests
- Topography
- Fluorescein angiography
- CAT scan
- MRI

Any Thoughts About “Ghost Images”?

- Previous unremarkable tests
- Topography
- Fluorescein angiography
- CAT scan
- MRI

Warn hospital if suspicion for GCA

- 20% of stroke or heart attack within 3 years
- However of those who experienced CVA or MI
  - 80% were within 24-48 hours; those remaining
  - 50% occurred in 2 weeks
  - Majority within the next 90 days

- Not PCP, not retinologist, just the Acute Stroke Ready Hospital!
How I felt when I finally realized keratoconus starts posteriorly

Forme Fruste Keratoconus
- Treatment
- RGP lens in office and trial frame over refraction
  - Eliminated “ghost image”
- Patient currently only in spex
  - Not interested in RGP lens
- RTC 1 year, BVA and topographies

Advanced Keratoconus

Topography OD
What happens when the posterior cone gets too steep and Descemet’s membrane ruptures?

Hydrops

The following video is rated "E" for Educational

Case 3

28 year old man
- Had LASIK 14 months ago
- His right eye is now very blurry
- He tried calling for an appointment the center is now closed
Current Correction
R +0.50-7.00 x 040
L -0.25 sphere

EOMS: full, unrestricted    PERRL (API)APD
CL: ortho D/N    CF: full by FC OU

- SLE-trace fibrosis at flap edges, no stain
- SLE-few multi-directional striae OD>OS
- SLE-clean interface OU
- Fundus-unremarkable

Case 4

43 year old man
- Called your office today
- Eye pain in the right eye since this morning
- OD 20/80 OS 20/20
- Externals: normal
- Review of Systems: unremarkable

43 year old male
- further history reveals

- Fourth time in past 24 months
- Uses Muro 128
  - Gits qid
  - Ung qHS

- Diagnosis:
  - Recurrent Corneal Erosion secondary to Epithelial Basement Membrane Dystrophy (EBMD)
Anterior and Posterior Segment Case Presentations

November 16, 2019

Greg Caldwell, OD, FAAO
Grubod@gmail.com  814-931-2030 cell

Treatment

- **Antibiotic**, Vigamox tid
- **Pain management**
  - Depending on severity
    - Bandage contact lens
    - Oral ibuprofen (200 mg) (16)
    - Maximum 3200 mg/day
    - Oral amoxicillin (500 mg) (8)
    - Maximum 1000 mg/day
    - Oral narcotics (need DEA number)
      - Lorcet (15/5)
        - This provides pain relief
        - A degree of sedation
        - Tend to minimally impact the digestive system and kidneys
        - Not as potent as OTC analgesics like aspirin, acetaminophen, diclofenac or ibuprofen
  - Topical NSAID

Treatment Options
(Once Abrasion Resolved, to Help Prevent Recurrence)

- **Medically**
  - Hypertonics
  - Gels
  - Use
  - Bandage contact lens
  - Nostril
  - Doxycycline/Minocycline
  - Amniotic membrane (PROKERA™)

- **Surgical/Procedures**
  - Anterior stromal micropuncture
  - Debridement
    - Chemically
    - Mechanically
  - Excimer phototherapeutic keratectomy (PTK)

Review of Map-Dot-Fingerprint

The Amniotic Membrane

- The amniotic membrane is the innermost lining of the placenta (amnion)
- Amniotic membrane shares the same cell origin as the fetus
- Stem cell behavior
- Structural similarity to all human tissue

The CRYOTEK™ Method

- Patented and proprietary cryopreservation
- Ensures key active components of the Extracellular Matrix (ECM) are retained
- The only method that retains both:
  - The integrity of the tissue structure
  - The key active (ECM) components
- Safe and effective
  - Supported by over 300 peer-reviewed articles
  - Over 100,000 implanted
- Bio-Tissue Cryopreserved Amniotic Membrane is the ONLY AM granted wound healing indication by the FDA.
Impressive regenerative platform that possesses natural growth factors and optimal scaffolding properties within a complex extracellular matrix that are:

- Anti-inflammatory
- Anti-scarring
- Anti-angiogenic

**Therapeutic actions:**
- Promotes Stem Cell Expansion
- Suppresses pain
- Promotes cellular migration
- Expedites recovery

**Technology Highlights**

- PROKERA® utilizes the proprietary CryoTek™ cryopreservation process that maintains the active extracellular matrix of the amniotic membrane which uniquely allows for regenerative healing.
- PROKERA® is the only FDA-cleared therapeutic device that both reduces inflammation and promotes scar less healing.
- PROKERA® can be used for a wide number of ocular surface diseases with severity ranging from mild, moderate, to severe.

**PROKERA®: Biologic Corneal Bandage**

- An Active Amniotic Membrane

**PROKERA®**:

- **BIOLOGIC CORNEAL BANDAGE**
- **Active Amniotic Membrane**

- (Microbial, HSV)
- Recurrent Corneal Erosions
- Corneal Abrasions / Wounds
- Neurotrophic PED
- Severe Infectious Keratitis
- Post DSEK for Bullous Keratopathy
- Corneal Wounds
- Severe Adnexal Infections
- Severe Corneal ulcers
- Corneal Wounds

**Excimer Phototherapeutic Keratectomy (PTK)**

- **Corneal Opacities**
  - Scarring
  - Granular dystrophy

- **Surface Irregularity**
  - Saltzman nodules

- **Surface Breakdown**
  - Epithelial basement membrane dystrophy

**PTK Procedure**

- Removal of epithelium
- Manual debridement
- Polish with excimer

**PRK**
PTK

Post op Regimen

- Vigamox and Pred-Forte q2°
- Until wound is closed
- Bandage contact lens (BCL)
- Vitamin C, 1000 mg/day x 1 month
- NP-artificial tears
- Sunglasses in any UV

Before & After

84 year old woman

- Right eye red and painful
- Started about 10 days ago
- See photos for discussion

Case 5

Diagnosis?

Treatment?
1 Week Later

Treatment Plan?
- Continue with topical and oral antibiotics
- Surgical consult for dacryocystorhinostomy (DCR)

Reminder 1 week ago

After Dacryocystorhinostomy (DCR)

Tube Removal

35 year old man

- Wants another opinion due to “hemorrhage on my right eye”
- Happened 3 days ago after vomiting
  - Claims food poisoning from chicken Caesar salad
  - Still feels a little nauseated
- Saw ophthalmologist 3 days ago, told he had a bruise on his eye and it should go away in 1-2 weeks

Case 6

Wanted another opinion due to “hemorrhage on my right eye”

Happened 3 days ago after vomiting

- Claims food poisoning from chicken Caesar salad
- Still feels a little nauseated

Saw ophthalmologist 3 days ago, told he had a bruise on his eye and it should go away in 1-2 weeks
35 year old man

- BVA 20/100 OD, 20/70 OS
- Hx of amblyopia OD
- Current Rx OD +5.50 OS +4.50
- Any concerns?
- Patient noticed blurry vision OS
  - Started 2 weeks ago
  - Did not mention because he is more concerned about the blood on his right eye
- Headaches for 2 weeks, decrease if patient stands up
- ROS: unremarkable
- Decide to dilate OU

Retinal Findings

Discussion

Differential Diagnosis

- Hypertensive retinopathy
- Blood dyscrasia
- Terson’s syndrome
- Valsalva retinopathy
- Purtscher’s retinopathy
- Shaken baby syndrome

Terson’s Syndrome

- Terson’s syndrome originally was defined by the occurrence of vitreous hemorrhage in association with subarachnoid hemorrhage.
- Terson’s syndrome now encompasses any intraocular hemorrhage associated with intracranial hemorrhage and elevated intracranial pressures.
- Intraocular hemorrhage includes the development of subretinal, retinal, subhyaloidal, or vitreal blood.
- The classic presentation is in the subhyaloidal space.

Treatment

- Emergency referral to neurologist due to high suspicion of intracranial hemorrhage and elevated intracranial pressure
- Intracranial hemorrhage confirmed with MRI
- Patient later diagnosed with Hairy Cell Leukemia and cryptococcal meningitis

Case 7
Case 8

8 year old girl

- Mom noticed the left eyelid has become red and has pimples
- Started two days ago
- Slowly getting more pimples on the eyelid
- Globe not affected

Slit Lamp Evaluation

- Diagnosis
  - Herpes simplex blepharitis
- Treatment
  - 400 mg Acyclovir 5x/day
  - Call to pediatrician

58 year old woman

- VA OD 20/200 OS 20/400
- Longstanding history of macular degeneration
- Anything suspicious here?
  - ?? Longstanding AMD in 58 year old?!
- History of cataract surgery OU
- Glasses Rx OD -1.00 OS -1.00

Axial length 29.85 mm

OD -18.00 OS -18.50 prior to cataract surgery

At what dioptr value is a patient considered a degenerative or pathological myope?
Degenerative Myopia

- Differs from refractive myopia
  - There is an alteration of globe structure that is progressive
  - Primary alteration is a posterior elongation of eyeball as a result of progressive thinning of sclera
    - Posterior staphyloma

Findings

- Lacquer cracks
- Posterior staphyloma
- Fuch’s spot
- RPE and choroidal atrophy
- Scleral crescents
- Vessel straightening
- Disc tilting
- Peripheral retinal changes

Conditions Associated With Degenerative Myopia

- Fetal Alcohol Syndrome
- Ocular albinism
- Down’s Syndrome
- Low birth weight
- Infantile glaucoma
- Retinopathy of Prematurity
- Marfan’s Syndrome

Treatment

- BVA with glasses/contact lenses
- Education regarding trauma and possible eye hazards
- Monitor for neovascularization and peripheral retinal changes
- Follow-up at least yearly

Which patient is at higher risk of retinal detachment?

- Two patients are in your office
  - 8.00 D refractive myope
  - 14.00 D degenerative myope

- Refractive myopia
  - Peripheral retina concerns

- Degenerative myopia
  - Posterior pole concerns
Clinical Pearl

- **Refractive myopia**
  - Peripheral retina is general concern
- **Degenerative/Pathological myopia**
  - Posterior pole is general concern
  - Posterior staphyloma

Peripheral Fundus Findings

- Pavingstone Degeneration
- Pigmented Holes
- Lattice Degeneration

Case 9

88 year old man
I see faces of friends that I have not seen for years, wheels of cars and at times pine trees

- BVA: Count fingers at 2 feet OU
- Current Correction:
  - R: plano
  - L: -1.00 sphere

EOMS: full, unrestricted
CE: ortho D/N by Hirschberg
CF: central defect OU

Recommend psyche consult?

- Alert and Oriented x 3
  - Person
    - Knows who he is, who is with him
  - Place
    - Knows where he is, knows where he lives
  - Time
    - Knows what month, day, date and year

Diagnosis and Treatment?
Charles Bonnet Syndrome

“Release Hallucination”

VISUAL HALLUCINATIONS

Irritative (brief)
- Epilepsy
- Migraine

Release (continuous)
- Stroke
- Sensory deprivation

Treatment

Reassurance
- That this is normal for patient with severe vision loss to experience hallucinations

Clinical Pearl

Is there a difference between Geographic Atrophy and Disciform Scar

Case 10

65 year old woman

Referred by an optometrist due to corneal edema and map-like anterior opacities. Impression is EBMD versus corneal degeneration.

Patient reports decreasing vision over past 6-9 months. Especially at near

Vision 20/50 OU
Cornea OD

Patient's Medications
- Baby ASA
- Lanoxin
- Synthroid
- Glucophage
- Pravochol
- Amiodarone
- Neurotin
- Zoloft
- Vitamin E

Topography

Called Primary Care Physician to Discuss Findings
- D/C amiodarone
- Primary Care Physician switcher patient to diltiazem

<table>
<thead>
<tr>
<th>Class</th>
<th>Action</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Sodium channel blockade</td>
<td>Quinidine, Procainamide, Dimpyramide, Bretylium, Mexiletine, Phenytoin</td>
</tr>
<tr>
<td>II</td>
<td>ß-adrenergic blockade</td>
<td>Propranolol, Atenolol, Carvedilol, Esmolol, ...</td>
</tr>
<tr>
<td>III</td>
<td>Prolong repolarisation</td>
<td>Amiodarone, Bretylium, Sotalol, Dofetilid, Azimilide</td>
</tr>
<tr>
<td>IV</td>
<td>Ca2⁺ antagonist</td>
<td>Verapamil, Diltiazem, Flecainide</td>
</tr>
</tbody>
</table>

6 Months Later

20/25 BVA
Amiodarone Ocular Side Effects

- Halos and colored lights, reported symptoms
- Corneal opacities
  - Epithelial basal cell layer
  - Bilateral, dose and duration related
  - Reversible
- Dot, Linear, cornea verticillata (whorl like pattern found later)
- Conjunctiva, lens, retina and optic nerve deposits
- Optic neuropathy has been reported
  - Unilateral and bilateral cases

http://www.optometry.co.uk/articles/20020517/patel20020517.pdf

Cornea Verticillata (Whorls)

- Drug-induced
  - Amiodarone
  - Chloroquine/hydroxychloroquine
  - Tamoxifen
  - Chlorpromazine
  - Indomethacin

Another Patient Complaining of Blurry Vision Taking Amiodarone
Case 11

67 year old man complains of vision slowly deteriorating over the past 8 months

- History of NA-ION 10 months ago OD
- Patient sees family physician for physical due to recent NA-ION
  - Patient has not been to PCP for 35 years
  - Patient started Cardarone
  - VA 20/80 OD 20/25 OS (9 months ago)
- VA 20/400 OD 20/200 OS (today)
- CF: severe constriction OU
- SLE: vortex corneal whorls OU

Amiodarone Optic Neuropathy
Case 12

Treatment

- Doxycycline
- Maxitrol
- Avenova
- Prokera
- Hydrocortisone
- Xiidra, Xiidra, Xiidra
- Reassurance
- Follow up 10 days

Thank You and Hope You Enjoyed

Greg Caldwell, OD, FAAO
Grubod@gmail.com
Thyroid Dysfunction and the Eye

Greg Caldwell OD, FAAO
Arizona Optometric Association
November 16, 2019

Learning Objectives
- Enhance clinical understanding of rheumatology and thyroid dysfunction and their ocular associations
- Enhance clinical diagnosis of ocular manifestations of rheumatologic diseases and thyroid disease
- Enhance clinical management and treatment of ocular manifestations of rheumatologic diseases and thyroid eye disease
- Increase comfort level when ordering or interpreting laboratory tests in rheumatologic and thyroid diseases
- Gain confidence in working closer with rheumatology and endocrinology

Thyroid Disease
and Thyroid Eye Disease

Thyroid
- Thyroid is an endocrine gland
- Two types of glands:
  - Endocrine
  - Exocrine
- Endocrine system is a control system of ductless endocrine glands that secrete hormones (chemical messenger) that circulate within the body via the bloodstream or lymph system to affect distant organs
  - Hypothalamus
  - Pituitary gland
  - Thyroid
  - Parathyroid glands

Disclosures- Greg Caldwell, OD, FAAO
- Will mention many products, instruments and companies during our discussion
- I don't have any financial interest in any of these products, instruments or companies
- Pennsylvania Optometric Association - President 2010
- POA Board of Directors 2006-2011
- American Optometric Association, Trustees 2013-2016
- I never used or will use my volunteer positions to further my lecturing career
- Lectured for: Aerie, Alcon, Allergan, BioTissue, OptoVue
- Advisory Board: Allergan, Sight Sciences, Sun, Takeda
- Envirole: PA-Medical Director, Credential Committee
- Optometric Education Consultants - Scottsdale, St. Paul, Quebec City, and Nashville, Owner

Thyroid
- Exocrine glands contain ducts. Ducts are tubes leading from a gland to its target organ
  - Digestive glands have ducts for releasing the digestive enzymes
  - Salivary glands, sweat glands and glands within the gastrointestinal tract
- Pancreas is both endocrine and exocrine
  - Exocrine (ducted gland) secreting digestive enzymes into the small intestine.
  - Endocrine (ductless gland) in that the islets of Langerhans secrete insulin and glucagon to regulate the blood sugar level
Thyroid

- Largest endocrine gland in the body
- Butterfly shaped
- Two lobes located on either side of the trachea in the lower portion of the neck
- Lies just below skin and muscle layer surface
- The thyroid is controlled by the hypothalamus and pituitary
- The primary function of the thyroid is production of the hormones thyroxine (T4), triiodothyronine (T3), and calcitonin

Thyroid

- Thyroid regulates: heart rate, ventilation rate, metabolic rate, and development of cells
- Thyroid disorder- approx 1 in 13 or 7.35% or 20 million people in USA, estimated 2 million undiagnosed
- Diabetes- approx 1 in 13 or 7.8% or 17.9 million people in USA, 5.7 million undiagnosed
- Pathophysiology: >40 postulates (thyroid)

Normal Thyroid Function

Thyroid Dysfunction

- What is the most common cause of thyroid dysfunction?
  A. Cancer
  B. Surgically induced
  C. Medication toxicity or side effect
  D. Pregnancy
  E. Autoimmune disease

- In autoimmune disease the body typically produces ______ that attacks itself, this can be systemic or organ specific
  ◆ Antibodies, immunoglobulins

Discussion

Thyroid Dysfunction

- Primary=Thyroid gland
- Secondary= Pituitary failure
- Tertiary= Hypothalamic
Antibodies of Thyroid Dysfunction

**TSH Receptor Antibodies**
- Stimulating TSH receptor antibody
- Thyroid stimulating immunoglobulin (TSI)
- Thyroid blocking antibody (TBAb)

**Thyroid Peroxidase Antibodies (TPOAb)**
- TPO is found in thyroid follicle cells where it converts the thyroid hormone T4 to T3
- TPOAb contributes to thyroid cellular destruction

Most autoimmune thyroid dysfunctions have a combination of thyroid antibodies, however depending on which AB is more abundant results in the outcome of the disease.

---

**Hyperthyroid**

- TSI attacks the thyroid
- T3 and T4 increase
- TSH decreases

**Hypothyroid**

- TBAb attacks the thyroid
- T3 and T4 decrease
- TSH increases

---

**Hyperthyroidism**

Primary-autoimmune
- Graves
  - Graves-Barré syndrome or von Basedow’s

Secondary/Tertiary
- Medication treatment for hyperthyroidism
- Toxic multinodular goiter
- Toxic adenoma
- Excess iodine
- Excess hormone production in ectopic tissue
- Thyroid carcinoma

---

**Hypothyroidism**

Primary-autoimmune
- Chronic autoimmune thyroiditis
- Autoimmune atrophic thyroiditis
  - Primary myxedema
  - Opposite of Graves disease

Secondary/Tertiary
- Lithium medication
- Pregnancy
- Surgically induced
- Disorders of the pituitary gland or hypothalamus

---

**GRAVE’S**

A multisystem disorder consisting of a triad
- Hyperthyroidism with diffuse hyperplasia of the thyroid gland
- Infiltrative dermopathy
- Infiltrative ophthalmopathy

Prevalence:
- 20-40 year old female (F:M = 7:1)
- Genetic link

Etiology:
- Autoimmune disease: hypersensitivity reaction with thyroid stimulation by the circulation of abnormal thyroid-stimulating immunoglobulins (TSI)

---

**Hashimoto’s Thyroiditis**

The most common cause of hypothyroidism in the United States
- It is named after the first doctor who described this condition, Dr. Hakaru Hashimoto, in 1912
- Autoimmune disease
- Goiter formation
- 5-10 times more common in women than in men
- The underlying cause of the autoimmune process still is unknown
  - Anti-TPO ab and Anti-TB recp ab present
Autoimmune atrophic thyroiditis (Hypothyroidism)
- Atrophic thyroiditis is similar to Hashimoto's thyroiditis
- A goiter is not present

Postpartum Thyroiditis (Hypothyroidism)
- These women develop antibodies to their own thyroid during pregnancy, causing an inflammation of the thyroid after delivery

Systemic Manifestations of Hyperthyroid (Primary or Secondary)
- Symptoms
  - Nervousness
  - Heat intolerance
  - Sweating
  - Fatigue
  - Palpitation
  - Insomnia
  - Early waking
  - Nocturia
  - Vestigio
  - Brittle nails
- Signs
  - Sweating
  - Muscle Weakness
  - Emotionally labile
  - Tremor
  - Tachycardia
  - Arrhythmia
  - Hypertension
  - Irk tension reflex
  - Diabetes
  - Triglycerides & Ca, CHO
  - Microcyticanemia
  - Possible goiter
  - Myxedema

Systemic Manifestations of Hypothyroid (Primary or Secondary)
- Symptoms
  - Cold intolerance
  - Weakness
  - Reduced energy
  - Lethargy
  - Muscle cramps
  - Constipation
  - Increased sleeping
  - Weight gain
  - Reduced appetite
  - Joint stiffness
  - Brittle nails
- Signs
  - Cool, scaling skin
  - Puffy hands and face
  - Deep voice
  - Myotonia
  - Delirium
  - Bradycardia
  - Slow reflexes
  - Obesity
  - Hypothermia
  - Myxedema

Thyroid Eye Disease (TED)
- Other names used
  - Grave's disease
  - Graves ophthalmopathy
  - Grave's orbitopathy
  - Exophthalmos in Graves Disease
  - Thyroid Associated Orbitopathy (TAO)
  - Thyroid Orbitopathy
  - Ophthalamic Graves Disease
  - Inflammatory Eye Disease
  - Endocrine Orbitopathy

Why is this so confusing?
- Thyroid Eye Disease
  - Is often seen in conjunction with Graves' Disease (hyperthyroid)
  - Is seen in people with no other evidence of thyroid dysfunction
  - Is seen in patients who have Hashimoto's Disease (hypothyroid)
- Most thyroid patients, however, will not develop thyroid eye disease
Why is this so confusing?
- The eye symptoms usually occur at the same time as the thyroid disease
- However, they may precede or follow the obvious symptoms of the thyroid abnormality
- The incidence of thyroid eye disease associated with thyroid dysfunction is higher and more severe in smokers
- There is no way to predict which thyroid patients will be affected

Why is this so confusing?
- While eye disease may be brought on by thyroid dysfunction
- Successful treatment of the thyroid gland does not guarantee that the eye disease will improve
- No particular thyroid treatment can guarantee that the eyes will not continue to deteriorate
- Once inflamed, the eye disease may remain active from several months to as long as three years
- There may be a gradual or, in some cases, a complete improvement

Thyroid Eye Disease
- Commonly known as Graves' ophthalmopathy
- About 80% of all patients with TED have the autoimmune hyperthyroid disorder known as Graves' disease
- Another 10% of all cases are seen in patients with autoimmune hypothyroidism, either Hashimoto's thyroiditis, atrophic thyroiditis or Hashitoxicosis
- Another 10% of all cases are seen in people with normal thyroid function
  - When thyroid function is normal, the eye condition is referred to as euthyroid Graves' disease
  - Euthyroid is a term meaning that thyroid function tests are normal. Most people with euthyroid Graves' disease develop a thyroid disorder within eighteen months of the emergence of the eye disorder
  - But some people with euthyroid Graves' disease never develop thyroid dysfunction

Thyroid Eye Disease
- What causes the Thyroid Eye Disease signs and symptoms?
- The high and low levels of T3 and T4
- The antibodies that are attacking the thyroid gland

Thyroid Eye Disease
- Thyroid Eye Disease has 2 phases
  - A phase secondary to abnormal thyroid hormone levels
    - Increased or decreased FT3 and FT4 levels
  - Congestive Autoimmune form of Thyroid Eye Disease
    - Active phase: stimulating or blocking TRAb are causing ocular activity
    - Plateau phase: reduced activity
    - Resolution phase: symptoms regress and eyes return to normal

Thyroid Eye Disease
- Hyperthyroidism eye symptoms
  - Excess hormone acting on the nerves that supply the eye
  - Usually spastic and include staring
  - Dryness
  - Eyelid retraction

- Hypothyroidism eye symptoms
  - Deficiency hormone causing varied congestion, impaired circulation and fluid stagnation
  - Periorbital edema

- This form of TED resolves within a few weeks after thyroid hormone levels (FT4 and FT3) are corrected and brought back into the normal range
- The pituitary hormone TSH can stay low or suppressed for many months during the course of treatment for hyperthyroidism and doesn’t mean that the patient is still hyperthyroid
- TSH also lags at least 6 weeks behind thyroid hormone levels and often remains elevated longer in people who have been hypothyroid
- Relying on the TSH level can be misleading and in treating TED...
Congestive Autoimmune form of Thyroid Eye Disease
(Active phase, Plateau phase, Resolution phase)

- Caused by both stimulating and blocking TSH receptor antibodies (TRAu) and also immune system chemicals known as cytokines
- Secondary targets appear to be TSH receptor antigens (epitopes) located on orbital fibroblasts as well as dermal fibroblasts
- Active "inflammatory" phase of TED varies
  - Symptoms resolve quickly although on average the active phase lasts about 12-18 months
  - TRAb levels are high, patients are smokers, nutrient deficiencies are present, or the patient continues to be exposed to environmental triggers such as excess dietary iodine; the active phase can last as long as 5 years
  - Avoid any lid, muscle or orbital surgery
- Plateau phase and Resolution "Passive" phase
  - An individual may be left with structural changes, such as eye protrusion, eyelid retraction, and in some cases, double vision
  - There are corrective procedures that can be performed to address these problems

Euthyroid Graves' disease

- If thyroid function is normal. How does one develop thyroid eye disease?

Similar receptors are found in the skin, fat and muscle of the orbit

General Ocular Symptoms

- Pronominate eyes, stare
- Pain
- Lacrimation
- Eyelid swelling
- Foreign-body sensation
- Double vision
- Photophobia
- Decreased vision in one or both eyes

Euthyroid Graves' disease

You're in the Know

Normal Values
- Thyroglobulin 20 IU/ml
- Peroxidase <35 IU/ml
- TSI 1.75 IU/ml

It does work!

NOSPECS: Grading System

1969 by S.C. Werner
- Class 0: No signs or symptoms
- Class 1: Only signs, upper lid retraction
- Class 2: Soft Tissue Involvement with symptoms
- Class 3: Proptosis
- Class 4: EOM Involvement
- Class 5: Corneal involvement
- Class 6: Sight Loss

Clas 2-6 document severity
- A: absent
- B: minimal
- C: marked

Within classes 2 to 6 the investigator has to differentiate the severity grades 0, A, B, C
- NOSPECS. classifies severity but not the activity or stage
  (active/inflammatory or passive/congestive)
**NOSPECS: Grading System**

- **0**: No symptoms or signs
- **1**: Only signs (upper lid retraction without lid lag or proptosis)
- **2**: Soft tissue involvement with symptoms (excess lacrimation, sandy sensation, retrobulbar discomfort)
  - Grade 0: absent
  - Grade A: minimal (edema of lids, injection, sandy feeling)
  - Grade B: moderate (edema of lids, injection, chemosis, FRI; pain behind eye)
  - Grade C: marked
- **3**: Proptosis associated with classes 2-6 only
  - Grade 0: absent
  - Grade A: minimal: 21mm - 23mm
  - Grade B: moderate: 24mm - 27mm
  - Grade C: marked: 28mm or more
  - Specify if inequality of ≥ 3 mm between eyes, or if progression of ≥ 3 mm under observation

**LEMO Classification**

- **1991-Boergen and Pickardt**
- Complements NOSPECS
- 4 finding-categories
  - Lid
  - Exophthalmos
  - Muscular
  - Optic nerve
- Grade between 0 and 4 depending on severity
- LEMO, classifies severity but not the activity or stage (active/inflammatory or passive/congestive)

**Lid (L)**

- **0**: missing
- **1**: lid edema only
- **2**: real retraction (impaired lid closing)
- **3**: retraction and upper lid edema
- **4**: retraction and global lid edema

**Exophthalmos (E)**

- **0**: missing
- **1**: eye closing not impaired
- **2**: conjunctival injection in the morning
- **3**: persistent conjunctival injection
- **4**: corneal complications

**Muscular (M)**

- **0**: missing
- **1**: detectable in imaging only
- **2**: Pseudoparesis
- **3**: Pseudoparalysis

**Optic Nerve (O)**

- **0**: missing
- **1**: regarding color vision only
- **2**: peripheral scotoma
- **3**: central scotoma

**Endocrine ophthalmopathy with lid edema, exophthalmos, pseudoparesis of external eye muscles, and no optic nerve involvement**

**Grading Scales**

New grading scales are trying to be developed to not only grade the severity but also help to determine if inflammatory or passive stage

**Grading System**

- **4**: EOM involvement (usually with diplopia)
  - **0**: absent
  - **A**: minimal (limitation of motion, patient reports diplopia but no obvious restriction
  - **B**: moderate (obvious restriction of motion)
  - **C**: marked (motion of globe is fixed)
- **5**: Corneal involvement (due to proptosis, incomplete closure, lagophthalmos)
  - **0**: absent
  - **A**: minimal: 21mm - 23mm
  - **B**: moderate: 24mm - 27mm
  - **C**: marked: 28mm or more
  - Specify if inequality of ≥ 3 mm between eyes, or if progression of ≥ 3 mm under observation
- **6**: Sight loss (due to optic nerve involvement)
  - **0**: absent
  - **A**: minimal (disc pallor or edema, or VF defect, vision 20/20 - 20/60)
  - **B**: moderate (same as A but VA 20/70-20/200)
  - **C**: marked (blindness, VA < 20/200)
Lid Involvement
- Lid Retraction
- Lid Lag
- Lagophthalmus

Lid Retraction
- Scleral show in primary gaze
- Occurs in ~90% of Grave’s patients:
  - Excess stimulation of Muller’s muscle
  - Fibrotic inferior rectus
  - Mechanical restriction or infiltration of levator
  - Increased orbital volume causes exophthalmos
- Normal lid position:
  - Upper lid intersects cornea at the 2 and 10 o’clock positions
  - Lower lid coincident or 1-2 mm below the limbus

Eyelid Lag: von Graefe’s Sign
- Immobility or lagging of upper eyelid on downward gaze
- Fibrosis of the inferior rectus muscle may induce lower lid retraction

Lagophthalmos
- Inability to form a complete lid closure with a normal blink due to Exophthalmos/Proptosis
- Often leads to corneal exposure

Soft Tissue Involvement
- Conjunctiva
- Chemosis
- Periorbital edema

Conjunctiva
- Conjunctival and epithelial injection
  - Especially near the horizontal recti insertions
- Chemosis
  - Edema of the conjunctiva and caruncle
- Superior Limbic Keratoconjunctivitis
  - 65% correlation between SLE and systemic thyroid disease
  - Rheumatoid arthritis
  - Sjögren’s syndrome
Rheumatology, Thyroid Dysfunction and the Eye

If it is Red think TED

Periorbital Edema

Inflammation of the subcutaneous connective tissue

May be first sign of thyroid eye disease

Greatest in the morning

Infiltrative Orbitopathy (Exophthalmos/Proptosis)

Thyroid Eye Disease is most common cause of unilateral and bilateral exophthalmos

The term exophthalmos is reserved for prominence of the eye secondary to thyroid disease

May need MRI to determine or obvious exophthalmos may be present

It is permanent in 70% of cases

Caused by increased volume of the extra ocular muscles

- Lymphocytic infiltration
- Proliferation of fibroblasts
- Edema within the interstitial tissue of the muscle

Infiltrative Orbitopathy (Exophthalmos/Proptosis)
Exophthalmometry

- Is race dependent (Asians versus Black men is statistically significant)
- Heredity or Luedde results
- Adults
  - Average reading 17 mm
  - 95% of population have readings between 13-21 mm
- General concerns
  - A difference of 2 mm or more between the eyes
  - A measurement of more than 24 mm

<table>
<thead>
<tr>
<th>Race</th>
<th>Mean Normal Value</th>
<th>Upper Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mm</td>
<td>mm</td>
</tr>
<tr>
<td>White women</td>
<td>15.4</td>
<td>20.1</td>
</tr>
<tr>
<td>White men</td>
<td>16.5</td>
<td>21.7</td>
</tr>
<tr>
<td>Black women</td>
<td>17.8</td>
<td>23.1</td>
</tr>
<tr>
<td>Black men</td>
<td>18.5</td>
<td>24.7</td>
</tr>
<tr>
<td>Asians</td>
<td>----</td>
<td>18.0</td>
</tr>
</tbody>
</table>

Restrictive Myopathy

- Secondary to edema and fibrosis of EOM’s
- Inferior Rectus (IR) muscle is most commonly involved
- Occurs in 30-50% of patients
- Diplopia may be transient but in 50% it’s permanent

IOP in Thyroid Eye Disease

- A rise in IOP has been reported with TED
- I would have higher suspicion when you see
  - Periorbital edema
  - Exophthalmos, proptosis
  - Restrictive myopathy
- Some literature reports IOP in up gaze to be part of the diagnoses of thyroid dysfunction

Restrictive Myopathy

Obvious restrictive myopathy but also note the periorbital edema, and conjunctival hyperemia

Corneal Exposure

- Exposure keratopathy secondary to exophthalmos and lagophthalmos
- Significant threat to visual function

Optic Neuropathy

- Affects 5% of patients
- Usually mild to moderate exophthalmos and shallow orbits
- Enlargement of the recti muscles compresses ONH or its blood supply at the apex of the orbit
- Compression MAY occur without significant proptosis
- Compressive and/or ischemic and/or toxic

Greg A Caldwell, OD, FAAO
grubod@gmail.com  814-931-2030 cell
Treatment of Thyroid Eye Disease

- Depends on what phase of the disease we are in:
  - Phase secondary to abnormal thyroid hormone levels
  - Active “inflammatory” phase
  - Plateau phase and Resolution “Passive” phase
- Depends on what orbital tissue or structures are involved
- Depends on the risk of vision loss
- Depends if primary, secondary or tertiary thyroid dysfunction
- Management consists of:
  - Control of inflammation
  - Prevention of ocular and visual damage
  - Addressing ocular motor abnormalities
  - Improving cosmetic disfigurement
- Patient education is essential
- Communication with an endocrinologist or internist will ensure proper patient care

Treatment of Thyroid Eye Disease

- Palliative (hormone imbalance, active, passive)
  - Lubricants
  - Topical anti-inflammatory (Lotemax/Restasis)
  - Prisms
- Steroids (active phase)
  - Orals
  - Peri-cular injections
  - IV with oral steroid taper
- Orbital radiotherapy (active phase)
- Orbital Decompression (passive phase)
  - Fat removal orbital decompression (FROD)
  - Large orbit
  - Bone removal orbital decompression (BROD)
  - Small orbit
  - Both FROD and BROD

Smoking causes the thyroid eye disease to be more severe
Smoking causes treatments to be less effective

Lid Retraction, Eyelid Lag, Lagophthalmos

- Must treat underlying thyroid dysfunction
- Abnormal hormone level and Active phase
  - Treat the exposure keratitis with lubricants
  - Tape eyelids shut at night
  - Lid weight
  - Moisture chamber at night
  - Antibiotic ointments
- Passive Phase
  - Surgical Management
  - Inferior rectus recession
  - Mulsatomy
  - Resection of lower lid retractors

Future

- Looking for better or different ways to treat the active phase of this disease

Lid Retractor Surgery

Topical lubricants
- Artificial tears
- Ointment at night
- Topical steroids
- Restasis?
- Tape eyelids closed at night or use mask
- Elevate head at night to decrease lid edema
- Oral diuretics Acetazolamide
- Oral steroids
- Xo-Diuretic for 3 months
- IV steroids
- Periorbital steroids
- Restasis last 1 month

Conjunctiva, Periorbital edema

- Topical lubricants
- Artificial tears
- Ointment at night
- Topical steroids
- Restasis?
- Tape eyelids closed at night or use mask
- Elevate head at night to decrease lid edema
- Oral diuretics Acetazolamide
- Oral steroids
- Xo-Diuretic for 3 months
- IV steroids
- Periorbital steroids
- Restasis last 1 month
Infiltrative Orbitopathy (Exophthalmos/Proptosis)
- Orbital Disease Consult
  - Systemic steroids to reduce inflammation
  - Low dose radiotherapy
  - Surgical orbital decompression

Restrictive Myopathy
- Non-surgical (while waiting for stability)
  - Teach proper head position to alleviate diplopia
  - Prism in spectacle correction (Fresnel or ground in)
  - Oral steroids
  - Botulinum toxin injection
- Surgical Consult
  - Recession of the rectus muscles involved
  - Diplopia in primary gaze, reading gaze or both
  - Stable angle of deviation for at least 6 months
  - No evidence of active disease
  - Binocular vision in at least primary and reading positions

Corneal Exposure
- Manage the corneal defect as first line
  - Lubricating and antibiotic
  - Lid taping
  - Moisture barrier
- Orbital Disease Consult
  - High dose oral steroids
    - 150-140mg/day x 7 days
  - Orbital decompression

Optic Neuropathy
- Systemic Steroids
  - If rapidly progressive and painful in the early stage of the disease
  - Only if no contraindications
  - Prednisolone 80-100mg, expect results within 48hrs. Taper dose and d/c within 3 mo
- IV Methylprednisolone
- Radiotherapy: if contraindication to steroid
- Orbital decompression

Orbital Decompression (Surgical/Cosmetic)
- Not effective if no medical treatment
  - Two-wall decompression
    - 3-6 mm retro-placement of the globe
  - Three-wall decompression
    - 6-10mm retro-placement
  - Four-wall decompression
    - 10-16mm retro-placement

Orbital Decompression
- Not effective if no medical treatment
  - Two-wall decompression
    - 3-6 mm retro-placement of the globe
  - Three-wall decompression
    - 6-10mm retro-placement
  - Four-wall decompression
    - 10-16mm retro-placement
Thyroid Eye Disease and Depression

When facial disfigurement occurs, thyroid eye disease is equivalent to the diagnosis of cancer and AIDS.

Orbital Decompression
(Medical/Vision Threatened)

IOP in Thyroid Eye Disease

A rise in IOP has been reported with TED.
I would have higher suspicion when you see:
- Periorbital edema
- Exophthalmos, proptosis
- Restrictive myopathy

Some literature reports IOP in up gaze to be part of the diagnoses of thyroid dysfunction...let's discuss.

Laboratory Testing

Thyroid Hormone Levels
- Serum TSH concentration
- Serum total T3 (Triiodothyronine)
- Estimation of the serum free T4 (or T3) concentration
- Thyroglobulin (Tg) level

Anti-thyroid antibodies
- Thyroperoxidase antibodies (TPO)
- TSH binding inhibiting immunoglobulins (TBI)
- Anti-TPO antibodies
- Thyroglobulin (Tg) Antibodies (TgAb)

Commonly used thyroid tests
- Basic T3 uptake test
- Sensitivity T3 test (Thyroid stimulating hormone)
- TSH stimulation test (Thyroid releasing hormone)
- Thyroid (T4) suppression test
- Scintigraphy
- Needle biopsy
- Thyroid scans

IOP in Thyroid Eye Disease

Hypothyroid
- Low FT4, High TSH indicates primary check antibodies
- Low FT4, Low TSH indicates secondary or tertiary, TRH stimulation, MI

Hashimoto’s (primary disease)
- Most common
- Low FT4, High TSH, High Anti-TPO Ab, High levels of Thyroglobulin (Tg) Antibodies (TgAb), Anti-TB Recp Ab (approx 10% present)
- Autoimmune atrophic thyroiditis
- Low FT4, High TSH, Low Anti-TPO Ab, Low levels of Thyroglobulin (Tg) Antibodies (TgAb), Anti-TB Recp Ab (approx 60% present)
- Treatment: Levothyroxine (Synthroid, Levothroid, Levoxyl, Unithroid)

Hyperthyroid
- High FT4, Low TSH
- TSH present

Greg A Caldwell, OD, FAAO
grubod@gmail.com  814-931-2030 cell
Signs in Thyroid Eye Disease

- Dalrymple's sign: Lid retraction
- von Graefe's sign: Upper lid lag on downward gaze
- Griffith's sign: Lower lid lag on downward gaze
- Boston's sign: Jerky irregular movement of the upper lid on downward gaze
- Jellinek's sign: Increased pigmentation of the lids
- Stellwag's sign: Infrequent blinking
- Kocher's sign: Increased lid retraction with visual fixation
- Enroth's sign: Puffy swelling of the lids
- Rosenbach's sign: Tremor of closed lids
- Modius' sign: Weakness of convergence
- Ballet's sign: Palsy of one or more extracocular muscles
- Suker's sign: Weakness of fixation on lateral gaze
- Cowen's sign: Jerky papillary constriction in consensual light
- Knies' sign: Unequal dilatation of the pupils
- Jeffrey's sign: Absence of forehead wrinkling on upward gaze

Questions
Rheumatology and the Eye

Rheumatology

- Specializes in the diagnosis and therapy of clinical problems involving
  - Joints
  - Osteoporosis
  - Musculoskeletal pain disorders
  - Soft tissues
    - Not connective tissue
      - Muscle, nerve, and blood vessels
    - Connective tissue
      - Tendons, ligaments, fascia, fibrous tissues, fat, and synovial membranes
- There are more than 200 types of these diseases, including rheumatoid arthritis, osteoarthritis, gout, lupus, back pain, osteoporosis, fibromyalgia, and tendinitis

Where the Eye and Rheumatology Overlap

- Connective Tissue Disease
- Vasculitides
- Spondyloarthropathies

Connective Tissue Disease

- Connective tissue disease is any disease that has the connective tissues of the body as a primary target of pathology
- The connective tissues are composed of two major structural protein molecules
  - Collagen
  - Elastin
- The collagen and elastin become injured by inflammation
  - Typically due to autoimmunity
- “Collagen vascular disease” is an antiquated term used to describe diseases of the connective tissues

Connective tissue diseases secondary to gene abnormalities

- Connective tissue diseases that are strictly due to genetic inheritance include
  - Marfan syndrome
    - Gene FBN1 on chromosome 15
    - Can have tissue abnormalities in the heart, aorta, lungs, eyes, and skeleton
  - Ehlers-Danlos syndrome
    - Many types with numerous genes
    - Typically have loose, fragile skin and hyperextensible joints depending on type

Connective tissue diseases secondary to autoimmunity

- Cannot be regularly defined by gene abnormalities
- The spontaneous over activity of the immune system
  - Results in the production of extra antibodies into the circulation
  - Systemic Lupus Erythematosus
  - Rheumatoid Arthritis
  - Sjogren Syndrome
  - Systemic Sclerosis
  - Polymyositis/Dermatomyositis
  - Mixed Connective Tissue
  - Wegner’s Granulomatous
Connective Tissue Diseases

- Systemic Lupus Erythematosus
- Rheumatoid Arthritis
- Sjogren's Syndrome
- Systemic Sclerosis
- Polymyositis/Dermatomyositis
- Mixed Connective Tissue Disease
- Wegener's Granulomatosis

Auto-antibody
- Anti-dsDNA, Anti-Sm
- RF, Anti-RA33
- Anti-Ro(SS-A), Anti-La(SS-B)
- Anti-Scl-70, Anti-centromere
- Anti-Jo-1
- Anti-U1-RNP
- c-ANCA

Similar Structures

- The connective tissues are composed of two major structural protein molecules
  - Collagen
  - Elastin

- Sclera - the opaque, white, fibrous, protective, outer layer of the eye containing collagen and elastin fibers

- Synovial membrane: A layer of connective tissue that lines the cavities of joints, tendon sheaths, and bursae and makes synovial fluid, which has a lubricating function.

- Tenon's Capsule - a layer of connective tissue which forms a thin membrane that envelops the eyeball from the optic nerve to the limbus, separating it from the orbital fat and forming a socket.

53 year old woman

- Referred for treatment for a red OS
- 3 weeks ago sudden onset of red eye
- No pain, just feels like eyestrain
- At times it’s worse at times it’s better
- 5 years ago same eye was red, it resolved without treatment

Discussion

Review of Systems

Knuckles
Treatment

- Lotemax qid OS
- Ibuprofen 400 mg qid PO
- Artificial tears
- Educate patient on finding and possible underlying etiologies
  - This reveals an uncle with severe arthritis, no definite diagnosis
- Blood work? If so what test?
  - Antinuclear antibody (ANA) and rheumatoid factor (RF)

6 days later

- Treatment
  - Lotemax
    - TID = 1 week
    - BID = 1 week
    - QD = 1 week
- Ibuprofen 200mg QID
- D/C
- Review of lab results

Lab Results

Referral to Rheumatologist

Final Outcome

- Diagnosed with rheumatoid arthritis
- Current treatment successful
- No ocular occurrence since treatment of rheumatoid arthritis

Episcleritis

- Typically occur in exposure zones
- Inflammation localized to episclera:
  - Radiate posterior from limbus
  - Vessels are moveable
  - Vessels blanch with sympathomimetics
- Types
  - Simple episcleritis: 80%
  - Nodular episcleritis: localized with variable tenderness
- Clinical Evaluation:
  - Sectoral injection 70%
  - Diffuse injection 30%
48 year old woman

- My OD eye has severe pain, it started as an ache about 1 week ago, but now is a throbbing pain
- It hurts to move my eye or touch my eye
- The pain is radiating to my cheek
- Patient does suffer from rheumatoid arthritis
- VA 20/20 OU
- EOMs full, but pain on movement OD
- PERRL (-) APD
- Confrontation fields: full OU
- Let's take a look

Diagnosis and Treatment?

Treatment

- Non-Necrotizing Scleritis
  - Depending on severity, one or combination of:
    - Oral Non Steroidal Anti Inflammatory agents
      - Ibuprofen or indomethacin (50 mg po bid)
    - Oral steroids
  - Communication/consult with rheumatologist
  - Sub-Tenon's steroid injection is contraindicated

Scleritis

- Severe inflammatory condition
- An immune mediated inflammation and destruction of the sclera
- Commonly associated with underlying systemic disease
- 4th to 6th decade of life
- Rare in children
- Female > male
- Greater than 50% are bilateral

Symptoms

- Gradual presentation (days)
- Deep boring pain
  - May worsen at night
- Reflected pain to head and jaw
- Eye is tender to the touch

Clinical Evaluation

- Sectoral or diffuse injection at all levels of vessels
- Blue hue in natural light
- Vessels do not blanch or move
Classification of Scleritis

<table>
<thead>
<tr>
<th>Location</th>
<th>Subtype</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior Sclera</td>
<td>Diffuse Anterior Scleritis</td>
<td>40%</td>
</tr>
<tr>
<td></td>
<td>Nodular Anterior Scleritis</td>
<td>44%</td>
</tr>
<tr>
<td></td>
<td>Necrotizing Anterior Scleritis with Inflammation</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>Necrotizing Anterior Scleritis without Inflammation</td>
<td>4%</td>
</tr>
<tr>
<td>Posterior Sclera</td>
<td>Posterior Scleritis</td>
<td>2%</td>
</tr>
</tbody>
</table>

Non Necrotizing Scleritis

- **Diffuse**
  - Portion involved in 60%
  - Entire sclera involved in 40%
  - Red/blue hue

- **Nodular**
  - Scleral nodule
  - Deep red-purple
  - Nodule is immobile and separate from episclera

Necrotizing Scleritis

- Most destructive form
- 60% develop ocular/systemic complications
- 40% have vision loss
- 30% mortality rate at 5 years

Necrotizing Scleritis Without Signs of Inflammation (Scleromalacia Perforans)

- Predominantly seen in patients with rheumatoid arthritis (55%)
- Signs of inflammation are minimal
- No pain
- Progressive scleral thinning
- Uvea becomes visible
- Eye may rupture

Posterior Scleritis
**Posterior Scleritis**
- May occur in isolation or with associated anterior involvement
- Presentation:
  - Pain (ocular/head)
  - Proptosis
  - Visual loss
  - Restricted motility
- Posterior Findings:
  - Choroidal folds
  - Exudative retinal detachment
  - Papilledema
- Easily missed if no associated anterior scleritis
- Diagnosis confirmed with ultrasound, CT, or MRI
- Hallmark: thickened sclera
- Most have no identifiable related systemic disease

**Management**
- Laboratory evaluation warranted
- Scleritis is often associated with systemic disease (some fatal)
- Common etiologies:
  - Rheumatoid Arthritis
  - Systemic Lupus Erythematosus
  - Ankylosing spondylitis
  - Wegener's
  - Gout
  - Polymyositis nodosum
  - Hansen disease

**Treatment**
- **Non-Necrotizing Scleritis**
  - Depending on severity, one or combination of:
    - Oral Non Steroidal Anti Inflammatory agents
      - Ibuprofen or indomethacin (50 mg po bid)
    - Oral steroids
    - Topical steroids and NSAID's ineffective
- **Necrotizing Scleritis**
  - Oral/IV steroids
  - Immunosuppressive/ cytotoxic agents
  - “Sub-Tenon’s steroid” injection is contraindicated

**Rheumatoid Arthritis**
- 1% of the population
- Women affected 2-3 X more than men
- Age of onset is 40-50
- Juvenile form

**Rheumatoid Arthritis: Diagnostic Criteria**
1. Morning stiffness (>1h)
2. Swelling of three or more joints
3. Swelling of hand joints (prox interphalangeal, metacarpophalangeal, or wrist)
4. Symmetric joint swelling
5. Subcutaneous nodules
6. Serum Rheumatoid Factor
7. Radiographic evidence of erosions or periarticular osteopenia in hand or wrists

Criteria 1-4 must have been present continuously for 6 weeks or longer and must be observed by a physician. A diagnosis of rheumatoid arthritis requires that 4 of the 7 criteria are fulfilled.
Rheumatoid Arthritis

tusiform synovitis

Early
Intermediate
Late

Rheumatoid Arthritis

Vasculitis

Rheumatoid Arthritis

Vasculitis / Digital Necrosis

Rheumatoid Arthritis

Disease Modifying Anti-rheumatic Drugs / DMARDs

- Methotrexate (MTX)
- Hydroxychloroquine
- Leflunomide
- Sulfasalazine
- Cyclosporine
- Parenteral/oral gold
- Azathioprine
- D-penicillamine
- Minocycline*

* Not approved by the FDA for the treatment of RA.

Rheumatoid Arthritis

(Biologic DMARDs)

- Enbrel (Fusion Protein)
  - 50-100mg SQ q week
- Remicade (chimeric MAB)
  - 3mg/kg, 10mg/kg Q 4-8 weeks
- Humira (humanized MAB)
  - 40mg SQ qow
45 year old woman
- Reports a black line in her vision OD
- "The line in my vision does not move like a floater"
- Vision 20/20 OU
- Externals: unremarkable
- SLE: unremarkable

Fundus Photo OD

Cotton Wool Spots
- Non-specific finding
  - Hypertension
  - Diabetes
  - Connective Tissue Disease
  - HIV Retinopathy
  - Blood dyscrasia
    - Leukemia
    - Anemia

Many Faces of CWS
- No underlying etiology
- History of uncontrolled HTN and DM

Laboratory Work-Up
- Sed rate
- ANA
- Rheumatoid factor
- ACE
- HLA-B27
- Fasting blood glucose (FBG)
- Lipid profile
- Complete blood count (CBC)

Results
- Complete blood count (CBC):
  - WBC: 2.9 low
  - Hemoglobin: 9.1 low
  - Hematocrit: 33.3% low
  - Platelet count: 110 low
- Sed rate: 48 high
- ANA: 1:640 speckled pattern
- Rheumatoid factor: negative
- ACE: normal
- HLA-B27: negative
- Fasting blood glucose (FBG): normal
- Lipid profile: normal
Referred to Rheumatologist

- Patient diagnosed with systemic lupus erythematosus (SLE) and treated with an immunosuppressant
- CWS have resolved and no other occurrences

Systemic Lupus Erythematosus

- General
  - Autoimmune multisystem disease
  - Prevalence 1 in 2,000
  - 9 to 1: female to male (1 in 700)
  - Peak age 15-25
  - Immune complex deposition
  - Photosensitive skin eruptions, serositis, pneumonitis, myocarditis, nephritis, CNS involvement

Systemic Lupus Erythematosus: Diagnostic Criteria

- Anti-Nuclear Antibodies (ANA)-positive
- Specific labs
  - dsDNA antibodies
  - Anti-Sm antibody
  - Anti-SSA and Anti-SSB – may also be positive

Systemic lupus erythematosus 1982 classification criteria definitions

- Malar rash: Fixed erythema, flat or raised, sparing the nasolabial fold
- Discoid rash: Raised patches, adherent keratotic scaling, follicular plugging; older lesions may cause scarring
- Photosensitivity: Skin rash from sunlight
- Oral ulcers: Usually painless
- Arthritis: Nonerosive, inflammatory in two or more peripheral joints
- Serositis: Pleuritis or pericarditis

Systemic lupus erythematosus 1982 classification criteria definitions

- Renal disorder: Persistent proteinuria or cellular casts
- Neurologic disorder: Seizures or psychosis
- Hematologic: Hemolytic anemia, leukopenia (<4,000/mm³), lymphopenia (<1,500/mm³), or thrombocytopenia (<100,000/mm³)
- Immunologic disorder: Antibodies to dsDNA or Sm or positive antiphospholipid antibodies (aPL) or SS-A or SS-B antibodies, lupus anticoagulant, or false-positive serologic test positive serologic test for syphilis
- Antinuclear antibody test: Positive
Systemic Lupus Erythematosus

- Discoid Lupus: Cutaneous manifestations
- Scar upon healing

Systemic lupus erythematosus

- Butterfly rash, discoid type

Systemic lupus erythematosus

- Photosensitivity

Systemic lupus erythematosus

- Interarticular dermatitis

Systemic lupus erythematosus

- Retinal vasculitis
Systemic Lupus Erythematosus

- Treatment: Rheumatologist involvement
- Avoidance of sun
- Use of sunscreens
- DMARDs

Systemic Lupus Erythematosus

- Methotrexate (MTX)
- Hydroxychloroquine
- Leflunomide
- Sulfasalazine
- Cytoglobin
- Cellcept
- Cyclosporine
- Parenteral/oral gold
- Azathioprine
- D-penicillamine
- Minocycline

* Not approved by the FDA for the treatment of RA.


37 year old woman

- Referred in for punctal plug insertion due to dry eyes, temporary plug outcome was successful
  - Currently using
    - Systane q2h OU
    - Restasis bid OU
    - Systane night PRN
  - She wants plugs to help decrease her usage of lubricants
  - SLE: confirms almost absent tear prism and mild to moderate Lissamine green staining
  - Anything suspicious here?

Results

- Excellent outcome to permanent plugs RUL/RLL
- ESR: 33 mm/hr
- CRP: 1.7
- ANA: 1:320
- RF: positive
- SS-A: positive
- SS-B: positive
- Thyroid panel: normal

- Referral to rheumatologist for diagnosis and treatment

Treatment

- Permanent plugs RUL/RLL
- Labs ordered:
  - ESR, CRP, ANA, RF, SS-A, SS-B and thyroid panel

Diagnosis

- Sjögren’s Syndrome
**Definition of Sjögren’s Syndrome**

A chronic systemic autoimmune disease characterized by lymphocytic infiltration of salivary and lacrimal glands leading to dry mouth (xerostomia) and dry eyes (keratoconjunctivitis sicca) as a consequence of progressive glandular destruction and dysfunction.

- 1-2 million Americans affected
- 90% women
- 2nd most common autoimmune rheumatic disease
- A major women’s health problem

**Sjögren’s Syndrome**

- Primary or secondary
- Dry mouth and dry eyes
- Serum autoantibodies
  - RF, anti-Ro/SSA, anti-La/SSB
- Glandular and extraglandular manifestations
- Overlap with other autoimmune rheumatic diseases
- Women > Men (9:1)

**Sjögren’s Syndrome**

(Ocular signs)

- Reduced tear production
  - Measured by Schirmer test
- Decreased tear breakup time
- Epithelial staining with diagnostic dye
- Filamentary keratitis by biomicroscopy

**Sjögren’s Syndrome**

(Oral features)

- Dry mouth
- Sore or burning mouth
- Intolerance to acidic or spicy foods
- Abnormalities of taste
- Difficulty with chewing and swallowing dry foods
- Difficulty with phonation (speaking)
- Difficulty wearing dentures

**Dental Caries (Decay) in Sjögren’s Syndrome Patients**
Why Can Muscarinic Agonists Be Used to Stimulate Saliva?
- The severity of salivary dysfunction is disproportionate to the amount of lymphocyte infiltration.
- Most Sjögren’s syndrome patients have remaining acinar cells in their salivary glands.
- Muscarinic receptors on these cells are still capable of responding to stimulation.
- In sufficient dosages, muscarinic agonists can increase secretion of exocrine glands.

Salivary Glands
Sjögren’s Syndrome

Normal Salivary Gland
Salivary Gland SS

Evoxac
- Mechanism of Action:
  - A cholinergic agonist that binds to muscarinic receptors and stimulates exocrine glands.
  - Muscarinic receptor subtypes:
    - Evoxac has high affinity for M1 and M3 subtype
    - Secretion from salivary glands and stomach
    - Evoxac has a lower affinity for the M2 subtype
    - Slow heart rate, reduce contractile forces of atrium, reduce conduction velocity of AV node
- Sufficient dosages, muscarinic agonists can increase secretion of exocrine glands.

Connective tissue diseases secondary to autoimmunity
- Systemic Lupus Erythematosus
- Rheumatoid Arthritis
- Sjogrens Syndrome
- Systemic Sclerosis
- Polymyositis/Dermatomyositis
- Mixed Connective Tissue
- Wegner’s Granulomatous

Vasculitides
The vasculitides are a group of diseases characterized by non-infectious necrotizing vasculitis and resultant ischemia.

Connective tissue diseases secondary to autoimmunity
- Cannot be regularly defined by gene abnormalities
- The spontaneous over activity of the immune system
  - Results in the production of extra antibodies into the circulation.
Rheumatology, Thyroid Dysfunction and the Eye

Vasculitides
- Polyarteritis Nodosa
- Churg-Strauss Syndrome
- Hypersensitivity Vasculitis
- Wegener’s Granulomatosis
- Giant Cell Arteritis
- Behcet’s Disease
- Cogan’s Disease
- Kawasaki Disease

32 year old man
- “I have bleeding in my eyes”, patient requests 3rd opinion
- “I have been tested for high blood pressure and diabetes 4 times, I don’t have either one”
- Vision 20/20 OU

Fundus Reveals

Work Up
- CBC/diff normal
- ACE normal
- FTA ABS negative
- VDRL negative
- HLA-B27 negative
- PPD normal
- ANA negative
- RF negative

Results and Fundus 3 Weeks Later

Ask and You Shall Receive

Greg A Caldwell, OD, FAAO
grubod@gmail.com  814-931-2030 cell
Refer to Rheumatologist

- Testing and examination reviews Behcet’s diagnosis
  - Vascular with triad of oral and genital ulcers and uveitis or iritis
  - Ulcers, covered in pale pseudomembrane
    - Painful, on lips, gingiva, buccal mucosa, tongue, palate and oropharynx
  - Genital ulcers similar in appearance
  - Heal in days to weeks with scarring
- The treatment of Behcet’s syndrome depends on the severity and the location of its manifestations in an individual patient
  - This patient oral steroids and Remicade

Spondyloarthropathies

- Prevalence is similar to Rheumatoid Arthritis, 1-2%
- Share similar clinical, radiographic, and genetic features
- A cluster of overlapping forms of inflammatory arthritis
  - Are distinct from rheumatoid arthritis
  - Affect the spine
  - Affect the entheses (insertions of tendons and ligaments)
- The syndromes include
  - Ankylosing spondylitis
  - Reactive arthritis (Reiter’s syndrome)
  - Psoriatic arthritis
  - Enteropathic arthritis
- Syndromes sometimes included (controversial)
  - Whipple’s disease
  - Behcet’s syndrome

Seronegative Spondyloarthropathy

- Seronegative refers to the absence of the specific antibodies (or substance) that were being tested for
  - Rheumatoid factor
- Spondyloarthropathies are inflammatory joint diseases of the vertebral column associated with the major histocompatibility complex (MHC) Class I molecule
  - HLA-B27

Spondyloarthropathy

- The major histocompatibility complex is encoded by several genes located on human chromosome 6
- Most (but not all) patients with spondylitis carry a gene called HLA-B27
- People carrying the HLA B27 gene
  - Are at increased risk of developing spondylitis
  - The majority (over 75%) will never develop the disease
- HLA-B27 is not helpful in prognosis
**HLA-B27 & Uveitis**

- **Features**
  - Marked or severe presentation
  - Anterior iritis
  - Unilateral
  - Acute onset, < 3 months
- Can occur as a HLA B27 uveitis
- Can occur with a spondyloarthropathy

**Ankylosing Spondylitis**

- Ankylosing spondylitis is a chronic, usually progressive, disease involving the articulations of the spine and adjacent soft tissues
- HLA B27 positive 90%
- Uveitis 20-40% chance

**Reactive Arthritis**

- A spondyloarthropathy following enteric (GI tract) or urogenital infections and occurring in individuals who are HLA B27 positive
- What was once referred to as “Reiter syndrome” and is now referred to as reactive arthritis
- Can cause inflammation in the joints of the spine, legs and arms and in other parts of the body
- The syndrome usually begins with urethritis followed by conjunctivitis and rheumatological findings
- Arthritis begins within 1 month of infection in 80% of patients
- HLA B27 positive 40-80%
- Uveitis 20-40% chance

**Psoriatic Arthritis**

- Patients with psoriasis have a 5-42% chance of developing psoriatic arthritis
- About 20% of people who develop PsA will eventually have psoriatic spondylitis
  - The inflammation in the spine can lead to complete fusion
  - Spondylitis associated with psoriasis
    - 60-70% are HLA-B27 positive
    - Psoriatic arthritis without spondylitis 15% HLA B27 positive
- Uveitis 7% chance

**Enteropathic Arthritis**

- A form of chronic, inflammatory arthritis associated with the occurrence of an inflammatory bowel disease (IBD)
  - Ulcerative colitis
  - Crohn’s disease
- About one in five people with Crohn’s or ulcerative colitis will develop enteropathic arthritis
  - Approximately 50-60% of patients with spondylitis in association with IBD have HLA-B27
- The most common areas affected are the peripheral (limb) joints
  - In some cases, the entire spine can become involved as well
- Uveitis 3-11% chance

**Undifferentiated Spondyloarthropathy (USpA)**

- To describe symptoms and signs of spondylitis in someone who does not meet the criteria for a definitive diagnosis of AS or related disease
  - Unrecognized by many physicians
  - Initial diagnosis of Spondyloarthropathy or Unclassified
    - Spondyloarthropathy if certain symptoms are present but are not enough to make a specific diagnosis
    - Over time, most people with USpA will develop a well-defined form of spondylitis such as ankylosing spondylitis
Revised Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy

- **Recommendations were 2002 by the American Academy of Ophthalmology.**
- **Improved screening tools and new knowledge about prevalence of toxicity have prompted the change.**
- **Major points include:**
  - Improved Retinal Imaging (Optical coherence tomography, ERG, FAF).
  - Visual fields.
  - Fundus autofluorescence.
  - Retinal thickness.
  - Minimum levels, and the importance of annual screening validated with additional procedures to avoid unnecessary cessation of valuable medications.
  - **The recent publication of a large demographic study has been associated with the idea that toxicity is not rare among long-term users of anti-malarial drugs.**

**Screening Schedule:**

- **American Academy of Ophthalmology Statement:**
  - Begin annual screening after 5 years for patients on acceptable doses and without major risk factors.
  - **Major Risk Factors:**
    - Renal disease.
    - Hepatic disease.
    - Pulmonary disease.
    - Any RPE loss.
  - **Screening Schedule:**
    - **Dose:**
      - Hydroxychloroquine (HCQ) 2.3 mg/kg real weight.
      - Chloroquine (CQ) 5.0 mg/kg real weight, which correlates better with risk.
    - **Algorithm:**
      1. Fundus autofluorescence.
      2. Fluorescein angiography.
      3. Spectral domain optical coherence tomography.
      5. If fields are abnormal, perform Superficial Nerve Fiber Layer OCT.
      6. **If OCT shows evidence of toxicity:** Cross-validate with electrotoretinography.

**Background:** The American Academy of Ophthalmology recommends on screening for chloroquine (CQ) and hydroxychloroquine (HCQ) toxicity, and now being considered for new applications in diabetes toxicities. Retinopathy is not reversible, and there is no present therapy. Recognition at an early stage (before it is visible in the macula) is important to prevent irreversible visual loss. Therefore must be caught early.

- Screening for the earliest hints of functional or anatomic change.
- Plaquel toxicity is not well understood.

**Screening Schedule:**

- **Major Risk Factors:**
  - Renal disease.
  - Hepatic disease.
  - Pulmonary disease.
  - Any RPE loss.

- **Screening Schedule:**
  - Begin annual screening after 5 years for patients on acceptable doses and without major risk factors.
  - **Major Risk Factors:**
    - Renal disease.
    - Hepatic disease.
    - Pulmonary disease.
    - Any RPE loss.
  - **Screening Schedule:**
    - **Dose:**
      - Hydroxychloroquine (HCQ) 2.3 mg/kg real weight.
      - Chloroquine (CQ) 5.0 mg/kg real weight, which correlates better with risk.
    - **Algorithm:**
      1. Fundus autofluorescence.
      2. Fluorescein angiography.
      3. Spectral domain optical coherence tomography.
      5. If fields are abnormal, perform Superficial Nerve Fiber Layer OCT.
      6. **If OCT shows evidence of toxicity:** Cross-validate with electrotoretinography.

**Evidence:** The recent publication of a large demographic study has been associated with the idea that toxicity is not rare among long-term users of anti-malarial drugs. Although the locus of toxic damage is parafoveal in many eyes, Asian patients often show an extramacular pattern of damage. There is no treatment for this condition. Therefore, it must be caught early.

**Plaque Toxicity:**

- Plaque toxicity is not reversible, and there is no present therapy. Recognition at an early stage before it is visible in the macula is important to prevent irreversible visual loss. Therefore must be caught early.

**Screening:**

- Patients and prescribing physicians should be informed of the risk of toxicity, proper dose levels, and the importance of regular annual screening. Ophthalmology 2016;123:1386-1394.
**1-1.5 MM PERIMACULAR GCC THINNING THE FIRST SIGN OF PLAQUENIL TOXICITY**

*WHY? THICKEST LAYER OF GANGLION CELLS AND SMALLEST GANGLION CELLS AT THAT LOCATION. VERY SENSITIVE TO TOXICITY*

---

**WHAT DO YOU SEE ON THE SCANS?**

A. THINNING OF THE GCC IN THE PLAQUENIL ZONE
B. MACULAR EDEMA
C. COMPROMISED PIL
D. NOTHING OF IMPORT

---

**DO YOU SEE ANY PROBLEM IN THE PLAQUENIL ZONE?**

---

**WHAT DO YOU SEE ON THE SCANS?**

A. THINNING OF THE GCC IN THE PLAQUENIL ZONE
B. MACULAR EDEMA
C. COMPROMISED PIL
D. NOTHING OF IMPORT

---

**DO YOU SEE ANY PROBLEM IN THE PLAQUENIL ZONE?**
WHAT DO YOU SEE ON THE SCANS?
A. THE FLYING SAUCER SIGN
B. MACULAR EDEMA
C. INCREASED PERIMACULAR RETINAL THINNING
D. A AND C

THE END GAME...ONCE YOU DISCONTINUE PLAQUENIL IT STAYS AROUND A WHILE TO CREATE DAMAGE..LONG ½ LIFE
71 yo woman

With Lupus and hypertension

Medications:
- Colazapam
- Plaquenil 200 mg BID, 15 years
- 81 mg ASA
- Prednisone
- Losartin

VA 20/25 OD/OS (mild cataracts)
Patient was told to see an ophthalmologist in 2013

Thank You!
814-931-2030
grubod@gmail.com