SUMMARY OF TREATMENT AND RESEARCH, JUNE 2009 THROUGH MAY 2010

IMDSG Presentation
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Introduction

If I were to describe the past twelve months in a word, it would be “progress.” No spectacular breakthroughs have occurred during that time to make big news in the AMD world, but a lot of persistent work has been reaping promising results. moving us ever closer to effective treatments. Even the cure we hope for is now being thought of more in terms of “sooner” than “later.”

This summary is a brief overview of the news that has been of interest to us during the period of June 2009 through May 2010. More details about the reports from the 2009 Meeting of the American Academy of Ophthalmology (AAO) may be found at www.mdsupport.org/library/aao2009.html. Other reports in this summary are annotated with sources for further reference.

I’ll begin by mentioning two studies in the area of nutrition, since nutraceuticals are currently our most immediate hope for slowing the progression of vision loss from AMD.

NUTRACEUTICAL

1. Omega-3 Lowers AMD Risk

For the past couple of years, we have been made aware of the benefits of Omega-3 fatty acids in our diet, and nutritionists have been recommending several servings of fish each week or supplementation with fish oil. To further confirm these benefits, 671 subjects in the 2009 ALIENOR Study were given eye examinations seven years after plasma fatty acid measurement. As hoped, lower risk of geographic atrophy (advanced dry AMD) was associated with higher plasma levels of total omega-3 fatty acids, in accordance with previous studies of dietary intake.

Ref: AAO 2009 Paper: "Plasma Omega 3 Fatty Acids and Risk for Age-Related Maculopathy: The ALIENOR Study" (Presenting Author: Jean-Francois Korobelnik MD)

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2. Saffron Improves Vision

Another interesting finding was reported in March 2010, when clinical trials in Italy and Australia showed that the spice, saffron, can improve vision in people with AMD.

Subjects experienced up to 2 lines of improvement in their vision while taking saffron pills, but the effect quickly disappeared when the dose was discontinued. This indicates that it may improve the vision function of surviving cells but it does not reverse the damage that is already present.

If you intend to add saffron to your diet, be sure you are actually purchasing saffron, not safflower, which is sold as saffron by some unscrupulous dealers.

Ref: www.mdsupport.org/library/saffron.html

SURGICAL

Seven surgical procedures headed the news during these past 12 months.

1. FDA Considering Approval of IMT

The investigational implantable miniature telescope (IMT), discussed here last year, is designed to be a solution for moderate to profound vision loss due to advanced, end-stage forms of AMD that have no current surgical or medical treatment options.

If you remember, the telescope prosthetic device, which is smaller than a pea, is implanted in one eye during an outpatient surgical procedure. In the implanted eye, the device renders enlarged central vision images over a wide area of the retina to improve central vision, while the non-operated eye provides peripheral vision for mobility and orientation. On March 27, 2009, the FDA Ophthalmic Devices Advisory Panel unanimously recommended that the FDA approve, with conditions, the premarket application of the IMT for End-Stage AMD. The device has received CE Mark approval in Europe, but we are still waiting for approval in the US at this time. No explanation has yet been given for the delay.

Ref: AAO 2009 Session: "Implantable Miniaturized Telescope" (Presenter: Mark R. Wilkins, MD)

Ref: www.mdsupport.org/library/imt.html

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2. LMI Approved in Europe

In 2007, Optolight Vision Technology announced success from implantation of the LMI, which is a second generation of the implantable miniature telescope. They reported that the LMI may be an effective solution for optical rehabilitation of patients with ARMD or other macular pathology by increasing the central image on the retina while preserving peripheral vision. This preservation of the peripheral field is the main difference between the LMI and the IMT, allowing it to be implanted in both eyes.

On June 17, 2009, OptoLight Vision Technology announced that it received CE mark approval in Europe, which allowed OptoLight to immediately begin marketing the implant in Europe and other markets outside of the United States.

Ref: www.mdsupport.org/library/lmi.html

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3. Skin Cells Changed Into Retina Tissue

In August 2009, scientists at the University of Wisconsin-Madison reported that they had reprogrammed skin cells and turned them into different kinds of retinal cells. The work added to a growing weight of evidence that stem cells made by reprogramming have similar, if not the same, abilities as the more controversial embryonic stem cells.

Scientists may now be able to take a skin biopsy from someone with a vision ailment, create retinal cells, and observe how the disease unfolds and how the cells die over time. They hope to also use reprogramming as a way to generate damaged or diseased cells on which pharmaceutical companies can test their drugs and to find ways to correct genetic defects.

Farthest off, but most exciting to many researchers, is the possibility of using reprogramming to produce healthy cells that can replace those that have died.

Ref: "Skin Cells Changed Into Retina Tissue," by Mark Johnson (Journal Sentinel Online. August 24, 2009)

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4. UCI Researchers Create Retina

As recently as the end of May 2010, University of California Irvine scientists have created an eight-layer animal retina from human embryonic stem cells. This is the first three-dimensional tissue structure to be made from stem cells, and it could be a big step toward retina replacement in eyes affected by macular degeneration. It is an advancement over creation of single cell layers, since the multi-layered human retina might then be replaced in its entirety in one procedure.

The researchers are testing the early-stage retinas in animal models, in hopes that success will lead to human clinical trials.

Ref: today.uci.edu

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5. Brachytherapy May Improve Vision

Epimacular brachytherapy involves radiation treatment delivered by a small plaque sewn to the sclera (the white covering of the eyeball). In November 2009, NeoVista, Inc. announced results from a study designed to examine the company's brachytherapy procedure when used in patients undergoing anti-VEGF drug injections for wet AMD.

Preliminary study results suggest that a single procedure of epimacular brachytherapy can further improve visual acuity in a majority of this patient population while decreasing the number of injections required. Most importantly, they researchers reported, 63% of patients enrolled in the study experienced improvement in their visual acuity, while 50% of patients gained 5 or more letters of visual acuity at 6 months.

Ref: www.neovistainc.com/meritage.html

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6. New Radiation Treatment Under Study

Another radiation therapy system entering trials this past year was the Oraya IRay system. This delivers a robotically controlled dose of low-energy X-ray radiation to the retina. Oraya Therapeutics, Inc. began enrolling patients at seven European sites to demonstrate the safety and effectiveness of radiation therapy for the treatment of wet AMD. According to the company, the radiation dosages close inflammation mediated capillaries and further stop the inflammatory process that leads to wet AMD. In this study, the procedure is used in conjunction with anti-VEGF injections."

Ref: www.orayainc.com/clinicaltrials.asp

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7. Tinted IOLs May Slow AMD

A 2009 study showed that implantation of a blue light-filtering intraocular lens (IOL) at the time of cataract surgery increases macular pigment in the retina. This increase may provide protection against the development and/or progression of AMD.

Macular pigment is thought to protect against AMD by absorbing blue light before it reaches

the photoreceptors in the retina. The retina is exposed to as much as six times the amount of blue light in a person having the lowest level of macular pigment when compared to a person with the highest level. This gives rise to the belief that blocking blue light with replacement IOLs and other types of protective lenses may help slow down the disease process.

Macular Pigment Research Group: www.mprg.ie

PHARMACEUTICAL

The pharmaceutical industry leads the way this year, with nine newsworthy headlines.

1. Fenretinide Granted Fast-Track Status

Fenretinide (ST-602), a drug that has been used to treat certain cancers, rheumatoid arthritis, acne, and psoriasis, has been found to also slow the production and accumulation of a toxin called A2E that leads to buildup of lipofuscin (waste deposits) in the retina, resulting in vision loss in people with dry AMD. If the drug proves effective with dry AMD patients, it may then also be used off-label for treatment of Stargardt's disease, a juvenile form of macular degeneration.

The trials, which began in 2006, were granted fast-track designation in April 2009, based

upon strong results from phase 2.

Ref: ARVO 2009 Paper: "Fenretinide for the Treatment of Geographic Atrophy in Patients with AMD: One-Year Interim Analysis" (Presenting Author: Roger Vogel MD)

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2. Lucentis Still the Gold Standard

Incidence of ocular and non-ocular safety events continues to be low and consistent with prior Lucentis trials. For 600 patients who received Lucentis in prior trials, the most common ocular adverse events over 2 years have been worsening macular degeneration (35%), retinal hemorrhage (25%), and conjunctival hemorrhage (25%). Lucentis is still showing excellent results, and it is still considered the gold standard for treatment of wet AMD.

Ref: AAO 2009 Paper: "Safety Outcomes Over 2 Years in the HORIZON Extension Trial of Ranibizumab (Lucentis) in Neovascular AMD" (Presenting Author: Matthew S Benz MD)

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3. POT-4 Found Safe and Effective

POT-4 is a synthetic peptide that has been found to inhibit a genetic process that can lead to local inflammation, tissue damage (as in dry AMD) and the resulting blood vessel growth in wet AMD. Inflammation is thought to be the cause of AMD in as many as 50% of cases, so a good deal of research is being done in this area.

It was reported in 2009 that phase 1 studies found POT-4 to be well tolerated, safe, and effective in improving macular edema.

Ref: AAO 2009 Paper: "Phase 1 Results of the Complement C3 Inhibitor POT-4 in AMD" (Presenting Author: Philip J Rosenfeld MD PhD)

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4. VEGF Trap-Eye Completes Phase 2

AAO 2009 Poster: "VEGF Trap-Eye Vision-Specific Quality of Life Through 52 Weeks in Patients With Neovascular AMD in CLEAR-IT 2: A Phase 2 Clinical Trial" (Presenting Author: Allen C Ho MD)

VEGF Trap-Eye is a molecule which has been shown to block choroidal neovascularization (blood vessel growth) in eyes with wet AMD. Two studies were reported in 2009 to have been successful in both improvement of the affected retina and improvement in patients' quality of life.

AAO 2009 Poster: "OCT and Fluorescein Angiography Outcomes Through 1 Year for a Phase 2 Study of Intravitreal VEGF Trap-Eye in Neovascular AMD" (Presenting Author: Peter K Kaiser MD)

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5. Oral Drug For Dry AMD Enters Phase 2

Following the success of the Phase I clinical trial, Acucela Inc. has begun recruiting participants with dry AMD for a Phase II study of the oral drug ACU-4429 for dry AMD. Known as the ENVISION Clarity Trial, Acucela is planning to enroll at least 56 participants at multiple sites throughout the U.S. Participants will receive either the drug or a placebo.

Ref: www.medicalnewstoday.com/articles/149919.php

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6. Alzheimer's Disease Treatment May Benefit AMD Patients

Copaxone (glatiramer acetate) injections are given in Alzheimer's disease to decrease destructive beta-amyloid deposits. These deposits are similar to the proteins seen in drusen found in dry AMD, so researchers are trying copaxone for treatment of dry AMD. In week 12 of a small preliminary study, 4 eyes (3 patients) treated with copaxone showed a

total reduction of drusen area from baseline of 66%. Two eyes receiving sham injection had essentially no significant change in drusen area.

Ref: www.medscape.com/viewarticle/564015_2

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7. MC-1101 Eye Drop For Wet AMD Proves Safe

MC-1101 is an eye drop which affects the blood flow in the choroid, hopefully stopping the progression of AMD. So far, a small Phase 1 study by MacuCLEAR, Inc. has established the safety of seven dosages over three days, and plans for further trials are underway.

Ref: www.macuclear.com

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8. Aspirin May Aggravate AMD

We have been told that aspirin might help to inhibit the inflammation process, thereby slowing the progression of AMD. But here is frustrating news of a study just completed that suggests aspirin might actually be somehow associated with progression of the disease.

4691 patients 65 years and older were asked about their use of aspirin and about other possible risk factors for aging macula disorders. The results showed that odds ratios for all grades of early aging macula disorder rose with increasing aspirin intake frequency for subjects who reported daily use. The researchers, therefore, concluded that frequent aspirin use seems to be harmful for aging macula disorder in older populations.

Study leaderDr. Paulus de Jong said, however, that patients with cardiovascular disease should not stop taking aspirin. “But if they are taking it as a pain killer, there are other medications they can use."

Of course, more study is needed before definite conclusions can be drawn, and other studies have shown no correlation, even beneficial correlations, between aspirin and macula disorders. But moderate intake of aspirin might be something we need to consider until more is known.

Ref: Association for Research in Vision and Ophthalmology (AAO) 2010 Annual Meeting: Abstract 1620. Presented May 3, 2010.

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9. Studies Show Lucentis and Avastin to be Equal

In February 2010, investigators at Kaiser Permanente Southern California in Pasadena reported that Avastin and Lucentis performed equally. Of 452 patients treated for wet AMD, 22.9 percent of Avastin patients and 25.0 percent of Lucentis patients attained visual acuity better than or equal to 20/40 after a year of treatment. Similar numbers of patients in each group also showed some degree of vision improvement at 12 months.

The Kaiser Permanente study is one of several comparing the two drugs. The largest, and probably most definitive, study is the National Eye Institute's ongoing Comparisons of Age-Related Macular Degeneration Treatments Trials (CATT), with results expected next year. Avastin, originally designed as a cancer drug, is administered off-label, but research like the Kaiser study has been showing it to be at least as safe and effective as Lucentis for use in treatment of wet AMD.

We should remember that the comparison trials will not lead to FDA approval of Avastin for treatment of wet AMD. It may or may not confirm what we already know, but the drug will, in either case, remain on off-label status. Since large scale Avastin trials by the parent company, Genentech, are not likely, this will still be considered a safety issue.

Ref: Ophthalmology (Feb 2010)
Ref: www.mdsupport.org/library/catt.html

Drugs Under Study For Wet AMD

Here is a list of drugs currently under study for treatment of wet AMD. Three of them (Macugen, Lucentis and Avastin) have already entered clinical use, but followup studies continue to confirm their safety and efficacy.

Macugen
Lucentis (ranibizumab)
Avastin (bevacizumab)
Verteporfin PDT (in combination)
Tryptophanyl-tRNA synthetase (TrpRS)
AdPEDF
VEGF-TRAP-EYE
AG-013958
JSM6427
TG100801
ATG3
Perceiva
Endostatin
Pazopanib
siRNA

Ref: www.mdsupport.org/library/anti-angio.html

Drugs Under Study For Dry AMD

Here is a shorter list, but still encouraging, of drugs under study for potential treatment of the dry form of AMD:

ACU-4429
Copaxone
Fenretinide (ST-602)
Iluvian (fluocinolone acetonide)
MC-1101
OT-551
POT-4
Retinylamine

Ref: www.mdsupport.org/library/treatments.html

So there are at least 23 chances for treatments or cures from the pharmaceutical industry.If I haven't mentioned them in this summary, it's because most are still in the trial process, with no significant findings to report as yet. We may not hear very much about this work in the daily news, but rest assudred that the race is on, and no matter who reaches the finish line first, we, the patients--or at least our children and grandchildren--are going to be the eventual winners.

GENETICS

A great deal of research is being carried out in the field of genetics, as this is very likely where the cures for most diseases will be found. Two developments have stood out during the past 12 months.

1. RPE65 Gene Therapy Showing Promise

First, three young adults who received gene therapy for Leber congenital amaurosis (LCA), a blinding eye condition, remained healthy and maintained previous visual gains one year later. One patient also noticed a visual improvement that helped her perform daily tasks.

In this study, researchers injected healthy copies of the RPE65 gene under a healthy area of the retina in an attempt to repair the visual cycle. One year after the procedure, evidence shows that the newly introduced gene is functional and is increasing the light sensitivity of the retina.

This is the first study that reports the one-year safety and effectiveness of successful gene therapy for LCA. It paves the way for similar techniques, which can eventually be applied to other genetic diseases such as AMD.

Ref: www.mdsupport.org/library/breakthrough.html

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2. PEG-POD: A New Gene Delivery Tool

The second bit of news came in January 2010, when researchers reported having developed a new tool for gene therapy which significantly increases gene delivery to cells in the retina compared to other carriers and DNA alone.

A peptide called PEG-POD provides a safe and effective vehicle for transferring DNA into cells without using a virus, currently the most common means of DNA delivery. PEG-POD protects DNA from damage in the bloodstream, allowing for gene therapy treatments that can be administered through an IV and directed to many other parts of the body.

The researchers found that gene expression in specimens injected with PEG-POD was 215 times more effective than two other carriers tested.

Ref: www.mdsupport.org/library/PEG-POD.html

Envisioning A Cure For AMD (by Rick Trevino, OD)

I woul like to quote from an article by Dr. Rick Travino, who is active in our online community and who hosts one of the most informative web sites about vision research and developments. In his commentary, “Envisioning A Cure For AMD,” he wrote:

“One of the most exciting developments in the field of AMD research has been the discovery of a relatively small number of genes that seems to control a large amount of the risk of developing the disease.

“Most of the genes that are known to influence the risk of developing AMD involve various components of the complement cascade. Most prominent among these is complement factor H (CFH); however, variants in genes coding for other components of the complement system have also been discovered and shown to be associated with AMD risk and protection. The complement system is very important in regulating the body's immune system and directing inflammatory processes. Several lines of evidence suggest that dysregulation of inflammation plays a key role in the development of AMD.

“Now, thanks to these discoveries, we are beginning to see treatments that are specifically tailored to address abnormalities in the complement system. This raises the very real possibility of a truly preventative treatment, or even a cure, for the disease. . . Many . . complement pathway-modulating compounds are currently being considered for, and/or are under, preclinical development for possible use in AMD.

“One could imagine a day when persons are screened at an early age to determine whether they harbor the genes that will ultimately lead them to develop AMD later in life. Then, based upon their specific genetic make-up, persons could take medications, or perhaps undergo gene therapy, that will prevent AMD from ever occurring. In this scenario, the eradication of AMD is a real possibility.”

Thank you, Dr. Trevino for reinforcing our hope for the future.

Ref: www.myvisiontest.com

GOOD NEWS

Incidence of AMD Declining

And finally, to continue on a positive note, I reported last year that a recent study found a lower 5-year incidence of early AMD in patients born or examined more recently, compared to similarly aged persons born or examined in an earlier period. That study included 2,968 participants with early AMD and 3,588 participants with late stage AMD, all of whom were examined at 5-year intervals between 1988 and 2005 as part of the Beaver Dam Eye Study.

Now we have more good news along those same lines. A new study reported this year has shown a 68% lower incidence of macular degeneration in the Baby Boom population. The research suggests that improvements in environment, behaviors, and other such modifiable factors may have contributed to the results. The "birth cohort" effect remained even after adjusting for AMD risk factors such as obesity, heavy drinking, and sunlight exposure.

More study is necessary as the younger population continues to age, but the results further emphasize the importance of environmental and lifestyle factors to retinal health.

Source: Karen J. Cruickshanks, MD (University of Wisconsin School of Medicine and Public Health in Madison) and reported at the Association for Research in Vision and Ophthalmology (AAO) 2010.

Conclusion

One of the worst aspects of living with macular degeneration is that there is little we can do about our inevitable loss of vision. To alleviate some of the frustration that causes, we want to leave no stone unturned in our daily battle to maintain our healthiest eyesight.

I hope our news updates and annual summaries are serving that purpose by providing you with some comfort in knowing about all the good research being done. With this kind of information in hand, we no longer have to say, “Why didn’t someone tell me?”

Now, please accept the challenge of passing this information along. Educating others is one of the best ways to keep from being victimized by this disease, and your help is greatly appreciated!