Ophthalmology™ ROUNDS

FEBRUARY 2004
Volume 2, Issue 2

AS PRESENTED IN THE ROUNDS OF THE DEPARTMENT OF OPHTHALMOLOGY AND VISION SCIENCES, FACULTY OF MEDICINE, UNIVERSITY OF TORONTO

Age-related Macular Degeneration

By Michael H. Brent, M.D.

Age-related macular degeneration (AMD) is the leading cause of irreversible severe vision loss in North America and developed countries throughout the world.[1] AMD patients, 55 years of age and older, often present to the office with a variety of visual symptoms. A targeted diagnostic approach can help determine and stage the disease process. Results from recent clinical trials and emerging technology are changing the way AMD is managed.

Classification

AMD is the leading cause of blindness in the population aged ≥55 years. The risk of developing some form of AMD increases with age and, by age 75, the risk approaches 40%. AMD is classified into two clinical entities: atrophic (dry) and exudative (wet).

Atrophic AMD

Atrophic AMD comprises approximately 85% of all patients suffering from AMD and is responsible for 10%-20% of cases of blindness caused by this disease (Figure 1). Vision loss tends to be gradual and the amount of vision loss is determined by the number, size, morphology, and location of drusen in the macula, as well as the amount and location of associated retinal pigment epithelium (RPE) atrophy. Drusen size can be categorized as small (<63 µm), intermediate (63 µm-124 µm), or large (≥125 µm).[2] Small, hard drusen are at low risk of progression to advanced AMD, especially when in low numbers (eg, <5). Intermediate and large drusen, and confluent drusen are signs of more advanced AMD that could progress to exudative AMD. Pigmentary clumping is often associated with drusen. Non-central geographic RPE atrophy is an indicator of more advanced atrophic AMD. Maculae with at least one large druse and/or extensive intermediate drusen are more likely to develop RPE atrophy. In patients with advanced atrophic AMD, up to 43% of eyes progress to exudative AMD within 5 years.

Exudative AMD

Exudative AMD comprises approximately 15% of all patients suffering from AMD, yet is responsible for 80%-90% of cases of blindness caused by this disease (Figure 2). Vision loss tends to be rapid – over days to months – and is determined by the amount of subretinal and intraretinal blood, lipid, and fluid, as well as resultant submacular scarring. The conventionally accepted pathophysiology involves proliferation of abnormal new blood vessels in the choroid that leads to the development of a choroidal neovascular membrane (CNVM). This penetrates through Bruch's membrane into the sub-RPE and subretinal space. Exudation, hemorrhage, and fibrovascular scarring damage and destroy paramacular photoreceptors, resulting in severe central visual loss.

More recently, Yannuzzi et al described an alternate pathophysiologic process called retinal angiomatous proliferation (RAP) that can also result in severe central vision loss and is included in the exudative AMD category.[3] In RAP, capillary proliferation begins in the paramacular region within the deep capillary plexus of the retina. Neovascular proliferation proceeds both anteriorly and posteriorly. Posterior proliferation eventually invades the subretinal space and a subretinal neovascular membrane and a serous RPE detachment is formed. Further proliferation causes vessels to invade the choroid to form a CNVM. Vessels proliferating anteriorly form an anastomosis with the retinal circulation. Thus, a chorioretinal anastomosis is formed. The end result appears clinically and angiographically similar to, and is often indistinguishable from, AMD where neovascularization begins in the choroid rather than the retina. The two entities may respond differently to available treatment modalities at different stages of their development.

FACULTY OF MEDICINE
University of Toronto

Department of Ophthalmology and Vision Sciences

Department of Ophthalmology and Vision Sciences, Faculty of Medicine, University of Toronto,
60 Murray St.
Suite 1-003
Toronto, ON M5G 1X5

The editorial content of *Ophthalmology Rounds* is determined solely by the Department of Ophthalmology and Vision Sciences, Faculty of Medicine, University of Toronto

Figure 1: Atrophic AMD

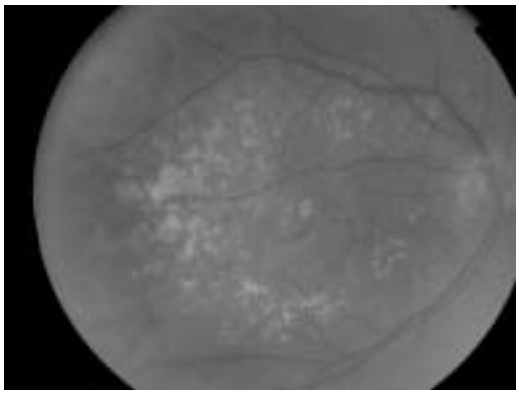
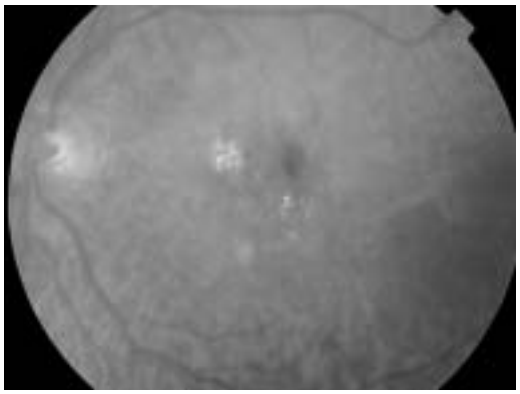


Figure 2: Exudative AMD



AMD = Age-related macular degeneration

Clinical presentation

Patients, aged ≥55 years, presenting with blurred or distorted vision, should be suspected of having AMD. Other symptoms may include difficulty reading or difficulty with vision under conditions of limited illumination. There may be long periods of stable vision interspersed with shorter periods of further deterioration. When assessing patients for possible AMD, the history should elicit the age of onset, duration of symptoms, location of distortion/paracentral scotomata, and degree of contrast sensitivity loss. Risk factors for AMD should be reviewed, including age, race, gender, light iris colour, family history, coronary artery disease, hypertension, history of smoking, poor diet, and prolonged ultraviolet light exposure. Races with lightly pigmented skin are at a higher risk of developing exudative AMD, females have twice the risk for its development over their male counterparts, and smokers are at 6 times the risk. Patients should be asked about medications that could have an adverse effect on macular function (eg, chloroquine derivatives, phenothiazines, and tuberculosis medications).

The ocular examination

The ocular exam should establish the presence of decreased vision and rule-out a refractive error as the underlying cause, either by refraction or pinhole visual acuity.

- Amsler Grid testing should be performed for all AMD assessments as it is simple to perform and, if positive, can help direct attention to a specific area during the biomicroscopic examination.
- If there is significant lenticular opacity present, macular function testing with laser interferometry or a potential acuity meter may help determine how much vision loss is secondary to cataract versus macular pathology.
- A visual field assessment is recommended to rule-out concomitant peripheral visual field loss or neurological causes for central vision loss.
- If available, Pelli Robson contrast sensitivity charts are quick and reliable for evaluating and following visual function in AMD.
- Examination of the macula should be performed using biomicroscopy with a biconvex indirect (60-90 D) or a Hruby lens. Although the image is inverted, good stereopsis is achieved. During macular biomicroscopy, the size, location, and morphology of drusen should be noted. Pigmentary clumping and areas of geographic RPE atrophy should also be noted since they may be indicators of more advanced atrophic AMD. Subretinal blood, lipid, or fluid are suspicious signs for the presence of a CNVM.
- Direct ophthalmoscopy fails to provide stereopsis and is inadequate to properly assess the macula in AMD.
- The best optical view of the macula can be achieved with a macular contact lens. This, however, requires topical anaesthesia and viscous fluid to eliminate the air-cornea interface. The viscous fluid can interfere with the quality of photography/angiography if these are to be performed shortly after examination.

Patients with acutely decreased vision, Amsler grid distortion, and clinically evident subretinal blood, lipid, or fluid require an urgent referral to a retina specialist with fluorescein angiographic capabilities. The algorithm for determining the best course of action to reduce vision loss in a patient with CNVM is based on interpretation of fluorescein angiography. It can determine whether the patient might benefit from thermal laser, photodynamic therapy with Visudyne® or simply followed with periodic observation.

Natural history

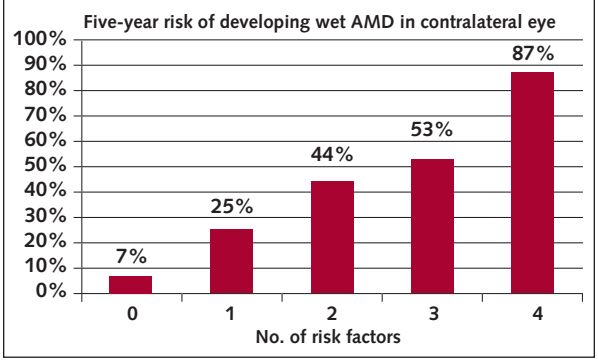
In the natural history of AMD, several factors are associated with the progression of atrophic to exudative AMD (Table 1). Eyes with large and/or extensive intermediate drusen or non-central geographic atrophy are most likely to progress to CNVM. If one eye has already developed subfoveal CNVM, there are major prognostic factors for vision loss in the fellow eye, secondary to the development of a CNVM. These factors are based on the type of late AMD documented in the first eye and include >5 drusen, large soft drusen, pigment clumping, and systemic hypertension. As the number of risk factors increase, the risk of developing exudative AMD in the fellow eye approaches 90% (Figure 3).[4]

Table 1: Progression of atrophic AMD to exudative AMD

Composition and number of drusen in dry AMD are factors associated with a greater risk of progression to wet AMD:

- Eyes with bilateral drusen
- Soft drusen, with poorly defined, non-discrete borders
- Numerous (>20) soft drusen associated with RPE pigment change
- Five or more large drusen (>63 µm)
- Focal hyperpigmentation of the RPE
- Pigmentary abnormalities including clumping
- Patients with geographic atrophy (late-stage dry AMD)

Figure 3: Progression to exudative AMD in second eye[4]



Age-related eye disease study

The Age Related Eye Disease Study (AREDS) examined the role of micronutrient supplementation in altering the natural history of atrophic AMD.[5] It demonstrated the effectiveness of high-dose antioxidants and minerals in reducing the risk of progression of intermediate and unilateral advanced AMD by 25% and moderate vision loss (≥3 lines) by 19% at 5 years. Patients with no AMD or only early AMD did not derive any benefit. The study formulation consisted of 500 mg vitamin C, 400 IU vitamin E, 25,000 IU beta-carotene, 80 mg zinc oxide, and 2 mg cupric oxide.

The AREDS Update II examined risk factors for AMD and the role of dietary lipids in the pathogenesis of AMD.[6] It reported that higher intakes of the dietary lipids omega-3 long-chain polyunsaturated fatty acids (LCPUFA)/fish and lutein/zeaxanthin were associated with a decreased risk of developing neovascular AMD. Seddon et al found that higher total fat intake increased the risk of progression to advanced forms of AMD.[7] Higher intake of vegetable fat and, to a lesser extent, animal fat increased rates of progression. Processed baked goods, in particular, were found to produce a higher rate of progression, while nuts demonstrated a protective effect. Therefore, modification of fat intake could potentially alter the course of disease in patients with early and intermediate forms of AMD.

Diagnostic evaluation

The following tests are valuable in determining and staging the presence of AMD.

Amsler Grid

Amsler Grid testing is an excellent monocular macular function test to determine the presence of macular pathology. Each 5 mm square on the grid subtends a visual angle of 1° when the chart is held at 30 cm. Therefore, the entire chart tests 10° on either side of fixation, in both horizontal and vertical meridians. Amsler Grid testing should be performed prior to pupil dilation and applanation tonometry. With their reading glasses on, patients should be asked to cover one eye and concentrate on the central dot on the grid. If all lines are visible without distortion and all boxes are observed to be present, then the testing result is considered to be normal and the fellow eye is tested. If the patient notices distortion, blurring, or paracentral scotomata, these should be recorded on the grid and stored in the chart. They may be useful for future comparison, to document progression or regression of disease.

Fluorescein angiography

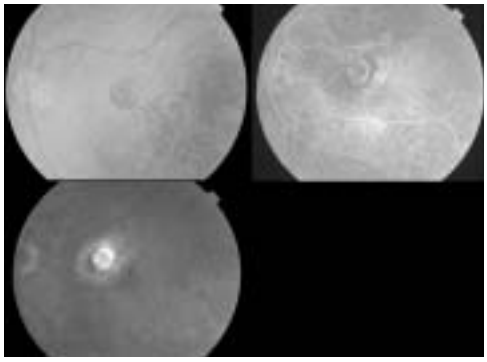
Fluorescein angiography is currently the gold standard for assessing retinal and choroidal circulation in AMD. After performing colour fundus photographs, sodium fluorescein dye is injected intravenously. The dye is excited by light from the camera flash passing through a blue excitatory filter. The 490 nm wavelength of the blue light is absorbed by the fluorescein molecules in the choroidal circulation and then the retinal circulation. The dye is stimulated to emit a yellow-green light (530 nm) and this passes back to the camera through a yellow-green barrier filter, blocking reflected blue light, allowing the fluorescence to be photographed. Photographs are taken as the dye transits through the choroidal and retinal circulation. Drusen may fluoresce, RPE atrophy is demonstrated as window defects, and choroidal neovascularization leaks dye and hyperfluoresces. Choroidal neovascularization is interpreted and classified by its leakage pattern.[8] Classic CNV is seen as an area of bright, well-demarcated hyperfluoresence identified in the early phase of the angiogram, with progressive dye leakage into the overlying subretinal space in the late phase of the angiogram (Figure 4).

Occult lesions can have 2 angiographic patterns:

- Fibrovascular retinal pigment epithelial detachment (RPED) demonstrates a speckled hyperfluoresence that is not as bright or discrete as classic CNV, 1-2 minutes after fluorescein injection, with persistent staining or leakage of fluorescein dye within 10 minutes of injection.
- The second pattern is that of late leakage from an undetermined source. This occurs only in the late phase of the angiogram, without evidence of classic CNV or fibrovascular RPED in the early or mid-phase of the angiogram to account for the leakage (Figure 5).

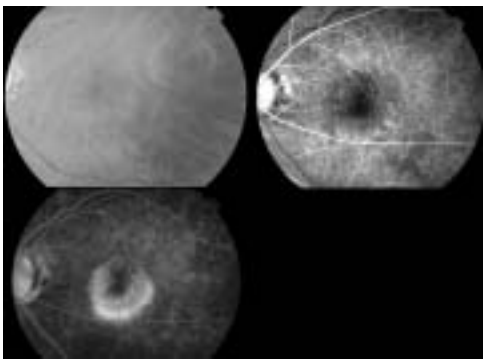
Until recently, most fundus photographs and fluorescein angiography were recorded on film. With advances in technology, digital capture and storage of images has

Figure 4: Predominantly classic subfoveal CVNM in AMD



CVNM = choroidal neovascular membrane

Figure 5: Occult CNVM in AMD



become popular. Instantaneous results are provided and lesions can be more accurately measured for size. Components of CNV lesions can be quantitatively assessed for suitability for treatment.[9] Digital images are easily stored inexpensively and the digital process is conducive to building databases to aid in research.

Indocyanine green

Indocyanine green (ICG) angiography is an important diagnostic adjunct in the evaluation of CNVM in AMD. ICG is a tricarbocyanine dye that absorbs light at 790-805 nm and has a peak emission at 835 nm, which is in the infrared spectrum. It is injected intravenously, and digital infrared video-angiography is used to photograph the retinal and choroidal vasculature. ICG is 95% plasma bound and therefore, remains largely intravascular, facilitating visualization of the choroidal vasculature. ICG can be visualized through thin blood, serous fluid, and pigment. ICG, in conjunction with fluorescein angiography, can better delineate the full extent of a lesion in patients with occult or minimally classic CNVM. This translates into better treatment success and reduced rates of retreatment. ICG is safe for general use and is less toxic than sodium fluorescein. It contains approximately 5% iodine by weight and is removed by the liver. ICG is therefore contraindicated for patients with iodine or shellfish allergies or significant liver disease.

Optical coherence tomography

Optical coherence tomography (OCT) is a technology similar to ultrasound, but it uses light waves rather than sound waves to produce high-resolution cross-sectional images of the posterior pole. This non-invasive technology enables micron-scale imaging of tissue microstructure *in situ* and in real time. The Stratus OCT3 from Zeiss Humphrey is a 3rd generation model with 7-8 µm axial resolution. False colour is added to tissues with different optical scattering properties enhancing image quality. Ultrahigh resolution OCT has been developed, but is not yet commercially available. It provides axial resolution as fine as 1-2 µm. The OCT is a useful tool for diagnosing macular pathology and monitoring treatment success; it is capable of measuring retinal thickness and can image intraretinal fluid (CME) and subretinal fluid (blood, serous fluid, CNVM). It is also excellent for demonstrating traction on the macula (epiretinal membranes), vitreomacular traction, and macular hole formation. Once treatment has been initiated, OCT is extremely useful to monitor and quantify post-operative response and assist in re-treatment decisions. It is quickly becoming an important diagnostic tool in the assessment and management of AMD.

Clinical management

Atrophic AMD

After clinical examination, patients deemed to have atrophic AMD and a normal Amsler Grid usually do not require fluorescein angiography. They should be given an Amsler Grid to monitor at home, on a daily basis. They should be reminded to wear their reading correction and to perform the test under consistent lighting conditions. Patients should be counselled to call the office if they notice a significant change in their grid lasting ≥3 days. Urgent reassessment should be provided and, if exudative AMD is suspected, urgent referral to a retina specialist is warranted. Patients should be counselled to eat a diet rich in vegetables and to increase their fish intake to 1-2 servings per week. Reducing dietary fat intake may also be helpful.

Non-smoking patients with extensive intermediate drusen (63-124 µm), at least 1 large druse (≥125 µm), non-central geographic atrophy in one or both eyes, or advanced AMD or vision loss due to AMD in one eye, may benefit from micronutrient supplementation as reported in AREDS. Currently, there are 2 commercially available preparations in Canada that match the AREDS study dosage. Vitalux® AREDS by Novartis Ophthalmics, requires 2 pills per day to match study dosage; it also contains lutein and

zeaxanthein. Ocuvite PreserVision® by Bausch & Lomb, requires 4 pills per day to match study dosage and does not contain lutein and zeaxanthein. Smokers are at a higher risk of developing lung cancer if they take beta-carotene. They should be informed about this and should stop smoking, if possible. There is no consensus about how long a smoker must stop smoking prior to safely taking beta-carotene. Some smokers with AMD may wish to take the AREDS formula without the beta-carotene component. This is commercially available as Vitalux-S®, by Novartis Ophthalmics, 2 pills per day. Patients with AMD may also benefit from ultraviolet protection by wearing wrap-around sunglasses whenever outdoors in daylight.

Exudative AMD

Patients suspected of having exudative AMD require further investigation. Fluorescein angiography is currently the diagnostic test of choice for assessing exudative AMD as it provides information regarding the location, composition, and extent of the lesion. CNVMs that are well-demarcated and extrafoveal or juxtafoveal in location benefit from thermal laser as opposed to having no treatment.[11] Lesions that are poorly demarcated do not generally benefit from thermal laser. CNVMs that are subfoveal in location may benefit from photodynamic therapy (PDT) with Visudyne®, depending on baseline visual acuity, lesion composition, and size.

The Treatment of Age-Related Macular Degeneration with Photodymanic Therapy (TAP) study demonstrated a statistically significant beneficial effect of PDT with Visudyne versus placebo for subfoveal lesions that are predominantly classic, with baseline visual acuity 20/40 to 20/200.[12] The Verteporfin in Photodynamic Therapy (VIP) trial demonstrated a clinically significant treatment benefit of PDT with Visudyne on visual function for patients who had occult without classic subfoveal CNVM, and a demonstrated recent progression of disease.[13] Eyes with baseline visual acuity ≤20/50 and lesion size ≤4 disc areas had the best results. There was no statistically significant treatment benefit of PDT with Visudyne demonstrated for eyes with minimally classic subfoveal CNVM. For predominantly classic lesions, or occult with no classic lesions that are juxtafoveal, photodynamic therapy with Visudyne should be considered when the lesion is so close to the foveal center that conventional thermal laser photocoagulation would likely extend under the center of the foveal avascular zone.[14]

However, more recently, a multiple linear regression analysis of data from TAP and VIP trials found that lesion size was a more significant factor affecting treatment benefit than either lesion composition or baseline visual acuity.[15] Patients with smaller lesions (≤4 disc areas) were found to lose less vision and a similar treatment benefit was found regardless of whether the lesion was predominantly classic, minimally classic, or occult with no classic.[15]

Currently, provincial health plans cover the cost of treating patients with predominantly classic CNVM secondary to AMD, with the exception of Prince Edward Island and Newfoundland. British Columbia and Quebec health plans cover the treatment of all types of CNVM, at the discretion of the treating ophthalmologist. In all other provinces, patients with minimally classic or occult lesions without classic subfoveal CNVM secondary to AMD, who wish treatment, must pay for off-label use of PDT with Visudyne. This is expensive and requires an average of 4-6 therapy sessions to close the CNVM. Patients need to be informed that the treatment goal is vision stabilization, although some patients do notice modest visual improvement at endpoint. Over the course of repeat PDT, lesions that initially present as minimally classic, or occult with no classic, may convert to become predominantly classic in nature. Unfortunately, the decision of provincial health plans to cover the cost of PDT is based on the initial fluorescein angiographic presentation.

Investigational treatments

There are several new treatment options for AMD that are in various stages of clinical trials.

- Rheopheresis for atrophic AMD is currently in Phase III clinical trials. This process filters out macromolecules (eg, macroglobulin, fibrinogen, LDL-cholesterol complexes, and IgA) that are thought to have deleterious effects on microvascular circulation, leading to the atrophic, degenerative process.
- The Transpupilary Thermal Therapy for occult CNVM in AMD (TTT4CNV) trial is complete, but results have yet to be released. TTT uses 810 nm diode infrared laser to treat subfoveal CNVM. Treatment protocol involves using a low irradiance, long exposure duration, and large spot size to gradually raise the temperature of blood vessels in the choroid. The goal is to close the CNVM without causing thermal damage to the overlying retina.[16]
- Vascular endothelial growth factor (VEGF) is a protein that stimulates vascular permeability and angiogenesis. High levels of VEGF have been found in diseases such as AMD, in which active blood vessel formation is evident. Inhibition of VEGF is an approach to treating these diseases. Anti-VEGF therapy for subfoveal CNVM, involving a series of intravitreal injections, is a very exciting area of research that should yield trial results over the next few years.
- Anecortave Acetate is currently in clinical trials and involves placing a posterior juxtascleral injection onto the posterior scleral surface. Its action is to inhibit blood vessel growth by inhibiting the proteases necessary for vascular endothelial cell migration.
- The Submacular Surgery Trials (SST) are evaluating the benefit of surgical removal of subfoveal CNVM in AMD. Enrollment was completed in 2001, follow-up was completed in September 2003, and the results should be published soon.
- Macular translocation is a surgical approach to treat patients with subfoveal CNVM secondary to

AMD. This procedure involves detaching the retina and rotating it in order to move the macula to a new location where the RPE is healthier. The CNVM, no longer subfoveal in location, is therefore amenable to thermal laser photocoagulation.

• Finally, there are trials underway for visual prostheses for visual rehabilitation, including the implantable miniaturized telescope (IMT) and artificial vision provided by epiretinal and subretinal microchips.

In conclusion, new approaches to AMD and rapidly evolving technology are changing the way AMD is assessed and managed. Exciting new treatment modalities will help us to meet the challenge of this devastating disease and improve the quality of life for our patients with AMD.

***Michael H. Brent, MD, FRCSC**, is Assistant Professor of Ophthalmology and Vision Sciences, University of Toronto, and a staff Ophthalmologist at Mount Sinai Hospital, Toronto and William Osler Health Centre, Brampton Campus.*

References

1. National Advisory Eye Council. Vision Research- A National Plan: 1999-2003, Vol 1. *A report of the National Advisory Eye Council*. Bethesda, Md: National Institute of Health; 1999. NIH publication 98-4120.
2. The Age-Related Eye Disease Study Research Group. *The Age-Related Eye Disease Study (AREDS): Design Implications*. AREDS Report No. 1. *Control Clin Trials* 1999; 20:573-600.
3. Yannuzzi LA, Negrao S, Iida T, et al. Retinal angiomatous proliferation in age-related macular degeneration. *Retina* 2001;21:416-434.
4. Klein R, Klein BEK, Linton KLP. Prevalence of age-related maculopathy. *Ophthalmology* 1992;99:933-943.
5. The Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta-carotene, and zinc for age-related macular degeneration and vision loss. AREDS Report No. 8. *Arch Ophthalmol* 2001;119:1417-1436.
6. Chew E. The Retina Debates 2003. New Technology and Controversies from the Posterior Segment. A presentation at the American Academy of Ophthalmology, Anaheim, California; November 14-15, 2003.
7. Seddon JM, Cote J, Rosner B. Progression of age–related macular degeneration. Association with dietary fat, transunsaturated fat, nuts, and fish intake. *Arch Ophthalmol* 2003;121:1728-1737.
8. Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin. One-year results of 2 randomized clinical trials – TAP Report no.1. *Arch Ophthalmol* 1999;117:1329-1345.
9. Brent MH. Fluorescein angiography interpretation and quantitative assessment of lesion area. A presentation at the PDT Users Meeting, Mt. Tremblant, Quebec; May 26, 2001.
10. The alpha-tocopherol, beta-carotene cancer prevention study group. The effect of vitamin E and beta-carotene on the incidence of lung cancer and other concerns in male smokers. *N Engl J Med* 1994;330:1029-1035.
11. Macular Photocoagulation Study Group. Argon laser photocoagulation for neovascular maculopathy: five year results from randomized clinical trials. *Arch Ophthalmol* 1991;109:1109-1114.
12. Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: two-year results of 2 randomized clinical trials: TAP Report no. 2. *Arch Ophthalmol* 2001;119:198-207.
13. Verteporfin in Photodynamic Therapy (VIP) Study Group. Verteporfin therapy of subfoveal choroidal neovascularization in age-related macular degeneration: two year results from a randomized clinical trial including lesions with occult with no classic choroidal neovascularization: Verteporfin in Photodynamic Therapy Report no. 2. *Am J Ophthalmol* 2001;131:541-560.
14. Verteporfin Roundtable 2000 and 2001 participants, Treatment of Age-related macular degeneration with Photodynamic therapy (TAP) Study Group Principal Investigators, and Verteporfin In Photodynamic therapy (VIP) Study Group Principal Investigators. Guidelines for using verteporfin (Visudyne®) in photodynamic therapy to treat choroidal neovascularization due to age-related macular degeneration and other causes. *Retina* 2002;22:6-18.
15. Treatment of Age-Related Macular Degeneration with Photodynamic Therapy and Verteporfin in Photodynamic Therapy Study Groups. Effect of lesion size, visual acuity, and lesion composition on visual acuity change with and without verteporfin therapy for choroidal neovascularization secondary to age-related macular degeneration: TAP and VIP Report no. 1. *Am J Ophthalmol* 2003;136:407-418.
16. Mainster M A, Reichel E. Transpupillary thermotherapy for age-related macular degeneration: Principles and techniques. *Semin Ophthalmology* 2001;16(2): 055-059.

Upcoming Scientific Meeting

4-5 June 2004
Age-related Macular Degeneration Update 2004
Baltimore, Maryland
CONTACT: Tel.: 410-955-5880
Email: cmenet@jhmi.edu

Upcoming Department Events

April 2, 2004
Jack Crawford Day Hospital for Sick Children
Contact: Karen Martin 416-813-8942 or karen.martin@sickkids.ca

April 22, 2004
VPP – Dr. Donald Fletcher, Birmingham, Alabama
Advances in Low Vision Rehabilitation

Aprill 29, 2004
VPP – Dr. Douglas Coster, Australia
Cornea

May 6, 2004
VPP – Dr. Kathleen Digre, Salt Lake City, Utah
Neuro-ophthalmic changes in pregnancy

May 13, 2004
VPP – Dr. Shaun Singer, Toronto, ON
Quality Assurance Rounds

May 20, 2004
VPP – Dr. David Apple, Charleston, North Carolina
U of T & TOS combined Rounds

Note: Visiting Professors Programme (VPP) site address: Toronto Western Hospital, West Wing, Room 401, 399 Bathurst Street, Toronto.

Change of address notices and requests for subscriptions for *Ophthalmology Rounds* are to be sent by mail to P.O. Box 310, Station H, Montreal, Quebec H3G 2K8 or by fax to (514) 932-5114 or by e-mail to info@snellmedical.com. Please reference *Ophthalmology Rounds* in your correspondence. Undeliverable copies are to be sent to the address above. Publications Post #40032303

This publication is made possible by an unrestricted educational grant from

Novartis Ophthalmics