

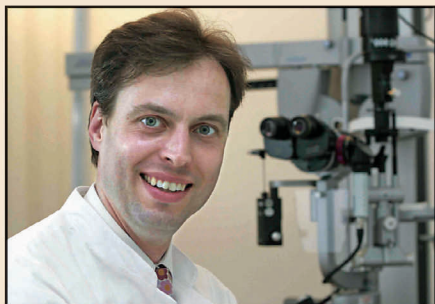
RetinaReview

A newsletter from the Wilmer Eye Institute at Johns Hopkins

SPRING 2011



Welcome Hendrik Scholl, M.D.



Following an international search, the Wilmer Eye Institute is pleased to welcome Hendrik Scholl, M.D. to the Retina Division Faculty. In the Spring of 2010, Scholl joined the faculty to serve as the first ever vitreoretinal surgeon dedicated primarily to clinical care, research, and education in inherited retinal degenerations at Wilmer. He also oversees the Division's Visual Neurophysiology Service providing state-of-the-art procedures in the management of retinal degenerations.

Scholl comes to Wilmer from the University of Bonn in Germany where he served as a lecturer, surgeon, and retina specialist. His research focuses on using the latest imaging technology to determine how the structure and function correlate in genetic retinal degenerations.

The Wilmer Eye Institute is excited to have Scholl as a part of their team. "With Dr. Scholl on board, we hope to be the premier site for initiating early and definitive clinical trials in retinal degenerations that will change how we treat patients with these conditions previously not relegated such a high priority for research around the world," says Neil Bressler, M.D., Chief of the Retina Division and The James P. Gills Professor of Ophthalmology. One of our first goals in securing this position is to identify a source of funding for an endowed professorship for Dr. Scholl's position to insure that this research will continue unabated well into the future. ◦

Progression of AMD After Cataract Surgery

A recent study conducted at the Wilmer Eye Institute by Drs. Susan Bressler, Sharon Solomon, Walter Stark, and Neil Bressler has contradicted previous reports that treating one cause of vision loss will worsen another eye problem. Cataract is the leading cause of blindness worldwide and the wet (neovascular) form of age-related macular degeneration (AMD), left untreated, is the leading cause of irreversible blindness among Americans age 65 and older. Surgery is the most effective and common vision-restoring treatment for cataracts. Since both conditions are strongly age-related, many individuals with cataract also have AMD.

In the past, many clinicians have argued that undergoing cataract surgery could negatively affect eyes with AMD. Many have even questioned whether cataract surgery increases the risk of progression to neovascular AMD.

A study funded by the Jack Valenti Research Fund at the Wilmer Retina Division studied eyes of 108 individuals with AMD who underwent pre-operative assessments for cataract surgery in collaboration with the Anterior Segment Service of the Wilmer Eye Institute between 2000 and 2002. Photographs of the retina were taken and fluorescein angiography, which uses a special dye (not an x-ray) to investigate blood vessels in the eye, was performed. A total of 86 evaluated eyes had AMD but no evidence of the wet form before surgery, and 71 had follow-up assessments between one week and one year after surgery.

The wet form of AMD was observed in nine (13%) of these 71 eyes at one or more follow-up assessments by one year. However, 5 of these cases were "uncovered" at one week, suggesting that only three eyes, or less than 5% truly developed wet AMD between 1 week and 1 year after cataract surgery. The rate of progression to wet AMD, thus, seemed similar to what would have been expected without cataract surgery.

These findings suggest that previous reports of the association or progression of AMD without the wet form to the wet form AMD after cataract surgery could be biased due to failure to recognize the wet form immediately before surgery. Subtle signs of the wet form of AMD or even extensive atrophy or loss of retina tissue from AMD (often termed an advanced dry form) may be obscured by cataract just prior to cataract surgery. In such cases, uncovering pre-existing wet form or advanced dry form after cataract surgery may be ascribed erroneously to the false belief that the cataract surgery somehow contributed to the progression, leading to withholding surgery in subsequent patients unnecessarily for falsely placed fear that the cataract surgery causes progression of AMD and additional vision loss. The discoveries made possible by generous contributors to the Jack Valenti Research Fund may allow people with AMD and cataract to proceed with cataract surgery with less fear and potentially lead to more people with both conditions able to benefit from cataract surgery. ◦

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Results Aid in Treatment of Diabetic Retinopathy

The national, multi-center READ-2 Study (Ranibizumab for Edema of the macula in Diabetes), funded in part by the Juvenile Diabetes Research Foundation (JDRF), has shown that a drug treatment for diabetic macular edema (DME, a condition characterized by swelling of the central portion of the retina, or macula, at the back of the eye) may be superior to the current standard treatment using laser surgery. This study was coordinated at the Wilmer Eye Institute and led by investigators in the Retina Division, Drs. Quan Dong Nguyen, Diana Do, and Peter Campochiaro.

The READ-2 Study showed that eyes treated with ranibizumab, a drug that blocks vascular endothelial growth factor (VEGF), gained more letters of visual acuity compared to eyes treated with laser over a six month study period. In addition, approximately 25% of the patients treated with ranibizumab gained 15 or more letters of visual acuity at six months.

VEGF is abnormally elevated in eyes with diabetic retinopathy and DME; therefore, blocking the effects of VEGF with a drug such as ranibizumab may be beneficial. The READ-2 Study results have the potential to alter the treatment regimen for DME, a leading cause of vision loss in the working-age population. The READ-2 Study was designed in 2006 to evaluate the long-term safety and potential effectiveness of injections of the drug ranibizumab (Lucentis, Genentech) in patients with DME.

The Diabetic Retinopathy Clinical Research Network (DRCR.net., see p.3) recently published a report definitively determining that ranibizumab should be considered in the management of diabetic macular edema. The advances made by this trial also were cited by the U.S. Senate Appropriations Committee in 2010 as justification, in part, for a requested

increase in funding to the National Eye Institute (NEI):

The Committee recognizes the NEI's leadership in conducting several comparative effectiveness clinical trials to improve ophthalmic care, including the Diabetic Retinopathy Clinical Research Network's comparison of drug therapies as an alternative to laser treatment for diabetic macular edema and proliferative diabetic retinopathy.

In a statement released by Jeffrey Brewer, JDRF President and CEO, the DRCR.net results were cited as an example of "tangible scientific and clinical results" that aided in Congress's passage of a \$300 million renewal of the Special Diabetes Program:

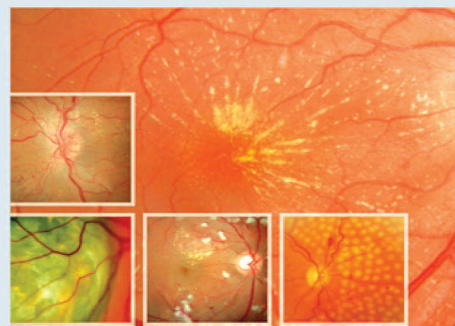
The pivotal data showed that after one year, nearly half of patients in the trial treated with drug and laser therapy improved their vision by at least two lines on a standard eye chart, ... this is really good news for those with diabetes and for the productivity of our workforce as a whole.

As ranibizumab at the standard dose has demonstrated superior efficacy in eyes with DME involving the center of the retina with some vision impairment (as well as wet age-related macular degeneration), it is hypothesized that a higher dose of ranibizumab may be more helpful. Thus, under the leadership of Drs. Nguyen, Campochiaro, and Do, the Wilmer Eye Institute, again in major collaboration with JDRF, is leading another multi-center, national trial, the READ-3 Study (www.read3.net), to evaluate various doses of ranibizumab for DME. The READ-3 Study has begun and is expected to provide informative results that may help the many patients who suffer from this devastating diabetic eye disease. ◊

The Retina in Systemic Disease

A Color Manual of Ophthalmoscopy

Homayoun Tabandeh, MD
Morton F. Goldberg, MD



Thieme

Dr. Goldberg's Picture Perfect Diagnoses

Former Wilmer Director Morton F. Goldberg, M.D. and former Wilmer resident, Homayoun Tebandeh, joined together to write a book titled: *The Retina in Systemic Disease: A Color Manual of Ophthalmoscopy*. Published in December 2009, this book is intended to be a quick reference guide for residents as well as practicing physicians of all specialties to aid them in making general systemic diagnoses (of a general disease) simply by looking at the inside of the eye with an ophthalmoscope. The 339 full-color illustrations and detailed index make it easy for physicians to make a diagnosis without invasive injections or lab tests.

"No injections, no lab tests. You can make a diagnosis on the spot," says Goldberg.

What is the Diabetic Retinopathy Clinical Research Network?

The Diabetic Retinopathy Clinical Research Network (DRCR.net) is a National Eye Institute (NEI) sponsored collaboration which involves over a thousand community and academic-based investigators who are working together to find treatments for diabetic retinopathy. Diabetic retinopathy is one of the leading and growing causes of vision impairment and blindness in the world.

The results of this collaboration are groundbreaking. They discovered that intravitreal steroids for diabetic macular edema was not superior to laser treatment and that one sitting of laser for the bleeding complications of diabetic retinopathy appears as safe as multiple sittings. New treatment studies planned through at least 2013, including definitive results which will determine whether ranibizumab is superior to laser treatment and should be considered in the management of diabetic macular edema.

In the summer of 2009, the DRCR Network was recognized by the United States House of Representatives in House Resolution 366 and the United States Senate in Senate Resolution 209 for its series of trials which have contributed to the NEI's overall savings of approximately \$1.6 billion each year in blindness and vision impairment disability costs.

The clinical site at Wilmer for the DRCR Network is overseen by Dr. Sharon Solomon as Principal Investigator. Drs. Diana Do and Adrienne Scott also participate actively. Johns Hopkins University also receives the Operations Center grant from the NEI to support Dr. Neil Bressler as the DRCR Network Chair (see www.drcr.net for further public information) while Dr. Susan Bressler is one of three Vice Chairs for the Network. "It is our hope that through this collaborative effort, we will more quickly get to the bottom of this blinding eye disease by discovering and testing innovative treatments," says Neil Bressler. ◦

Evidence that Cigarette Smoke Can Trigger AMD

With over three million people expected to develop advanced Age-Related Macular Degeneration (AMD) by 2020, Dr. James Handa and his team of researchers at the Wilmer Eye Institute are dedicating their time and energy to get to the bottom of this disease. It has long been believed that smoking has been a factor causing AMD, and Handa's research is designed to provide scientific results to further understand this connection.

Initial results, made possible by the generous support of Ken and Jo Merlau and other private philanthropists, have shown evidence that cigarette smoke can trigger AMD. Due to the success of this initial study, Handa and his team were awarded a National Institutes of Health (NIH) grant to further this research. Their proposal was the number one ranked grant in the application pool to the NIH. Handa's team was also recently awarded a Thome Foundation grant to study different aspects of how cigarette smoking causes AMD. These grants will provide funding to continue the study and gather more results.

The studies use a smoking chamber to create an oxidatively stressful environment. Mice, aged to represent a 50 year old person, are in the chamber for a period of time that is equivalent to a person exposed to a heavy secondary smoke environment. Initial results show that cigarette smoke inhibits the actions of Nrf2, a small molecule necessary in the body to protect against injury from oxidative stress, and possibly against the development of macular degeneration. Handa and his team plan to use these results to learn where and by how much Nrf2 is inhibited by cigarette smoke. The ultimate goal with this understanding, is to develop treatment for early AMD because at present, none exists.

When Dr. Handa is not in the lab, he continues his multifaceted contributions to the Retina Division, with expertise both in intraocular tumors and pediatric retina surgery, as well as overseeing the Division's ultrasound interpretations obtained under the direction of fellow faculty member, Ms. Cathy Dibernardo. ◦

Recent NIH Awards in Retina at Wilmer

Dr. Akrit Sodhi is the most recent recipient of a prestigious, competitive National Institutes of Health (NIH) training grant, following in the footsteps of fellow Division faculty members Drs. Peter Gehlbach and Howard Ying, who previously had received similar awards from the NIH. The awards provide the foundation to compete for subsequent independent research grants from the NIH, whose allocations continue to be threatened by Congressional budget restraints, creating an even greater need to supplement these awards with outside foundation or private philanthropic support.

Diabetic Retinopathy Screening at Primary Care Physicians' Offices

Approximately 50% of patients with diabetes in the United States do not undergo recommended ocular evaluations for diabetic retinopathy. Wilmer researchers Ingrid Zimmer-Galler, M.D. and Ran Zeimer, Ph.D. have collaborated to develop the DigiScope, a cost-effective and practical telemedicine digital imaging system used to screen for diabetic retinopathy in the primary care physician's (PCP) office.

At the PCP's office, patients with diabetes who have not undergone an eye examination in the past two years are imaged with the DigiScope. The images are transmitted to a reading center where the need for a referral to an ophthalmologist is determined. Non-urgent and urgent referrals are then recommended to the patients based on the level of sight-threatening disease that is found in the image before they even see an ophthalmologist. If the referral is urgent, it is recommended that the patient be evaluated by an ophthalmologist within 72 hours.

A recent study of the effectiveness of the DigiScope

indicated that the implementation of this device in the primary care setting is practical and allows accurate screening of patients with diabetes who are otherwise not receiving recommended eye examinations. ◦

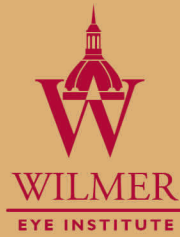


Ingrid Zimmer-Galler, M.D. takes a break from reading the results of the diabetic retinopathy screening done at primary care physician offices with the DigiScope.

If you are interested in supporting the doctors in the Retina Division and the research they are conducting at the Wilmer Eye Institute, please contact:

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