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THE PACE AND PROGRESS OF VISION SCIENCE IS HURTING FORWARD AT MOMENTOUS SPEED, SPURRED ON BY A HOST OF EXCITING NEW RESEARCH DISCOVERIES, AN UNPRECEDED CULTURE OF COLLABORATION, AND THE UNFLAGGING EFFORTS OF OUR CLINICIANS, SCIENTISTS, AND EDUCATORS.”

— JOAN W. MILLER, MD

MESSAGE FROM THE CHAIR

Welcome colleagues, friends and supporters to the Harvard Medical School (HMS) Department of Ophthalmology’s inaugural edition of Frontiers in Ophthalmology. I am proud and excited to share with you this first report, which highlights significant clinical, scientific, and educational milestones of the department’s world-class affiliated hospitals and research institutions. Our report reflects on two decades of discovery and progress in the field of vision science, and the tools and technologies that are transforming the lives of people and patients across the globe.

From Boston to Bangladesh, improving ophthalmic care and its delivery to millions of people worldwide is a shared vision and singular goal of the HMS ophthalmic community. Advancing technology, expanded global connections, and thriving new alliances among HMS affiliates and across the broader scientific community are fueling gains in vision science, education, and medicine. As you’ll read in the following pages, HMS scientists, physicians, and academics from all ophthalmic disciplines and across every subspecialty are brainstorming in the lab, the classroom, and the clinic. Their shared knowledge is driving ideas forward and, ultimately, improving care to patients.

**Educating the next generation of leaders**
The HMS Department of Ophthalmology has a proud history of teaching, training, and mentoring generations of students who become leaders in their field. In the last several years, we’ve reinvented, refined and retooled our educational program to challenge and inspire students at every level of their medical education.

Our training program features a newly restructured surgical curriculum for residents, which now integrates lectures and customized wet lab sessions supervised by attending physicians. Groundbreaking faculty efforts are reshaping resident education with the development of revolutionary, computer-simulated technologies that fine-tune surgical knowledge and skills outside the operating room. Innovative courses and conferences—including our nationally recognized cataract course and new vitreoretinal course—offer students added lenses of scientific inquiry and learning, and attract prominent, international speakers. We continue to forge strong alumni ties through our expanded lecture series, a robust visiting professors program, a new AMD symposium, and a newly revamped and expanded three-day Annual Meeting & Alumni Reunion. Across the HMS community and abroad, our expanded alliances with affiliates and partners have sparked unprecedented opportunities for surgical, clinical, and research training. All of these endeavors offer an unparalleled educational experience for our brilliant young trainees.

**Advancing science**
Thanks to a paradigm shift in collaboration among basic researchers and clinician scientists, insights gained in the lab are accelerating bench-to-bedside discoveries faster than ever before. The last decade has seen groundbreaking advances in human genetics, regenerative medicine, and inflammation and immunology; these, in turn, have led to a host of new treatments, technologies, and therapies aimed at alleviating the suffering associated with eye diseases and blindness.

HMS researchers have focused intensely on these areas, and are beginning to unravel some of the mysteries surrounding disease processes, and the biological mechanisms or environmental influences that may cause them to go awry.

For example, you’ll read about advances in age-related macular degeneration (AMD) pioneered by the HMS Angiogenesis Research Group. The foundations of the group’s work not only illuminated how new blood vessel formation in the eye (neovascularization) contributes to severe forms of AMD, but also spurred revolutionary clinical treatments that halt and sometimes reverse pathological blood vessel growth. Today, anti-VEGF inhibitors and therapies developed in our labs have saved or improved the sight of nearly a million people around the world. Recent and exciting results from a large-scale, phase III clinical trial for treating macular edema in diabetic patients showed dramatic visual improvement using the anti-VEGF drug Lucentis®. These groundbreaking efforts represent a quantum leap in treatment for patients with diabetes—the first in 25 years—and are rapidly establishing new standards of care.

In cornea, HMS faculty members are pursuing novel translational research that has shed new light on the roles of angiogenesis and inflammation in ocular disease. Clinical trials in these areas are providing a robust baseline of data—facilitating the development of therapies to combat these diseases. HMS cornea scientists are also leading industry efforts to harness powerful, new imaging technologies that more precisely target,
track, and treat corneal disease, and ultimately improve patient outcomes. You’ll also read about advances to our Boston Keratoprosthesis (KPro)—the most widely used corneal prosthesis in the world—coupled with aggressive outreach efforts to make it available to patients worldwide. To date, some 5,000 people in 50 countries, including the 72 here, have benefitted from the clinical advances of our KPro programs.

In 2005, significant advances in whole-genome screening technologies, coupled with increasingly powerful computing capabilities, are enabling us to explore DNA inheritance with unimaginable precision and speed. This first-time opportunities to examine gene-gene and gene-environment interactions will help us determine who may be at increased risk for specific diseases. Efforts within the department are already underway to exploit this potential: we are currently integrating information and expertise across the department through new centers of excellence, building a massive biorepository of donor tissue and DNA samples, integrating vast amounts of genetic and clinical information, and launching our new Ocular Genomics Institute. All of these efforts welcome a new era of personalized medicine—which ultimately means better care for everyone.

Pursuing excellence in patient care
The cornerstone of our mission is the quality of care we provide to patients. Significant efforts by HMS faculty are impacting our full spectrum of patient care—from prevention to treatment to rehabilitation. For example, cutting-edge technologies are giving us better prognostic information that enables us to diagnose and treat ocular diseases faster and more efficiently. More targeted and less invasive drug treatments and therapies are preventing, saving, and sometimes restoring sight in diseases that were once considered untreatable. Recent and exciting developments in lens technology—already helping to improve quality of life for many millions of people—will continue to play a key role in the future of vision care.

Pioneering advancements in rehabilitative medicine are enabling us to maximize their patients’ vision—sometimes even restoring sight—with new cutting-edge technologies already helping to improve patient outcomes. You’ll also read about advances to track, and treat corneal disease, and ultimately improve patient outcomes. You’ll also read about advances to treat AMD

Joan W. Miller, MD
Henry Willard Williams Professor of Ophthalmology
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The pace and progress of vision science is hurtling forward at momentous speed, spurred on by a burst of exciting new research discoveries, an unprecedented culture of collaboration, and the unflagging efforts of our premier group of clinicians, researchers, and educators. As you’ll find in these pages, our affiliate institutions that comprise the HMS Department of Ophthalmology and its affiliated programs have made remarkable gains in medical science and ophthalmic practice that are both broad in scope and high in impact.

Despite these gains, there is much to accomplish and a growing imperative to do so as; our population grows older, we can expect a significant rise in the number of people who become blind or visually impaired due to age-related diseases such as macular degeneration, glaucoma, and cataracts. An epidemic rise in the United States of type 2 diabetes is also triggering a surge in diabetic retinopathy—a leading cause of blindness in American adults. According to a study sponsored by the National Eye Institute in 2007, an estimated 3.3 million Americans age 40 or older in 2004 by 2020, that number is projected to rise to 5.5 million Americans. These sobering statistics underscore the relevance of our mission and the call to action that we cherish.

Thanks to you, our generous friends and supporters, our quest for imaging and non-invasive methods continues unabated across the HMS ophthalmic community. As you read on, I hope you’ll share our excitement, understanding, and support that our vision scientists have made to date and of the discoveries yet to come. It’s a marvelous, inspiring, and empowering time to be at the forefront of vision science.

Welcome to our world of vision.
“Academic medical institutions like the HMS Department of Ophthalmology attract an intellectually curious faculty—individuals who push the boundaries of medicine and science in their often tenacious pursuit of answers.”

—Janey Wiggs, MD, PhD, Associate Director of the Howe Laboratory, Massachusetts Eye and Ear Infirmary
The Harvard Medical School (HMS) Department of Ophthalmology is one of the leading and largest academic departments of ophthalmology in the nation. Formally established in 1871, the department has been built upon a strong and rich foundation in medical education, research, and clinical care. Through the years, HMS faculty and alumni have profoundly influenced ophthalmic science, medicine, and literature—helping to transform the field of ophthalmology from a branch of surgery into an independent medical specialty at the forefront of science. Today, the department continues its legacy as one of the finest academic medical institutions in the world—teaching and mentoring future leaders, turning laboratory insight into cures, and bringing the fruits of its labors to patients’ bedside.

**HMS’s unique architecture**

Since its inception, the department has evolved into an academic institution with a multi-institutional structure and a broad base of clinicians and scientists. This decentralized structure is unique among other U.S. academic medical schools, which are typically integrated—physically and financially—into their affiliated universities. Unlike other medical schools, HMS does not own a teaching hospital; instead, the school comprises a network of formal hospital and research affiliations that provide the teaching, training, and research environment for medical and graduate education. Through a system of faculty titles and cross-appointments, the hospitals and the school are closely linked.

The HMS Department of Ophthalmology is comprised of 40 full-time faculty members who carry out the majority of the department’s teaching, research, and patient care activities. An additional 90 faculty members (mostly private practitioners) hold part-time HMS faculty appointments in ophthalmology and participate in various academic endeavors of the department.

Throughout the years, the department’s ophthalmic network has grown in both scope and intellect. The department has recruited some of the finest clinician scientists in ophthalmology, and established key affiliations with many of the world’s leading academic medical schools and research institutions. These affiliations have added significant depth and breadth to the department’s core capabilities, and have created a rich and robust infrastructure steeped in multidisciplinary investigations, educational collaborations, and clinical enterprises.

**Formula for success**

Though administratively complex, the department’s network structure has proven highly successful for a variety of reasons. Affiliates and partners are firmly united in their commitment to educational excellence. Stimulating residency and fellowship opportunities abound throughout the HMS network—offering broad clinical and surgical exposure, as well as rewarding mentorship opportunities, to the faculty and trainees. The collaborative environment also supports a wide array of preclinical and clinical research, and inspires robust scientific partnerships among divergent yet complementary research programs; these unified efforts have led to landmark advances in patient care, many of which are highlighted in this report. Collectively, the broad clinical expertise and deep fund of knowledge allows the Department of Ophthalmology to provide sophisticated diagnostic and therapeutic care for patients, thus ensuring the best possible outcomes.

The Department of Ophthalmology also wholeheartedly embraces the vast diversity of the HMS community, which forms the intellectual backbone of the department. Students and faculty, who represent a myriad of geographical and cultural backgrounds, and are selected based on their accomplishments and future potential. Women represent 45 percent of the full-time faculty, and fill numerous senior-level positions within the department, including Chair. In no small way, the cultural and academic diversity of the HMS community prepares the students and faculty to lead with fresh vision and purpose as they take on the challenges of an increasingly global healthcare environment.

**HMS Ophthalmology historic milestones**

1869 - Henry Willard Williams, AM, MD, presents at HMS the first course of lectures ever given in an American medical school by an ophthalmologist. Two years later, he is appointed to Professor of Ophthalmology, marking the formal establishment of the HMS Department of Ophthalmology in 1871.

1891 - Williams’ successor, Oliver Fairfield Wadsworth, AM, MD, joins the staff of the Massachusetts Charitable Eye & Ear Infirmary (established in 1841). Soon after, the hospital becomes the hub of Harvard’s ophthalmic training.

1926 - Frederick H. Verhoeff, MD, HMS Professor of Ophthalmology and Mass. Eye and Ear’s first full-time researcher and pathologist, establishes the first endowed ophthalmic research unit, the Howe Laboratory, at Mass. Eye and Ear.

1949 - The world’s first retinal service, and first retinal disease fellowship, is established at Mass. Eye and Ear by famed HMS retinal pioneer and innovator, Charles L. Schepens, MD. Dr. Schepens is also credited with establishing the vitreoretinal subspecialty.

1958 - Claes H. Dohlman, MD, PhD, considered to be the founder of modern corneal science, establishes the world’s first organized cornea subspecialty, and the first structured cornea fellowship program at Mass. Eye and Ear.

1966 - Deborah Pavan-Langston, MD becomes the first woman to be accepted into the HMS Ophthalmology residency program. Unlike her male colleagues, Dr. Langston is required to complete a two-year pre-residency fellowship. In 1973, she is appointed the first woman director of Mass. Eye and Ear’s Cornea and External Disease Service.

1974 - The Berman-Gund Laboratory for the Study of Retinal Degeneration formally opens. The laboratory was conceived as a multidisciplinary research effort between Mass. Eye and Ear and Harvard with the goal of understanding the disease mechanisms involved in retinitis pigmentosa and the more than 30 related diseases that affect the retina.

2003 - Joan W. Miller, MD, is named Chair of the HMS Department of Ophthalmology and Chief of Ophthalmology at Mass. Eye and Ear. She is the first woman to hold this dual role.
John I. Loewenstein, MD

Vice Chair for Medical Education, Department of Ophthalmology, Harvard Medical School
Associate Professor of Ophthalmology, Harvard Medical School
Director, Department of Ophthalmology Residency Training Program, Harvard Medical School
Associate Chief for Graduate Medical Education and Associate Clinical Chief of Ophthalmology, Massachusetts Eye and Ear Infirmary

A graduate of Massachusetts Institute of Technology, Dr. John Loewenstein received his medical degree from the State University of New York at Buffalo and completed his ophthalmology residency at Boston University (BU) School of Medicine. This was followed by a two-year clinical and research fellowship at BU. He initially joined the HMS Department of Ophthalmology as a part-time member of the Retina Service at Mass. Eye and Ear while continuing to practice privately in the Boston area. After a decade, he missed teaching and the academic environment, and in 1994, was invited to join Mass. Eye and Ear/HMS as a full-time faculty member of the Retina Service. He quickly became an integral part of the training program for medical students, residents, and fellows.

In 1996 and 2001, Dr. Loewenstein earned high accolades from HMS ophthalmology residents who honored him as Teacher of the Year. He was also a 2007 nominee for the HMS Prize for Excellence in Teaching. In 2002, with the vigorous support and unanimous approval from residents and administration alike, Dr. Loewenstein was named Director of the Residency Program. A gifted teacher, clinician, surgeon, and manager, Dr. Loewenstein has used his exceptional abilities to enhance the residency program in numerous ways. He has modified and streamlined residency rotations to improve continuity of experience, and to maximize clinical and surgical teaching. He has collaborated with colleagues at the Boston Veterans Administration Hospital to enhance the resident experience, and strengthened communication and feedback among HMS-affiliated teaching hospitals. He is also a strong advocate of achieving progress through collaboration; in this regard, he chairs a biweekly Residency Steering Committee meeting, which provides residents and faculty with a forum where they may address concerns and brainstorm about continuous improvements to the program.

Together with Associate Residency Program Director, Carolyn Kloek, MD, Dr. Loewenstein has created a structured surgical curriculum that enhances the overall training experience for residents. This invigorated curriculum includes faculty-proctored wet-lab in cataract surgery, retinal surgery, glaucoma surgery, cornea surgery, and oculoplastics surgery. A step-wise introduction to phacoemulsification (cataract surgery) boosts cognitive learning and reduces resident stress, and a state-of-the-art virtual reality eye surgery simulator enables residents to practice and hone their surgical skills.

In 2008, Dr. Loewenstein was appointed Vice Chair for Medical Education. In this expanded educational role, he continues to cultivate and fine-tune the HMS Residency Program and works closely with the Fellowship Committee Chair to coordinate fellowships across HMS affiliate sites. He also collaborates with the Director of Medical Student Education and the Vice Chair of Academic Programs to identify new educational initiatives and program improvements. Since becoming Vice Chair, he has pursued a strategic vision that ensures a cohesive, challenging, and inspiring experience for students at every level of their medical education.

Dr. Loewenstein has pioneered revolutionary teaching tools to improve surgical competency in ophthalmology. Beginning in 2003, he collaborated with colleagues and experts in cognitive psychology, computer programming, and ophthalmology to develop an interactive, computer program for teaching the complex art of cataract surgery. This virtual surgical tool, called the Mass. Eye and Ear Cataract Surgery Mentor, allows residents to gain critical cognitive skills in a safe, forgiving environment and eliminates risk to patients. So far, eight of 10 modules on phacoemulsification have been completed. Current efforts focus on developing the remaining modules and establishing licensing agreements to distribute the program to residents nationwide.

Dr. Loewenstein’s newest initiative in resident education development is a formal study of the effect of trainee fatigue on surgical learning. Working with Drs. Carolyn Kloek, James Gordon, Director of the Gilbert Program in Medical Simulation at HMS, and Charles Caesler, Stephen Lockley, and Brian Abaluck from the sleep medicine program at HMS and Brigham and Women’s Hospital, he is evaluating retention of surgical learning in rested and sleep-deprived states using a commercial, virtual reality eye surgery simulator. He is also developing a computer-based training tool to teach residents, fellows, and practicing ophthalmologists how to screen for retinopathy of prematurity (ROP), a disease that can cause premature infants to go blind. For this effort, he is collaborating closely with Dr. Rodrigo Alvarez and other clinicians who have expertise in ROP, and leveraging the techniques used to develop the Mass. Eye and Ear Cataract Surgery Mentor.
Reza Dana, MD, MPH, MSc

Vice Chair for Academic Programs, Department of Ophthalmology, Harvard Medical School
Claes H. Dohlman Professor of Ophthalmology, Harvard Medical School

Dr. Reza Dana is a leading international expert in corneal and ocular inflammation, and his studies have greatly elucidated the cellular and molecular mechanisms of ocular surface biology. Dr. Dana has made substantial contributions to the bodies of knowledge in both basic science and clinical research.

After receiving college-preparatory education at St. Paul’s School in Concord, New Hampshire, Reza Dana pursued his baccalaureate degree at Johns Hopkins University School of Arts and Sciences, where he was elected to Phi Beta Kappa. Dr. Dana continued his postgraduate training at Johns Hopkins, where he received both his MPH and MD degrees. He performed his residency in ophthalmology at the Illinois Eye and Ear Infirmary at the University of Illinois, followed by a clinical fellowship in cornea and external diseases at Wills Eye Hospital in Philadelphia. Dr. Dana then received additional fellowship training in immunology and uveitis at Mass. Eye and Ear, and in ocular immunology and transplantation at Schepens Eye Research Institute.

Dr. Dana was appointed Instructor in the Department of Ophthalmology at HMS in 1995; he ascended to the rank of Assistant Professor in 1995, Associate Professor in 2000, and Professor and Co-Director of the Cornea and Refractive Surgery Service at Harvard Medical School in 2008. In 2009, he was named Co-Director of Research at Schepens. With numerous ongoing projects in his laboratory and multiple collaborations with other researchers, Dr. Dana is rapidly expanding his list of scientific accomplishments and publications—over 270 publications, including 175 peer-reviewed articles to date. In addition to leading laboratory research, Dr. Dana has served on the Cornea and Refractive Surgery Service of Mass. Eye and Ear since 1996.

In 2005, Dr. Dana earned his MSc degree in Health Care Management from Harvard University; this, complemented by his scientific and clinical expertise, gives Dr. Dana a unique capacity for leadership. As Director of the Cornea and Refractive Surgery Service at Mass. Eye and Ear, a position he has held since 2006, Dr. Dana leads the world’s largest and most esteemed group of clinician-scientists dedicated to cornea research and treatment. Dr. Dana became Vice Chair of Academic Programs in the Department of Ophthalmology at HMS in 2006, and was named Co-Director of Research at Schepens in 2009. With leadership appointments at both Mass. Eye and Ear and Schepens, Dr. Dana has promoted collaborative efforts in translational research between the two institutions. Committed to the advancement of clinician scientists, Dr. Dana is a Principal Investigator of the Harvard Vision Clinical Scientist Development Program funded by the NIH, and has helped provide unparalleled training opportunities for junior investigators.

In addition to publishing numerous original research articles in top-tier scientific journals such as Nature Medicine, Proceedings of the National Academy of Sciences, and Journal of Clinical Investigation, Dr. Dana is dedicated to the dissemination of scientific knowledge. He serves on the editorial board of journals such as Cornea, Investigative Ophthalmology and Visual Science, Ophthalmology, and The Ocular Surface. He has served as Editor of the Eye and Systemic Disease volume of The Principles and Practice of Ophthalmology, and as Senior Editor of The Encyclopedia of the Eye, published in 2010 by Elsevier.

Dr. Dana has delivered more than 120 invited and named lectures, and has been the recipient of multiple awards, including the William and Mary Greve Special Scholar Award and the Physician-Scientist Merit Award from Research to Prevent Blindness (RPB). In 2009, he was honored with the Lew R. Wasserman Award from RPB. Dr. Dana’s honors also include the Achievement Award of the American Academy of Ophthalmology, the Cogan Award of the Association for Research in Vision and Ophthalmology, and the Alcon Research Institute Award.
Patricia D’Amore, PhD, MBA

Vice Chair for Basic Research, Department of Ophthalmology, Harvard Medical School
Professor of Ophthalmology, Harvard Medical School
Professor of Pathology, Harvard Medical School
Co-Director of Research, Senior Scientist, and Ankeny Scholar of Retinal Molecular Biology, Schepens Eye Research Institute

Dr. Patricia D’Amore is an internationally recognized expert of vascular growth and development, and has been at the forefront of angiogenesis research for over three decades. Investigations conducted in her laboratory have helped form the foundations of vascular-targeting therapies, which are currently used to treat various cancers and vascular diseases of the eye. Dr. D’Amore’s studies have also uncovered important physiological roles of vascular growth factors—yielding crucial insight into the safe use of antiangiogenic therapies.

Dr. D’Amore received her PhD in biology from Boston University School of Medicine in 1980. Dr. D’Amore returned to Boston in 1981 to join the Department of Surgery. At HMS, Dr. D’Amore became Associate Professor of Pathology in 1989, and was promoted to Professor of Ophthalmology (Pathology) in 1998. Dr. D’Amore also joined Schepens Eye Research Institute as a Senior Scientist in 1998, where she is the Ankeny Scholar of Retinal Molecular Biology.

To complement her scientific achievements, Dr. D’Amore obtained her MBA degree from Northeastern University in 1987, and has parlayed her knowledge and superb management skills into numerous leadership roles. Since 2001, Dr. D’Amore has served as Co-Chair of the Program in Development in Angiogenesis, Invasion & Metastasis at the Dana Farber/Harvard Cancer Center. At Schepens, she was appointed Associate Director of Research in 2002, and assumed the role of Co-Director of Research in 2009. In 2008, Dr. D’Amore became HMS Ophthalmology Vice Chair of Basic Research.

Over 50 predoctoral students and postdoctoral fellows have benefited from the outstanding teaching and thoughtful mentorship of Dr. D’Amore. At HMS, Dr. D’Amore serves on numerous committees that promote educational and research opportunities for future and established scientists; these include but are not limited to the Minority Recruitment Committee, Joint Committee on the Status of Women, Faculty Committee on Student Research, Summer Honors Undergraduate Research Program (SHURP), Henry K. Beecher Prize in Medical Ethics Committee, Selection Committee for the Eleanor and Miles Shore Fellowship Program for Scholars in Medicine, and the Faculty Diversity Committee. Since 2003, Dr. D’Amore has served as Co-Chief Director of the Leder Human Biology & Translational Medicine Program at HMS. For her efforts in training future leaders in research, Dr. D’Amore was honored in 2006 with the A. Clifford Barger Excellence in Mentoring Award. Dr. D’Amore is also committed to fostering scientific discussion and communication. She founded the Boston Angiogenesis Meeting, now in its 13th year; this meeting continues to be a highly regarded forum for presenting new findings and promoting collaboration, understanding, and advancement in angiogenesis research. She has held editorial roles for many scientific journals, including Executive Editor of Experimental Eye Research, Associate Editor of American Journal of Pathology, and Editor-in-Chief of Microvascular Research. For her scientific and academic achievements, Dr. D’Amore was elected to The Academy at Harvard Medical School in 2004, and received the Senior Scientific Investigator Award from Research to Prevent Blindness in 2006. In 2009, she was elected a Gold Fellow by the Association for Research in Vision and Ophthalmology. Dr. D’Amore delivered the 2010 Lerner Lecture for the Jeffrey M. Lerner Endowed Memorial Lectureship, a venue for cutting-edge, thought-provoking discussions on basic and translational research. She is also the recipient of the 2012 Rous-Whipple Award from the American Society of Investigative Pathology.
Lloyd P. Aiello, MD, PhD

Vice Chair for Centers of Excellence, Department of Ophthalmology, Harvard Medical School
Professor of Ophthalmology, Harvard Medical School
Vice President of Ophthalmology and Head of Joslin’s Section on Eye Research, Joslin Diabetes Center
Director, Beetham Eye Institute

Dr. Aiello received his PhD in biochemistry and MD from Boston University School of Medicine. He completed residency in ophthalmology at the Wilmer Ophthalmological Institute at Johns Hopkins University and Hospital before coming to the Joslin Diabetes Center, where he completed both a clinical vitreoretinal and a research fellowship. He joined the Joslin staff in 1994.

A third-generation Joslin ophthalmologist, Dr. Aiello is committed to eliminating vision loss due to diabetic retinopathy and other related retinopathies, which account for the majority of blindness among working-age individuals in the United States and other developed countries. His research aims to determine the underlying biochemistry and molecular mechanisms of these diseases, then develop and test novel therapeutic interventions through rigorous translational and clinical trial research.

Dr. Aiello and collaborating Joslin scientists—including George L. King, MD, Head of the Section on Vascular Cell Biology and Director of Research at Joslin—were key members of the HMS teams working on angiogenesis research, a field founded by Dr. Judah Folkman. Their pioneering work demonstrated the role of vascular endothelial growth factor (VEGF) in diabetic retinopathy and the therapeutic potential of VEGF inhibitors. In related research, Dr. Aiello’s laboratory made significant progress toward understanding and manipulating the expression, regulation, and signaling functions of VEGF and its receptors. Dr. Aiello published the first evidence that protein kinase C-beta (PKC-beta) is involved in excessive blood vessel growth and vascular leakage in diabetic retinopathy. The team went on to develop a PKC-beta inhibitor that interrupts the actions of this protein—thus opening a new therapeutic avenue for diabetic and other retinopathies.

Dr. Aiello is recognized internationally for his leadership in diabetic retinopathy research. In 2002, he founded and served as the inaugural chair for the Diabetic Retinopathy Clinical Research Network (DRCR.net), a national collaborative network dedicated to facilitating multi-center clinical research for diabetic retinopathy, diabetic macular edema, and related disorders. Funded by the National Eye Institute, DRCR.net is now comprised of 150 centers nationwide representing academic medical institutions and private practice groups.

In 2008, Dr. Aiello was named Vice Chair for Centers of Excellence (COE) in the HMS Department of Ophthalmology. These centers are designed to coordinate the department’s efforts in patient care, research, and training in key areas of ophthalmology in order to leverage the expertise and core strengths of faculty across affiliates. As Vice Chair, Dr. Aiello brings a wealth of collaborative insight, experience and energy to this role. Initial COE targets include diabetic eye disease, AMD, cornea, and glaucoma.

Dr. Aiello is the author of over 150 original papers and 215 publications, including contributions to the New England Journal of Medicine, Nature Medicine, PNAS, Journal of Biological Chemistry, Journal of Clinical Investigation, Diabetes, Lancet, and many others covering a wide range of topics in diabetic eye disease. Dr. Aiello has received 40 national and international awards and honors, including the Alcon Research Institute Award, the ARVO/Pfizer Ophthalmics Translational Research Award, the Award of Merit in Retina Research from the Retina Society, the Senior Achievement Award from the American Academy of Ophthalmology, the Charles Schepens Award in Research, the Outstanding Foreign Investigator Award from the Japan Society of Diabetic Complications, and the Novartis Award in Diabetes. The Research to Prevent Blindness Foundation has awarded Dr. Aiello the Dolly Green Scholar Award, the Special Research Scholar Award, and the LeW R. Wasserman Merit Award; from the Macula Society, Dr. Aiello has received the Rosenthal Foundation Award and the Paul Henkind Memorial Award.
David G. Hunter, MD, PhD

Vice Chair for Promotions and Reappointments, Department of Ophthalmology, Harvard Medical School
Professor of Ophthalmology, Harvard Medical School
Richard and Robb Chair of Ophthalmology, Children’s Hospital Boston
Ophthalmologist-in-Chief, Children’s Hospital Boston

Dr. Hunter received his MD and PhD degrees at Baylor College of Medicine, and completed an ophthalmology residency at Massachusetts Eye and Ear Infirmary, HMS. Dr. Hunter furthered his training with a pediatric ophthalmology fellowship at Wilmer Eye Institute of Johns Hopkins Medical School, where he joined the faculty in both Ophthalmology and Biomedical Engineering. He returned to HMS in 2002 as Ophthalmologist-in-Chief of Children’s Hospital.

During his tenure, Dr. Hunter has encouraged both clinical excellence and research innovation within the Ophthalmology division at Children’s. He created the first international fellowship in Pediatric Ophthalmology, and led the development, initiation, and funding of the Children’s Hospital Boston Visiting Professorship lecture series. Since its establishment in 2006, this lecture series has brought four to six internationally recognized visiting professors to Boston each year.

A devoted mentor and teacher, Dr. Hunter was nominated for the Harvard Medical Student Teaching Award in 2004, and received the Robert Petersen Pediatric Ophthalmology teaching award in 2005. As HMS Vice Chair for Promotions and Reappointments, Dr. Hunter facilitates the academic advancement of department faculty across all HMS affiliates. He also has added to the wealth of academic strength and collaboration within the Department by rigorously recruiting faculty with dual fellowship training—combining pediatric ophthalmology and subspecialty training in neuro-ophthalmology and oculoplastics.

Dr. Hunter is best known for his expertise in complex strabismus (misalignment of the eyes) in adults and children. He is exploring and publishing innovative techniques in strabismus surgery, including the “short tag nose” adjustable suture and transposition procedures for paretic strabismus. His research also focuses on developing more accurate ways to help pediatricians identify eye problems in children.

In collaboration with Elizabeth Engle, MD, HMS Professor of Neurology and Ophthalmology, Dr. Hunter has established new clinical systems and protocols for studying the genetics of common strabismus disorders, including simple esotropia, exotropia and anisometropic amblyopia. These new protocols—which include clinical exams and sampling of affected and non-affected family members to ensure proper phenotyping—will serve as models for ongoing and future genetic studies at HMS affiliates.

A preeminent expert in optics and refraction, Dr. Hunter delivers lectures worldwide and via podcast, he has also authored numerous scientific articles, editorials, and book chapters. He co-authored Last Minute Optics, a widely used optics review book, and serves as Editor-in-Chief of Journal of the American Association for Pediatric Ophthalmology and Strabismus. For his outstanding contributions to clinical ophthalmology, Dr. Hunter has received numerous honors, including the Richard Starr Ross Clinician Scientist Award from Johns Hopkins University and the Research to Prevent Blindness Lew R. Wasserman Merit Award.
Massachusetts Eye and Ear Infirmary

Founded in 1824, the Massachusetts Eye and Ear Infirmary is a pre-eminent specialty, teaching, and research hospital caring for disorders of the eye, ear, nose, throat, head, and neck. Mass. Eye and Ear is the main primary and tertiary care facility of the HMS Department of Ophthalmology, and the hub of its teaching and research activities. The hospital’s dedicated staff provides a full range of primary and subspecialty medical and surgical care to nearly 225,000 patients each year, and serves as a major referral center throughout the northeast. With a medical staff that tops nearly 130 full-time physicians and some 325 community-based physicians, Mass. Eye and Ear encourages multi-disciplinary and interdisciplinary pursuits across patient care, education, and research. Seminal contributions to these three mission-critical areas span nearly a two hundred year history and have shaped the hospital’s reputation and success as a national and global center of excellence in ophthalmology and otolaryngology.

In 2011, the Scheie Eye Research Institute became a member of the Massachusetts Eye and Ear Foundation—forming the world’s largest and most robust basic and clinical ophthalmology research enterprise. Both institutions are long-time collaborators in vision research, with complementary areas of expertise and technology. Together, this scientifically rich and diverse union is uniquely primed to solve the problems of and to find cures for blinding diseases.

Educating future leaders in ophthalmology

As the flagship academic center for the HMS Department of Ophthalmology, Mass. Eye and Ear is deeply committed to providing a superb education and an exciting, fruitful learning experience to the next generation of ophthalmology health care leaders. Innovative medical training programs prepare young physicians and scientists to excel as leaders in today’s increasingly complex and global health care environment. Broad clinical and surgical exposure, a first-rate mentoring program, and unparalleled research opportunities combine to offer a world-class medical education experience. Each year, the department’s progressive training programs attract 60-70 of the highest-caliber physician applicants from around the world to match in its eight residency and 14 fellowship positions.

Graduates of the department’s training programs are well prepared to be tomorrow’s leading clinicians, researchers, and academicians. In fact, a significant number of graduating residents—nearly 60 percent—pursue academic careers after fellowship rather than establishing a full-time private practice. Today, about one in six ophthalmology chairmen in academic institutions across the United States and Canada are HMS postdoctoral alumni—striking testimony to the caliber of the department’s graduates and the strength of its programs.

Thriving patient care

Mass. Eye and Ear strives to enhance every patient’s quality of life by providing the best possible care. Central to this mission is the hospital’s highly skilled and compassionate team of physicians, many of whom are global leaders in their fields of specialty. Every physician specializes in at least one area of ophthalmic care; some physicians are cross-trained in multiple specialties, and nearly all have completed subspecialty fellowship training. Most conduct active laboratory and/or clinical research programs; this knowledge contributes immeasurably to their clinical, surgical, and diagnostic expertise. The talented faculty, together with scientifically advanced medical care and dedicated support staff, keeps Mass. Eye and Ear at the forefront of care.

The Comprehensive Ophthalmology and Cataract Consultation Service (COS) handles more than 20,000 patient visits each year. In addition to serving walk-in patients, COS serves as a key resource for timely referrals from across the HMS network of 17 hospitals and affiliates, as well as referrals from private practitioners from all over New England. The service specializes in cataract extraction with intraocular lens implantation. Between July 2008 and June 2009, COS performed 2,498 cataract surgeries at Mass. Eye and Ear’s main Boston campus. Surgical results exceeded national and international benchmarks (Cataract and Refractive Surgery Today Europe, May 2009, and Cole Eye Institute, Outcomes 2008) with 92 percent of patients achieving within 1 diopter of target refraction after surgery.

Mass. Eye and Ear’s Eye Trauma Service has developed highly successful, standardized protocols for treating emergency eye injuries. According to a recent review of all open globe injury cases treated at Mass. Eye and Ear from January 2000 to July 2007, the post-surgical infection rate of endophthalmitis was less than 1 percent. By comparison, the endophthalmitis rate in the United States is 6.0 percent after open globe repair, according to the U.S. National Eye Trauma Registry. The service also has exceeded benchmark outcomes with some of the lowest enucleation (eye removal) rates nationwide, and some of the lowest rates reported for sympathetic ophthalmia—a devastating and vision-threatening complication that can occur in the non-injured eye after open globe surgery.


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Best-of-class services spur best outcomes

As a preeminent center of ophthalmic care, Mass. Eye and Ear establishes global standards for quality patient care while pushing the envelope internally to achieve the highest levels of excellence. In 2010, the hospital published its first Quality and Outcomes report, which documented clinical and surgical outcomes data for 13 subspecialty procedures. The initial impetus for this effort was to determine the quality of care and how well the patient experience is managed; ultimately, however, the report also showed that the hospital is leading the medical community in the development of outcomes measures in ophthalmic care.

Reaching out to patients and partners

In 2008, Mass. Eye and Ear launched a strategic and collaborative plan for growth, which was designed to streamline services and expand its expertise and resources to as many people as possible. Since that time, the hospital has forged several highly successful alliances with its HMS affiliates and partners that will directly benefit patients by nurturing an environment for improved patient care, research activities, and educational programs.

Mass. Eye and Ear has added ophthalmic services in multiple satellite offices beyond Boston’s city limits, providing thousands of patients with easy access to world-class care. Mass. Eye and Ear has also established a veteran’s eye care program in MGH’s Chelsea Health Center to screen patients for diabetic eye disease. Numerous expansions and modernizations to its physical facilities—including a new state-of-the-art surgical center, renovated pediatric and rehabilitation suites, and a renovated radiology department with significant equipment upgrades—have added capacity and comfort for patients. In 2010, the hospital kicked off an ambitious expansion plan that will add approximately 70,000 square feet to its central Charles Street clinical facility and a 90,000 square foot research center to its main Boston campus. Additionally, an outpatient surgical center will be developed in Boston’s Longwood Medical Area. To support its new service partnerships and department expansions, the hospital has added more than a dozen external physicians and researchers to its full-time staff in just the last two years. Aggressive recruitment efforts are ongoing at Mass. Eye and Ear to keep pace with its accelerated growth.

Advancing ophthalmic science & discovery

For nearly two centuries, Mass. Eye and Ear faculty members have pioneered advances in ophthalmic medicine and research, many of which have set standards of care in the United States and abroad. The pursuit of knowledge has driven numerous groundbreaking discoveries; scientists have developed new drugs and devices, perfected new techniques, identified disease-causing genes, and translated groundbreaking laboratory research into clinical treatments that benefit scores of people. Today, the department remains at the forefront of discovery, aggressively tackling new areas of research and developing next-generation tools and technologies to combat blinding diseases. Mass. Eye and Ear provides a first-rate setting for scientists who facilitate a broad and aggressive program of basic, translational, and clinical research. Key areas of study focus on retinal degenerations, including age-related macular degeneration and retinitis pigmentosa, glaucoma, keratopathy, corneal infections and ocular tumors. During the last several years, the department also has made significant inroads in the specialty areas of ocular genetics, regeneration, and repair.

Bringing personalized medicine to Mass. Eye and Ear

Delivering highly targeted care to patients based on their unique genetic makeup is now an exciting possibility thanks to modern genomics and powerful new computing technologies. At Mass. Eye and Ear, transforming the hope of personalized medicine into a 21st-century reality is now a vigorous focus of the department. In 2011, the department launched the Ocular Genomics Institute, which combines clinical information from a patient’s electronic medical records and clinical samples from Mass. Eye and Ear’s expanding biobank. Relating clinical information to tissue and DNA samples, coupled with advanced DNA sequencing and analysis technologies, will allow investigators to unravel disease mechanisms and develop new interventions at an accelerated pace. The department’s ten-year goal is to have personal genome sequences embedded into the electronic medical records of the nearly 200,000 patients treated annually at Mass. Eye and Ear.

Eric Pierce, MD, PhD

Lecturer on Ophthalmology, Harvard Medical School

Associate Director, Berman-Gund Laboratory for the Study of Retinal Degenerations, Massachusetts Eye and Ear Infirmary

Director, Ocular Genomics Institute, Massachusetts Eye and Ear Infirmary

Dr. Pierce, a clinician, educator, and preeminent leader in the area of retinal degenerations, recently joined Mass. Eye and Ear and HMS as Associate Director of the Berman-Gund Laboratory for the Study of Retinal Degenerations. As Director of the new Ocular Genomics Institute, he will direct the Genetic Therapies Program—accelerating the department’s growth into advanced studies in genomic research and gene therapy. Dr. Pierce is working in close collaboration with Berman-Gund Laboratory Director Eliot L. Berson, MD, and Janey Wiggs, MD, PhD, who directs the Genetic Diagnostics section of the Institute.

Dr. Pierce’s scientific efforts have resulted in groundbreaking ways to address retinal degenerations using genetic sequencing and gene therapy methods. Recently, he has used next-generation DNA sequencing to identify new retinal degeneration disease genes and to improve genetic testing for patients with inherited retinal degenerative disorders. He has also demonstrated that it is critical to functionally test DNA sequence variants to accurately identify specific disease-causing mutations. Dr. Pierce is also applying his genetic expertise to therapeutic discovery and helped demonstrate the safety and efficacy of gene therapy for the RPE65 genetic form of Leber congenital amaurosis, an early onset form of retinal degeneration.

Dr. Pierce earned a PhD in biochemistry at the University of Wisconsin-Madison and his MD at HMS/NMIT Health Sciences and Technology Division. He completed his ophthalmology residency at Mass. Eye and Ear/HMS, followed by a combined research-clinical fellowship in pediatric ophthalmology at Children’s Hospital Boston. He joined the faculty of Children’s Hospital Boston working in clinical care and angiogenesis research for three years before being recruited to the University of Pennsylvania. In 1999, Dr. Pierce joined the F.M. Kirby Center for Molecular Ophthalmology in the Scheie Eye Institute of the University of Pennsylvania School of Medicine. He focused his work on retinal degenerations and was a member of the Division of Ophthalmology at Children’s Hospital of Philadelphia, where he attained an appointment as Associate Professor of Ophthalmology.
**Schepens Eye Research Institute**

In 1947, World War II hero Charles L. Schepens, MD, joined the HMS Howe Laboratory as a research fellow. Recognizing the need for a dedicated eye research organization, Dr. Schepens established the Retina Foundation in 1950, representing a handful of researchers working out of a modest Boston tenement. This collaboration was renamed the Eye Research Institute of Retina Foundation in 1974 to better represent its active research program, and became formally affiliated with HMS in 1991. Today, the Institute bears the name of its influential founder, who is regarded as “the father of retinal surgery.” In a cutting-edge facility just a short walk from the main campuses of Mass. Eye and Ear and Massachusetts General Hospital, Schepens researchers advance the understanding of eye disease and facilitate the transfer of scientific knowledge into clinical use. Since its inception, Schepens has trained over 600 post-doctoral fellows and produced nearly 5,000 scientific papers and books on the eye. Schepens Eye Research Institute became a subsidiary of the Massachusetts Eye and Ear Foundation in 2011.

**Leadership**

In 1993, J. Wayne Streilein, MD, joined Schepens Eye Research Institute as Ankeny Director of Research. He became President in 1995, and was responsible for the Institute’s substantial growth in size and impact. After Dr. Streilein’s sudden passing in 2004, renowned microbiologist Michael Gilmour, PhD, was recruited as President and Ankeny Director of Research. Dr. Gilmour led the Institute for five years before joining the Howe Laboratory at Mass. Eye and Ear to focus on research. In 2009, Kenneth Fischer, MBA, was named President and Chief Operating Officer. Co-Directors of Research, Patricia A. D’Amore, PhD, MBA; Rena Dana, MD, MPH, MSc; and Eli Pell, OD, MSc, form the Institute’s triumvirate research directorate.

**Unique centers of excellence**

**Schepens Eye Research Institute**

Scientific endeavors carried out at Schepens span all levels of research, from developing novel concepts to conducting clinical testing in various forms of eye diseases. Extensive preclinical investigations carried out by Schepens researchers often dovetail with ongoing basic and translational efforts at HMS affiliates. These collaborations have led to innovative pathways for ocular diseases and therapies. To advance these efforts, Schepens has formed distinct Centers of Excellence to streamline the transfer of scientific knowledge into clinical application:

- **The Mobility Enhancement and Rehabilitation Center**
  Directed by Dr. Pelli, an expert in vision rehabilitation, the Mobility Enhancement and Rehabilitation Center aims to improve eyesight in visually impaired patients. Researchers are developing novel and innovative techniques to enhance vision—and thus quality of life—for people with various forms of vision loss, including strabismus, amblyopia, age-related macular degeneration (AMD), and hemianopia.

- **Center for Corneal & External Eye Disease Research**
  The interdisciplinary research in the Center for Corneal & External Eye Disease Research focuses on multiple conditions that affect the cornea, such as dry eye disease, corneal dystrophies, infections, and injuries. Dr. Dana, a renowned immunologist and forerunner in corneal research, directs this center, which has helped develop numerous pharmacological treatments and innovative therapeutic methods.

- **Center for Age-Related Macular Degeneration (AMD) Research**
  Among retinal diseases, AMD is of particular concern as it becomes more and more prevalent with increasing life expectancies. Led by Dr. D’Amore, a world-renowned authority in AMD, the Center of Excellence for AMD Research brings together outstanding scientists, engineers, and clinicians to decipher the mechanisms of AMD and combat this growing cause of vision loss.

- **Minda de Gunzburg Center for Ocular Regeneration**
  The Minda de Gunzburg Center for Ocular Regeneration forms an arena for developing revolutionary methods to regenerate eye tissues. Michael Young, PhD, a leading expert in tissue and stem cell transplantation, leads the effort to develop regenerative therapies for various diseases, including AMD, glaucoma, corneal disease, and ocular cancer.

- **Children’s Hospital Boston**

A leader in pediatric healthcare for more than 130 years, Children’s Hospital Boston first opened in 1869 as a 20-bed facility in Boston’s South End. Since then, scientists at Children’s Hospital have made important contributions in eradicating some of the major illnesses that have threatened young lives. Today, the hospital stands out as a preeminent institution for pediatric care by utilizing cutting-edge research from disciplines such as genomics, proteomics, and informatics. Children’s Hospital has also revolutionized treatment options for infections, congenital disorders, and other childhood diseases.

The Department of Ophthalmology at Children’s Hospital Boston is the largest group of full-time practicing pediatric ophthalmologists in the United States. Here, children and families receive the most advanced testing and treatment available for all types of visual impairments. Specialized services are available for misaligned eyes (strabismus), cataract and retinal degenerative conditions, as well as comprehensive evaluation and treatment of patients with eye muscle problems or refractive concerns. The Department of Ophthalmology is a collaborative environment that includes clinicians at the top of their field, award-winning principal investigators, and trainees from around the world.

**Innovative treatments for pediatric eye disease**

Led by Ophthalmologist-in-Chief David G. Hunter, MD, PhD, the Ophthalmology Department is known internationally for its innovative research, clinical outcome, and cutting-edge work in the most common pediatric vision problems. Ophthalmologists at Children’s Hospital have extensive experience performing cataract surgery, intraocular lens implantation, and laser treatments of strabismus in infants and children. In some cases, Botulinum Toxin A (a powerful injection that can paralyze muscle) is used in young children to correct strabismus instead of eye muscle surgery. When eye muscle surgery is needed, ophthalmologists can use adjustable sutures, which allow for adjustments to be made in the position of the eye after surgery. Children’s is also at the leading edge of treatment for complex strabismus in children, and recently presented a webinar for management of Duane syndrome using transposition surgery and adjustable sutures.

**Multidisciplinary programs**

Collaboration is central to the success of Children’s Hospital, and multidisciplinary programs allow teams of physicians and scientists with training in different scientific fields to work together to address specific medical problems. Located in the John F. Enders Pediatric Research Laboratories and in the Karp Family Research Laboratories, the Multidisciplinary Programs uniquely position Children’s Hospital to be a pioneer in the applications of vascular biology, bioinformatics, genomics, clinical research, neurobiology, translational research, and stem cell research.

**Expanding partnerships: a model for growth**

In 2009, the Department of Ophthalmology of Children’s Hospital Boston began a formal relationship in patient care with Mass. Eye and Ear and Children’s Hospital Ophthalmology Foundation (CHOF). This unique arrangement furthers the mission of both institutions to increase access to patient care in a seamless fashion and integrate training and research programs.

**World-changing research**

The research mission of Children’s Hospital encompasses clinical research, basic research, postdoctoral training of new scientists and community service programs. With over $825 million in annual funding, Children’s Hospital Boston is home to the world’s most dynamic research enterprise at a pediatric center. Significant ophthalmologic advancements have been made at Children’s in the field of retinopathy of prematurity, revealing the important role of growth factors in this vision-robbing childhood disease. Studies conducted in collaboration with Mass. Eye and Ear have shed new light on the etiology of vision loss in glaucoma, revealing the chain of molecular and cellular events that damage the optic nerve. During the last two decades, intense research at Children’s has uncovered some of the genetic underpinnings of strabismus, revealing the underlying genetics of seven inheritable forms of the disorder.
BEETHAM EYE INSTITUTE AT THE JOSLIN DIABETES CENTER

Joslin Diabetes Center is the world’s premier diabetes research and clinical care institution, and is dedicated to improving the lives of people with diabetes. Joslin Diabetes Center owes its existence to Elliott Proctor Joslin, MD, who is widely considered to be the pioneer of modern diabetes management. When Dr. Joslin began his private practice in 1928, he became the first physician in the United States to specialize in diabetes—which was still a poorly understood disease with few treatment options. In 1952, Dr. Joslin’s practice became formally known as the Joslin Clinic, which moved to its current location in the Longwood Medical Area in 1956.

With the discovery of insulin in the 1920s came substantial growth in the life span of patients with diabetes. Unfortunately, increased life expectancy also brought an increased risk of vascular complications—including diabetic retinopathy. By the 1990s, diabetic retinopathy had become the leading cause of blindness in the United States.

Combating diabetic eye complications at the Beetham Eye Institute

In the 1960s, Joslin physicians Lloyd M. Aiello, MD, and William P. Beetham, MD, noticed that retinal scarring (caused by diabetes) could prevent retinal blood vessels from proliferating, bleeding and detaching—and thus prevent vision loss—in patients with diabetic retinopathy. Drs. Aiello and Beetham developed a method that used lasers to create scars in retinas. This technique, laser photocoagulation therapy, reduced the risk of blindness in diabetic retinopathy by over 75 percent to less than 4 percent. Three decades later, this approach remains the “gold” standard of care for treating proliferative diabetic retinopathy and has saved the sight of hundreds of thousands of people worldwide.

To combat diabetic eye complications, the Joslin Clinic formed The William P. Beetham Eye Institute (BEI), a dedicated on-site eye research center that fosters close partnerships between physicians and scientists at Joslin and BEI. Through the years, this model of collaboration has accelerated the introduction of new diagnostic and therapeutic modalities to prevent vision loss in diabetes, and has led to preeminent discoveries and improvements in diabetes eye care that have preserved vision for more than nine million people worldwide. Today, the Institute participates in virtually every major medical trial for diabetic retinopathy in the United States, some 24–46 trials at any given time.

A new wave of discoveries

Despite advances in eye-care, some patients with diabetes still suffer visual loss. Today, Joslin clinicians and researchers from the BEI continue their quest to develop new and improved methods to prevent diabetes-related eye complications. HEMS Professor of Ophthalmology, Dr. Lloyd P. Aiello, MD, PhD, is Head of Joslin’s Section on Eye Research and Director of the Beetham Eye Institute. In recent years, Dr. Aiello and other BEI members have been at the forefront of several key discoveries that may soon yield better treatments and therapies. These include the development of inhibitors to stop pre- liferation, bleeding, and detachment of blood vessels in the back of the eye, as well as the development of treatments that prevent the activation of a molecule called protein kinase C (PKC). Previously, BEI researchers found PKC to be a major signaling pathway that, when activated, can trigger early cellular changes in the eye leading to diabetic retinopathy. Investigators have also identified a new molecular path to diabetes; for example, the thickness of the retina and changes in blood flow in the back of the eye—that may enable clinicians to better predict who may be at risk for the disease.

Preventing blindness through patient participation

Dr. Elliott P. Joslin believed that patient participation and empowerment were vital in the effort to control diabetes. Fulfilling this vision is the Joslin Vision Network (JVN), implemented by Joslin researchers in 1995. This initiative uses advanced video technology to detect abnormal retinal blood vessels, and not only allows regular and noninvasive screenings of diabetic retinopathy (at over 70 sites in the United States and abroad), but also allows patients in the network to participate in clinical trials. Through its 50-Year Medalist program, the Joslin Diabetes Center also recognizes individuals who live with diabetes for 50 years or more without complications. Many Medalists are participating in a long-term study that is yielding important clues into the prevention of diabetic retinopathy.

MASSACHUSETTS GENERAL HOSPITAL

Massachusetts General Hospital consistently ranks in the top 1 percent of the nation’s medical institutions and is second in U.S. News & World Report’s most recent, “America’s Best Hospitals Survey.” Working collabora- tively within Harvard’s broad network, the clinicians and researchers in this world-class institution are bringing scientific breakthroughs to ophthalmic practice.

Allies in comprehensive eye care

In close collaboration with multiple HMS affiliate and partner institutions, Massachusetts General Hospi- tal (MGH) offers comprehensive and expert care for a broad range of eye conditions. In 2009, the hospital teamed with Mass. Eye and Ear to establish the Mass. Eye and Ear/Massachusetts General Hospital Department of Ophthalmology, an innovative alliance that formalized the centuries-old clinical and academic partnership between the two world-class institutions. The department is staffed by Mass. Eye and Ear physicians under the direction of HMS Ophthalmology Chief and Chair, Joan W. Adams, MD. Deeper collaboration and joint programmatic planning is enhancing the quality of care, research, and teaching at both institutions. Patients, in particular, will benefit from this closer connection with seamless access to the most innovative care available anywhere in the world.

The proximity to Mass. Eye and Ear also allows access to advanced diagnostic tests, such as optical coherence tomography, optic nerve imaging, and fundus imaging. The Mass. Eye and Ear/MGH Children’s Hospital provides pediatric services in collaboration with oph- thalmologists from Children’s Hospital Boston—both primary pediatric teaching sites for HMS. These valuable alliances allow the ophthalmology specialists at MGH to determine the best possible course of treatment for each patient.

Neuro-ophthalmology consultation

Because visual function is closely integrated with neuro- logical function, many conditions that affect the brain may also affect vision. Through a streamlined consulta- tion process, physicians from Mass General’s neurology, neurosurgery, and inpatient services work jointly with Mass. Eye and Ear’s Neuro-ophthalmology Service to provide unparalleled services to patients with neuro-visual complications, as well as patients with primary neurological conditions that may cause visual distur- bances. This service is widely recognized for handling rare neuro-ophthalmic conditions, and receives many referrals from general ophthalmologists and optometrists. In addition, the service coordinates ophthalmic inpatient consultation for urgent patient care.

Cooperative pathology programs

The Mass General Hospital Surgical Pathology Service and Mass. Eye and Ear’s David G. Cogan Laboratory of Ophthalmic Pathology collaborate extensively to provide enhanced diagnostic services. The staff and full spectrum of diagnostic methods from MGH’s surgic- al pathology services are available to facilitate the diagnostic and research work undertaken in the Cogan Laboratory. Cooperative programs between MGH and ophthalmic pathology specialists also support clinico-pathology research projects and enhanced educational and training initiatives throughout the HMS Ophthalmology campus.

Teleretinal screening program

Another vital alliance between Mass General Hospi- tal and Mass. Eye and Ear was realized in 2008 when a teleretinal imaging program was established at MGH’s Chelsea Health Center. The program provides expanded, preventive care to high-risk patients with diabetes. Retinal images are sent electronically to Mass. Eye and Ear and screened for diabetic retinopathy and other pathologies, enabling early intervention and potential sight-saving diagnosis and treatment. This program also provides primary care practices with key diabetes screening results that are central to meeting major performance measures of health care insurers.
Type I Keratoprosthesis (KPro) surgery pioneered by HMS Emeritus Professor, Claes Dohlman, MD, PhD; other innovative procedures include Descemet’s striping endothelial keratoplasty and treatments for choroidal melanoma.

### Training partners

The VA Boston Healthcare System has a strong educational partnership with Mass. Eye and Ear and HMS. Residency training is a key mission area of VA ophthalmology. Guided by Dr. Daly, the department has significantly improved the quality and depth of its training program in just the last few years, which has evolved into a highly structured curriculum comprised of surgical conferences, weekly faculty lectures and journal clubs, with greater participation from residents. HMS residents complete one six to seven week block rotation at the VA each year of residency with exposure to general and subspeciality clinical care in retina, cornea, glaucoma, oculoplastics, and neuro-ophthalmology, as well as hands-on surgical training. Third-year residents receive intensive cataract training and serve as primary surgeons on a large volume of cataract and glaucoma surgeries. The department utilizes state-of-the-art equipment, including two Eyetsi virtual reality simulators to help residents hone their surgical skills.

### Supporting innovations in research

Historically, the U.S. Department of Veterans Affairs has supported innovative R&D efforts in many areas of healthcare to improve the lives of Americans. This same spirit of purpose drives ongoing research efforts at the VA Boston. Since 2002, the VA has supported the efforts of HMS Professor of Ophthalmology, Dr. Joseph Rizzo III, MD, in the Boston Retinal Implant Project. In this endeavor, Dr. Rizzo leads a team of physicians, scientists, and engineers to develop an implantable microelectronic retinal prosthesis that can essentially restore some vision to people blinded by retinitis pigmentosa and age-related macular degeneration (AMD). This highly challenging and multidisciplinary research is being carried out by the Center for Innovative Visual Rehabilitation located at the VA.

Mary K. Daly, MD

Lecturer on Ophthalmology, Harvard Medical School
Associate Professor of Ophthalmology, Boston University School of Medicine
Chief of Ophthalmology, Veterans Affairs Boston Healthcare System
Associate Director, HMS Ophthalmology Residency Training Program, Veterans Affairs Boston Healthcare System

Dr. Mary K. Daly obtained her BA from Harvard College in 1994 and her MD degree from Johns Hopkins University in 1998. After completing an ophthalmology residency at the Wilmer Eye Institute at Johns Hopkins in 2002, she conducted fellowship training in cornea and external eye disease at Moorfields Eye Hospital, London. Dr. Daly specializes in complex cataract, anterior segment, and corneal surgery including keratoprosthesis and Descemet’s stripping endothelial keratoplasty.

Since 2005, Dr. Daly has championed transformative changes within the Department of Ophthalmology at the Boston VA, boosting continuity and quality of patient care, expanding research efforts, and creating an enhanced training rotation for HMS residents. Under her guidance, the department’s staff, programs, and services continue to grow at a rapid clip. She has recruited superb clinical and research talent to the department, including clinician scientists from Mass. Eye and Ear and the Boston University School of Medicine, tripling the number of full-time staff in the last two years. She credits VA Boston Leadership—including Dr. Kamal Itani, Chief of Surgery, Dr. Michael Charness, Chief of Staff; and Dr. Michael Lawson, Medical Center Director—for their tremendous support of Ophthalmology at VA Boston and for always putting the patient first. “Today, I’m proud to say that our staff and capabilities are at the leading edge of technology, and we are providing premier ophthalmic services to our veterans. It’s unbelievably rewarding to work here and with this particular patient population,” says Dr. Daly. “I know everyone, including the residents, consider themselves lucky to be taking care of this wonderful group of people.”

Dr. Daly is also a clinical champion of the Ophthalmic Surgical Outcomes Data Committee (OSOD) under the direction of Mary Lawrence, MD, Deputy Director of the Boston Integrated Ethics Committee, which strives to ensure ethical practices in the Veterans Healthcare Administration and foster a strong ethical culture through ethical leadership.

Dr. Daly is also a clinical champion of the Ophthalmic Surgical Outcomes Data Committee (OSOD) under the direction of Mary Lawrence, MD, Deputy Director of the Vision Center of Excellence. The VA Boston is one of five OSOD pilot sites tracking ophthalmic surgery data in order to establish a prospective outcome-based program for comparative assessment and enhancement of the quality of cataract surgery across the VA system.

VETERANS AFFAIRS BOSTON HEALTHCARE SYSTEM

The Veterans Affairs Boston Healthcare (VHA) System—one of 171 VA health care facilities across the country—is a full-service tertiary care center that provides a broad spectrum of medical, surgical, and rehabilitative care to veterans across New England and the Veterans Integrated Service Network 1. The medical center encompasses three main campuses and five outpatient clinics located within a 40-mile radius of Boston.

### Providing world-class care to veterans

Affiliated with Boston University and Mass. Eye and Ear/HMS, the VA Boston Ophthalmology Department provides veterans with a full complement of eye care and services with specialization in vitreoretinal diseases, glaucoma, neuro-ophthalmology, oculoplastics, cataract, strabismus, and corneal/external eye diseases. In recent years, under the leadership of Chief of Ophthalmology, Mary K. Daly, MD, the department’s reputation for delivering excellence in patient care has flourished; today, it is a premier provider of ophthalmic care within the VA national network. The busy department offers 24/7, on-call access to more than 20,000 patients every year; a number that has steadily climbed in recent years along with an influx of ophthalmic referrals from other VA centers across the country. The department continually strives for innovation and, for example, is one of a handful of VA medical centers nationwide that offers certain highly specialized procedures such as the Boston
Converging disciplines
In conjunction with the Department of Ophthalmology, the Neuro-Ophthalmology Service, under the direction of Nurhan Torun, MD, employs a wide range of ophthalmologic and neurologic evaluative techniques to provide care for patients with neurologic difficulties. The Eye Movement Laboratory provides quantitative assessment of difficulties with eye movements and visual perception, both for research and for patient care needs.

BIDMC partners with the nearby Joslin Diabetes Center, a preeminent diabetes research and clinical care organization, to provide patients with a spectrum of multidisciplinary care for diabetes and endocrine disorders in both inpatient and outpatient settings. The BIDMC/Joslin Collaborative Eye Care Program offers diabetes-specific ophthalmic care focused on preventing and treating eye disease. Ophthalmologists in this program are specially trained to treat complex eye conditions associated with diabetes.

Highly lauded teachers and mentors
Using outstanding depth of knowledge and experience, BIDMC’s esteemed team of mentors, educators, and clinicians play a key role in the education of HMS ophthalmology residents and fellows. All second-year residents rotate through BIDMC and participate in comprehensive ophthalmology and subspecialty clinics, including retina, glaucoma, and neuro-ophthalmology. Surgical experience is also a primary focus of this rotation, and residents spend a significant amount of time participating in cataract, retina, and glaucoma surgeries. Drs. Berson and Arroyo, and Mark Kuperwaser, MD, have received teaching awards from Mass. Eye and Ear; HMS ophthalmology residents, most recently Dr. Kuperwaser in 2010.

BET ISRAEL DEACONESS MEDICAL CENTER
Beth Israel Deaconess Medical Center (BIDMC) is one of the nation’s preeminent academic medical centers, committed to providing excellence in clinical care, teaching, research, and community outreach. A major teaching hospital of Harvard Medical School with more than 1,250 full-time medical staff, BIDMC is ranked each year as a “Best Hospital” by U.S. News & World Report in multiple specialties. BIDMC’s focus on safe and quality patient care has helped establish them as a national leader in health care quality, safety and transparency. BIDMC’s thriving research programs, state-of-the-art clinical care and unparalleled medical education are recognized worldwide.

The BIDMC Division of Ophthalmology
Located within the Longwood Medical Eye Center, the BIDMC Division of Ophthalmology provides comprehensive medical and surgical treatment of eye diseases.

Dr. Frank Berson, Chief of the Division of Ophthalmology, leads an exceptionally trained team of ophthalmologists, all of whom hold academic appointments in the HMS Department of Ophthalmology. In research and clinical care, the Division collaborates with other HMS affiliates, including Beth Israel Eye Institute at Joslin Diabetes Center and Mass. Eye and Ear.

Under the direction of Jorge G. Arroyo, MD, MPH, the Retina Service serves an international patient base, and handles some of the most complex vitreoretinal cases utilizing a complete array of state-of-the-art equipment and intraocular instruments. Dr. Arroyo is a sought-after authority in complex vitreoretinal and other surgical techniques and has participated in research studies on age-related macular degeneration (AMD), retinal detachment, and diabetic retinopathy.

BIDMC Division of Ophthalmology provides comprehensive medical and surgical treatment of eye diseases. Ophthalmologists in this program are specially trained to treat complex eye conditions associated with diabetes.

Frank G. Berson, MD
Associate Professor of Ophthalmology, MD
Chief, Division of Ophthalmology, Beth Israel Deaconess Medical Center

As Chief of the Division of Ophthalmology at BIDMC, Dr. Berson is an integral member of the world-renowned surgical staff in the HMS Department of Ophthalmology. He holds an academic appointment as Associate Professor in Ophthalmology at HMS. Dr. Berson was recently recognized by BIDMC for his milestone anniversary of 30 years of service.

Board-certified in ophthalmology, Dr. Berson received his MD degree from HMS in 1971. After completing an internship in surgery at Beth Israel Hospital, he went on to complete his residency and fellowships in ophthalmology at Mass. Eye and Ear. Dr. Berson’s clinical interests are focused on glaucoma and cataracts. For more than two decades (1982–2004), he served as Director of Medical Student Education for Mass. Eye and Ear/HMS Department of Ophthalmology. From 1982 to 1992, he was the Director of the HMS Ophthalmology Residency Training Program.

Dr. Berson currently serves on the Executive Committee and the Subcommittee for Promotions and Reappointments in the HMS Department of Ophthalmology. At BIDMC, he is a member of the Board of Overseers and Treasurer of the Beth Israel Surgical Foundation.
BRIGHAM AND WOMEN’S HOSPITAL

Brigham and Women’s Hospital (BWH) is committed to upholding the best practices in eye care. Centrally located in Boston’s Longwood Medical Area, BWH has established a strong partnership with the Mass. Eye and Ear Department of Ophthalmology to ensure that their patients have convenient and direct access to best-in-class eye care providers and services.

The hospital’s guiding philosophy is to utilize an exceptionally trained and experienced team of eye care providers, resources, and technology to achieve an optimal outcome for every ophthalmology patient.

Comprehensive care through collaboration

BWH offers comprehensive ophthalmology services and most subspecialty eye care through this clinical affiliation with Mass. Eye and Ear, which offers world-renowned expertise and diagnostic and treatment capabilities unmatched in the region.

As the result of a comprehensive partnership, Mass. Eye and Ear began providing inpatient subspecialty ophthalmic care and emergency eye trauma coverage to BWH patients in 2009. Trauma care at BWH is coordinated by the director of the Mass. Eye and Ear Ophthalmic Trauma Service and is reinforced by its unique around-the-clock, dedicated Eye Emergency Department. This creative alliance has helped to streamline and boost quality of care for patients who can now receive 24/7 on-site treatment at BWH from an outstanding group of physicians who rank as one of the leading eye trauma management teams in the country.

Integrated clinical services and training

A second innovative alliance in 2009, led by Mass. Eye and Ear and the Beetham Eye Institute at Joslin Diabetes Center, has enabled continuity of follow-up care (post discharge) for BWH patients with the establishment of a new, outpatient comprehensive ophthalmology service (COS) at One Joslin Place. Located in the heart of the Longwood Medical Area the service is directed by Lloyd Paul Ayllo, MD, PhD, and staffed by Mass. Eye and Ear ophthalmologists with participation from Joslin retina specialists and BWH neuro-ophthalmologist director, Dr. Don Brienfang. The service provides BWH with outpatient patient services, as well as inpatient consultations and marks yet another important milestone in collaborative service development among HMS affiliates. Patients can receive routine annual eye and vision exams as well as spectacle and lens correction. Comprehensive evaluation and treatment of complex and systemic disorders, such as cataract, glaucoma, diabetes, macular degeneration, retinal detachment, conjunctivitis, and dry eye are also provided.

The Neuro-Ophthalmology service of the Brigham and Women’s Hospital Department of Neurology diagnoses and treats disorders involving the visual pathways and eye movements. A number of neurological conditions affect the areas of the brain devoted to vision. Disturbances of these important visual areas may produce debilitating symptoms, and often require high-quality, specialized care.

ARAVIND EYE HOSPITALS

The Aravind Eye Care System of India is the world’s largest provider of eye care services, encompassing five hospitals, three managed eye hospitals, an international research foundation, an ophthalmic product manufacturing center, and a training center. Committed to the prevention of needless vision loss, the Aravind Eye Hospitals are revolutionizing the concept of efficient and sustainable eye care across the developing world.

Upon his retirement in 1976, Govindappa Venkataswamy, MD, established the GOVERN Trust to support an alternate health care model. Under this Trust, the Aravind Eye Hospitals were created as a self-sustaining system that not only provides affordable high-quality care for millions of individuals, but also serves as a model example of sustainable health care.

For its remarkable impact, the Aravind Eye Care System has been honored with several prestigious awards, including the 2007 The António Champalimaud Vision Award, the 2008 Gates Award for Global Health, and the 2010 The Conrad N. Hilton Humanitarian Prize.

International partnership

Since 1988, HMS senior residents have had the option of an elective rotation at Aravind Eye Hospital in Madurai. This unique training experience offers residents an unparalleled learning experience in international eye care, and the opportunity for hands-on clinical and surgical exposure to many ophthalmic conditions rarely encountered in the United States. Since the program’s inception, more than 100 seniors have opted to experience an Aravind rotation.

Expanding on this educational partnership, HMS Ophthalmology and Aravind leadership recently conducted two joint grand rounds teleconferences. These interactive, high-tech events have allowed faculty from both institutions the opportunity to present grand rounds cases in real time, and share observations and insights.

Research and development

Several Aravind programs, catering to all levels of ophthalmic teaching and training, are designed to meet the demands of a growing ophthalmic health care system. More recently, Aravind has expanded its research facilities and created PhD programs for medical and non-medical graduates. In 2010, there were 24 research projects being conducted in the department, with significant growth predicted for coming years.

Telemedicine: remote care and communication

As part of its comprehensive success, Aravind utilizes telemedicine to reach out to remote rural areas using computers, video-conferencing and the Internet. Through these technological services, eye care service is made accessible and affordable by reducing travel cost and time for the patients. In addition, telemedicine provides a network for eye care providers to share their knowledge and expertise.
Look forward to a productive relationship, which will rations.

With investigators to explore potential research collabora
dency training program. Shanghai ophthalmologists

of the team was to learn about the department’s resi
and Ear in the operating room and clinic. Another goal
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mology team from Shanghai. The two-month visit gave

This initial exchange proved highly successful, and HMS

HMS Department of Ophthalmology Residency Training

well as details about the organization, structure of the

as well as the needs of

HMS faculty provided an overview of ongoing research

efforts within the HMS Ophthalmology Department, as

Beginning an international dialogue

HMS Ophthalmology faculty and Chinese colleagues

from Shanghai Eye and ENT Hospital have begun a
dialogue aimed at exploring potential research and edu-
cational opportunities. This endeavor began in earnest

in December 2010, when several HMS faculty members

taveled to Shanghai Hospital on a five-day international

outreach trip. The group received a tour of the institu-
tion and presentations on its clinical and research ef-
forts. Faculty gained a solid perspective of the hospital’s

ophthalmology training process, as well as the needs of

the population they serve; today, for example, there are

only 600 phacoemulsion/cataract surgeons to serve the

country’s population of 1.3 billion. During their visit,

HMS faculty provided an overview of ongoing research

Collaborations aim to advance science

and education

This initial exchange proved highly successful, and HMS

Ophthalmology reciprocated in the spring of 2011 when

the faculty welcomed to Boston a five-member ophthal-

mology team from Shanghai. The two-month visit gave

team members first-hand exposure to a full range of

learning opportunities, including general ophthalmol-

ogy and subspecialty training practices. With specialties

in glaucoma, retina, cornea, and cataracts, each Shang-

hai physician shadowed a faculty mentor from Mass. Eye

and Ear in the operating room and clinic. Another goal

of the team was to learn about the department’s resi-
dency training program. Shanghai ophthalmologists

attended educational programs and lectures, and met

with investigators to explore potential research collabo-

rations.

Ultimately, faculty members from both institutions

look forward to a productive relationship, which will

advance academic programs and scientific endeavors in

various subspecialty fields in China.

**SHANGHAI EYE AND ENT HOSPITAL**

**TOGUS VETERANS AFFAIRS MEDICAL CENTER**

**History**

On March 21, 1866, Congress established the National

Homes for Disabled Volunteer Soldiers (NHDVS) to

provide care for wounded soldiers; soon thereafter, the

Eastern Branch of NHDVS in Togus, Maine was estab-

lished. In 1990, the Togus NHDVS became a part of the

Veterans Administration, which provides benefits to

veterans and their dependents. Since its inception in

1866, Togus VAMC has grown to be recognized locally,

regionally, and nationally as a leader in quality patient

care. Today, the Department of Veterans Affairs Medi-
cal and Regional Office Center has an operating bed

capacity of 796 beds, with a staff of approximately 500

full-time and part-time employees.

**Ophthalmic care**

As a regional referral center for ophthalmology in the

state of Maine, Togus VAMC provides various clinical

services, including general surgery, ophthalmology,

neurosurgery, pain management, and optometry. Here,

senior residents work with staff ophthalmologists in

surgical procedures for a broad range of ocular disease

(including cataracts and glaucoma) as well as retina

laser procedures. Togus VAMC is an academic affiliate

of Mass. Eye and Ear and the New England College

of Optometry.

**Telemedicine: medical care at a distance**

Togus VAMC contributes greatly to the growing suc-

cess of telemedicine programs, such as the Joslin Vision

Network (JVN). Implemented in 1990, the JVN uses

advanced digital video technology to detect abnormal

retinal blood vessels. In 2005, over 1,200 patients from

Togus VAMC were selected to participate in a clinical

trial through JVN. This study demonstrated the utility of

JVN for identifying the severity of wide-ranging ocular

conditions, thus determining the appropriate treatment

priorities for eye care and allowing clinicians to provide

“care at a distance.”

HMS Instructor in Ophthalmology, Joseph Ciolino, MD, and Mass. Eye and Ear Clinical Fellow, Houman Hemmati, MD, PhD at the Massachusetts Institute of Technology (MIT). Drs. Ciolino and Hemmati are collaborating with Professor Robert S. Langer (David H. Koch Institute Professor), Daniel Kohane, MD, PhD (MIT and Children’s Hospital), Claes Dohlman, MD, PhD (Mass. Eye and Ear) in efforts on long-term delivery systems for use in a wide range of ophthalmic conditions.
HMS Department of Ophthalmology researchers and clinician scientists are continuously turning insights into cures that benefit scores of people. Many discoveries and developments, past and present, are helping to enhance the knowledge and practice of ophthalmology worldwide. Here are some of these outstanding achievements:

**RETI NA**
- Isolated the gene governing retinoblastoma, a potentially fatal eye tumor affecting young children. This gene is also a prototype for an entire class of genes relating to cancers of the breast, bone, bladder, and lung.
- Pioneered the use of proton beam therapy for successfully treating intraocular malignant melanoma with minimal or no damage to surrounding tissue.
- Isolated the gene that causes a form of retinitis pigmentosa, a hereditary and degenerative blinding disease of the retina.
- Made the first diagnosis of retinopathy of prematurity, a form of blindness caused by excessive amounts of oxygen given to premature babies.
- Introduced scleral buckle surgery for retinal detachments (to North America).
- Developed laser photocoagulation therapy, which revolutionized the diagnosis and treatment of diabetic retinopathy, and has remained the gold standard of therapy for more than 25 years.
- Developed photodynamic therapy (PDT) with verteporfin (Visudyne®), the first FDA-approved drug treatment for neovascular “wet” age-related macular degeneration (AMD).
- Discovered the role of vascular endothelial growth factor (VEGF) in ocular neovascularization in two of the most common causes of blindness: AMD and diabetic retinopathy.
- Participated in the development of anti-VEGF drugs for treating AMD and diabetic retinopathy. Given by intraocular injection, this new class of inhibitors has been shown in clinical trials to help 90 percent of patients avoid moderate vision loss, while one-third experienced gains in vision.
- In collaboration with Swedish colleagues, developed an algorithm called WINROP, based on measures of postnatal weight gain, this algorithm can predict retinopathy of prematurity nine weeks before development of disease.
- Identified genetic pathways that increase the risk of advanced diabetic retinopathy. A collaboration with the University of San Diego demonstrated that a polymorphism in the promoter region of the cry topsin gene increases the risk for proliferative diabetic retinopathy.
- Developed (with MIT and MGH researchers) optical coherence tomography, the most widely used and non-invasive imaging modality in retina.

**CORNEA**
- Developed the Boston Kerato- prosthesis (BKP), the world’s first and most popular artificial cornea, with more than 5,000 implantations to date in 50 countries.
- Discovered the first drug to cure the virus infection, Herpes Simplex, which causes severe damage to the cornea.
- Elucidated the molecular and physiological mechanisms of corneal swelling and edema that contribute to corneal edging. These discoveries laid the groundwork for many techniques currently used to restore corneal clarity and visual acuity in patients.
- Discovered the mechanism (by which the cornea remains avascular (without blood vessels)). This body of work formed the basis for ongoing clinical trials of novel therapies to treat graft rejection and other inflammatory disorders, including dry eye diseases, which affects millions of people worldwide.
- Demonstrated the protective role of certain molecules (called mucins) to prevent infections on the cornea and surrounding tissue. This key discovery had multiple crossovers to other areas of investigation, including human reproduction and infectious diseases.

**DISCOVERIES**

**OPTIC NERVE/GLAUCOMA**
- Demonstrated (in postnatal mice) successful full-length regeneration of the optic nerve.
- Identified several genetic, hormonal, and environmental factors associated with various forms of glaucoma, a diverse group of conditions that can potentially damage the optic nerve.
- Identified novel targets for potential neuroprotective strategies in glaucoma management.

**MAKING A DIFFERENCE**
- Paul A. Chandler, MD, and W. Morton Grant, MD, describe clinical features of glaucoma, and form definitive concepts in the management of the disease. Their book Chandler and Grant’s Glaucoma remains an authoritative reference text since its first publication in 1965.
- Discovered seven different forms of strabismus arising from a variety of genetic errors in brainstem motor neuron development. This body of work defined a new category of congenital disorders that leave children unable to move their eyes in specific directions.
- Discovered that earlier intervention in unilateral corona syn- opticous (by way of endoscopic strip cranioctomy) can prevent sight-threatening strabismus and strabismus.
HMS Ophthalmology Centers of Excellence drive collaboration

From novel clinical and research partnerships to new educational venues, many exciting initiatives in recent years are transforming “business as usual” within the HMS Department of Ophthalmology. Contributing to this momentum, the HMS Department of Ophthalmology has launched Centers of Excellence (COEs) in key subspecialty areas that draw on the exceptional talent and resources of the HMS community. These efforts are advancing scientific discovery, expand training opportunities, and bringing new innovations into the clinic. COEs are underway in the areas of diabetic eye disease, age-related macular degeneration (AMD), corneas, and glaucoma.

“Momemtous leaps in science, biotechnology, and medicine in the last decade have brought the future of healthcare to our doorstep—creating unprecedented opportunities for advancement,” says Lloyd P. Aiello, MD, PhD, HMS Ophthalmology Vice Chair for Centers of Excellence and Director of the Beetham Eye Institute at Joslin Diabetes Center. “Centers of Excellence allow us to lead by design and create communities of collaborators that will bring the next generation of advances to fruition. COEs also provide the framework for moving information and ideas across campus with improved speed and access, helping us to accelerate progress in all aspects of our mission.”

COEs integrate the clinical, research, and academic objectives of HMS’s six ophthalmology affiliates and broad faculty base of 145 full-time clinicians, scientists, and academicians—creating an information network that links ideas, resources, and people in pursuit of common goals. Each center is a catalyst for collaboration—creating a multidisciplinary “think tank” that identifies new training opportunities, broadens the scope of research at every juncture, and elicits the highest benchmark standards in all aspects of clinical care.

Core Concepts

- Utilize inherent leadership and expertise to build the key structure, components, and mechanisms of each center for maximum results.
- Identify communication strategies that integrate academic, clinical, and research objectives, and spark cross-institutional involvement.
- Develop unified and readily accessible standards and metrics to improve patient care across the HMS campus and to lead national benchmark standards of care.
- Establish, maintain, and share preferred practice patterns through an ongoing clinical quality program that utilizes robust, evidence-based surgical and outcomes review.
- Facilitate vital research, educational, and clinical partnerships within HMS and in collaboration with community and academic institutions across the United States.
- Expand training opportunities and boost recruitment efforts through stimulating and supporting mentorship, resident, and fellowship programs.
- Create a focus for new funding opportunities that attract sponsorship from government, industry, foundation, and private donors.

As the HMS COEs continue to evolve, department Chair Joan Miller, MD, anticipates that they will be a global resource for innovation. “As our world becomes increasingly connected, we need to embrace strategic partnerships that advance collaboration and connections in our three mission-critical areas,” she said. “COEs represent a scalable healthcare model that will help forge these synergies and usher in advancements that resonate here and around the world.”
CENTERS OF EXCELLENCE

HIGHLIGHTS

Diabetic eye disease
- BEI clinical research program (DRCR.net)
- Joslin Vision Network (model for preferred practice patterns)
- Latino diabetes initiative

Age-related macular degeneration (AMD)
- Public symposia and outreach
- Biennial AMD International Symposium
- Experimental models for ocular research

Ocular Surface Imaging Center (OSIC)
- Increased ten-fold thanks to high-tech imaging equipment and enhanced diagnostic methods developed by OSIC Director, Pedram Hamrah, MD.
- BEI clinical research program (DRCR.net)
- Translational research center
- Ocular Surface Imaging Center
- Monthly cornea conference

Glaucma
- Clinical research faculty focus groups
- State-of-the-art glaucoma laboratory
- Glaucma COE newsletter

Optimizing eye care
The aim of evidence-based data helps identify the best eye care delivery systems. The Diabetes COE, for example, is using data-driven management practices for its acclaimed international imaging program, the Joslin Vision Network (JVN), to evolve standards across other areas of diabetic eye disease. Lessons learned from the JVN can now be used to improve screening techniques, rigorously validate imaging methods, establish detailed metrics, and engage in multi-institutional collaboration. All of this information can be fed continuously to other faculty engaged in related research within HMS and with outside collaborators.

Delivering care in real time
In just one year, patient referrals to the department’s new Ocular Surface Imaging Center (OSIC) have increased ten-fold thanks to high-tech imaging equipment and enhanced diagnostic methods developed by OSIC Director, Pedram Hamrah, MD. These optimized tools and techniques enable real-time and non-invasive imaging, allowing our physicians to diagnose, monitor and track disease progression and treatments with unprecedented speed and precision. These methods also eliminate the need for invasive biopsies and slow cultures, and reduce the wait time for results from three to seven days to less than 24 hours. In many cases, results can be read during the patient’s visit. For thousands of patients each year, this means better diagnosis, treatment, and outcomes.

Tools of the trade
- Medil ConfoScan 4 and the Heidelberg HRT 3
- Rostock Cornea Module confocal microscopes
- Haag- Streit IM 900 digital slit lamp camera, and a Optovue Ocular Coherence Tomographer with cornea module.

Focus for funding
COEs create new funding opportunities in every aspect of the mission of the Department of Ophthalmology. For example, researchers in the AMD Center of Excellence conduct preclinical investigations using a variety of animal models, and carry out small-scale clinical trials to establish a foundation for proof-of-concept in humans. In recent years, work with these models has led to revolutionary treatments for macular degeneration, including the photodynamic therapy and a number of antiangiogenic agents. Today, HMS investigators use models for angiogenesis, diabetic retinopathy, retinal detachment, glaucoma, intracranial tumors, and retinis to develop novel pharmaceutical, biological, and gene-therapy approaches to treat eye diseases. Investigators are also developing the first dry AMD primate model to better understand the pathophysiology of the disease, as well as potential therapeutic targets. To learn more, contact Kim Fechtel at kim_fechtel@mgh.harvard.edu.

Making connections
COEs provide a scalable platform for expanding collaboration, education, and training opportunities. For example, a monthly glaucoma focus group was the first point for merging the research efforts of Louis Pasquale, MD, from Mass. Eye and Ear and Emmanuel Buys, PhD, from Mass General.

During a recent meeting, Dr. Buys spoke to the group about his research on a knockout mouse model that turned out to have direct relevance to Dr. Pasquale’s epidemiology research on primary open-angle glaucoma. Finding common ground, they teamed up with Scheepens scientists Bruce Kramers, PhD, and Meredith Gregory Kramers, PhD, to validate that the mouse model is applicable to POAG in humans. The group has submitted an R21 grant application to NIH. “This cross-fertilization of ideas is an exciting hallmark of the glaucoma Center of Excellence,” says Dr. Pasquale. “We learn first-hand about ongoing work across the department, and how our clinically relevant findings may have direct application to what our colleagues are discovering in the lab.”

One size does NOT fit all
Ten years ago, the Human Genome Project provided a genetic blueprint of the DNA code that ushered in a revolution in personalized medicine. The goal at HMS is to capture genetic variations that contribute to human disease and use it to improve patient care for every disease we treat. COEs provide an integrated framework for delivering personalized medicine to every patient. By merging clinical data (electronic medical records) with a biorepository of donor DNA and tissue samples, HMS clinician scientists can draw unprecedented insights into how diseases manifest, and the best route to intervention based on a patient’s unique genetic and biological make-up.

Tear down those walls!
COEs engender a disease-driven approach that break down traditional research silos, and engage basic researchers and clinician scientists in direct and focused dialogue. Pertinent clinical opportunities can then be identified and moved from bench to bedside with greater speed. “At any given time, ophthalmology faculty members are leading investigations for 50 to 75 clinical trials in various phases, and pursuing vital grant research,” notes Dr. Joan Miller, HMS Ophthalmology Chair. “COEs simplify our communication structure and open the floodgates for scientific inquiry and discovery across the department in complementary areas. What’s happening in AMD research, for example, may yield critical insight into diabetic eye research, and vice versa. It may also embolden scientists to take their research in entirely new directions.”
the study aims to better understand the natural history of intermittent exotropia. Using rigorous study protocols, the Pediatric Ophthalmology Visiting Professor Lecture at Children’s Hospital in Boston has built one of the country’s premier practices in ophthalmology. Integrating their depth of experience into our core services enables us to deliver seamless and integrated care to our most vulnerable patients. “This partnership is a significant milestone in keeping a top-tier pediatric care provider,” says David Hunter, MD, PhD, Ophthalmologist-in-Chief at Children’s Hospital Boston. “It reinforces our already deep commitment to quality patient care by making our world-class services increasingly accessible to patients including treatment for the most complicated eye and vision problems.”

Raising the bar on research
By pooling resources and a patient base that combines pediatric eye and adult strabismus cases, the new alliance also enhances investigative teamwork carried out internally, and brings more opportunity for the department—and patients—to participate in benchmark clinical studies on an international scale. Melanie Kazlas, MD, Medical Director of the Children’s Hospital Ophthalmology Department Foundation at Mass. Eye and Ear, describes one such study that involves the Pediatric Eye Disease Investigative Group (PEDIG), a collaborative network funded by the National Institute of Health that facilitates multicenter clinical research in strabismus, amblyopia and other eye disorders that affect children. Housed in each Children’s Hospital Ophthalmology, Susanne Johnston, MD, is Principal Investigator of a randomized clinical trial comparing observation vs. occlusion therapy for intermittent exotropia. Using rigorous study protocols, the study aims to better understand the natural history and progression of intermittent exotropia (wandering eye) and determine the best method of managing the disease in young patients. Until now, there have been no studies to verify the efficacy of our current treatment,” says Dr. Kazlas. “Studies like this provide important public health implications because they help establish standards for solving common childhood problems in eye disease using evidenced-based medicine.”

Currently, more than 60 sites comprising 225 pediatric ophthalmologists and optometrists in the United States, Canada, and the United Kingdom participate in the PEDIG network on various studies. “Forward-thinking consortiums like PEDIG help generate new ideas that can then be pursued in a collaborative, well-designed study. Integrating Mass. Eye and Ear and CHOF pediatric services gives us the scalable patient base required to participate, as well as the vital research resources and support staff we need to carry out a long-term study,” noted Dr. Kazlas.

Patient empowerment
Bringing PEDIG to Mass. Eye and Ear also affords patients more opportunities to participate in ongoing investigations. Some patients, for example, have contributed clinical information in the form of blood, tissue, and DNA samples that have helped to elucidate the genetics of common forms of strabismus. Study participation is empowering for many patients whose vital contributions can help pave the way for new treatments or lead to a cure for their disease.

Enhancing resident education
The clinical alliance between CHOF and Mass. Eye and Ear also has enhanced resident education with added exposure to important pediatric ophthalmology and strabismus topics through lectures at both institutions. The Pediatric Ophthalmology Visiting Professor Lecture Series, organized by Dr. Anne Fulton, HMS Professor of Ophthalmology, invites faculty who are leaders in the field of pediatric eye disease and strabismus to lecture and interact with faculty, residents, and students. These lectures are televised remotely to Mass. Eye and Ear’s main campus and CHOF’s Waltham location.

Instructor in Ophthalmology, Harvard Medical School Medical Director, Children’s Hospital Ophthalmology Foundation, Massachusetts Eye and Ear Infirmary

Dr. Melanie Kazlas received her BS degree cum laude at Rensselaer Polytechnic Institute in 1989. Following completion of her MD in 1996 and an internship in 1999, both at Albany Medical Center, Dr. Kazlas completed her residency in ophthalmology at Manhattan Eye, Ear and Throat Hospital (MEETH). She went on to complete an ophthalmology and strabismus fellowship at MEETH in 1994. She served as Acting Director of the Pediatric Ophthalmology and Strabismus Service at Mass. Eye and Ear from 2000 until 2009, at which time she was appointed Medical Director of the Children’s Hospital Ophthalmology Foundation at Mass. Eye and Ear.

Dr. Kazlas provides comprehensive evaluation and treatment for babies, children, and adults of all ages with strabismus (otherwise known as misaligned eyes or crossed eyes). In addition to pediatric and adult strabismus, Dr. Kazlas specializes in amblyopia (commonly known as lazy eye), retinopathy of prematurity, and all other areas of pediatric ophthalmology. Exceptionally trained in delicate surgical techniques required for difficult cases of strabismus, Dr. Kazlas has earned a stellar reputation for her compassionate and innovative diagnostic and treatment approaches. Dr. Kazlas is an active health educator, and serves as a leading expert in strabismus and pediatric ophthalmology for ABCNews.com. Dedicated to providing the pediatric community with the best care possible, Dr. Kazlas has teamed with Mass. Eye and Ear’s Outreach staff to provide eye screening to at-risk pediatric populations at Boston’s Camp Harbor View and Neighborhood House Charter School. A member of the New England Ophthalmologic Society, Dr. Kazlas has also co-authored several papers including historical and current practices in pediatric intracranial lens implantation, ocular injuries in shaken baby syndrome, and diplopia after surgical repair of facial trauma.

**Pedig network on various studies.**
As the world becomes increasingly connected, there is a greater need to build viable global healthcare partnerships. In 2005, an initiative funded by the National Institute of Health led to one such collaboration: the US INDOS Joint Working Group, a vision research partnership between the U.S. National Eye Institute (NEI) and the Indian government’s Department of Biotechnology (DBT). Co-Chair of the initiative is Janey Wiggs, MD, MPH, Associate Director of the Howe Laboratory of Ophthalmology, Associate Chief for Clinical Research at Mass. Eye and Ear Infirmary, and Director of the Genetics Diagnostics section of the department’s new Ocular Genomics Institute. As Co-Chair, Dr. Wiggs oversees the U.S. effort, which includes research projects from physicians and researchers from academic medical institutions throughout the U.S.

The exploratory vision science group first met in India in 2005 to identify and facilitate research opportunities between the two countries. The group visited three institutions that deliver high quality eye care and conduct active, vibrant research programs: Aravind Eye Hospital in Madurai, the largest eye care provider in the world and a long-standing educational partner of the HMS Department of Ophthalmology, Sankara Nethralaya in Chennai, and LV Prasad Eye Institute in Hyderabad. Through a series of meetings and workshops, the U.S. team and Indian colleagues paired research interests and skills, which spanned several areas of the molecular genetics of eye disease, including clinical aspects and harmonization of clinical measurement techniques and terminology. Additional areas included translational physiology and the identification, development, and exchange of research resources.

Today, several projects are well underway. For her part, Dr. Wiggs teamed with David Friedman, MD, MPH, PhD, from Johns Hopkins University and Ronnie George, MD, a clinician scientist from Sankara Nethralaya, to study the application of consanguineous pedigrees to mapping of complex genetic traits.

In 2008, Dr. Wiggs received a grant for a National Eye Institute study entitled India-US Genetics Study of Ocular Quantitative Traits. The purpose of the project is to determine the viability of consanguinity for quantitative trait mapping, and to identify genes that are associated with specific ocular characteristics that are risk factors for common, complex eye diseases. During the last several years, Drs. Wiggs and George have worked together to develop project logistics and strategies and to execute each phase of the study, from identifying study participants, to collecting blood samples and analyzing data. The underlying hypothesis of the study is that consanguineous families—compared to nuclear families—may provide a more powerful way to identify genetic factors responsible for quantitative traits. For example, optic nerve size is a quantitative trait that is passed from generation to generation, and larger optic nerves may carry an increased risk of developing glaucoma. In the long term, this information may provide a rich source of genotype/phenotype data that can be mined for genetic insights into blinding diseases such as glaucoma. Analysis of data gathered from the study is currently underway.

Besides having the potential for advancing vision science, the study demonstrates the growing importance of cross-border collaboration. “If our underlying hypothesis proves correct—that consanguineous pedigrees do, indeed, provide a more robust genetic roadmap for flushing out faulty genes—then we’ll have the information needed to accomplish two important goals: helping to pave the way for new diagnostic and therapeutic capabilities, and applying that knowledge to reduce the burden of blindness worldwide,” notes Dr. Wiggs. “It’s a win-win for the U.S. and India, with positive global consequences.”

**THE TEAR FILM & OCULAR SURFACE SOCIETY BUILDS A GLOBAL EYE RESEARCH COMMUNITY**

During the past several decades, a significant international research effort has focused on understanding the composition and regulation of the ocular surface tear film. This effort was motivated by the recognition that the tear film is critical for maintaining corneal and conjunctival integrity, protecting against microbial challenge, and preserving visual acuity. In addition, research has been stimulated by the knowledge that deficiency of the tear film—commonly called “dry eye”—occurs in innumerable individuals throughout the world and over 40 million people in the United States alone. Dry eye may lead to desiccation of the ocular surface—potentially resulting in visual disability and vision loss.

To promote further progress in this field of vision research, David A. Sullivan, MD, MPH, PhD, HMS Associate Professor in Ophthalmology, founded and created a global eye research community that became known as the Tear Film & Ocular Surface Society (TFOS). The mission of TFOS, which was incorporated as a non-profit organization in 2000, is to advance the research, literacy, and educational aspects of the field of tear film and ocular surface. Since incorporation, TFOS has launched numerous initiatives, including:

- Organization of a special experts’ meeting, entitled “Global Treatments for Dry Eye Syndrome: An Unmet Need,” in Florence in 2010. This meeting addressed accepted and emerging clinical endpoints of dry eye with regulatory authorities from around the world.
- Organization of the International Dry Eye Workshop (DEWS), and publication of the DEWS report in The Ocular Surface (2007). The DEWS Report updated the definition, classification, and diagnosis of dry eye disease, and assessed its etiology, mechanism, global impact, management, and therapy. This report, termed the “Regulatory Bible” in Europe, required a 3-year effort of more than 65 experts—from who are associated with the HMS Department of Ophthalmology.

**“TFOS embraces Harvard’s 1650 Charter and mission statement, in that it strives to create knowledge, to advance the sciences, to educate leaders and to pursue excellence in a spirit of productive cooperation.”**

—Dr. David Sullivan, TFOS President

**TFOS TV, which features many important diagnostic procedures cited in the DEWS Report.**

**Sponsorship of TFOS, and facilitation of its growth into the 3rd highest ranked ophthalmic journal in the world.**

**Organization of the International Workshop on Meibomian Gland Dysfunction (MGD), and publication of this TFOS MGD report in March 2011 in IOVS.**

**The TFOS MGD Report provides evidence-based evaluation of meibomian gland dysfunction in health and disease. MGD is very likely the most frequent cause of dry eye. The report required over 2 years of effort from more than 10 leading clinical and basic research experts and is being translated into 12 languages.**

**Collaboration with the ARVO, EYER, MEACDO, ICO, AAO/tips, AOPA, BCLA, British Royal Society of Ophthalmology, Japanese Dry Eye Society, Asian Pacific Academy of Ophthalmology, International Symposium on Ocular Pharmacology and Therapeutics, and Sao Paulo Federal University in organizing scientific sessions.**

**Awards of more than 120 Young Investigator Travel Awards.**

Dr. Sullivan, TFOS President, notes that “TFOS activities have significantly helped to promote increased international awareness of external eye diseases, enhance governmental funding for tear film and ocular surface research, stimulate the development of therapeutic drugs and diagnostic devices, and influence the design and conduct of clinical trials of new and unique treatments for ocular surface disorders.” At present, TFOS has a distribution to thousands of basic scientists, clinical researchers and industry representatives in more than 80 countries. For more information, visit: www.tearfilm.org.
“I am still in awe of what I see every day! As a visual artist and photographer, everything I do is about light and the way it reflects off an object. This operation has given me my creative life back; my sight, I feel, is that of a newborn’s sight, but with a lifetime’s experience in which to use what I now see in artistic ways. I am forever grateful to Dr. Daly and her staff for the professionalism they have shown, and the follow-up care they have given me. Your system works amazingly well. Thank you!”

—Joseph Puleo, Navy Veteran, Photographer and Visual Artist
The brain receives more environmental input from the eyes than from any other sensory system. While most of us enjoy healthy vision, 314 million people around the world live each day with blindness or low vision. For many individuals, loss of vision can have devastating social and economic consequences, leading to a significant loss of independence, mobility, and productivity. In some cases, vision loss is accompanied by significant eye pain or discomfort.

In the United States, blindness or low visual acuity affects 1 in 28 Americans older than 40, or 3.3 million people, according to a 2004 study of age-related eye disease sponsored by the National Eye Institute (NEI). Authors of the study project a significant increase in age-related ophthalmic disease—including cataracts, macular degeneration (AMD), glaucoma, and diabetic retinopathy—as the population ages. By 2020, the number of blind persons in the U.S. is projected to reach 5.5 million—a 70 percent jump—with a similar projection for low vision.

Beyond individual suffering, the economic backlash of blindness and low vision on societies around the world is staggering. In April 2010, AMD Alliance International released a landmark report with the first-ever estimates of the global cost of vision loss—nearly $3 trillion dollars (USD) in 2010 for the millions of people worldwide living with low vision and blindness. According to the study, these costs will rise dramatically through 2020, unless effective prevention and treatment strategies are adopted worldwide.

**Dedicated stewards of vision health**

Working the front lines of vision care every day, HMS Department of Ophthalmology physicians understand the extent to which blindness and low vision can compromise a patient’s quality of life. Fueled by this knowledge, HMS clinicians practice exacting standards of care along the vision health continuum—from well-visits to rehabilitation—combining their expertise with innovations that aim to prevent, mitigate, or cure blinding eye diseases. Each year, the HMS network of physicians draws thousands of patients from around the country and the world seeking treatment for some of the most challenging and complex eye diseases. Collectively, they form a clinical ophthalmic powerhouse, offering an extensive array of the world’s best tertiary and specialty care for patients of all ages and across every ophthalmic subspecialty.

The preceding section of this report, People & Partners, highlights the unique attributes, expertise, and strengths of HMS affiliates and partners. This section focuses on their inspiring clinical innovations and treatments, which have given hope and sight to millions of people around the globe, and credence to the possibility that one day blinding diseases will be relics of the past.
Advanced Clinical Resources

The HMS Department of Ophthalmology continually invests in people, technology, and resources to facilitate a wide spectrum of clinical services, advance quality of care, and enhance every patient’s experience.

Clinical teams

Each clinical area is staffed by teams of highly skilled ophthalmic professionals, including dedicated faculty, fellows, residents, nurses, technicians, and clinical coordinators.

Dedicated eye emergency department

Mass. Eye and Ear’s 24/7 Emergency Department is a unique Center of Excellence that offers unparalleled resources for emergency ophthalmic care and trauma.

Morse laser center

The center performs advanced laser procedures using state-of-the-art refractive, glaucoma, retinal, and anterior segment lasers.

Enhanced imaging and diagnostics center

HMS Ophthalmology affiliates utilize highly sophisticated imaging and diagnostic equipment for precise diagnostic capabilities.

At Mass. Eye and Ear, the Ocular Surface Imaging Center is equipped with confocal microscopy that enables rapid, non-invasive, corneal biopsies, and potentially earlier detection and treatment of disease.

Around the world, an adult goes blind every five seconds and a child goes blind every minute.

— National Eye Institute

FOCUS:

AGE-RELATED MACULAR DEGENERATION

Revolutionary AMD therapies reshape the landscape of patient care

Age-related macular degeneration (AMD) is the leading cause of blindness in adults over age 55 in the United States, and affects some 10 million Americans. The disease causes the macula, the central portion of the retina, to progressively deteriorate; left untreated, it eventually robs patients of their vision.

There are two types of AMD: Dry AMD makes up about 90 percent of all cases, and involves the degeneration of the retinal pigment epithelium (RPE), which is a thin layer of supportive cells beneath the macular photoreceptors. This corresponds with atrophy of the macular photoreceptors and loss of central vision. Although dry AMD is a slow process, this vision loss occurs without deposits in the retina. Biobank

Plans underway to develop a centralized data registry and tissue repository of DNA samples that will be collected from patients and stored electronically. Genetic information will be collected and stored electronically through electronic medical records, enabling clinicians to compare and contrast genetic differences for a host of ocular diseases.

International programs

HMS affiliates’ hospitals offer extensive medical and non-medical coordination services to ensure a friendly and seamless experience for international patients. Services range from assistance with appointments, transportation and accommodations, to language translation assistance.

Contact lens services

Mass. Eye and Ear’s full-service center specializes in therapeutic, bandage lenses, and a range of specialty contact lens uses that address numerous eye diseases and conditions, including astigmatism, bifocal, dry eye, and prosthetics.

Children’s Hospital Boston also provides complete contact lens care for newborns and infants, and specializes in fittings for children with cataract removal, keratoconus, astigmatism, and other conditions.

Around-the-clock pharmacy

Mass. Eye and Ear’s 24/7 pharmacy specializes in ophthalmic medications.

Dedicated social work department

The Social Work and Discharge Planning Department at Mass. Eye and Ear is staffed by licensed clinical social workers and nurses registered in social work and case care. Services are designed to help families cope with medical issues, improve social, and practical concerns related to their illness and treatment.

The status quo began to change in the 1970s when angiogenesis pioneer, Judah Folkman, MD, first proposed the groundwork for the concept that angiogenesis is central to the development and growth of tumors. Dr. Folkman theorized that it was possible to identify specific factors that induce and inhibit angiogenesis, thus providing a way to arrest tumor growth and develop new treatments for cancer. In the decades to follow, Dr. Folkman and other scientists conducted intensive research to identify specific promoters driving angiogenesis. In particular, the efforts of the nine-member HMS Angiogenesis Research Group (HM SARG, see footnote on page 86), led to key studies that elucidated the role of vascular endothelial growth factor (VEGF) in ocular neovascularization, and its potential as a target pathway for treating neovascular AMD.

Studies directed by Joan Miller, MD, and Evangelos Gragoudas, MD, in the Mass. Eye and Ear Retina Research Institute and HMSARG led to the first FDA-approved drug treatment for neovascular (wet) AMD. Photodynamic therapy (PDT) with Visudyne®. Now, with more than 15 years of data, Visudyne® was a revolution in patient care. Injected systemically and activated by light, the drug targets and destroys pathogenic blood vessels in the eye. A relatively painless and quick treatment, Visudyne® marked a significant milestone in patient care by slowing and limiting vision loss without damaging surrounding healthy tissue.

Photodynamic therapy laid the foundation for the second wave of pharmacologic treatments that soon followed. Anti-VEGF drugs Macugen®, Avastin®, and Lucentis® represented a novel attack on the underlying cause of wet AMD. Given by intravitreal injection, this class of inhibitors prevents specific VEGF proteins from binding to receptors, thus thwarting the growth and leakage of destructive new blood vessels that can lead to the disease. These new therapies represent a quantum leap in patient care—not only saving but restoring vision in many patients.

In particular, clinical trials of the drug Visudyne® approved by the FDA in 2006, showed nine out of 10 patients avoided moderate vision loss, while one-third of patients experienced gains of three lines or more on an eye chart. Forty percent of these patients achieved vision of 20/40 or better on a monthly treatment regimen lasting one year.

Today, these pioneering discoveries—coupled with a passion and talent to translate them into vision-saving therapies—have ushered in a new era of patient care for treating wet AMD. Physicians now have powerful anti-VEGF therapies at their disposal that can slow or arrest vision loss in patients—or even markedly improve vision in some cases. In the last decade, nearly one million AMD patients around the globe have avoided vision loss thanks to these therapies.

The unprecedented and rich tapestry of angiogenesis research supported by a translational work pursued by HMS ophthalmologists has established new paradigms of patient care, given hope—and sight—to millions of people, and set forth a promising precedent that is helping to shape the vision of the future. Research efforts continue at full throttle as the HMS Department of Ophthalmology continues the quest to solve some of the most complex genetic and epidemiologic puzzles in retinal science.

“We’ve made some dramatic gains in AMD research and clinical care that serve as an exciting platform for discovery on which to forge ahead,” said department chief and chair, Joan Miller. “Our research mandates today of follow the biology” take aim at several different AMD targets that potentially could lead to better therapies and preventive measures in the years ahead.”

$3,000,000,000,000 (U.S. dollars) The estimated cost of global vision loss today.

— AMD Alliance

*$DBS*
Transforming AMD: Treatment restores vision

**PATIENT PROFILE**

Gloria Cohen, an avid tennis player and golfer and now a youthful 72, was diagnosed with AMD at the age of 49. Reading one evening, she noticed that the words on the page were blurred. Gloria made an appointment with an optometrist to get reading glasses. During her exam, the optometrist noticed tiny accumulations of drusen (deposits) beneath the retina—an early finding of AMD. The optometrist referred Gloria to the Mass. Eye and Ear Infirmary for further examination, and she was diagnosed with dry AMD.

Thankfully, Gloria’s vision did not change for many years. Then, in 2014, two decades after her diagnosis, she noticed while playing golf one day that another person on the tee appeared to have “squinting eyes.” She realized that she was not seeing objects that were in her center of vision. “When I met with a retina specialist, I learned my condition had changed from dry to wet AMD,” Gloria said. This progression occurs only in 15% of all AMD cases. The retina specialist suggested that she undergo laser treatment to destroy the blood vessels and stop the leakage. Uncomfortable with this suggestion, Gloria decided to research other options. She read an article in AARP Magazine about Joan Miller, a retina specialist who was working with a new drug called Lucentis®. In November, 2014, Dr. Miller examined Gloria and found that her visual acuity had decreased to 20/200 on the eye chart. Dr. Miller recalls, “When I met Gloria, I was conducting a clinical trial investigating Lucentis® here at Mass. Eye and Ear. Gloria was a good candidate for the treatment.” The studies found that Lucentis® slowed or helped prevent vision loss in patients. According to Dr. Miller, “The number of patients showing significant vision improvement. In fact, 30% of the patients who were given Lucentis® gained three or more lines of vision improvement on an eye chart. Forty percent of patients achieved driving vision of 20/40 or better.”

The U.S. Food and Drug Administration (FDA) approved the new drug in June 2006. Lucentis® is administered in small doses, injected directly into the eye through the sclera (white coating) of the eye. Gloria remembers the procedure. “The treatment was quick and I didn’t feel a thing.”

“We haven’t seen any serious side effects with Lucentis®, ” Dr. Miller says. Gloria was given three injections of Lucentis® over a three-month period. “When I saw Dr. Miller after the third injection, I had a wonderful surprise,” she said. “My vision had been restored to 20/20 with correction. I didn’t notice the vision improvement because it happened slowly.” Two months later, she had a fourth injection and her vision improved to 20/20.

“Lucentis,” Dr. Miller notes, “is the first treatment that, taken fortnightly, can maintain the vision of more than 90 percent of patients with wet AMD.” This is good news for the 150,000 Americans who are diagnosed each year with the disease. However, Lucentis® is expensive and some people are not covered by insurance, or they are burdened with high co-pays. For others, getting to a doctor’s office for treatment each month can be difficult. “To make treatment easier,” Dr. Miller says, “we are looking at ways to slowly release Lucentis® into a patient’s eye without injections as well as combination of more convenient drug therapies with other drugs that might lead to good results with fewer treatments. We’re also part of a multicenter trial (Comparison of AMD Treatments Trials) to compare Lucentis® and Avastin®, a less expensive and anti-VEGF drug.”

Lucentis® treatments and excellent ophthalmic care from Dr. Miller have transformed Gloria’s life. “I no longer feel handicapped,” she says. “That’s a very good feeling.”

**HMS scientists forge ahead**

Crucial gains in AMD research and treatment, pioneered by Mass. Eye and Ear scientists during the last two decades, mean that millions of people diagnosed with neovascular AMD will potentially retain their vision for life. While this is exciting and remarkable progress, much work remains. In the United States, wet AMD is still the leading cause of blindness in older adults, and is expected to rise dramatically as the population ages and adults live longer. Also, there are currently no FDA-approved treatments for treating the atrophic or “dry” form of AMD. While there are now studies at Mass. Eye and Ear examining anti-VEGF therapy for dry AMD, there are currently no FDA-approved treatments for neovascular AMD. Patients need to receive injections every few months with either prompt or deferred laser treatment—significantly improved vision in many patients with DME, and is quickly emerging as a potential and powerful first-line treatment for people with the disease. The lead author of the study is Lloyd P. Aiello, MD, PhD, Director of the Beetham Eye Institute at Joslin Diabetes Center, and the inaugural chair of the NIH-funded DRCR network. Nearly three out of four people with DME have diabetes and a leading cause of vision loss in the working-age population. Since the introduction of laser photocoagulation for diabetic eye complications, millions of people worldwide have benefited from this treatment, which can preserve vision and reduce the risk of blindness in 90 percent of patients. Now, findings from the DRCR.net study demonstrate that anti-VEGF therapy coupled with the leading standard laser therapy by further reducing diabetic eye complications could be achieved at a substantially lower cost.

The ongoing, five-year study involves a total of 814 eyes of 691 people diagnosed with type 1 or 2 diabetes and diabetic macular edema involving the center of the retina (macula). At one year of follow-up, participants who received anti-VEGF therapy gained an average of nine letters (nearly 2 lines) in visual acuity—a three-fold improvement over laser treatment alone. The percentage of people who experienced a three lines or more gain in vision gain also jumped dramatically, from 28 to approximately 30 percent with anti-VEGF treatment (with prompt or deferred laser) compared to laser treatment alone. Conversely, the number of individuals treated with anti-VEGF medication versus laser alone who experienced two or more lines of vision loss also fell sharply from 13 percent to fewer than 5 percent of people, representing a significant reduction in the number of people who experienced adverse effects.

Few participants experienced eye-related complications, and there were no serious systemic events such as heart attack or stroke associated with treatment. Results from the trial were published online April 2020 in Ophthalmology. Two-year follow-up data are available for 57 percent of study participants, and these results are consistent with the one-year findings.

The results from this clinical trial also show that anti-VEGF treatments for diabetic macular edema are substantially effective, providing substantial improvements in vision and substantial reductions in vision loss,” said Dr. Lloyd P. Aiello. “Anti-VEGF treatments represent a full bench-to-bedside cycle of translational science, with eye-related complications, millions of people worldwide have benefited from this treatment, which can preserve vision and reduce the risk of blindness in 90 percent of patients. Now, findings from the DRCR.net study demonstrate that anti-VEGF therapy could be achieved at a substantially lower cost and the National Institute of Diabetes and Digestive Kidney Diseases.

Initially designed as a three-year study to investigate whether anti-VEGF treatments for diabetic macular edema could result in significant vision improvement, the trial ran until three years had been extended to five years, and is supported by additional funding from the National Institute of Diabetes and Digestive Kidney Diseases.
therapy is saving sight

Kevin England, a 32-year-old participant in the DRCR.net-sponsored diabetic macular edema (DME) study, was diagnosed with type 1 diabetes at the age of five. In October of 2005, he first sought the help of Drs. Jennifer Sun and Lloyd P. Aiello, ophthalmologists at Joslin’s renowned Beetham Eye Institute. At the time, Kevin already had lost sight in his right eye due to complications from diabetic retinopathy. Substantial retinal swelling in his left eye, caused by DME, had reduced his vision to 20/200, the legal definition of blindness.

Fortunately, Kevin’s left eye met the criteria for study participation and he was enrolled in the clinical trial the following January. He was randomly assigned to the study group receiving up to once-monthly injections of the anti-VEGF drug ranibizumab (Lucentis®) in combination with prompt laser therapy. Kevin remembers feeling hopeful that the treatment would arrest the ravaging progress of the disease and save the sight in his left eye. “Even though there were no guarantees, I was happy to be accepted,” he said.

From the outset, participation in this study has involved rigorous evaluation and careful follow-up of patients. For the first 13 months of the study, Kevin traveled once or twice a month from his home in Connecticut to the Beetham Eye Institute to receive treatment and/or an eye exam to check his progress. In Kevin’s case, Dr. Sun gave him intravitreal injections during nine of his first 13 visits and Dr. Aiello performed laser treatment every four months.

Within two months of treatment, Kevin’s vision began to improve. As the DME-induced swelling decreased in his eye, his vision continued to show dramatic improvement. Thirteen months into the study, Kevin’s visual acuity had climbed an average eight to nine letter gain. “Kevin’s left eye has done remarkably well in this study and, despite minor variations month-to-month, his vision has remained strong and intact,” she said. “And he hasn’t experienced any serious side effects, which is consistent with the results from his treatment group.”

For Kevin, who works in construction, the treatments have opened up a whole new world—literally. “I don’t even remember how I managed before,” he says. “I struggled to read a newspaper, watch TV, or see any distance. Now, life is just a whole lot easier.”

Dr. Sun adds, “Our ultimate goal for all of our patients, including as Kevin, is to maintain vision so that they’re not limited by diabetic eye disease. The results in Kevin’s case are especially exciting because he is a young person with many years ahead of him. Saving the vision in his left eye, hopefully, will give him maximum quality of life so he remains independent and continues to have a bright, productive future.”

FOCUS
Ocular Oncology

Ocular oncology involves the study and treatment of tumors that occur in or around the eye. These tumors may cause vision loss or even loss of the eye itself; some ocular tumors are potentially fatal, while others benign yet severely disfiguring.

The HMS Department of Ophthalmology provides unparalleled care for patients with various forms of ocular tumors. Ocular oncologists at Mass. Eye and Ear regularly perform life-changing procedures, and researchers throughout the department are actively pursuing new and improved ways to treat tumors of the eye.

Proton beam therapy: the gold standard of treatment for uveal melanoma

Between the sclera (the “white” of the eye) and the retina lies the uveal tract, which consists of the iris, the ciliary body, and the choroid. Melanomas, which are tumors that arise from melanin-producing cells (melanocytes), sometimes develop in the uveal tract. Uveal melanoma is the most common type of eye cancer that affects adults, and about 25 percent of cases are fatal.

The earliest treatment for uveal melanoma was enucleation, or removal of the eye. Radiotherapy is now the standard of care, and can allow patients to retain their eyes as well as visual function. Proton beam therapy (“PBT”), a very precise form of radiation therapy that was developed by Dr. Evangelos Gragoudas at Mass. Eye and Ear, is particularly effective for treating tumors near critical parts of the eye, such as the optic disc (where the optic nerve joins the retina) or the macula (area of the retina that provides central vision).

Presently, with more than 30 years of follow-up, PBT has proven to have the lowest local recurrence rate of any radiation therapy. There are now 20 proton beam facilities in North America, Europe, South Africa, and Japan. More than 15,000 patients have been treated worldwide. Not surprisingly, the Mass. Eye and Ear Retina Service has become a major center for the treatment of this tumor, as well as a center of investigation for related areas of study in epidemiology, diagnosis, treatment, experimental models, new therapies, and basic research.

Dr. Gragoudas played a pivotal role in the development of PBT for uveal melanoma, and performed both preclinical studies and the first clinical studies in patients. For his invaluable contributions to the field of ocular oncology—as well as the development of vascular-targeting therapies for numerous eye disorders—Dr. Gragoudas received the esteemed Mildred Weisenfeld Award in 2006. In his Weisenfeld lecture entitled “Proton Beam Irradiation of Uveal Melanomas: The First 30 Years,” Dr. Gragoudas describes the evolution of charged-particle tumor therapy from its conception in a Harvard physics laboratory in 1946 to its inaugural use for choroidal melanoma in 1975 at Mass. Eye and Ear. Despite the clinical success of this therapy, Dr. Gragoudas emphasized the need for further optimizing PBT—particularly for complicated tumors and for prevention of metastasis. Along with Drs. Ivana Kim and Demetrios Vavvas of Mass. Eye and Ear’s Retina Service, Dr. Gragoudas continues to refine PBT, and has taken a multidisciplinary approach to developing new strategies for managing uveal melanoma.

By investigating the epidemiology, genetics, and molecular biology of uveal melanoma, Dr. Gragoudas and colleagues may uncover innovative therapies and diagnostic methods for this prevalent and potentially deadly cancer.
Evangelos S. Gragoudas, MD
Charles Edward Whitman Professor of Ophthalmology, Harvard Medical School
Director, Retina Service, Massachusetts Eye and Ear Infirmary

Dr. Evangelos Gragoudas completed his medical training in Athens, Greece and his ophthalmology residency at Boston University School of Medicine. He was a clinical fellow in diabetic retinopathy at the Elliott F. Joslin Research Laboratory at Harvard Medical School (HMS), and subsequently a retina fellow under Dr. Charles Schepens at Mass. Eye and Ear. He was promoted to HMS Professor of Ophthalmology in 1994. Director of the Retina Service since 1985, Dr. Gragoudas has helped transform the service into the preeminent academic and clinical service that it is today. Under his leadership, the service has grown from two clinicians to nine clinicians and clinician scientists pursuing vigorous research activities. The number of retina fellows also increased from two to six, and the fellowship expanded from one to two years. Dr. Gragoudas has trained more than 100 clinical retina fellows, many of whom have gone on to leadership roles in medicine, academics, and industry. The Retina Service also serves an important role in training the 24 residents in the Harvard Medical School Department of Ophthalmology Residency Training Program.

Dr. Gragoudas is an international authority in retinal diseases and intraocular tumors. His early translational work focused on uveal melanoma, for which he pioneered the use of proton beam irradiation—a highly successful treatment that has been in over 15,000 patients to date as approved and safe alternative to enucleation. Along with refining proton beam therapy, Dr. Gragoudas has studied the epidemiology, genetics, and molecular biology of uveal melanoma to further improve diagnosis and treatment for this potentially fatal disease.

Making treatments safer for retinoblastoma patients
Retinoblastoma is the most common primary ocular tumor that affects infants. This cancer develops in the retina, which is the light-collecting tissue at the back of the eye. In advanced cases, the affected eye must be removed; if the cancer spreads to other tissues, retinoblastoma can be fatal. If retinoblastoma is detected early enough, there is a good chance of survival, and it is often possible to save the eye as well as vision.

Ongoing studies in the Department of Ophthalmology aim to improve existing approaches for retinoblastoma, as well as to develop novel therapeutic strategies.

Chemotherapy is often used to treat retinoblastoma. Unfortunately, the existing chemotherapeutic treatments for retinoblastoma can be highly toxic, and may even increase the risks for other forms of cancer. Drs. Demetrios Vavvas, Joan Miller, and Evangelos Gragoudas set out to find safer treatments for retinoblastoma. They focused on a cellular protein called AMP-activated protein kinase (AMPK), which helps tumor cells grow and multiply. Along with colleagues, they found that they could inhibit retinoblastoma cells with a chemical that inhibits AMPK. This chemical, called 5-aminooxazole-4-carboxamide-1-beta-guanosinenucleotide (ACG), holds enormous potential in treating retinoblastoma because it not only inhibits cancer cell growth, but also has very low toxicity. This study, published August 2010 in The FASEB Journal, provides evidence that safer, non-toxic treatments for retinoblastoma may soon be possible.

Several ongoing collaborations between several HMS affiliates are also aiming to improve the methods of treating retinoblastoma. Dr. Shinzo Miki, a pediatric retinal specialist at Mass. Eye and Ear, has helped develop collaborations with Mass General Hospital, Dana Farber Cancer Institute, and Children’s Hospital Boston to test combination chemotherapy and radiotherapy for retinoblastoma. In addition to fine-tuning proton beam therapy techniques, Dr. Miki is also examining the possibility of inducing the body’s own immune defenses to fight retinoblastoma. In a study led by Dr. Bruce Ksander of the Children’s Eye Research Institute, Dr. Mukai and colleagues used the membrane bound, pro-inflammatory form of Fas ligand (Fasl) in a mouse model of intraocular tumors. Fasl induced a potent inflammatory response in mice with tumors of the eye; this resulted in tumor regression, reduced metastasis, and lower mortality. This study, reported July 2005 in the Journal Investigative Ophthalmology and Visual Science, helped form the basis of potential immune-based therapies for retinoblastoma and other intraocular tumors.

Life-changing surgery for patients with vascular malformations
About 10 percent of all babies have vascular birthmarks that develop either before birth or during the first few weeks of life. Most common vascular birthmarks are known as hemangiomas, which are actually non-cancerous tumors made almost entirely of abnormal blood vessels. Hemangiomas are generally not harmful, and many go away without treatment. However, some hemangiomas continue to grow and develop into life-long deformities that may cause significant complications. Such was the case with Alicia Loshkin, a young girl who developed a hemangioma near her eye when she was an infant. When Alicia came to Mass. Eye and Ear in 2009 as a 17-month-old toddler, her hemangioma had grown so large that it was obstructing vision in one eye. Alicia was treated by Dr. Aaron Fay of Mass. Eye and Ear’s Ophthalmic Plastic and Reconstructive Surgery Service.

In collaboration with the Vascular Birthmarks Foundation, Dr. Fay coordinated his consultation and services to remove Alicia’s hemangioma, thus restoring her vision. “When we intervene, it’s almost like—overnight—they’re back to normal,” Dr. Fay says of the surgery. “You can’t even put it in words; it’s really a great feeling to be able to participate in that experience.”

Dean Elliott, MD
Dr. Dean Elliott is Associate Director of the Mass. Eye and Ear Retina Service and a full-time clinical and research faculty member of the HMS Department of Ophthalmology. Dr. Elliott is an accomplished and nationally renowned vitreoretinal surgeon. He is active in clinical trials for retinal disease, with a strong interest in translational research on diabetic retinopathy, AMD, and non-diabetic vascular disease. Prior to joining the department, Dr. Elliott was Professor of Ophthalmology, Director of Clinical Affairs and Director of the Vitreoretinal Fellowship Program at the USC Keck School of Medicine’s Doheny Eye Institute in Los Angeles. Dr. Elliott has been awarded a Heed fellowship, an American Academy of Ophthalmology 2004 Achievement Award, and the Vitreous Society’s 2003 Honor Award.
Drug delivery: envisioning alternatives to eye drops

Approximately 90 percent of ocular medications are delivered to the eye topically—often in the form of eye drops. Because drops are administered periodically, they do not provide sustained drug levels. Drops are also inefficient because reflexive blinking washes away much of the medication; typically, the eye absorbs less than 10 percent of each dose, and the rest may be absorbed by other tissues and result in unwanted side effects. Moreover, studies show that many patients often don’t follow their medication schedules. This is of particular concern as the population ages and the frequency of age-related ocular disorders continues to rise.

Drug delivery is thus an increasingly intense focus of translational ophthalmology research—particularly for conditions that require repeated, long-term pharmacologic intervention. Two new methods of drug delivery, currently in development in the HMS Department of Ophthalmology, may overcome many of the limitations of eye drops.

Drug-eluting contact lenses

Some recent innovations have multiple therapeutic applications that may directly benefit a wide range of patients. This may very well be the case with a novel drug-eluting contact lens—developed in a collaboration between Children’s Hospital Boston and MIT—that directly releases medications into the eye. Inspired in part by the needs of keratoplasty (KPro) patients, Drs. Joseph Ciolino, Daniel Kohane (MIT and Children’s Hospital Boston), Claus Dohlman, and colleagues published a paper describing the development of a drug-eluting contact lens, which can potentially improve surgical outcomes by both protecting the ocular surface of the eye and by preventing post-operative infections. The prototype lens consists of a thin polymer film (containing the pharmaceutical agents) that is encapsulated within a hydrogel material that is used in standard contact lenses. The lens is characterized using scanning electron microscopy and drug-release studies, and showed a steady release rate of an antibiotic (ciprofloxacin) that effectively inhibited bacterial growth for more than four weeks. The design and characterization of the drug-eluting contact lens was reported in July 2009 in Investigative Ophthalmology and Visual Science. Although the contact lens could benefit KPro patients, this technology may potentially also benefit a wide range of ophthalmic conditions. It also lays the groundwork for developing additional sustained ocular drug delivery systems.

Implants for intraocular drug delivery

More than three million people in the United States undergo cataract extraction each year. This procedure involves replacing a clouded lens with an artificial lens, and is the most common type of intraocular surgery. Patients usually require eye drops for a short period of time to combat post-operative inflammation and antibiotic medications for at least one month after cataract surgery. Dr. James S. Steinemann, a collaborator in Sweden, has developed an algorithm currently in trial called WINROP (‘Weighted IGF-I’ Neonatal ROP) that can predict ROP nine weeks before development of the disease based on postnatal weight gain indicative of postnatal IGF-I (protein) levels. In prior research, a collaborative group of researchers identified IGF-I levels as a key predictor of whether or not an infant would develop ROP. This simple surveillance model can eliminate the need for costly and stressful eye exams in infants by as much as 75 percent. Identifying children at risk for the disease early on also can lead to more timely interventions, and possibly prevent loss of vision.

Strabismus treatments benefit children and adults

“It’s hard enough to convince adult strabismus patients to get corrective surgery, because doctors may have told them ‘it’s too late,’” says Dr. David Hunter, Ophthalmologist-in-Chief at Children’s Hospital Boston. “So imagine how hard it is to convince grown ups to come to a hospital for kids.” He laughs. “Commonly known as ‘lazy eye’ or ‘crossed eyes,’ strabismus occurs when a person’s eyes are misaligned because the muscles of the nerves that control them are weak or don’t function properly. Some people are born with strabismus, while others can develop the condition in adulthood as a result of illness or injury. People who develop strabismus as adults may also suffer from double vision, which can be severe enough to cause functional disability. Even so, many adults are hesitant to get corrective surgery for strabismus. Children’s Hospital Boston and Mass. Eye and Ear Infirmary are home to a group of surgeons who specialize in evaluating, diagnosing, and treating all forms of adult strabismus, including Dr. Linda Dagli, Director of Adult Strabismus at Children’s. The group’s highly skilled pediatric ophthalmologists perform delicate muscle surgery in patients of all ages, routinely handling difficult cases and correcting the condition in patients who have experienced failed surgeries elsewhere. Dr. Dean Cestari, Neuro-ophthalmologist and adult strabismus surgeon at Mass. Eye and Ear, notes that there are many causes of the disorder, including very subtle medical or neurological disease. “Some people are under the false impression that strabismus correction is a vanity procedure,” he said. “However, strabismus isn’t just a cosmetic issue—it’s a genuine medical condition that sometimes requires reconstructive surgery.” Drs. Hunter, Cestari, and Gena Heidary, Children’s Hospital’s dedicated pediatric neuro-ophthalmologist, are currently preparing a case-based textbook on strabismus, which is slated for publication in early 2012.

With recent advancements like adjustable sutures and non-surgical alternatives, strabismus correction can be far less invasive and have greater long-term success than more traditional procedures. Dr. Hunter has led efforts to improve the utility and surgical success of adjustable sutures. He developed an adjustable...
suture procedure called the “short tag noose,” which allows physicians to wait up to one week after initial surgery to make final suture adjustments in the office if needed; prior to this, corrections were required within 24 hours of surgery. The short-tag noose procedure widens considerably the window of opportunity to ensure exact and proper positioning of the eye muscle(s) and, often times, eliminates the need for subsequent surgeries.

For some patients, Botox injections offer a viable, permanent, and non-surgical solution for treating strabismus. Physicians at Children’s Hospital Boston and Mass. Eye and Ear use Botox to successfully treat a variety of complex strabismus cases. Dr. Hunter and colleagues also have used Botox to correct residual strabismus in adults for whom previous multiple incisional surgeries have failed, as well as strabismus in children with cerebral palsy or developmental delays.

**Going live: new imaging techniques are patient-friendly**

In recent ophthalmic practice, many standard diagnostic procedures are invasive, slow, and yield only limited insight into the pathology of corneal diseases. To better understand the underlying mechanisms of corneal physiology and pathology, Dr. Pedram Hamrah has applied live corneal imaging techniques that may be used to examine nerves, vessels, and immune cells of the ocular surface. As director of the newly formed Ocular Imaging Center, Dr. Hamrah aims to standardize the use of in vivo confocal microscopy (IVCM) in clinical practice. IVCM is far less invasive than traditional biopsy tests, and may facilitate earlier detection and treatment for patients with corneal diseases—ultimately benefiting the quality of care given to patients and imposing less of a burden on the health care system. IVCM may also help shorten the treatment periods with medications (some of which can have harmful side effects), enabling more targeted medical treatment, decrease the need for surgery, and delay disease progression—resulting in an overall improvement in visual acuity.

Recently, Dr. Hamrah, in collaboration with Drs. Deborah Langston and Rena Dana, used IVCM to measure corneal innervation, in patients with herpes simplex keratitis (HSK). Corneal innervation is a marker of disease severity in HSK and other corneal conditions, including dry eye syndrome and keratoconus. This study, and more recent studies, not only demonstrated that corneal innervation (as measured by IVCM) correlated with corneal sensation, but has also demonstrated that both corneal innervation and immune cells are altered bilaterally in unilateral corneal diseases. Prior to this study, clinicians could only measure corneal sensation using subjective and invasive methods. These prospective studies, the first of which was published September 2010 in the journal Ophthalmology, presents a rapid, quantitative, qualitative, and reproducible method for measuring corneal innervation and inflammation, and assessing disease progression in clinical practice.

**Surgical advances benefit glaucoma patients**

Glaucoma is the second leading cause of irreversible blindness in the United States, affecting an estimated three million Americans—and the principal cause of blindness for people of African and Latino descent. This “silent thief of sight” progresses slowly and painlessly, leaving half the people affected by the disease unaware of it. Left untreated, glaucoma’s signature risk factor of high fluid pressure within the eye—a known as intracocular eye pressure (IOP)—can eventually destroy the optic nerve, robbing people of their sight. There is no cure and early detection is critical; glaucoma can be controlled with eye drops, laser therapy, and surgery, but any vision lost to the disease is lost forever.

Fran Hall is one of the most active octogenarians you’ll ever meet. At 82, she still works professionally as a psychotherapist, skis in the winter, and plays tennis year-round. She also finds time to sing in a chorus, restore furniture, and participate in a book club. Amazingly, Fran maintains this lifestyle 15 years after she was first diagnosed with glaucoma, and just two and a half years after sight-saving surgery at Mass. Eye and Ear.

For ten years, Fran successfully controlled her glaucoma pressure with medicated eye drops and laser treatments. Over time, however, the pressure in both of Fran’s eyes continued to rise, and the treatments gradually became less effective. Fran sought the advice of glaucoma specialist Dr. Douglas Rhee at Mass. Eye and Ear. They discussed her busy lifestyle, and Dr. Rhee suggested they forego traditional trabeculectomy surgery in favor of a newer, less invasive procedure—trabectome surgery—that offers patients shorter recovery times and a lowered risk of complications.

Trabectome surgery works by treating the eye’s primary “drain,” called the trabecular meshwork, which helps to remove fluid from the eye. The procedure is appropriate for patients with open-angle glaucoma, the most common form of the disease in the United States. Dr. Rhee was the first physician in New England to perform the trabectome procedure, and is currently one of the most experienced physicians in the world performing the procedure.

In April 2008, Dr. Rhee performed the surgery on both of Fran’s eyes. As expected, Fran’s recovery time was short and the pressure in both eyes is now under control. Aside from regular check-ups at the hospital’s Glaucoma Service, Fran is back to an active lifestyle, swinging her tennis racket and spending time with her grandchildren.

Besides trabeculectomy surgery, Mass. Eye and Ear is also the first academic medical center in New England to offer canaloplasty—another new and innovative surgical option for pediatric and adult glaucoma patients. While the trabectome procedure utilizes an internal approach and removes part of the trabecular meshwork, canaloplasty utilizes an external approach with a rapid, noninvasive, quick access to the interior of the eye. During canaloplasty, surgeons dilate the canal behind the trabecular meshwork and place a suture to keep the canal open. As with trabeculectomy surgery, canaloplasty helps to provide better drainage in the eye. It also speeds recovery time and lowers the risk of complications compared to traditional surgical interventions. “With a number of surgical procedures available under one roof, we can offer glaucoma patients options for the best, most individualized care, and ultimately, the best outcomes,” says Dr. Rhee.

Fran agrees. “I’m one happy camper,” she says.
FOCUS: KERATOPROSTHESIS

Boston KPro offers a second chance at sight

There are an estimated eight million people in the world—including 1.5 million children—who are blind from corneal disease. In many severe cases of corneal disease, corneal transplants are the only hope for restoring vision. However, because transplantation facilities and suitable donor corneas are not always accessible, only a fraction of patients who need corneal transplants actually receive them. Standard, corneral transplants are not successful in many corneal conditions—such as recurrent graft failure, congenital corneal dystrophies, ocular burns, or autoimmune diseases.

The Boston Keratoprosthesis (KPro), an artificial cornea developed at Mass. Eye and Ear, is an economically sustainable option for many cases that cannot be treated with classic donor cornea tissue transplants. First conceived of by Drs. Claes Dohlman in the 1960s, the Boston KPro received FDA approval in 1992, and is now the most successful artificial cornea in the world with over 5,000 implantations worldwide. Dr. Dohlman, now working with Dr. James Chodosh and a number of colleagues, continues to lead advancements in Boston KPro design and postoperative management, and the device continues to grow in clinical success and worldwide demand.

The Boston KPro is made of medical grade poly(methyl methacrylate) or PMMA, a clear plastic with excellent tissue tolerance and optical properties. The three parts of the device form a collar-button shape when assembled. The device is inserted into a corneal graft and when fully assembled, the device forms a collar-button shape. The device is made of medical grade poly(methyl methacrylate) or PMMA, a clear plastic with excellent tissue tolerance and optical properties. The three parts of the device form a collar-button shape when assembled. The device is inserted into a corneal graft and when fully assembled, the device forms a collar-button shape.

Improved postoperative care has been central to the clinical success of the Boston KPro. Common complications such as inflammation and infection are becoming more rare with new prophylactic drug regimens. Innovative devices also have significantly improved postoperative management. KProsologists contact lenses are now worn continuously to improve graft retention, prevent irriation and evaporative damage; with the current efforts of Dr. Joseph Ciolino and colleagues at MIT and Mass. Eye and Ear, contact lenses may soon be used for drug delivery as well. Dr. Dohlman, with the help of Drs. Cynthia Grosskreutz, Teresa Chen, and Louis PASquale, recently developed shunts that allow direct aqueous humor away from the anterior chamber to an epithelialized cavity (sinus, etc); these have been shown to reduce IOP after KPro surgery, and may eventually prevent glaucoma. Dr. Samir Melki is spearheading the development of a technique to insert a pressure transducer into the eye, which allows the intraocular pressure to be read from the outside via radio wave telemetry. The Boston KPro is now the primary therapeutic option for a growing number of conditions. Studies using combined immunomodulatory therapy with the Boston KPro, led by Drs. Chodosh, Stephen Foster, and George Papaliodis, may continue to improve the outcome in autoimmune disease in cases where the disease makes corneal allograft failure inevitable. A series of case reports by Drs. Dohlman and Deborah Langston demonstrated the Boston KPro’s effectiveness in treating corneal damage caused by herpetic keratitis. At Mass. Eye and Ear, Dr. Kathryn Colby pioneered the use of the Boston KPro to treat certain corneal conditions in pediatric patients. Use of the Boston KPro has grown rapidly—from only 46 procedures in 2002 to 1,200 procedures worldwide in 2010—as corneal surgeons become increasingly aware of the device’s numerous advantages.

The Boston KPro continues to evolve. A large number of research fellows are working with Dr. Dohlman to improve the device and expand its potential. Soft research in collaboration with Dr. Eli Peli at Scopenso Eye Research Laboratory, utilizes soft contact lenses in various Boston KPro models. The goal is to studying ways to prevent postoperative retinal detachment, and Dr. Elena Gipaldon leading an effort to inhibit enzymes that can cause tissue melt and perforation around the Boston KPro. Dr. Isimag Dahlhaus and colleagues are examining antagonistic coatings for the device surface at the Khaneh lab at MIT; Dr. Daniel Kohane is directing further development of a titanium port by Drs. Dohlman and Deborah Langston. Researchers at the Boston KPro are spearheading a major effort to prevent infection are becoming more rare.

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Focus: vision rehabilitation

Technology and tools shaping the future of vision—today

Despite many breakthrough treatments for eye disorders, millions of Americans suffer from irreversible vision loss that restricts their productivity, independence, and quality of life. By 2020, there will be an estimated 35 million Americans aged 65 and over who will suffer some form of visual impairment—a number that will rise as America ages. One of the goals of the HHS Department of Ophthalmology is to develop and implement new tools and technologies that can help patients make the best use of their remaining eyesight.

Maximum impact

It’s 1968. Imagine that you’ve been diagnosed with advanced age-related macular degeneration (AMD) or diabetic retinopathy; a time when there are few vision-saving tools, technologies, and therapies to prevent you from going blind or slowing the progression of these diseases. As you are studying ways to prevent postoperative retinal detachment, and Dr. Elena Gipaldon leading an effort to inhibit enzymes that can cause tissue melt and perforation around the Boston KPro. Dr. Isimag Dahlhaus and colleagues are examining antagonistic coatings for the device surface at the Khaneh lab at MIT; Dr. Daniel Kohane is directing further development of a titanium port by Drs. Dohlman and Deborah Langston. Researchers at the Boston KPro are spearheading a major effort to prevent infection. It’s 1968. Imagine that you’ve been diagnosed with advanced age-related macular degeneration (AMD) or diabetic retinopathy; a time when there are few vision-saving tools, technologies, and therapies to prevent you from going blind or slowing the progression of these diseases. As you are studying ways to prevent postoperative retinal detachment, and Dr. Elena Gipaldon leading an effort to inhibit enzymes that can cause tissue melt and perforation around the Boston KPro. Dr. Isimag Dahlhaus and colleagues are examining antagonistic coatings for the device surface at the Khaneh lab at MIT; Dr. Daniel Kohane is directing further development of a titanium port by Drs. Dohlman and Deborah Langston. Researchers at the Boston KPro are spearheading a major effort to prevent infection.
Claes Henrik Dohlman, MD, PhD, Emeritus Professor of Ophthalmology at Harvard Medical School, was born in 1922 in Uppsala, Sweden. Dr. Dohlman earned his MD and a Doctorate of Medical Research (biochemistry) from the University of Lund in Sweden, and completed his residency in ophthalmology in the Eye Clinic of the University of Lund. In 1958, he was recruited to work at The Retina Institute of Boston by former mentor and world-renowned retina surgeon, Dr. Charles Schepens, founder of the Institute (now Schepens Eye Research Institute). He was also asked by Dr. Edwin Dunphy, then Chief of Staff at Mass. Eye and Ear, to establish a Cornea Service at the Infirmary. In 1974, the same year he achieved HMS professorial status, Dr. Dohlman was appointed Chairman of the Department of Ophthalmology of Harvard Medical School, Director of the Howe Laboratory of Ophthalmology, and Chief of Ophthalmology at Mass. Eye and Ear.

In a career that now spans six decades, Dr. Dohlman stands as one of the most highly honored ophthalmologists in the world. Recognized as the founder of modern corneal science, his work is considered “classic” literature on understanding corneal biology. His investigations of corneal physiology laid the groundwork for modern clinical practice in dry eye disease, management of corneal burns, wound healing, corneal transplantation, and keratoprosthesis.

His career reflects a remarkable number of firsts: Dr. Dohlman was first in the world to create an organized cornea subspecialty (Mass. Eye and Ear), first to create a formal structured cornea fellowship program (Mass. Eye and Ear and Schepens), first to recruit full-time cornea fellows to HMS, and first to pioneer surgical innovations in keratoplasty and keratoprosthesis. His most notable achievement is the Boston Keratoprosthesis (KPro), an artificial cornea he first conceptualized in the 1960s and is now the most successful artificial cornea in the world with over 9,000 implantations to date. During his career, Dr. Dohlman has trained first-hand over 600 cornea specialists—more than any other ophthalmologist in the world. His “real” contributions to ophthalmic education are incalculable considering the hundreds of second- and third-generation cornea specialists who have trained under his protégées, and the thousands more who have benefited from his prolific contributions to corneal literature and science.

In 2007, the American Academy of Ophthalmology named Dr. Dohlman recipient of the Laureate Award—the highest honor possible to bestow by the Academy—in recognition of his contributions spanning 50+ years of continuous service to the profession. The following year, he was again honored for his lifetime accomplishments in a named Harvard Professorship whose first incumbent is Dr. Reza Dana, famed for his pioneering science in corneal immunology and transplantation biology. “Dr. Dohlman’s opus of research and clinical work set the stage for a world-class cornea center of excellence at Harvard,” remarked chief and chair Joan W. Miller. “His work has benefitted millions of people around the world, and his legacy of knowledge thrives today in the hundreds of fellows, students and colleagues he has trained and mentored over the years. Harvard Medical School—and indeed, the whole world—is a far better place today because of his remarkable talent, contributions, and character.”

Dr. Dohlman retired from formal administrative roles in 1989. Today, at the age of 88, he continues to advise and mentor students and colleagues, run a special KPro patient clinic, and pursue multi-disciplinary research to enhance clinical KPro outcomes. Despite a lifetime of achievements, Dr. Dohlman is remarkably self-effacing. While he acknowledges his numerous accomplishments, he prefers not to focus on what he has achieved, but rather what still needs to be accomplished—particularly in the area of KPro development. He continues to shape and set new standards for the field, and remains an inspiration to everyone in the Harvard community—and beyond.

An interview with Dr. Claes Dohlman begins on page 160.

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— Joan W. Miller, MD
Mary Louise Jackson, MD
Assistant Professor of Ophthalmology, Harvard Medical School
Director, Vision Rehabilitation Center, Massachusetts Eye and Ear Infirmary

Dr. Mary Louise Jackson is a vision rehabilitation expert, committed to helping patients with impaired vision make the best use of their remaining eyesight. As Director of the Vision Rehabilitation Center (VRC) at Mass. Eye and Ear, Dr. Jackson aims to provide optimal treatment through rehabilitation techniques and visual aids. A graduate of York University in Toronto, Dr. Jackson completed her MD and internship at McMaster University in Hamilton, Ontario. She completed a residency in ophthalmology at the University of Toronto, and practiced in Victoria, British Columbia prior to joining the HMS Department of Ophthalmology in 2006.

One of Dr. Jackson’s research interests is Charles Bonnet hallucinations, which are recurrent visual hallucinations seen by otherwise healthy individuals with significant vision loss. She is examining patients referred to the VRC to determine the frequency of these hallucinations, why patients experience them, and how they affect quality of life. She is involved with national research collaborations, and is currently conducting a trial of the impact of using a video magnifier on reading performance. Dr. Jackson’s focus is clinical practice and resident education. At Mass. Eye and Ear, she has restructured the multi-disciplinary VRC to follow a patient-centered model of rehabilitation. Under her direction, the VRC has seen significant growth in patient referrals, and is rapidly emerging as a national leader in the field. Dr. Jackson is the Secretary on the Executive Committee of the International Society for Low Vision Research and Rehabilitation. She serves on the American Academy of Ophthalmology’s Vision Rehabilitation Committee; as Chair, she leads the development of a national vision rehabilitation residency curriculum and a web-based vision rehabilitation course for ophthalmology residents.

Tiny telescope restores vision to some AMD patients

Jo Ann Preece has a spring in her step and a sparkle in her eye despite living with end-stage age-related macular degeneration (AMD). The vibrant 84-year-old had a miniature telescope implanted in her eye in 2003 during a clinical trial at Mass. Eye and Ear. At a recent check up, JoAnn peered out of a sixth-floor window and saw the cars driving by below. Before the surgery, these cars—and everything else—would have appeared blurry: “It’s like you’re in a fog,” JoAnn explains. “I stopped driving and reading.”

The CentraSight® Implantable Miniature Telescope (IMT), a new option for some AMD patients, gave JoAnn a new outlook on life—literally—by restoring central vision to one of her eyes. This innovative device is surgically implanted in one eye, where it magnifies and projects central images onto a healthy portion of the retina. This enables patients to see objects in fine detail, and perform “near” activities like reading, watching TV and recognizing faces. The non-implanted eye is then used for peripheral vision.

Post-surgery rehabilitation helps patients develop the skills needed to make their eyes work together to achieve the best possible vision. Dr. Kathryn Colby has played a key role in optimizing methods for implanting the miniature telescope in AMD patients, and described the surgical procedure in the August 2007 issue of Archives of Ophthalmology. Dr. Colby was also an investigator in a multicenter clinical trial that showed the IMT significantly improved vision in most patients who received the implant. She describes the pea-sized technology as a true “breakthrough” for millions of patients with end-stage AMD, whose treatment options, until now, have been limited. But she also cautions that the telescope, approved by the FDA in July 2010, will not work for everyone, and is geared specifically for patients 75 years and older with blind spots (bilateral central scotomas) associated with end stage AMD. For many of these patients, however, the device is life-changing. “Over 90 percent of patients in the clinical trial improved two lines in vision as measured in the doctor’s office, but what really matters is how this technology impacts quality of life,” Dr. Colby said. “Can you write out a check! Watch TV! See your grandson’s face? That’s significant improvement.”

Restoring peripheral visual function with prisms

Peripheral vision loss makes it extremely difficult for patients to navigate safely around objects and other people. This occurs in retinitis pigmentosa, which causes gradual loss of eyesight starting from the outside edges of the visual field. Another condition that affects peripheral vision is homonymous hemianopia, which causes loss of half of the visual field on one side in both eyes—not due to a problem with the eyes themselves, but rather due to brain injury. Stroke, trauma, brain tumors, and surgery are common causes of this condition, which affects over one million people in the United States. Hemianopia can severely impact activities of daily living, such as driving or even walking.

Dr. Eli Peli, Co-Director of Research at Schepens Eye Research Institute and Professor of Ophthalmology at HMS, has devised a solution using prism lenses. Mounted on eyeglasses, the prisms redirect images from a blind side and project them onto functional parts of the visual field. This causes objects from the blind side to appear as “ghost images” in the remaining visual field. People wearing these special prism glasses can then be aware of objects in their blind side, and make adjustments to either examine them further or move to avoid collision. So far, the prism lenses have been tested in two multi-center clinical trials directed by Dr. Peli, who is also an optometrist and Director of the Vision Rehabilitation Service at the New England Eye Center. In the first trial, published in the May 2008 issue of Archives of Ophthalmology, 43 patients with hemianopia reported that the prism glasses were “very helpful” in navigating around obstacles. These results were confirmed in a later randomized control study of 61 patients, presented at ARVO 2010. At around $600 for glasses with permanently mounted prisms—and even less for temporary stick-on prisms—these lenses represent an affordable breakthrough for people with hemianopia and other conditions that cause peripheral vision loss.

Life-Transforming Care
67 Vision Rehabilitation

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Astonishing. Miraculous. Life altering. This is how some patients...
Emerging retinal prosthetics technology aims to restore sight to the blind

A state-of-the-art retinal prosthesis, designed to help some people blinded by retinal disease to regain a portion of their vision, may soon be within reach. In many retinal disorders, such as retinitis pigmentosa and age-related macular degeneration (AMD), the image-sensing photoreceptors (rods and cones) eventually die—resulting in vision loss. However, even in patients who become legally blind, cells in the optic nerve—which connects the retina to the brain—may still be alive and functional.

Hoping to take advantage of the surviving nerve cells, Dr. Joseph Rizzo III and scientists of the Boston Retinal Implant Project are developing an implantable microelectronic prosthesis that will deliver visual information to the brain through the remaining retinal circuits. This highly sophisticated “bionic eye” will consist of internal electronic components that will be implanted around and behind the eyeball. Users wear a small camera, mounted to eyeglasses, that captures visual scenes and converts them into electrical impulses. The impulses are transmitted wirelessly to a prosthesis that stimulates the healthy nerve cells. The nerve cells, in turn, carry the visual impulses to the brain for image processing—helping patients with macular degeneration or retinitis pigmentosa regain some vision. Special innovations to the prostheses include an ultra-low power design and a geometric architecture that minimizes that amount of hardware that is placed into the eye. The team has also developed a minimally invasive surgical method of implantation.

The retinal implant may not work for all blind patients—particularly those with significant optic nerve damage, or those who were born blind because the visual centers in the brain have not developed. Furthermore, it’s still too early to tell exactly how much vision can be restored by the retinal prosthesis. Nonetheless, many blind patients maintain that even the smallest improvements to their eyeglasses can dramatically improve their quality of life. This technology represents a major milestone toward restoring some vision in many patients blinded by retinal disease.

Dr. Rizzo, Director of the Center for Innovative Visual Rehabilitation, Department of Veterans Affairs, Boston, MA

Professor of Ophthalmology, Harvard Medical School

Director, Neuro-Ophthalmology Service, Massachusetts Eye and Ear Infirmary

Founder and Co-Director, Boston Retinal Implant Project

Dr. Joseph Rizzo III is a clinician scientist dedicated to understanding the mechanisms of vision loss, and his decades-long mission has focused on improving the diagnostic and treatment methods for blinding diseases. A native of New Orleans, Dr. Rizzo received his undergraduate and medical training at Louisiana State University. Following an internship in adult medicine at UCLA Medical Center, Dr. Rizzo completed both a neurology residency at Tufts University/New England Medical Center and an ophthalmology residency at Boston University. He completed a clinical fellowship in neuro-ophthalmology at Mass. Eye and Ear before joining the faculty of the HMS Department of Ophthalmology.

As a clinician, Dr. Rizzo specializes in visual disorders that result from damage to the eye or brain. He is Director of the Neuro-Ophthalmology Service at Mass. Eye and Ear, which houses three of only a handful of dually trained neuro-ophthalmologists worldwide. Dr. Rizzo evaluates roughly 40 percent of all patients referred to the service, and collaborates closely with neurologists at MGH to deliver high-quality care for patients with visual disorders. As Professor of Ophthalmology at HMS, Dr. Rizzo is directly responsible for training clinical fellows, residents, and medical students in neuro-ophthalmology. He regularly delivers lectures on diverse ophthalmic issues, and directs the neuro-ophthalmology section of the Lancaster Course, which is the oldest and largest training course for ophthalmologists.

Dr. Rizzo devotes a major portion of his professional focus to developing new therapeutic options for vision disorders. He is Director of the Center of Innovative Visual Rehabilitation at Boston Veteran’s Administration Hospital and Co-Director of the Boston Retinal Implant Project (BRIP), an initiative he founded in 1988 to develop a retinal prosthesis for patients with acquired blindness. This interdisciplinary and international research collaboration now includes scientists and clinicians from over 20 institutions worldwide. For his significant contributions to visual science, Dr. Rizzo was presented with the Senior Achievement Award by the American Academy of Ophthalmology in 2007.
“Imagination is truly the key to any discovery, and science to cure blindness is no exception. It is the constant reexamination of the facts along with creative leaps of thought that give birth to innovation in every field.”

— Michael Young, PhD, Associate Scientist, Schepens Eye Research Institute

This Research & Discovery section highlights some of the many scientific contributions made in recent years by the dedicated scientists in the HMS Department of Ophthalmology, whose investigations have resulted in major advancements in medical science and ophthalmic practice. Discoveries made in various fields—including genetics, immunology and ocular biology—have reshaped the foundations of ophthalmology and formed many new paradigms for the repair, regeneration, and rehabilitation of countless disorders.

Today, using a uniquely synergistic approach that combines both laboratory research and applied medicine, this pioneering team continues to advance clinical care for the eye. Fields under intensive study span several areas: physiology, ocular inflammation and immunology, neovascularization optic neuropathies; ocular prostheses; new approaches to drug delivery; laser surgery, and; ocular therapeutics and surgery. Investigations have also expanded to include the specialty fields of genomics, proteomics, gene-gene and gene-environment interactions, gene therapies, and stem cell therapy.

HMS investigators also conduct preclinical investigations using a variety of disease models, and carry out small-scale clinical trials to establish a foundation for “first proof in man.” In recent years, this work has led to revolutionary treatments for macular degeneration, including the development of photodynamic therapy as well as a number of anti-angiogenesis agents. Current work focuses on the development of novel pharmaceutical, biological, and gene-therapy approaches for the treatment of blinding diseases.

With ample collaborative dialogue between talented researchers and clinicians, scientific advances are being rapidly transformed into cutting-edge clinical practice.
As the eye’s most powerful focusing structure, the cornea is essential for acute vision. Injuries, infections, and genetic disorders can rob vision by disrupting normal corneal function. The HMS Department of Ophthalmology houses the world’s largest and most esteemed group of scientists and physicians—nearly 80 MDs and PhDs in all—committed not only to understanding corneal biology, but also to treating or preventing corneal disease. With a potent arsenal of tools, technologies, and knowledge, the department is continually applying laboratory discoveries to clinical practice. With increasing success, we’re treating or averting the potentially devastating effects of corneal disease, infections, and injury.

**CORNEAL INFECTIONS**

The cornea protects the rest of the eye from many pathogens, such as bacteria, fungi, or viruses; however, because it is constantly exposed, the cornea itself is susceptible to infections that may cause keratitis, or corneal inflammation. Besides causing irritation, pain, and blinding vision, keratitis can damage or scar the cornea, and may lead to permanent vision loss. Several scientists in the HMS Department of Ophthalmology are conducting research and improving treatments for this potentially blinding condition.

**Inflammatory responses in epidemic eye infections**

Adenovirus keratitis (commonly known as “pink eye”) refers to inflammation of the mucus membranes covering the surface of the eye, including the cornea and conjunctiva. There are many causes of keratoconjunctivitis, including allergens, microbes, and chemicals, however, adenoviral keratoconjunctivitis is particularly contagious and spreads so rapidly that it commonly causes epidemic keratoconjunctivitis (EKC). Although EKC infections generally resolve on their own, the inflammatory immune responses in the cornea may lead to corneal clouding that may linger for several weeks, months, or even years in severe cases.

James Chodosh, MD, MPH and his team generated the first mouse model of adenoviral keratitis, as well as the first whole genome sequences of EKC-causing adenoviruses. Bioinformatic analyses performed by his group provided evidence for new emergent adenoviral serotypes in EKC. His laboratory also studies how cells called keratocytes in the cornea respond to adenoviral infections, and how signals produced by these cells lead to inflammation.

Because the inflammatory response is a well-conserved host defense mechanism against injury or infection, there are numerous common causes of corneal infections, yet both are difficult to treat and can be visually devastating when they occur. Kathryn Colby, MD, PhD, in collaboration with other colleagues within HMS and nationwide, has examined the changing landscape of these atypical pathogens, both at Mass. Eye and Ear, and throughout the United States. These studies demonstrated an increase in both fungal (supported by Yehia and Colby, June 2019 issue of the journal Cornea), and Acanthamoeba (Tanhehco and Colby, Cornea, September 2010) infections at Mass. Eye and Ear in recent years, paralleling nationwide trends. In addition, filamentous fungi were found to have replaced yeasts as the predominant pathogen in fungal keratitis at Mass. Eye and Ear. Soft contact lens wear was a major risk factor for fungal infection by pinpointing the major pathogens and risk factors involved in atypical keratitis, this work may lead to improved prevention and treatment strategies for these potentially blinding infections.

The changing landscape of atypical keratitis

Fungi and Acanthamoeba (a genus of protozoa) are now more common causes of corneal infections, yet both are difficult to treat and can be visually devastating when they occur. Kathryn Colby, MD, PhD, in collaboration with other colleagues within HMS and nationwide, has examined the changing landscape of these atypical pathogens, both at Mass. Eye and Ear, and throughout the United States. These studies demonstrated an increase in both fungal (supported by Yehia and Colby, June 2019 issue of the journal Cornea), and Acanthamoeba (Tanhehco and Colby, Cornea, September 2010) infections at Mass. Eye and Ear in recent years, paralleling nationwide trends. In addition, filamentous fungi were found to have replaced yeasts as the predominant pathogen in fungal keratitis at Mass. Eye and Ear. Soft contact lens wear was a major risk factor for fungal infection by pinpointing the major pathogens and risk factors involved in atypical keratitis, this work may lead to improved prevention and treatment strategies for these potentially blinding infections.

**CORNEAL CLARITY**

The focusing power of the cornea relies on its clarity. Many conditions—from injuries to infections to dietary or genetic disorders—can cause the cornea to lose transparency, and thus its ability to properly refract light. Inflammatory responses to infections, injury, or even corrective surgery can also cause the cornea to become cloudy; moreover, inflammation can induce corneal neovascularization which can also impair vision. Understanding the factors that promote corneal clarity is a major area of study in the HMS Department of Ophthalmology, where scientists have defined many of the molecular and physiological mechanisms that maintain corneal transparency, as well as the pathological processes that cause corneal clouding.

The focus of the cornea is maintained by the ability to continuously remove the extracellular matrix that supports the epithelial cells in the cornea, where it acts as a “sink” for factors that induce blood vessel growth in response to inflammation. These findings presented an effective and novel mechanism for suppressing inflammation-induced CNV.

Dr. Dana is also examining the
Deborah P. Langston, MD, FACS
Professor of Ophthalmology, Harvard Medical School
Director of Virtue Service, Massachusetts Eye and Ear Infirmary

Dr. Deborah Langston was the first woman to complete ophthalmology residency training at Harvard, and the first female fellow in Dr. Claes Dohlman’s corneal fellowship program. She was also among the first to study the efficacy and toxicity profiles of antivirals in animal models, later translating these findings successfully to humans. Her expertise is sought quite prominently in national and international health policy for the treatment of ophthalmic disease, including issues of viral latency, diagnosis, public health and clinical treatment. Dr. Langston is now principally a clinician-educator, focusing on patient care, clinical research, committee work and teaching appointments. Former Chair of the FDA Ophthalmic Drug Advisory Committee, she now serves on the President’s Commission on Bio-terrorism Preparedness and Response Committee.

Kathryn A. Colby, MD, PhD
Assistant Professor of Ophthalmology, Harvard Medical School

Dr. Kathryn Colby is HMS Assistant Professor of Ophthalmology and a corneal specialist at Mass. Eye and Ear and Children’s Hospital, Boston. Dr. Colby’s research and clinical interests involve advancing new surgical techniques for various corneal diseases. Dr. Colby was one of the first surgeons in Boston to perform selective endothelial transplantation, which replaces only the diseased endothelial cells of the cornea in conditions such as Fuchs’ corneal edema. She has been performing different forms of this surgery since 2006. She was the first surgeon in the area to implant the Boston Keratoprostheses (KPro) in children, and she is currently evaluating new therapies for keratoconus. Dr. Colby has been pivotal in optimizing the surgical technique for the implantable miniature telescope for restoring vision in patients with end-stage age-related macular degeneration (AMD). She has the largest ocular surface tumor practice in the New England region, and is currently evaluating the biology of conjunctival melanoma, one of the few ophthalmic conditions capable of causing death.

CORNEAL DYSTROPHIES
Corneal dystrophies form a diverse group of conditions that involve gradual deterioration of the cornea. Diseased corneas may become cloudy or abnormally curved, which results in impaired vision. Most corneal dystrophies are inherited; many have no symptoms for decades, and vision loss may vary widely from mild to severe. Researchers in the HMS Department of Ophthalmology are advancing therapeutic strategies for corneal dystrophies by understanding their genetic causes and developing improved treatment and surgical interventions.

Finding molecular clues in Fuchs Endothelial Corneal Dystrophy
In Fuchs’ endothelial corneal dystrophy (FECD), the endothelial layer of the cornea deteriorates and eventually leads to corneal swelling and loss of vision. FECD accounts for over 10,000 corneal transplants (roughly one-third of all corneal transplantations) each year in the United States. Corneal transplantation is currently the only modality to treat FECD because the exact cause of endothelial cell degeneration is unknown. Even though FECD is an inherited condition, the genetic defects underlying this common and age-related condition have not been clearly identified. HMS Assistant Professor Ula Jurkunas, MD, a full-time member of the Cornea Service at Mass. Eye and Ear, is spearheading efforts to understand the complex interaction between the environmental stressors and the genetic factors that, in turn, cause the development of FECD. Dr. Jurkunas is leading a laboratory effort at Schepps Eye Research Institute to evaluate the role of oxidative damage to endothelial cells as an underlying cause of FECD. They found that that reactive oxygen species are involved in the development and progression of FECD, and these novel findings were published November 2012.

Dr. Jurkunas has received approval from PACT (Production Assistance for Cellular Therapeutics) for support in the manufacture of cultivated corneal and oral epithelial stem cells for corneal transplantation. Drs. Jurkunas and Dana are collaborating with researchers from Harvard’s Immune Disease Institute and the Dana Farber Cancer Institute.

D R Y E Y E D I S E A S E
The triple-layered tear film, which covers the ocular surface, is a critical component of the eye and visual system; any component of the tear film may be disrupted in dry eye disease. Although it rarely leads to severe vision loss or blindness, dry eye disease can lead to extreme discomfort and significant disability. Tens of millions of people have persistent or severe dry eye disease in the United States—making it a major public health concern. In the HMS Department of Ophthalmology, the efforts of several researchers have contributed to the development of new therapies for this widespread and potentially debilitating condition.

Inflammation, immunity, and dry eye disease
For the past decade, the pathology of dry eye disease has been known to involve inflammation and immunity; however, until recently, these disease mechanisms have been...
Reza Dana, MD, MPH, MSc
Dr. Reza Dana studies how the immune, lymphatic, and vascular systems interact during ocular inflammatory responses, and how inflammation contributes to transplant rejection, corneal neovascularization (CNV), and other pathologic processes in the eye. At HMS, Dr. Dana is Professor of Ophthalmology and holds the Claes R. Jacobson Chair in Ophthalmology. He also serves as Associate Chief of Ophthalmology and Vice Chair for Academic Programs, Senior Scientist and Co-Director of Research at Schepps Eye Research Institute, Principal Investigator for the Harvard Vision Clinical Scientist Development program (K12), and Director of the Cornea and Refractive Surgery Service at Mass. Eye and Ear. With numerous ongoing projects in his laboratory and multiple collaborations with other researchers, Dr. Dana has made substantial contributions to the bodies of knowledge in both basic science and clinical research.

You are Principal Investigator of the Department’s Harvard Vision Clinical Scientist Development Program, a federally funded K23 program. Explain what the K23 program is, and how it’s contributing to Harvard’s translational research in ophthalmology.

RD: We’ve made a huge effort to recruit clinician scientists to the HMS Department of Ophthalmology K23 program, which is a mentored learning and career development program funded by the National Eye Institute (NEI) of the National Institutes of Health. It awards 4-year career development grants that provide exceptional junior faculty with financial support, mentorship and 75 percent protected research time to pursue and build independent research careers. The program has numerous benefits: it bridges the translational gap between research and clinical activities, helps us attract and retain the best and brightest talent, and enriches our clinical, teaching and research programs. For trainees, it provides an unparalleled learning and research experience not typically nurtured in an academic research institution. Straight from training, the program helps jump start their careers as independent, leading clinician scientists in an amazingly supportive environment. Our K23 “alumni” have included Pedram Hamrak, Ula Jurkunas and Joseph Colino in cornea research, and Lucia Sobrin in retina and uveitis. Our first K23 recipient, Jennifer Sun, is conducting diabetic eye research with Lloyd P. Aiello at the Beetham Eye Institute at Joslin. This program has allowed enormous growth in our translational science program. I’m pleased to say that NEI has approved the Harvard Department of Ophthalmology’s five-year grant renewal.

What is “translational research” and how is it carried out among the Harvard Department of Ophthalmology’s core specialties?

RD: Translational research helps move a basic scientific discovery or idea from the lab to the clinic so patients benefit directly. There’s a clinical side and a preclinical side, and both avenues of investigation are carried out by our HMS Ophthalmology affiliates; much of this work is complemented by the extensive preclinical laboratory work at Schepens. Combined, our prodigious team of nearly 80 HMS principal investigators and research fellows represent the world’s largest group of scientists dedicated to corneal research, and they are working beyond “collaboration” in the usual sense. We’ve also maintained longstanding and fruitful collaborations with many of our HMS faculty who maintain private practices in the community—including Dr. Marc Abelson at Ora, Inc., and Drs. Perry Rosenthal and Deborah Jacobs at the Boston Foundation for Sight. Their work has contributed significantly to corneal translational research.

What are some of the latest developments in Cornea’s infrastructure at Mass. Eye and Ear Infirmary?

RD: In the last four years, we’ve doubled the cornea faculty at Mass. Eye and Ear, all of whom are clinician scientists with active research programs. We’ve developed a corneal research infrastructure with five full-time corneal research managers and research technicians. We’ve also established a Cornea and Ocular Surface Imaging Center that utilizes an incredible collection of hardware and software geared toward corneal imaging, making it the leading front-of-the-eye imaging center anywhere. We’re using these new technologies in cutting-edge clinical care, as well as in our clinical and translational research. At the moment, corneal research at Mass. Eye and Ear involves more than 20 investigator-sponsored translational and clinical studies—a growth of more than 400 percent compared to just a handful of years ago.

What are some examples of your most novel translational Cornea research programs and initiatives?

RD: There are several active programs to highlight, including regenerative medicine and stem cell medicine, corneal angiogenesis, corneal inflammation and dry eye, corneal transplantation, corneal imaging, drug delivery and corneal infections, and a large keratoprosthesis program. For example, we’ve among the few programs that have applied for several investigational new drug applications (INDs) to the FDA to develop novel therapeutic agents. Corneal angiogenesis and inflammation are major causes of blindness worldwide, so we’re looking at new ways of suppressing growth of blood vessels in cornea using topical therapies. We have active and ongoing trials related to this, and some of our findings are now published.

We’ve also made great advances in the field of imaging as well. Eight or nine years ago, using preclinical models, we identified a new class of immune cells that are present in the cornea. Now we’ve taken our research to the clinic. We’re currently using precise high-powered confocal imaging instruments to look at the corneas of live patients. This gives us a better sense of the degree of neuropathy and immune cell activation in the cornea. The experience we gained in our earlier lab work has proven invaluable to our understanding of the clinically relevant metrics of imaging.

Another interesting development is in the field of drug delivery. Along with colleagues at MIT, we’ve developed an innovative lens design for contact lenses that elute or release drugs, representing a novel venue for sustained drug delivery. This addresses a big problem in ophthalmology, since many people can’t use eye drops. Right now, we’re looking at preclinical models, and the next stage will be to apply it to clinical practice.

As Director of the Cornea and Refractive Surgery Service at Mass. Eye and Ear, and Co-Director of Research at Schepens, what are your goals for the translational research program?

RD: I’ve tried to develop a seamless process between the two institutions—lab to clinic and clinic to lab—to understand at a cellular and molecular level what is happening to patients. We study the fundamental biological processes in the lab and define potential therapeutic targets. For example, we’ve among the few programs that have applied for several investigational new drug applications (INDs) to the FDA to develop novel therapeutic agents. Corneal angiogenesis and inflammation are major causes of blindness worldwide, so we’re looking at new ways of suppressing growth of blood vessels in

“We study the fundamental biological processes in the lab and define potential therapeutic targets, bringing these findings to the clinic for testing and proof of concept—it’s very much a circle.”

—Dr. Reza Dana
The uvea refers to the structures (iris, ciliary body and choroid) that form the middle, pigmented layer of the eye. Because uveal tissues contain many blood vessels, they are susceptible to inflammation and other immune responses from a variety of eye disorders. Inflammation of the uvea, or uveitis, can be caused by many conditions, including injuries, infections, autoimmune disorders, and systemic inflammatory diseases. If left untreated, uveitis can lead to other conditions—such as glaucoma, macular edema, and cataract—that may result in profound vision loss.

The HMS Department of Ophthalmology offers a unique combination of scientific and clinical expertise in ocular inflammatory disorders like uveitis. Multiple clinics within Mass. Eye and Ear and Massachusetts General Hospital (MGH) form the Ocular Immunology and Uveitis Service, which is one of the busiest uveitis services in the country. Outfitted with state-of-the-art diagnostic and examination equipment, the Ocular Immunology and Uveitis Service is establishing a patient information database that will allow case series, epidemiologic studies, genetic analyses, and assessments of treatment efficacy and clinical outcomes for uveitis. These combined efforts have optimized existing treatments for uveitis, and have yielded potential novel therapeutic strategies for protecting eyesight in ocular inflammatory disorders.

Expanding treatment options for ocular inflammation

Uveitis is usually treated with corticosteroids, which themselves can have serious side effects (including cataract and glaucoma). Immune-suppressing drugs, such as cyclosporine and mycophenolate mofetil, may also be used to treat some forms of uveitis; however, vision loss can still occur despite treatment with standard immunosuppressants. Thus, Dr. Sobrin and other clinic immunologists in the HMS Department of Ophthalmology are working to expand the therapeutic options for uveitis. Daclizumab and infliximab, which are immune-modulating drugs that specifically target inflammatory cytokines, have been used to effectively treat some forms of uveitis that were resistant to traditional immunosuppressants. Bevacizumab (Avastin®), a prominent anti-angiogenic drug, has shown success in treating cystoid macular edema (CME) caused by posterior uveitis. Intravitreal injections of clindamycin represent a novel use of this antibiotic for treating uveitis caused by toxoplasmosis infections. Case studies conducted by Dr. Sobrin and colleagues serve as evidence-based decision support tools for uveitis, particularly in cases that are resistant to standard therapies.

A novel non-invasive treatment for anterior uveitis

Anterior uveitis, which affects the front of the eye, can cause swelling of the iris (iritis), and the painful condition known as “red-eye.” Like other forms of uveitis, anterior uveitis is usually treated with corticosteroids via eye drops, local injections, or systemic delivery. A potential non-invasive treatment option is the ActiPatch® device, which is based on pulsed electromagnetic field (PEMF) technology.
By emitting a low-frequency electromagnetic field, the ActiPatch® device is thought to restore the tight junctions between endothelial cells, which may in turn minimize inflammation within the eye. In an ongoing randomized, double blinded, placebo-controlled trial led by George Papaliodis, MD, patients with anterior uveitis will wear the ActiPatch® (or a placebo device) over the affected eye for eight hours per day. Inflammation, redness, and pain will then be assessed after a one-week course of treatment. This prospective trial is expected to be complete by December 2011, and may lead to larger clinical trials of PEMF therapy for uveitis. The PEMF device has great potential to reduce the dose or duration of corticosteroid treatment—thus representing a safer adjunct or alternative to standard drug therapy.

**Keratoprosthesis and autoimmune disease**

The Boston Keratoprosthesis (KPro) artificial cornea, developed by Claes Dohlman, MD, PhD at Mass. Eye and Ear, is highly successful in most patients—even those with failed corneal allografts. However, in patients with autoimmune disorders, current surgical treatments—including the Boston KPro—remain marred by complications and prosthetic failure. In this subset of patients, ocular inflammation and neovascularization are common concerns; the tissues adjacent to the prosthesis may also break down, which can lead to prosthetic failure. At Mass. Eye and Ear, these issues in keratoprosthesis implantation were highlighted by two recent cases of corneal blindness secondary to autoimmune disease. The team of C. Stephen Foster, MD; Jessica Ciraksky, MD; George Papaliodis, MD; Claes Dohlman, MD, PhD; and James Chodosh, MD, MPH, reviewed these cases to better understand the underlying mechanisms of keratoprosthesis failure in autoimmune patients. Because prosthetic dental and orthopedic implants have been successful in autoimmune patients, this team of clinician scientists looked to previous reports of prosthetic complications to find unifying mechanisms of prosthetic failure. Upon systematically reviewing the published literature, the team found that prosthetic failure is clearly linked to inflammation and immune activation in autoimmune patients. Keratoprosthesis materials, such as polymethylmethacrylate (PMMA) and titanium, generally have low potential for inducing immune responses; however, the available literature suggested that in autoimmune patients, these materials themselves might stimulate inflammatory cascades that may damage recipient tissues. These findings called for further study of keratoprosthesis materials and the underlying mechanisms of autoimmunity and inflammation. Because more and more treatment options are becoming available for autoimmune diseases, ongoing efforts in the HMS Department of Ophthalmology will produce new, targeted approaches to restoring vision in autoimmune patients.

The retina, which lines the inside of the back of the eye, contains highly specialized cells that convert visual images into electrical signals. The retina then transmits the signals to the brain via the optic nerve. Genes, lifestyle, and age-related factors can all affect the retina, which is susceptible to numerous disorders. In the United States, the leading causes of adult blindness—age-related macular degeneration (AMD) and diabetic retinopathy—are diseases of the retina.

For patients with retinal disease, vision loss may be slowed or even reversed with therapies pioneered by the members of the HMS Department of Ophthalmology. Today, translational research across the HMS campus continues at an intense pace. As scientific discovery is continuously translated into clinical practice, innovative sight-saving treatments are breaking ground in vision care.
Continuing his studies on dangerous multidrug-resistant infections that plague patients following surgery or associated with injuries, Dr. Gilmore and his former trainees Janet Manson, PhD, and Lynn Hancock, PhD, discovered a mechanism used by harmless gastrointestinal microorganisms to acquire multidrug resistance. They found that plasmids—circular pieces of DNA that replicate independently of the bacterial’s chromosomal DNA—facilitate the transfer of virulence and antibiotic-resistance genes from one bacterium to another. Infections from multidrug-resistant Enterococcus are leading complications of surgery, ranging from cataract extractions to knee replacements. Understanding the origins of these strains will help guide the judicious and effective use of antibiotics, and the development of new treatments. This groundbreaking article, published in the Proceedings of the National Academy of Science in 2010, was ranked by Faculty of 1000 as being in the top 1% of published articles in biology and medicine.

Dr. Richard H. Masland, PhD

Richard H. Masland, PhD

David G. and Jody J. Fishbowl Professor of Ophthalmology and Associate Professor of Neurobiology

Harvard Medical School

Director of the Howe Laboratory of Ophthalmology and Associate Chief of Ophthalmology Research, Massachusetts Eye and Ear Infirmary

Dr. Richard Masland is an accomplished scientist in basic and translational research in the retina. He completed his undergraduate studies at Harvard College, received his PhD from McGill University and conducted postdoctoral work at Stanford University and Harvard Medical School. Dr. Masland was an Investigator of the Howard Hughes Medical Institute from 1995 to 2006, and joined Mass. Eye and Ear in 2009 as Associate Chief for Ophthalmology Research and the Director of the Howe Laboratory, which houses much of the research in eye development and disease at Mass. Eye and Ear.

Masland’s laboratory focuses on the neuronal diversity of the retina, its cellular interactions, and the complex photoreceptor microcircuitry that codes visual input. Because the retina is a readily accessible extension of the central nervous system, the findings of Dr. Masland and colleagues are applicable to other neuronal processes. His ambitious and collaborative retinal atlas project is fundamental to the understanding of retinal degenerative disorders. For his outstanding contributions to the field of ophthalmology, Dr. Masland received the 2010 Proctor Medal, which is the highest honor bestowed by the Association for Research in Vision and Ophthalmology (ARVO). A former Howard Hughes investigator, Dr. Masland has also received Brian Boycott Prize for his retinal research. His honors for excellence in teaching include the Hoopes Prize and the Irving M. London award.
Constance L. Cepko, PhD
Professor of Genetics and Ophthalmology, Harvard Medical School
Investigator, Howard Hughes Medical Institute

Dr. Constance Cepko’s scientific career began with a seventh-grade science fair project in microbiology; this led to a weekend research internship that continued through high school, followed by baccalaureate studies in biochemistry and microbiology at the University of Maryland. At MIT, under the direction of Phillip Sharp, PhD, Dr. Cepko conducted her doctoral research on adenoviral proteins. As a postdoctoral fellow in the laboratory of Richard Mulligan at MIT, Dr. Cepko helped pioneer the use of retroviruses to express transgenes in cells. Recognizing the utility of retroviral vectors in developmental biology, Dr. Cepko used them to study retinal development when she became an independent investigator at HMS in 1985. Besides significantly advancing the basic science underlying retinal development, Dr. Cepko has applied the tools of genetics and molecular cell biology to understanding the basis of retinal disease. Dr. Cepko has received numerous honors for vision research, including the David Cogan Outstanding Young Investigator Award in Vision Research, the Alcon Institute Research Award for Vision, and the Bressler Prize for Vision from the Jewish Guild for the Blind. Dr. Cepko has been an Investigator of the Howard Hughes Medical Institute since 1994; she was inducted into the American Academy of Arts and Sciences in 1999 and the National Academy of Sciences in 2002. She is a member of the Society for Neuroscience and the Association for Research in Vision and Ophthalmology.

Dr. Cepko’s laboratory is currently studying how HDAC4 promotes rod survival, and is now developing gene delivery techniques that may someday be used to treat retinal degenerative disorders in humans.

Judah Folkman, MD
February 24, 1933 – January 14, 2008

The Father of Angiogenesis
As a young navy doctor in 1961, Dr. Judah Folkman noticed that tumors needed blood vessels to grow. Ten years later, Folkman published a controversial theory that is now widely accepted: targeting angiogenesis may potentially arrest cancer. Although others described tumor angiogenesis as early as 1945, Dr. Folkman’s paramount achievement was to lay the foundation of antangiogenic therapy, and he is unequivocally considered the “Father of Angiogenesis.” By the time Dr. Folkman passed away, an estimated 1.2 million people had received antangiogenic treatments. His scientific legacy endures through the HuFokans, scientists who were mentored or otherwise influenced by this visionary of translational research.
Angiogenesis

Because blood vessels play important roles in many human diseases (including cancer), they have become a major focus of translational research and drug development. Realizing that blood vessels are central to many blinding retinal diseases, scientists and clinicians of the Harvard Medical School Angiogenesis Research Group (HMSARG) have focused intense scrutiny on the underlying mechanisms of blood vessel development. HMSARG researchers have individually and collaboratively discovered many mechanistic features of vascular biology, thus forming new paradigms for diseases that involve neovascularization (the abnormal formation of new blood vessels) or angiogenesis (the growth of existing vessels). Efforts of the HMSARG have translated groundbreaking scientific discoveries into innovative treatments for millions of patients with vascular disease.

Vascular endothelial growth factor (VEGF)

Antiangiogenic therapy, first advocated by Judah Folkman, MD, in 1971, targets factors in the body that regulate blood vessel growth. One molecule, first discovered in 1987, was named vascular permeability factor (VPF) for its ability to make blood vessels leaky. In 1989, researchers realized that VPF could also make blood vessels grow. Unlike other angiogenic factors that stimulate the growth of many cell types, VPF’s potential effects were very specific for vascular endothelial cells. Moreover, VPF can be secreted into the bloodstream; thus, it can have effects distant from the cells of origin. Because of its specific and far-reaching effects on blood vessels, VPF was renamed vascular endothelial growth factor (VEGF), and is the primary target of current antiangiogenic therapies.

The genetics of angiogenesis

An individual’s genetic makeup can greatly affect many biological processes, including angiogenesis. Prompted by the fact that African-Americans rarely develop neovascular AMD or hemangiomas (benign tumors composed of endothelial cells), Robert D’Amato, MD, PhD, set out to identify genetic factors that modify the angiogenic response. In 2000, he demonstrated that genetic variations among different strains of mice may lead to differences in angiogenic response. In 2004, Dr. D’Amato mapped genetic regions that control the angiogenic response to basic fibroblast growth factor (bFGF) in mice. More recently, Dr. D’Amato’s team mapped genetic regions that control the degree of choroidal neovascularization induced by laser injury. This study, reported in the July 2009 issue of The AER Journal, identified several candidate genes that may regulate angiogenesis, which presents new targets for antiangiogenic therapies. These findings may also lead to the development of new screening tests that detect disease risk, as well as methods to predict a patient’s response to specific treatments.

The benevolent side of VEGF

With the advent of antiangiogenic therapies for cancer and other vascular disorders, VEGF is often viewed in an unfavorable light. However, VEGF also has numerous important physiological roles that HMS scientists have helped to define. For example, in 1999, Yvna Kim, MD, and colleagues demonstrated that the genes for VEGF and two VEGF receptors were constantly expressed in normal eyes, indicating that these genes play active roles in normal eye physiology. While working as an investigator with Patricia D’Amore, PhD, MBA, Magali Saint-Geniez, PhD, she showed that the normal adult retinal pigment epithelium (RPE) expresses VEGF abundantly. This suggested that VEGF is a survival factor for nonproliferating choroidal vessels. Dr. Saint-Geniez subsequently showed that endogenous VEGF is critical for lens development, and may even have neuroprotective effects on photoreceptors. Dr. Saint-Geniez demonstrated that abnormal VEGF expression in the RPE resulted in degeneration of the choroidal vessels, Bruch’s membrane, and the RPE itself. This study was published November 2009 in Proceedings of the National Academy of Sciences, and was featured in the February 2010 issue of EyeNet, the electronic journal of the American Academy of Ophthalmology. These studies highlight the importance of endogenous VEGF in normal eye health, and emphasize the need for strategies that selectively target pathological VEGF activity without disrupting normal VEGF function when using antiangiogenic therapies.

Original group of nine HMS angiogenesis researchers who conducted pioneering bench and translational research to elucidate the role of angiogenesis in blinding ocular diseases, and subsequently developed revolutionary clinical treatments. Much of their work was initiated under the mentorship of Judah Folkman, MD. HMSARG researchers include: Anthony Adams, MD; Lloyd P. Acklin, MD, PhD; Robert D’Amato, MD; Patricia D’Amore, PhD, MBA; Evangelos Gragoudas, MD; George King, MD; Joan Miller, MD; David Slowa, PhD, and Lois Smith, MD, PhD.
HMS ANGIOGENESIS RESEARCH Fuels a Revolution in Retinal Care

1971
- Judah Folkman and colleagues at Children's Hospital and Harvard Medical School describe the isolation of a “tumor angiogenesis factor” (TAF) in the February issue of Journal of Experimental Medicine.

1973
- Work from the HMSARG intensifies, and several studies led by Lloyd D’Amato, George King, Lois Smith, Evangelos Gragoudas, Robert D’Amore, and Joan Miller further explore VEGF and other angiogenic factors in ocular diseases. The investigators help define the role of hypoxia in regulating VEGF, and show how angiogenic inhibitors may block ocular neovascularization. These studies provide the scientific foundation for using anti-angiogenic therapies for vascular disorders of the eye.

1974
- A phase I clinical trial for pegaptanib (Macugen®), a VEGF inhibitor, begins in AMD patients.

1989
- George King demonstrates how protein kinase C, activated by elevated glucose levels, contributes to retinopathy and other vascular complications in diabetes. This mechanistic model of diabetic retinopathy is published in the July issue of Proceedings of the National Academy of Sciences.

1992
- The first tumor angiogenesis factor (VFP) is discovered in the laboratory of Harold Dvorak at Harvard Medical School, and described in the journal Science. Dvorak’s group demonstrated that this factor is a major driver of ocular tumors. VFP later becomes known as vascular endothelial growth factor (VEGF).

1994
- In the journal American Journal of Pathology, Joan Miller, Robert D’Amore, and colleagues correlate VEGF with ocular angiogenesis in primates. This is the first in vivo demonstration of VEGF’s role in ocular neovascularization.

1995
- Based on the work of Joan Miller and Evangelos Gragoudas, the first AMD patient in the world is treated with Visudyne.

1997
- Joan Folkman’s laboratory identifies endostatin, an endogenous inhibitor of angiogenesis, and shows that it inhibits tumor growth. These findings are published in the January issue of the journal Cell.

1998
- Photodynamic therapy (PDT) with verteporfin (Visudyne®) shows efficacy in treating wet AMD in Phase I clinical studies. Joan Miller and Evangelos Gragoudas lead investigators of these studies.

1999
- In studies led by Evangelos Gragoudas and Joan Miller using primate animal models, choroidal neovascularization is prevented by intravitreal injection of an anti-VEGF antibody fragment. The lead author, Magdalena G. Krysko, publishes the study in the Archives of Ophthalmology.

2000
- On April 13, 2000, PDT with Visudyne becomes the first FDA-approved direct treatment for wet AMD.

2002
- The phase I clinical trial for Macugen® shows promise for treating AMD. The results of this study are reported in the April issue of the journal Retina.

2004
- On December 13, Macugen® becomes the first FDA-approved anti-VEGF therapy for neovascular (wet) AMD. The approval is based on a large multi-center clinical trial published December 30 in New England Journal of Medicine. Evangelos Gragoudas is an investigator in this study.

2005–2006
- In a series of studies, Evangelos Gragoudas and Joan Miller examine the safety and efficacy of combination therapies of Lucentis® and Visudyne® in preclinical models.

2008
- Lucentis®, a fragment of the anti-VEGF antibody bevacizumab, enters clinical testing for AMD.

2010
- A landmark clinical trial shows that intravitreal Lucentis® injections remarkably improve the results of standard laser photocoagulation for diabetic macular edema. Lloyd D’Amato and Jennifer Sun are investigators of this collaborative study conducted at 53 clinical sites within the Diabetic Retinopathy Clinical Research Network and published in the June issue of the journal Ophthalmology.

2013
- In July, the FDA approved Lucentis® for the treatment of diabetic macular edema following retinal vein occlusion.
AGE-RELATED MACULAR DEGENERATION (AMD)

At the center of the retina is a photoreceptor rich region known as the macula, which processes images in the middle of the visual field. The macula has a high density of cones, which are the photoreceptors that distinguish color and fine detail in bright light. The fovea, which lies at the center of the macula, is made entirely of cones, and thus provides the most acute vision. As people age, their maculas may begin to degenerate, causing progressive loss of central vision. This condition is known as age-related macular degeneration (AMD). Some AMD patients retain enough peripheral vision to continue many activities of daily life; however, as the disease progresses, it can have devastating effects on quality of life as patients lose the ability to drive, recognize faces, or read. In the United States, AMD is the leading cause of blindness in people over the age of 50.

Photodynamic therapy: a breakthrough for patients with wet AMD

Studies initiated in the early 1990’s by Joan Miller, MD, and Evangelos Gragoudas, MD, have led to a breakthrough for patients with wet AMD: photodynamic therapy (PDT) with verteporfin (Visudyne®). In this procedure, verteporfin (a light-sensitive dye) is injected systemically; an acocl laser is then directed at the eye, which activates the drug specifically in the choroidal vessels. This blocks the leakage of the immune vessels and prevents further growth. This therapy allows targeted and non-invasive treatment for patients with CNV under the fovea, which is the cone-rich central portion of the macula. Approved by the FDA for treating neovascular AMD on April 13, 2000, Visudyne® was the first pharmacologic therapy for AMD and has also been used to treat CNV caused by other ocular conditions. Photodynamic therapy also laid the foundation for a new class of vascular-targeting therapies for AMD, altering the landscape of ophthalmic care.

Drs. Miller and Gragoudas are actively pursuing ways to improve standard PDT. Although this therapy blocks disease progression in most patients who receive it — and may even improve vision in some — PDT itself can cause damage to the retina by causing retinal cells to undergo apoptosis (cell suicide), which is the primary cause of vision loss in both the dry and wet AMD. In 2007, to better understand why this occurred, they showed that Visudyne® induced photoreceptor apoptosis. Drs. Miller and Gragoudas used animal models of AMD to identify the factors that control apoptosis in photoreceptors. In 2018, using the same models, they also showed several promising ways to prevent photoreceptor apoptosis after PDT, such as using a light-emitting sphere (a potent steroid) or L-NAME (a nitric oxide synthase inhibitor). These studies are helping to optimize current PDT protocols for treating CNV secondary to AMD.

Inspiring the development of VEGF inhibitors for AMD

Beginning in the early 1990s, HMSARG scientists began to research the role of VEGF in ocular neovascularization. In 1993, Patricia D’Amore, PhD, MBA, David Shima, PhD, Tony Adams, MD, Judah Folkman, MD, and colleagues showed that the blood vessels of mice with VEGF and in 1995 they found that VEGF expression results from the trial demonstrated low-oxygen (hypoxic) conditions. Using preclinical models, Drs. Miller and D’Amore showed that VEGF expression was virtually undetectable in healthy eyes, but dramatically increased with severity of retinal ischemia (lack of blood flow in the retina) and iris neovascularization. This 1994 discovery was the first time VEGF was implicated in ocular neovascularization. In a series of studies published between 1995 and 1996, several HMSARG members (including D’Amore, Gragoudas, Miller, Adams, Lloyd A. Aiello, MD, PhD, George King, MD, and Lois Smith, MD, PhD) showed that VEGF inhibitors could block neovascularization in preclinical models. In 1994, Drs. Adams, Miller and Folkman showed increased VEGF expression in patients with proliferative diabetic retinopathy. This study, published in the American Journal of Ophthalmology, directly linked VEGF with the development of diabetic retinopathy. The paper also demonstrated that the VEGF levels measured in blood alone to the eye was sufficient to produce neovascularization, again in a process of vision loss.

Moving from preclinical studies to clinical trials, Drs. Gragoudas and Miller led clinical safety studies of ranibizumab in 2005, and along with Ivana Kim, MD, tested its effectiveness in combination with Visudyne®. Recent and ongoing studies conducted by the HMSARG are expanding the role of VEGF in ocular diseases that may be treated with ranibizumab or other anti-angiogenic therapies. Dr. Kim contributed to a primate model of dry AMD, which typically progresses more rapidly and leads to profound vision loss.

HMS Ophthalmology researchers are aggressively pursuing new therapeutic strategies for the dry form of AMD, which still has no FDA-approved treatments. The first step involves defining the mechanism that underlies dry AMD and its progression to GA. Ivana Kim, MD, and Deme Trivissan, MD, PhD, are exploring animal models of dry AMD to better understand its pathophysiology.

By establishing preclinical models and delineating key mechanisms of vision loss in dry AMD, researchers can test novel interventions for this widespread condition.

Genes, smoking, and genetic smoking guns in AMD

AMD is a complex disease that often involves a combination of multiple genetic and environmental factors. Researchers in the Mass. Eye and Ear Molecular Genetics Institute seek to identify genes that contribute to AMD, and to understand how the interactions between genes and the environment may alter an individual’s risk of developing AMD. By studying pairs of siblings in which one had AMD and the other did not, Margaret DeAngelis, PhD, Thaddius Djrya, MD, and Dr. Miller identified cigarette smoking as a risk factor for wet AMD. In 2005, multiple groups identified complement factor H (CFH), a protein involved in immune responses, as a susceptibility locus for AMD. This study showed that the Y402H variant of CFH is associated with 60 percent of AMD risk in older adults. In a subsequent study that addressed both genetic and environmental factors, Drs. DeAngelis, Djrya, Miller and Kim showed that specific variants of the CFH gene, combined with
cigarette smoking, increased AMD risk 144-fold. Using powerful genetic studies combined with gene expression profiling and proteomic techniques, ongoing studies have identified several novel gene vari-
ations and gene-gene interactions that affect AMD risk.

Based on the genetic findings implicating the complement pathway in AMD pathogenesis, several complement-directed therapies are currently under clinical investiga-
tion. The Mass. Eye and Ear Retina Service is participating in a Phase I/ II study, sponsored by Genetech, of an anti-complement factor D an-
tibody for the treatment of advanced dry AMD or GA.

In March 2010, Alexandra Sil-
veira, PhD, and colleagues, working with Drs. Miller, Kim and DeAn-
gela, also identified variants in the retinoic acid receptor related orphan receptor alpha (RORA) gene that substantially contribute to an individual’s risk of AMD. Because the RORA gene codes for a recep-
tor that binds cholesterol and other hormones, this finding links new bio-
markers of risk to AMD, sug-
gesting new ways to prevent or po-
tentially treat AMD and other retinal disorders.

DIABETIC RETINOPATHY

Prior to the 1950s, type 1 diabetes was often fatal within a few years after diagnosis, usually due to keto-
acidosis, kidney failure, and other life-threatening complications of uncontrolled hyperglycemia. The discovery of insulin in 1921 allowed people with this type of diabetes to live longer lives; however, the increased life expectancies also revealed long-term vascular compli-
cations of chronic hyperglycemia, such as diabetic retinopathy. By the 1950s, diabetic retinopathy had be-
come the leading cause of blindness in the United States. Many patients with diabetes are now able to avoid

blindness thanks to laser photoco-
gagulation, a therapy developed in 1967 by researchers Lloyd M. Aiello, MD, PhD, and William P. Berthen, MD, at the Joslin Diabetes Center. Despite this revolutionary treat-
ment, diabetic retinopathy remains a major public health concern as the leading cause of blindness among working-age Americans. Researchers at the Beetham Eye Institute (REI) at Joslin are continually advancing available treatments for diabetic retinopathy, and have also contrib-
uted greatly to the development of antiangiogenic therapy for vascular eye disorders.

Picking PKC as a target of diabetic retinopathy treatment

George King, MD, HMS Professor of Medicine at HMS and Direc-
tor of Research at Joslin Diabetes Center, first detailed some of the cellular signaling pathways that underlie diabetic retinopathy over two decades ago. In his landmark report, published in July 1980 in Proceedings of the National Academy of Sciences, Dr. King proposed that elevated glucose levels activate protein kinase C (PKC), which in turn leads to vascular complications in diabetic retinopathy. Dr. King and his collaborator, Lloyd P. Aiello, MD, PhD, have continued to define the role of PKC in diabetic retinopathy. A report in the November 2009 issue of Nature Medicine showed how PKC-delta activation by hypergly-
cemia causes blood vessel cells to die—resulting in vascular complica-
tions in the early stages of diabetic retinopathy.

The cumulative findings of Drs. King and Aiello led to the develop-
ment of ruboxistaurin (Arzoxfen®), a PKC- beta inhibitor, which was demonstrated to inhibit vascular disorders in preclinical models of diabetes. Results of a Phase 3 clinical trial of ruboxistaurin were reported in 2006, compared to placebo, ruboxistaurin reduced risk of sus-
tained moderate vision loss by 40 percent in patients with moderate to severe non-proliferative diabetic retinopathy and those still undergoing clinical trials to further test the safety

and efficacy of this PKC inhibitor. Although endpoints to prevent the progression of diabetic retinopathy were not achieved in recently com-
pleted clinical trials, the secondary endpoints from these studies suggest that ruboxistaurin may still have some potential in preventing vision loss from diabetic retinopa-
thy. More importantly, these studies have advanced the understanding of the disease processes in diabetic retinopathy, and help to guide new approaches for developing potential therapeutics.

VEGF as a villain of diabetic retinopathy

Since diabetic retinopathy involves leaky blood vessels and pathologi-
cal neovascularization in advanced stages, it is not surprising that it involves VEGF; in fact, some of the earliest studies implicating VEGF in neovascular eye disorders conducted in patients with diabetes. In 1994, researchers at Mass. Eye and Ear, in collaboration with Drs. King and Adams) and at REI (including Drs. Aiello and King) found increased VEGF levels in the vitreous of patients with diabetic retinopathy. In No-

vember of 1995, Drs. Aiello, King, and Louis Sobrin, MD, PhD, published the first report that VEGF inhibitors could suppress retinal neovascular-
ization. In January of 1996, a team that included Drs. Adams, Shima, Gragoudas, Folkman, D’Amore and Miller published studies showing that VEGF inhibition with a mono-
clonal antibody could prevent neo-
vascularization. These studies were instrumental in the development of ranibizumab (Lucentis®), a retinoid acid receptor-related ophthal-
omy that binds cholesterol and other

biological pathways to AMD, sug-

gesting that certain traits make some individuals more prone to diabetic retinopathy. In a multi-

center clinical trial of 854 eyes in 681 patients with DME, laser combined with ranibizumab was more effec-
tive at slowing or reversing vision loss than using laser alone. At a two-year follow-up, vision was still dramatically improved in patients who received the combination treatment. This study was con-
ducted by the Diabetic Retinopathy Clinical Research Network and published June 2010 in Ophthalmol-
ogy. Expanded two-year results were published April 2011 in Ophthal-
mology, and confirmed the results of the previous report. Drs. Aiello and Sun

were among the lead investigators of this study, which gives promis-
ing evidence that antiangiogenic therapy can greatly benefit patients with diabetic retinopathy.

Genetics of diabetic retinopathy and the Jackson Heart Study

In the United States, African Americans have an increased risk of cardiovascular disease and related conditions, including diabetes. For reasons that are not entirely clear, diabetic retinopathy is not only more common in African Americans compared to other groups, but the disease also tends to progress more quickly. Because this disparity can’t be explained by differences in blood sugar control alone, research- ers suspect that other factors exist. Lucia Sobrin, MD, MPH, believes that genetics may explain why Afri-
can Americans are especially prone to diabetic retinopathy. Through a collaboration between Mass. Eye and Ear, the University of Mississip-
i Medical Center, and the Jackson Heart Study group, Dr. Sobrin hopes to uncover genes that may alter an individual’s risk of diabetic retinopathy.

The Jackson Heart Study fol-

ows African Americans living in the greater Jackson, Mississippi area, and is the largest study in history to examine the genetics of cardiovas-
cular disease and related conditions in African Americans. Researchers have collected DNA samples from over 15,000 African Americans who are living for genetic clues as to why certain people are more prone than others to develop diabetic retinopathy.

for treating diabetic macular edema (DME), new studies suggest that ranibizumab therapy may improve the visual outcomes of standard laser therapy for complications of diabetic retinopathy. In a multi-
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others to certain conditions. Dr. Sobrin has carefully examined the clinical signs and genetic maps of over 100 patients thus far, and will continue to enroll participants through 2023. Genetic mapping is being done at the Broad Institute in Cambridge, Massachusetts, where Dr. Sobrin has been working with David Altschuler, MD, PhD, and Mark Daly, PhD. By identifying genes that may affect retinopathy path and rate of progression, Dr. Sobrin hopes to improve monitoring, counseling, and therapeutic strategies for patients that may suffer vision loss from diabetic complications.

**Retinal Degenerations**

Retinal degenerations are diverse genetic conditions that progressively destroy the light-sensing photoreceptors of the retina. Those that are hereditary are known collectively as retinitis pigmentosa and allied diseases, and affect approximately 100,000 people in the United States and a million people worldwide. Most people affected by this condition become night blind in adolescence, lose side vision in young adulthood, develop tunnel vision, and become blind by age 60 if untreated, some individuals become virtually blind by age 30. Though vision loss in retinitis pigmentosa is irreversible, treatment regimens developed in the HMS Department of Ophthalmology may slow the course of disease, and postpone blindness for up to 40 years. Research is ongoing with the ultimate goal of restoring vision among those with early stages of this group of diseases.

**Treating hereditary retinal degenerations and deciphering their genetic origins**

Eliot L. Benson, MD, the William F. Charles Professor of Ophthalmology at HMS, has been at the forefront of research on retinal degenerations for more than four decades. In the 1960s, Dr. Benson discovered that electroretinography (ERG) could detect photoreceptor dysfunction years to a decade before vision starts to deteriorate in retinitis pigmentosa. Since then, ERG has been used routinely to diagnose this condition and to estimate visual prognoses. Dr. Benson and colleagues, working in the Berson and coworkers’ group at the German-Gund Laboratory for the Study of Retinal Degenerations, developed the first treatment regimens for retinitis pigmentosa: supplementation with vitamin A palmitate and a fish oil diet (of which docosahexaenoic acid, or DHA is a major constituent). They have recently shown that the supplementation slows middle-aged visual field loss (Archives of Ophthalmology, 2012).

In the early 1990s, Dr. Benson and his colleague Thaddeus Dryja, MD, discovered the first gene defects associated with retinitis pigmentosa—point mutations in the rhodopsin gene, which encodes a light-sensitive pigment in photoreceptor cells. Drs. Benson and Dryja have since pinpointed identified approximately 20 genes associated with retinitis pigmentosa—revealing numerous other retinopathies that are altered in this heterogeneous group of diseases. More recently Dr. Benson has collaborated with Carlo Rivolta, PhD, a former fellow of Dr. Dryja, to define further the mutation spectrum in these disorders. In the July 2020 issue of the journal Human Gene Therapy, Dr. Benson, Michael Sandberg, PhD, Basil Pawlyk and coworkers reported successful gene therapy of both rod and cone photoreceptors in an animal model of a severe form of retinitis pigmentosa (Leber congenital amaurosis) caused by loss of the RPGRIP1 gene. These genetic studies form the foundations for new disease models and developing targeted therapies for some of these other forms of retinobacterial disorders.

**Deciphering the genetic origins of retinitis pigmentosa**

The X chromosome also contains a gene that is often associated with retinitis pigmentosa; it codes for a protein called rhodopsin pigment GTPase regulator (RPGR), which is missing or nonfunctional in about 10 percent of all cases of the degenerative retinal disease. Studies conducted in the Benson-Gund Laboratory of Retinal Degenerations have significantly advanced the understanding of how RPGR functions in the retina, and have led to promising new therapies for retinitis pigmentosa.

In the early 2000s, Drs. Benson and colleagues used adeno-associated virus (AAV) to express RPGRIP in a mouse model of LCA. This gene therapy then restored photoreceptor function as confirmed by electroretinography (ERG). In a subsequent preclinical study, reported August 2010 in the journal Human Gene Therapy, Drs. Benson, Li, and Dryja used a similar strategy to restore photoreceptor function in LCA mice—a first time using the human RPGRIP gene. This provided proof-of-concept that gene replacement therapy is feasible for the human form of LCA, and called for clinical testing in patients with RPGR deficiencies. This study also suggested that RPGRIP, rather than other retinal degenerations caused by ciliary defects. Ongoing studies are testing AAV-mediated RPGR replacement therapy for X-linked retinitis pigmentosa.

**Optical coherence tomography (OCT): a revolutionary technique in evaluating retinal disease**

**Optical coherence tomography (OCT) is a non-invasive technique that uses light to produce high-resolution, three-dimensional images of fine ocular structures. OCT was developed in the early 1990s at Mass. Eye and Ear in collaboration with Massachusetts Institute of Technology and Massachusetts General Hospital. OCT is now used worldwide in routine clinical practice to diagnose and monitor numerous ocular conditions. In the retina, OCT was first used to characterize morphosis in the macula, and the term “morphe” was shortened expanded quickly into a role in the management of neovascular (wet) AMD.**

In a case series reported June 2006 in American Journal of Ophthalmology, researchers at Mass. Eye and Ear (including Teresa Chen, MD, Joan Miller, MD, and Eva-Britta Glaser, MD) demonstrated for the first time that histological changes in dry AMD can be detected in time domain OCT (TD-OCT) scans of the retina. OCT is now rapidly becoming the “gold standard” for diagnosing and monitoring both wet and dry forms of AMD, and HMS researchers are continually optimizing techniques for measuring retinal changes in this increasingly prevalent condition. TD-OCT detection in the classic and probably most widely used OCT technology. A newer form, based on spectral domain (SD) detection, has greatly improved the image quality for retinal morphology. SD-OCT has had a major impact in the diagnosis and management of patients with AMD, said Dr. Benson. Chromatic aberration in macular pigment in AMD OC techniques. Ongoing studies are using OCT to better understand the pathology of retinal disease, and to determine the effectiveness of novel therapeutic regimens.

As SD-OCT has become an integral part of AMD management, so has the need to better understand the implications of OCT findings and how they relate to other clinical findings. Andrea Gianini, MD, Daniel Esmaili, MD, and Dr. Miller of Mass. Eye and Ear, in collaboration with Giovanni Staurenghi, MD, and colleagues at the University of Milan, recently evaluated patients with classic CNV using SD-OCT, and correlated the findings with vessel leakage as determined by fluorescein angiography (FA). The researchers found that the absolute difference between CNV morphology and retinal pigment epithelial reflectivity (REF), as determined by SD-OCT, was significantly greater than previously treated (but still leaking) CNV. Moreover, the average difference between CNV material and REF was higher in leaky lesions than in those without leakage. This study, slated for publication in the journal Retina, demonstrates that SD-OCT findings may provide important information regarding vessel leakage measurements by FA. In a related study, published August 2001 in the journal Investigative Ophthalmology and Visual Science, Drs. Gianini, Esmaili, Miller, and Staurenghi, and colleagues tested whether SD-OCT may be used to predict FA leakage in CNV. Indeed, the researchers found that SD-OCT findings were significantly correlated with FA leakage in CNV with fluid present and with certain patterns of fluid presentation. These cumulative findings will establish the clinical relevance of OCT imaging and its use in managing...
mined by TD-OCT measurements (due to presumed edema) deter cell loss) and retinal thickening that both retinal thinning (due to less and detecting complications, OCT has proven to be extremely useful in evaluating and predicting visual acuity to be a clinically useful tool in evaluating and predicting visual acuity after treatment.

For retinal degenerative disorders like as retinitis pigmentosa, researchers showed that higher baseline measurements of retinal volume in a multicenter, trial of focal/grid photocoagulation for diabetic macular edema may have advantages over standard therapy for DME, and showed OCT to be critical in the development of ROP, and has defined novel strategies for treating and preventing this disease. In 2007, Dr. Smith, with John Paul San Giovanni, ScD, Jing Chen, PhD, and Kip Connor, PhD, showed that omega-3 fatty acids promote normal vessel growth in the retina while reducing abnormal neovascularization. This suggested that prenatal supplementation with omega-3 fatty acids may help prevent retinopathy in newborns. In a series of studies published in the past few years, Drs. Smith and Chen demonstrated that erythropoietin (EPO) and insulin-like growth factor 1 (IGF-1) are both deficient in the early stages of ROP when retinal vessels are insufficient—yet both contribute to the pathological angiogenesis that occurs during neovascular ROP. These studies not only present new pharmacological targets, but also demonstrate that timing is critical for preventing and treating ROP.

**Retinopathy of Prematurity**

If a baby is born too early, the retinal vessels—which grow outward from the center of the retina—may stop growing before they reach full length. This may lead to retinopathy of prematurity (ROP), and can deprive the developing peripheral retina of oxygen and nutrients. This early stage of ROP affects about 15,000 premature infants each year in the United States, while most recover without treatment, about 10 percent of ROP cases progress to a neovascular stage that can severely damage the retina and cause vision loss. VEGF plays a major role in both stages of ROP, and its regulation by oxygen is central to the disease process. VEGF is induced by low oxygen (hypoxia) but repressed by high oxygen (hyperoxia), so when a baby is exposed to the oxygen-rich environment outside of the womb, the relative hyperoxia may halt normal retinal vessel growth by suppressing VEGF. As a result, the blood-starved peripheral retina becomes hypoxic, and produces VEGF and other angiogenic factors to induce neovascularization.

The interplay between neural and vascular networks in the developing retina

In babies with ROP, the disease exists as an angiogenic process that is initiated at approximately 32 weeks of gestation, or about eight weeks short of full term. This happens to be the time when the photoreceptors (the rod cells in particular) undergo rapid maturation. Because nerves and blood vessels often grow side by side, the interplay between the neural and vascular networks in the retina may be important in ROP. This neurovascular interaction is the focus of Anne Fulton, MD, HMS Professor of Ophthalmology and Senior Associate in Medicine at Children’s Hospital Boston. Dr. Fulton’s recent studies have explored the possibility that the rapidly maturing photoreceptors, with their increased metabolic demands, create a hypoxic environment that promotes neovascularization; thus, photoreceptor function may actually occur before vascular abnormalities appear. Using non-invasive assessment techniques such as electroretinography (ERG) and OCT, Dr. Fulton showed that rod sensitivity could predict vascular outcome at a later age. These observations were confirmed in animal models of ROP, and suggest that rod dysfunction reflecting a causative role in the vascular problems of ROP. These studies may begin to unravel the mechanisms of retinopathy and suggest that the immature photoreceptors as potential pharmacological targets, and offer promise for early intervention in the treatment of ROP.

Understanding unique aspects of angiogenesis in the eyes of children

By studying ROP, Lois Smith, MD, PhD, has made several notable contributions to the field of angiogenesis research. In the 1990s, Dr. Smith worked with Patricia D’Amore, PhD, MBA, and Robert D’Amato, MD, PhD, to develop a mouse model of ROP that is widely used to study VEGF regulation and oxygen-induced retinopathies. In collaboration with George King, MD and Lloyd P. Aiello, MD, PhD, Dr. Smith was among the first to implicate VEGF in retinopathy and suppress ocular neovascularization using VEGF inhibitors. Dr. Smith has since shifted her focus to other factors that are also important in the development of ROP, and has defined novel strategies for treating and preventing this disease.
As a pediatric ophthalmologist, Lois Smith, MD, PhD, has cared for many extremely premature babies—some weighing less than one pound. Not only do these vulnerable infants face the threat of blindness, but many also suffer from retinopathy of prematurity (ROP). A number of years ago, Smith decided that she needed to find a way to help these babies preserve their vision.

Dr. Smith’s quest began by looking at the first ROP risk factor: oxygen delivery. She worked with newborn mice, which, like premature babies, have only partially developed retinas. When the mice were given supplemental oxygen at high levels, their retinal blood vessels stopped growing or disappeared. Moreover, retinal cells of VEGF were lost. For the mice, the VEGF levels were brought back into normal room air, VEGF levels surged and blood vessels resumed growth—sometimes abnormally.

Many years of follow-up experiments revealed that VEGF is actually involved in two biochemical pathways. Targeting one pathway could enhance the normal, “good” vessel growth in the first phase of ROP without affecting the abnormal second-phase vessel growth.

To discover other critical factors acting in these pathways, Dr. Smith began to investigate growth hormone (GH), which is produced by the pituitary gland and implicated in diabetic retinopathy. Her work gradually led her to another hormone known as insulin-like growth factor 1 (IGF-1), which works in concert with GH and is important for growth and development of the brain, lungs, intestines and other organs. Dr. Smith conducted a series of experiments in mice that could not produce IGF-1. The results showed that IGF-1 was critically important for normal vessel growth, Dr. Smith says. “If IGF-1 is low, vessels don’t grow.” The research quickly moved into humans, Dr. Smith’s group found that in the third trimester of pregnancy, IGF-3 levels in the ferum rise markedly because they get the factor from the mother in the womb. In very premature babies, however, this supply is cut off, and their levels of IGF-1 begin to decline.

This finding prompted Dr. Smith and Ann Helleström, MD, PhD, a collaborator in Sweden, to assess IGF-1 levels in 80 babies born at 24 to 36 weeks of gestation. They found that IGF-1 levels at the gestational age of 30 to 33 weeks were the most important predictor of whether a preterm baby would develop ROP. In babies who developed ROP, IGF-1 levels never rose to the level they would have achieved at 30 to 33 weeks in utero. In contrast, premature babies who did not develop ROP managed to make enough IGF-1 soon enough after birth to prevent disease.

Dr. Smith and Helleström next conducted a Phase 1 clinical trial in Sweden to see if supplementing IGF-1 in premature newborns would prevent ROP. Starting at birth, the babies received small amounts of IGF-1 intravenously until they were able to make sufficient levels of the growth factor on their own. Successful results from this trial have led to an expanded, multi-center Phase II trial in Sweden. “In science, you have to look at one thing at a time,” says Dr. Smith. “You try to find pathways that you can alter to make a difference, and you just keep on pushing.”

In children, retinopathy of prematurity (ROP) is a major cause of vision loss in the U.S. Each year, about 1,500 premature infants develop ROP severe enough to require medical treatment; approximately 500 children each year become legally blind from ROP.

(National Eye Institute)

Preserving vision: new agents for neuroprotection

Though blinding retinal diseases have many different origins, they often converge on pathways that trigger the death of photoreceptors (the light-sensing neurons of the retina), resulting in vision loss. Two well-characterized biological pathways, apoptosis (cell suicide) and necrosis (cell death caused by stress and other external factors), are controlled routes of cellular destruction. Therapeutic interventions that prevent photoreceptor cell death by both apoptotic and necrotic pathways may potentially preserve vision for a myriad of retinal diseases.

Thus, neuroprotection is an area of current research in the HMS Department of Ophthalmology.

In 2003, a collaboration between Cynthia Grosskreutz, MD, PhD, and Dr. Smith, demonstrated that photoreceptor cell death and apoptosis occurred in an experimental model of retinal detachment. In 2008, a group led by Dr. Smith showed that the class of anti-AIDS drugs known as protease inhibitors could protect against photoreceptor death in laboratory model species. In 2010, in an article published in the Proceedings of the National Academy of Science, Dr. Miller and Dementrós Vasvári, PhD, reported findings that, although the caspase pathway was activated and apoptosis occurred in the model, cell death also occurs through another pathway triggered by receptor interacting protein (RIP). In this study, they demonstrated that blockade of the Fas death receptor by the Fas death receptor inhibitor and necrostatin-1 (a RIP kinase inhibitor), was required to effectively prevent apoptosis, necrosis, and oxidative stress. Similarly, deficiency of Rip3 (a key activator of RIP1 kinase) prevented the necrotic changes. Thus, two pathways to cell death were triggered by retinal detachment in animal models, indicating that combination therapy to prevent both caspase-dependent apoptosis and RIP-mediated necrosis may help preserve vision.

Retinal research at the xenic retinal restoring vision

The convergence of research progress in many areas has created an unrivaled opportunity in retinal research. The retina, which is more accessible (and has a simpler neuronal structure) than the brain, is likely to yield the first successful neuroregenerative treatments using gene-targeting and stem cell therapies. Moreover, the retinal atlas project provides investigators with the complete cellular architecture of the retina, which complements new advances in gene therapy and stem cell research. Under current study are three distinct approaches to restoring vision: persuade healthy retinal cells to acquire photoreceptor functions, targeted gene therapies, and stem cell engraftment into the retina. These approaches are described as potential treatment options for patients with vision loss, and can be applied to a multitude of ocular diseases that cause blindness.

Gene therapy with help from retinal ganglion cells

Retinal ganglion cells relay visual information, in the form of electric impulses, from the photoreceptors to the brain. Some ganglion cells express the light-sensitive pigment melanopsin, which allows them to act as photoreceptors as well. Melanopsin is also known to impart photoreceptor-like qualities to cells that normally express it; thus, Richard Masland, PhD, wondered whether retinal ganglion cells, induced to express melanopsin using gene therapy techniques, could substitute for photoreceptors in eyes with retinal degeneration. In a mouse model of hereditary retinal degeneration caused by Dr. Masland used viral vectors to deliver the melanopsin gene to a large number of retinal ganglion cells. This treatment restored an appreciable degree of vision in mice that lacked rod and cone photoreceptors. This study, published in the October 2009 issue of Proceedings of the National Academy of Sciences, established melanopsin as a candidate gene therapy for retinal degenerations. More importantly, this work provides proof-of-principle that photoreceptor substitution is a viable approach for treating retinitis pigmentosa and other retinal degenerative disorders. Dr. Masland’s group is currently refining that technique for potential use in patients blinded by retinal disease.

Making stem cell therapy a reality for retinal disease

Tissue and stem cell therapies hold enormous promise for repairing the retina in diseases that cause photoreceptor destruction. This is the focus of Dr. Robert Young, Associate Professor of Ophthalmology at HMS, and Director of the Minda de Gunzburg Center for Ocular Regeneration at Schepens Eye Research Institute. Studies led by Dr. Young during the past few years have significantly advanced the understanding of tissue and stem cell transplantation in the retina particularly in terms of graft survival and the formation of functional neural connections after transplantation. Dr. Young’s laboratory has developed biomaterials that can be used for delivering neuroprotective agents or stem cells to the retina; the engineered biomaterials have also been shown to promote neuronal and functional growth of neurons after transplantation.

In 2007, Dr. Young established a novel role for matrix metallo-

Reprinted from the spring 2010 issue of Dreams: The Magazine of Possibilities, with permission of Children’s Hospital Boston. Original story by Nancy/’Flaherty. Content has been adapted and updated for this report.
proteases (MMPs) in promoting neural regrowth. Using a mouse model of retinal degeneration, Dr. Young showed that MMPs support the growth of transplanted neural progenitor cells in the retina. Subsequent studies showed that increased MMP levels create a permissive environment for neural regeneration. Recently, Dr. Young’s laboratory engineered a cell delivery system consisting of a biodegradable/bio-compatible polymer that provides a steady release of MMP to promote neural regeneration at sites of retinal injury. This technology represents a significant step toward making stem cell therapy a reality in the treatment of retinal disease.

A pharmacological approach to regenerating the retina

Another possible way to treat blindness is by stimulating the growth of new photoreceptors. For many optic neuropathies, the lack of suitable preclinical models has hindered efforts to improve existing treatments and develop novel therapeutic strategies. Dean Cestari, MD, a specialist in neuro-ophthalmology, is developing animal models of hereditary optic nerve disorders with the goal of preventing disease progression. Dr. Cestari also studies conditions that lead to secondary optic neuropathy, including giant cell arteritis and neurofibromatosis type 1. He is particularly interested in the inflammatory and pro-angiogenic factors that mediate cell death and visual loss during ischemia (lack of blood flow) in the optic nerve. With the knowledge gained from his studies, Dr. Cestari hopes to develop novel therapies for many optic nerve conditions.

GLAUCOMA

Glaucoma encompasses several conditions that cause optic neuropathy, and affects an estimated 60 million people worldwide. Primary open-angle glaucoma (POAG) is the most common form; it is associated with increased intraocular pressure (IOP), also known as ocular hypertension, which may in turn lead to retinal ganglion cell death and optic neuropathy. Secondary glaucoma occurs as a complication of eye surgeries, injuries, or other ophthalmic conditions. Glaucoma may even occur without increased IOP in normal tension glaucoma. Many kinds of glaucoma have strong genetic and/or environmental risk factors, and any form of the disease can cause irreversible blindness if left untreated.

GENETIC SCREENING AND PROGNOSIS

The most common forms of glaucoma have complex inheritance patterns that seem to involve multiple genetic and environmental factors. By identifying genes associated with glaucoma, scientists hope to develop screening tests that allow rapid risk assessment.
Nature, nurture, and glaucoma

For diseases that do not have straightforward inheritance patterns, finding a genetic basis is very much like searching for a needle in a haystack; thus, identifying glaucoma-causing genes in the human genome requires significant collaboration and the ability to search multiple genomes at once. One major collaborative project, now in its third year, is the NEIGHBOR Consortium—a multicenter cohort study organized by Janey Wiggs, MD, PhD, and Louis Pasquale, MD. This study includes case samples and controls from the Massachusetts Eye and Ear Infirmary, the Nurses’ Health Study (NHS), the Health Professionals Follow-up Study (HPFS), and thousands of additional subjects from 21 other investigators with eight different institutions, for a total of 4,960 cases with diagnoses and controls.

“The collaborative effort not only taps into the intellect and resources of multiple institutions, but also encourages a combination of genetically and statistically robust sample sizes needed to identify major genes that contribute to glaucoma.” Collaborations are essential for this type of study because no single hospital or glaucoma service can produce this many samples,” notes Dr. Pasquale. “It’s an incredibly exciting effort, and my expectation is that we’ll find some major genes that contribute to glaucoma.”

The NEIGHBOR Consortium and other related studies form the basis of several genetic and epidemiologic collaborations between John E. Pellegrino, MD, Louis Pasquale, MD, and Janey Wiggs. The highly anticipated results of these studies may ultimately allow at-risk patients to be identified through genetic screening tests. A genetic epidemiology study, published in early 2010 in the journal Investigative Ophthalmology and Visual Science, identified potential interactions between endothelial nitric oxide synthase 3 (eNOS3) gene variants and hormone replacement therapy in POAG. This study shows that the association between NO3 genotypes and POAG is modified by postmenopausal hormone use. Drs. Pasquale and Wiggs are currently collaborating with researchers at MGH and Schepens to validate a mouse model of POAG that may, in turn, be used to validate these epidemiologic findings.

Genomic studies have also identified candidate genes for pseudoexfoliation syndrome, a major risk factor for glaucoma. In a pseudoexfoliation fibrous buildup on the inner surfaces of the anterior chamber (including the lens) may exfoliate, or flake off, and block drainage of the aqueous humor. Pseudoexfoliation has been associated with LOXL1 gene variations in patients from Scandinavian countries, where the condition was first described. In 2008, researchers at Mass. Eye and Ear associated three LOXL1 variants with pseudoexfoliation in ethnically diverse patients in the United States. This study, published in the journal BMC Medical Genetics, suggested that certain variations in LOXL1 confer significant risk for adult-onset glaucoma worldwide.

The LOXL1 gene encodes an enzyme that helps build elastic fibers in numerous tissue types, and Mass. Eye and Ear researchers showed that the mutations potentially reduce LOXL1 gene expression. This study, slated for 2011 publication in Investigative Ophthalmology and Visual Science, increases the understanding of the pathology of exfoliation glaucoma, and reveals potential therapeutic targets for this widespread condition.

Data from over 100,000 subjects in the NHS and HPFS cohorts revealed interesting trends for exfoliation glaucoma; that disease is more common in higher geographical latitudes, risk increases with distance from the equator. When exfoliation glaucoma affects only one eye, it even appears to vary according to which side people sleep on. These results suggest that temperature and radiation exposure (such as UV light) are factors in exfoliation glaucoma. Though not yet published, these results highlight the importance of gene-environment interactions in various forms of glaucoma.

An NIH-funded study in India seeks to identify other genes and measurable traits (such as optic nerve size) that may affect glaucomatous optic nerve damage. This study focuses on certain large Indian populations with closely related members, particular because the condition often yields a wealth of genetic information. Data from these ongoing studies are currently being analyzed, and may yield new diagnostic tests for glaucoma.

OCT holds the most potential for glaucoma imaging technologies and was the principal clinical collaborator on the research team that first developed ultra-high resolution video-rate spectral domain OCT. Dr. Chen recently published a study which was the first comprehensive description of the full range of qualitative and quantitative characteristics of the optic nerve and RNFL in glaucoma. This paper also depicted the first spectral domain OCT images of an eye with glaucoma. This study was published December 2009 in the Journal of the American Ophthalmological Society. In a subsequent study, slated for publication in 2011, the Journal of Glaucoma, Dr. Chen and colleagues used spectral domain OCT to examine the eyes of 45 healthy subjects and 33 glaucoma patients. This study is the first to show that a spectral domain OCT machine with tracker has the best ability for reproducible RNFL thickness measurements. These studies provide a basis for further developing and optimizing this imaging technique in larger-scale clinical trials.

Dr. Teresa Chen is an Associate Professor of Ophthalmology and Visual Science at Schepens Eye Research Institute, and was the principal clinical collaborator on the research team that first developed ultra-high resolution video-rate spectral domain OCT. Dr. Chen recently published a study which was the first comprehensive description of the full range of qualitative and quantitative characteristics of the optic nerve and RNFL in glaucoma. This paper also depicted the first spectral domain OCT images of an eye with glaucoma. This study was published December 2009 in the Journal of the American Ophthalmological Society. In a subsequent study, slated for publication in 2011, the Journal of Glaucoma, Dr. Chen and colleagues used spectral domain OCT to examine the eyes of 45 healthy subjects and 33 glaucoma patients. This study is the first to show that a spectral domain OCT machine with tracker has the best ability for reproducible RNFL thickness measurements. These studies provide a basis for further developing and optimizing this imaging technique in larger-scale clinical trials.

Diagnosing glaucoma using psychophysics

Peter Bex, PhD, Assistant Professor of Ophthalmology and Associate Scientist at Schepens Eye Research Institute and Howe Laboratory Director Richard Masland, PhD, have led successful efforts to cultivate interdepartmental collaboration within HMS, as well as multicenter partnerships with other universities and hospitals in the U.S. and abroad. Dr. Bex is also a co-chair of the USINDO Joint Working Group, an international vision research partnership initiated in 2005 between the National Eye Institute and the Indian government’s Department of Biotechnology. The goal of the group is to advance vision science through collaboration of ideas, expertise, and resources. In 2011, Dr. Bex was also tapped to lead the Genetic Diagnostics Section of the department’s new Ocular Genomics Institute. In this role, she will closely collaborate with Dr. Eric Pierce, who has been recruited as Director, to develop the institute into a premier Center of Excellence for leading genomics-based advances in patient care.

Dr. Bex also collaborates internationally and is the recipient of numerous awards including, most recently, a Leroy Wasserman Merit award from Research to Prevent Blindness.

Janey L. Wiggs, MD, PhD
Associate Professor of Ophthalmology, Harvard Medical School
Associate Director of the Howe Laboratory and Associate Chief for Clinical Research, Massachusetts Eye and Ear Infirmary
Director, Genetic Diagnostics Section, Ocular Genomics Institute, Massachusetts Eye and Ear Infirmary

Dr. Janey Wiggs is an accomplished clinician-scientist specializing in the genetics of glaucoma. Using a uniquely collaborative and multidisciplinary approach, Dr. Wiggs’ overall research goal is to identify genetic factors that underlie various forms of glaucoma, including adult-onset primary open angle glaucoma, pseudoexfoliation glaucoma, juvenile open angle glaucoma, and others. Her research, which has been continuously funded by the National Eye Institute for over 15 years, has provided critical information regarding the biology of the disease. Ongoing studies may greatly improve current methods of diagnosis, and lead to more effective and specific therapies.

Dr. Wiggs is the Associate Director of the Howe Laboratory, Associate Chief for Clinical Research, and co-directs the Glaucoma Center of Excellence with Louis Pasquale, MD. Together, Drs. Pasquale and Wiggs, and Howe Laboratory Director Richard Masland, PhD, have led successful efforts to cultivate interdepartmental collaboration within HMS, as well as multicenter partnerships with other universities and hospitals in the U.S. and abroad. Dr. Wiggs is also co-chair of the USINDO Joint Working Group, an international vision research partnership initiated in 2005 between the National Eye Institute and the Indian government’s Department of Biotechnology. The goal of the group is to advance vision science through collaboration of ideas, expertise, and resources. In 2011, Dr. Wiggs was also tapped to lead the Genetic Diagnostics Section of the department’s new Ocular Genomics Institute. In this role, she will closely collaborate with Dr. Eric Pierce, who has been recruited as Director, to develop the institute into a premier Center of Excellence for leading genomics-based advances in patient care.

Dr. Wiggs’ work integrates clinically and scientifically and is the recipient of numerous awards including, most recently, a Leroy Wasserman Merit award from Research to Prevent Blindness.
One of the goals of optic nerve research is to develop novel therapies that ultimately protect the nerve from glaucoma. Dr. Rhee and Dr. Bex are currently working at the Neuroimmunology Institute, is studying how psychological testing methods and Dr. Bex is currently working with Dr. Pasquale to further develop this psychophysical testing method for use in clinical settings.

**PREVENTION & NEUROPROTECTION**

One of the goals of optic nerve research is to develop novel therapies that ultimately protect the nerve from glaucoma. Dr. Rhee and Dr. Bex are currently working at the Neuroimmunology Institute, is studying how psychological testing methods and Dr. Bex is currently working with Dr. Pasquale to further develop this psychophysical testing method for use in clinical settings.

**COMBATING OCULAR HYPERTENSION: SPARCING INTEREST IN THE EXTRACELLULAR MATRIX**

In an eye with normal IOP, aqueous humor production is balanced by its drainage through the trabecular meshwork, a spongy tissue structure that resides at the “open angle” where the cornea and the iris meet. The trabecular meshwork is impaired in many types of glaucoma (including POAG), and this can lead to changes in intraocular pressure (IOP). Current treatments focus on improving drainage through this tissue. It is known that deposits of extracellular matrix material on the trabecular meshwork can block the aqueous humor outflow, and Douglas Rh, MD, Associate Professor of Ophthalmology, is studying the role of matrix proteins in maintaining normal IOP. Dr. Rhee previously showed that human trabecular meshwork cells normally express high levels of the matrix protein SPARC (secreted protein, acidic and rich in cysteine), and hypothesized that this protein may be linked to regulatory IOP. Thus, Dr. Rhee and colleagues generated mice that are deficient for the gene that encodes the SPARC protein, and found that SPARC-null mice had significantly lower IOP than their wild-type counterparts. This suggests a pivotal role for SPARC in IOP maintenance, and establishes this protein as a novel therapeutic target for glaucoma. This approach presents a novel therapeutic strategy for inducing neuroregeneration in the central nervous system.

**OPTIC NERVE REGENERATION**

Like most neural tissues in the adult central nervous system, the optic nerve cannot regenerate appreciably once injured. Nonetheless, the optic nerve is readily accessible, and this is one of the standard laboratory models in neuroregenerative research. One of the ultimate goals of ophthalmology—and the entire field of neurobiology—is to uncover the mechanisms of optic nerve regeneration.

**OVERCOMING BARRIERS TO OPTIC NERVE REGROWTH**

Axons in the central nervous system can potentially regenerate after injury, but this normally happens only in the developing nervous system. Dong Feng Chen, MD, PhD, discovered that during development, optic nerve cells lose neuroregenerative abilities around the time they stop expressing Bcl-2, a regulator of cell survival. This also coincides developmentally with the maturation of astrocytes, which are cells that form scars around damaged nerves and prevent regeneration. Dr. Chen and colleagues used a pharmaceutical approach to promote optic nerve regeneration. They then used the effects of two drugs: lithium, which stimulates Bcl-2 expression, and alpha-amino adipate, which selectively kills astrocytes. While neither drug alone had significant effects on severed optic nerves, in combination they stimulated robust nerve regeneration in adult mice. These results present a novel therapeutic strategy for inducing neural regeneration in the central nervous system.

**LINKS BETWEEN INFLAMMATION, DEGENERATION, AND REGENERATION IN THE OPTIC NERVE**

In mature optic nerves, inflammation can have very divergent effects. On one hand, inflammation can lead to death of the retinal ganglion cells (RGCs) that form the optic nerve, while on the other hand, inflammation can actually stimulate regeneration to some extent. These phenomena are some of the main research interests of Larry Benowitz, PhD, Director of the Laboratories for Neuroscience Research in Neurosurgery at Children’s Hospital and Professor of Surgery and Ophthalmology at HMS.

In collaboration with Toru Nakazawa, MD, PhD, and Joan Miller, MD, Dr. Benowitz showed how inflammation might mediate the harmful effects of elevated IOP in a mouse model of glaucoma. In the retinas of mice, elevated IOP induced tumor necrosis factor-alpha (TNF-alpha), a major inflammatory molecule. The elevated TNF-alpha activated immune cells, which in turn killed the oligodendrocyte cells that produce the protective myelin sheath of nerve fibers. These events resulted in the death of RGCs that form the optic nerve. Using an antibody that blocked TNF-alpha action, these investigators and colleagues were able to prevent the RGC death caused by elevated intracranial pressure. Similar protection of RGCs was seen in mice that lacked either the gene that encodes TNF alpha or one of its receptors. This study suggested that inhibition of TNF-alpha function might be a novel target in elevated IOP. Because drugs that block TNF-alpha are already FDA-approved for treating other conditions, this approach presents significant promise for the treatment of glaucoma.

**REFERENCES**

A niche in eye-movement disorders sheds light on the developing nervous system

(continued from page 107)

a promising neuroprotective treatment for glaucoma. This study was published in 2006 in the journal of Neuroscience.

In 2006, Dr. Benowitz and colleagues discovered that certain immune cells produce a calcium-binding protein called oncomodulin in response to inflammation, and that this protein could actually stimulate regeneration of optic nerves and other neurons of the central and peripheral nervous systems. Subsequent studies led by Dr. Benowitz confirmed that oncomodulin was indeed a link between inflammation and axon regeneration in the optic nerve. While examining the molecular mechanisms of oncomodulin in nerve regeneration, Dr. Benowitz and colleagues observed that it activated Mst3b, a signaling protein that could also stimulate axon growth, but also overcoming scar formation and other barriers to nerve regrowth. Dr. Benowitz and colleagues are testing these nerve regrowth factors in combination with other cellular, molecular, and pharmaceutical agents to maximize axon regrowth.

Dr. Elizabeth Engle, HMS Professor of Neurology and Ophthalmology, and a Howard Hughes Medical Institute Investigator, never expected to land in her current specialized research niche. But deep curiosity and a single patient encounter led her to become the world’s primary researcher probing the genetics of strabismus, or misalignment of the eyes.

Her work, blending genetics with neuroscience, has defined a new category of congenital disorders that leave children unable to move their eyes in specific directions. These conditions impair vision and are often socially isolating; the eyes are fixed in abnormal positions, forcing children to hold their heads in odd positions just to see properly.

In 1992, as a neurology resident at Children’s Hospital Boston, Dr. Engle met a little boy with droopy eyelids. Over tea one night in the family’s home, she learned of another branch of the family with the condition and got permission to contact them. With enough family samples to do genetic studies, Engle realized she needed to make a foray into laboratory research. “I thought there was no way that I could ever run a lab,” she recalls. “I didn’t have a PhD and was never officially trained in the lab. I didn’t even know how to make chemical solutions.”

Nonetheless, Dr. Engle talked her way into a research fellowship in Children’s Department of Genetics with Louis Kunkel, PhD, and Alan Beggs, PhD. Aided by their mentorship and resources, she identified the location of the gene mutated in the boy’s disorder, then defined its neuropathology by conducting an autopsy of an affected family member. Eventually, she traced the boy’s disorder to a single amino acid change in a protein called KIF2A, which carries specific cargo to growing nerve fibers. The subtle change apparently left the cargo stranded—leaving two of the boy’s eye muscles without cranial nerve stimulation. Modeling the disorder—congenital foros of the extraocular muscles type—I in mice, Engle’s lab is now studying how the mutations disrupt KIF2A’s function, and will determine what its cargo is.

Since that first case, Dr. Engle has searched for other families with unusual congenital eye-movement disorders. She has built a database of more than 1,500 patients, which families with unusual congenital eye-movement disorders. She has built a database of more than 1,500 patients, which
“This is a program where learning is valued and the educational experience is tangible. You will learn a vocation, but it differs from many other schools in that HMS is a very academic environment. This is a place where a trainee can approach a faculty member and count on getting help. People coming from other institutions are simply struck by the emphasis we place on medical education.”

— SIMMONS LEESELL, MD, DIRECTOR OF OPHTHALMIC MEDICAL STUDENT EDUCATION, HARVARD MEDICAL SCHOOL

Medical education is integral to the HMS Department of Ophthalmology’s mission, and trainees receive the finest ophthalmic education in the world. The department supports full-time faculty in every ophthalmic subspecialty, giving residents a comprehensive grounding in ocular disease and management. Moreover, fellows have the opportunity to gain further clinical expertise or pursue in-depth research in one or more of nine subspecialty areas. Under the exceptional leadership of John I. Loewenstein, MD, HMS Ophthalmology Vice Chair for Medical Education and Director of the HMS Department of Ophthalmology Residency Training Program, recent program innovations have continued to strengthen the department’s continuum of medical education. These distinctions culminate in a superb educational experience that offers remarkable depth and breadth to the department’s cadre of medical students, residents, and fellows.

The department’s greatest asset is its dedicated community of educators. Through their wealth of collective experience, HMS faculty strive to create a supportive and stimulating learning environment at every opportunity; as teachers in the classroom, clinic or lab, and as mentors to students and trainees in their day-to-day interactions. Through close teamwork—and by serving as role models of effective leadership—their goal is to graduate well-rounded academicians and outstanding clinician scientists who become tomorrow’s leaders in ophthalmic medicine, science and education.

### Setting Standards for Medical Student Education

Within the ophthalmology community, there is general consensus of a need to improve the quality of ophthalmic education for medical students, residents, and primary care physicians. Even so, statistics show that ophthalmic education has fallen victim to tightening budgets and shifting priorities in many academic medical schools in the United States. According to a 2004 survey by the Association of University Professors in Ophthalmology, only 39 percent of medical schools nationwide require a formal ophthalmology rotation. Because physicians in many surgical and medical specialties often need to perform eye exams—especially if they are responsible for managing and triage patients who have ophthalmic complaints—this lack of formal ophthalmic training is of grave concern.

Diverging from this unsettling trend, the HMS Department of Ophthalmology continues to hone its medical student education program. In recent years, major innovations have been implemented, largely due to efforts championed by Simmons Lessell, MD, HMS Director of Ophthalmic Medical Student Education, and Deborah Jacobs, MD, Director of the Core Medicine Clerkship for Harvard Medical School students. Today, the program’s revitalized core and elective curriculum emphasizes a dynamic, integrated format that combines didactics with hands-on clinical and research training under a mentor’s watchful eye. Core requirements begin in the 2nd year of medical school, when students learn to perform the basic eye exam and use the direct ophthalmoscope in a small-group setting. During their 3rd year internal medicine rotation, students directly engage in clinical activity. Augmenting these activities, a revitalized Introductory Elective teaches fourth year medical students the principles of basic ophthalmology through hands-on clinical instruction, rather than a traditional lecture-based curriculum. This unique, modified apprenticeship system pairs each student with two active ophthalmic clinicians in different subspecialties, both of whom provide student supervision and feedback. During the four-week rotation, students accompany their mentors in a busy outpatient setting, in the operating room, and at conferences. Early in their rotation, students work in tandem with residents in the 24/7 emergency eye department and trauma center. Closely supervised by faculty, students have the opportunity to evaluate, triage, and manage patients, and learn how to use specialized ophthalmic equipment, including the slit-lamp biomicroscope, the tonometer and the ophthalmoscope. Students are also loaned a set of basic ophthalmology textbooks and encouraged to attend Grand Rounds and department lectures to reinforce their training. Faculty guidance and feedback throughout the rotation is an important part of the learning process. A pediatric ophthalmology elective is also available at Children’s Hospital-Boston for interested students, and directed by Ophthalmologist-in-Chief, David Hunter, MD, PhD. Students who satisfactorily complete the Introductory Elective may choose to take a four-week minimum Advanced Ophthalmology course. At this level, more than 30 electives representing a robust, cross-section of ophthalmic subspecialties are open to students who wish to participate in a focused clinical or laboratory investigation. Students may choose from many exciting areas of study. Some examples include:

- Pathogenesis of age-related macular degeneration (wet or dry)
- Antibiotic resistant bacterial infections
- Human and molecular genetics research with an emphasis on understanding the role of genes in the development of glaucoma
- Behavioral and imaging research to assess visual impairment and monocular visual disorders
- Diseases of the surface of the eye, including infections and dry eye diseases
- Glyobiology - an expanding field at the forefront of the biomedical sciences that studies the structure and function of the carbohydrate chains (glycans) present in all living organisms
- Ocular immune privilege and the pathogenesis of autoimmune uveitis

Today, about 1 in 6 ophthalmology department chairs in academic institutions across the U.S. and Canada conducted postdoctoral training at HMS.
“I’m honest. I acknowledge my shortcomings. I’ve also tried to be generous. If you have more pieces of the puzzle than the person you are teaching, the next criterion is generosity. What you are trying to do is to give to someone else everything you have acquired and the means of gaining more. You hope that each one will do even better than you do.”
— Simmons Lessell, MD

Simmons Lessell, MD

Paul A. Chandler Professor of Ophthalmology, Harvard Medical School

Director of Ophthalmic Medical Student Education, Harvard Medical School

Dr. Simmons Lessell is one of the department’s most respected faculty members, and is well known as a gifted clinician, teacher, and mentor. Educated at Amherst College, he attended Cornell Medical College, where neuro-ophthalmologist Dr. Edward Norton first kindled his interest in this specialty. He completed a year of residency in neurology at the University of Vermont under Dr. George Schumacher, followed by two years of neurology clinical practice and research at the National Institutes of Health. During this time, he spent a year in Guam conducting research on amyotrophic lateral sclerosis, and served as the sole neurologist for 60,000 civilians and military personnel. Dr. Lessell then spent two years doing research in the Howe Laboratory of Mass. Eye and Ear/Harvard Medical School, working with Dr. Toichiro Kuwabara. Upon completing his research, he entered the HMS Ophthalmology Residency Training Program, training under noted ophthalmologists David Cogan, MD and Paul Chandler, MD.

After residency, Dr. Lessell joined the new ophthalmology department at Boston University (BU) Medical Center under Dr. Ephraim Friedman, attaining the rank of Professor of Ophthalmology, Neurology and Anatomy. During his 18-year tenure at BU, he maintained a thriving consultative practice at the VA Hospital in Jamaica Plain, Carney Hospital, Dorchester, and the New England Medical Center in Boston. Dr. Lessell was a highly regarded teacher at Boston University Medical School, and was honored with the 1977 Metcalf Cup and Prize, an annual award presented to the most Outstanding Teacher at BU. In 1983, he was recruited to Mass. Eye and Ear as Director of the Neuro-Ophthalmology Service. Over the years, he built an outstanding clinical and teaching service. His first recruit to the faculty was Mass. Eye and Ear neuro-ophthalmology fellow Joseph Rizzo III, MD. Together, they have trained a premier group of internationally recognized neuro-ophthalmology fellows.

In 2004, Dr. Lessell retired as Director of the Neuro-Ophthalmology Service, and was appointed Director of Ophthalmic Medical Student Education for Harvard Medical School. During his tenure, he has transformed the HMS ophthalmic curriculum by radically redesigning the elective program to emphasize faculty mentorship, conference participation, and emergency room training. He is a master at leading weekly Grand Rounds, and has gained nearly legendary status for his keen insight and quick wit during his presentations.

Dr. Lessell ranks among the top neuro-ophthalmologists in the world, and is frequently sought for consultation by patients and physicians in the U.S. and abroad. During his career, he received NIH funding from the National Institutes of Health for 13 consecutive years, an objective indicator of his deep intellect and prolific contributions to his field. His depth of knowledge and clinical insight are unmatched, even while he maintains an approachable bedside manner and endearing sense of humor. He demands the best from his residents and fellows, and makes it his personal mission to improve their analytic and diagnostic skills. In describing Dr. Lessell, one resident stated: “To spend a [clinical session] with Dr. Lessell is to see the rare example of an ophthalmologist taking a thorough history and performing a complete exam. In the age of technicians, support staff, and shortcuts, Dr. Lessell knows only to do things completely and accurately himself.”

Dr. Lessell embodies the attributes of his teacher, Dr. Chandler, as a physician who exemplifies the highest standards of teaching and patient care. He received the Outstanding Teacher Award in 2004, and in 2006 he was honored as a Distinguished Alumnus at the HMS Department of Ophthalmology Annual Meeting. In 2006, when the Department of Ophthalmology completed funding for the Paul A. Chandler Professor of Ophthalmology, Dr. Lessell was named the first incumbent, reflecting a lifetime of major accomplishments and unparalleled excellence in academic medicine. Dr. Lessell has authored over 200 publications, chapters and reviews, and serves on the editorial board of two premier peer-reviewed journals, Archives of Ophthalmology and Journal of Neuro-Ophthalmology. At 78 years of age, he remains busy with clinical practice, teaching, and educational administration.
The HMS Residency Program: Training Ophthalmologists, Turning Out Leaders

The HMS Department of Ophthalmology Residency Training Program, directed by John Loewenstein, MD, and Associate Director, Carolyn Kloeck, MD is ACGME accredited and ranked by Ophthalmology Times as one of the top five programs in the country. With the program’s stellar reputation, securing one of the department’s eight junior residency slots is highly competitive. Each year, the program attracts an average of 450+ physician applicants from around the globe.

Mentored by some of the finest educators in ophthalmology, residents receive superb comprehensive and subspecialty training. Many faculty members are renowned internationally for their specialized expertise in ocular melanoma, macular degeneration, retinal degenerations, keratoconus, diabetic eye disease, ocular surface disease, glaucoma, ocular genetics, amblyopia, and ocular pathology. In this rich and dynamic teaching environment, our gifted academicians and clinician-scientists nurture, inspire, and challenge residents at every turn while carefully balancing the needs and safety of their patients. Residents complete this synergy by bringing vital contributions, energy, and insight to bear across the department.

Residents work closely with junior and senior faculty to pursue novel scientific and clinical investigations; their efforts often lead to publication of scholarly papers in peer-reviewed journals. Residents also gain experience at national meetings and conferences such as Association for Research in Vision and Ophthalmology (ARVO) and American Academy of Ophthalmology. In 2011, 70 percent of HMS ophthalmology residents were invited to present at ARVO’s annual spring meeting.

Broad Patient Exposure

With a strong emphasis on leadership development, the residency program is structured to give trainees broad patient exposure and increasing responsibility during their three years of training. Residency training is firmly integrated into all aspects of patient care so that trainees gain expertise in diagnosing and treating an extensive array of ocular conditions.

Residents develop finely tuned surgical and clinical skills as they rotate through the comprehensive and subspecialty programs of our world-class HMS affiliates, including Mass. Eye and Ear, Massachusetts General Hospital, Children’s Hospital Boston, Beth Israel Deaconess Medical Center, and the VA Boston Healthcare System. Residents also provide inpatient consultations and 24/7 emergency eye care and trauma coverage to patients at Mass. Eye and Ear, and many Harvard-affiliated hospitals. Additional clinical and surgical experience is gained through senior rotations at the Togus VA in Maine and elective rotations at Aravind Eye Hospital in India.

With 11 affiliate and partnering institutions, HMS’s broad-based organizational structure brings tremendous educational value to our residency program. Diverse patient populations give residents exposure to a myriad of pathologies and the opportunity to provide highly specialized care to patients both young and old. Residents derive benefit from international reputations of our faculty; patients come from around the world seeking specialized care, and residents work in tandem with faculty to diagnose and treat some of the most difficult and unusual ocular pathologies. Each affiliate setting is unique, and residents gain valuable insights from the varied philosophies of treatment and surgical techniques of individual institutions and their faculty.

24/7 Emergency Department

The Mass. Eye and Ear Emergency Department (ED) is one of only three dedicated eye facilities in the country, and New England’s only specialized referral center for eye trauma. This busy facility handles an average of 12,000 patient visits each year, and provides a tremendously valuable teaching environment for residents, complementing their already robust clinical exposure. During ED rotations, junior residents learn to function independently and manage the medical and surgical care of patients with various ocular pathologies, conditions, and injuries. By year three, senior residents perform open-globe repairs on patients under the supervision of the Chief Resident - who also serves as Director of the Eye Trauma Service – and supervise junior residents in minor procedures.

Aravind Eye Hospital, India

During senior year, most residents choose to do an international elective rotation at the Aravind Eye Hospital in India. This unique opportunity allows HMS ophthalmology residents to broaden their clinical and surgical experience in an international setting.

At Aravind, residents witness an impressive international health care system that delivers high-quality eye care to a large volume of patients in a cost-efficient manner. Residents have the opportunity to participate in the cornea, glaucoma, and uveitis clinics with exposure to end-stage inflammatory and infectious diseases that are uncommon in the United States. Residents also spend half of each day in the operating room, and serve as primary surgeons for cataract surgeries (both extra-capsular and phaco-emulsification). Residents also receive superb comprehensive and subspecialty training. Many faculty members are renowned internationally for their specialized expertise in ocular melanoma, macular degeneration, retinal degenerations, keratoconus, diabetic eye disease, ocular surface disease, glaucoma, ocular genetics, amblyopia, and ocular pathology. In this rich and dynamic teaching environment, our gifted academicians and clinician-scientists nurture, inspire, and challenge residents at every turn while carefully balancing the needs and safety of their patients. Residents complete this synergy by bringing vital contributions, energy, and insight to bear across the department.

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Hands-On Learning

Numerous program innovations have created a more effective learning environment for trainees. State-of-the-art training tools and technology enable residents to fine-tune their surgical skills outside of the operating room.

Progressive Surgical Curriculum

Beginning in the first year of residency, a progressive surgical curriculum provides a graduated learning process for trainees, as well as greater surgical exposure with a cataract rotation in Year 2. “We’re always looking at ways to give our residents the best experience possible,” says Carolyn Kloeck, MD.

Aravind Eye Hospital, India

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HMS resident graduate statistics

A Five-Year Review: Academic Years 2007-2011

95% seek fellowship training

57% choose HMS fellowships

60% pursue academic careers after fellowship

HMS Department of Ophthalmology national rankings

U.S. News & World Report

#4 “America’s best hospitals” (2011-12)

Ophthalmology Times

#5 “Overall best program” #3 “Best research program” (2010-11)

HMS residency highlights

Year 1: (PGY-2)

- Ophthalmology fundamentals gained through daily lectures, core clinical rotations, and “high-yield” exposure in the Emergency Department and Eye Trauma Service

- Observation in the operating room and serve as primary surgeon for several operative cases

Year 2: (PGY-3)

- Refine exam, diagnostic, and surgical skills rotating through subspecialty clinics

- Independently consult for HMS affiliates (with attending supervision)

- Emphasis on surgical skills (corneal, glaucoma, retinal, and cataract surgeries)

- Perform intravitreal injections, as well as retina and glaucoma laser procedures

Year 3: (PGY-4)

- Refine knowledge, judgment, technical skills, and professional maturity

- Intensive ophthalmic surgical training in cataract, glaucoma, anterior segment, open-globe, and vitrectomy surgeries

- Elective surgical rotation at Aravind Eye Hospital, India
Carolyn E. Kloek, MD
Associate Director, Residency Program in Ophthalmology, Harvard Medical School
Instructor in Ophthalmology, Harvard Medical School
Editor-in-Chief, Digital Journal of Ophthalmology

Dr. Carolyn Kloek is a comprehensive ophthalmologist at Mass. Eye and Ear who provides consultation and treatment for cataracts, eye injuries, and various other ocular disorders. A magna cum laude graduate of Dartmouth College, Dr. Kloek received her MD from Harvard Medical School and completed an internship in Internal Medicine at Brigham and Women’s Hospital. Dr. Kloek completed her ophthalmology residency at Mass. Eye and Ear, where she served as Chief Resident. Dr. Kloek is actively involved in medical student and resident education. She routinely serves as a lecturer at HMS, and is a preceptor for medical students rotating in ophthalmology at Mass. Eye and Ear. As Associate Director of the HMS Residency Program in Ophthalmology, Dr. Kloek assists residency program director, Dr. John Loewenstein, in the administrative leadership of the program, and serves on several HMS committees, including the Graduate Medical Education Committee and Residency Selection Committee. She developed and implemented the progressive Harvard Ophthalmology Residency surgical curriculum to improve the learning experience for trainees. She also spearheaded a PhD degree education track for residents. She continues to teach ophthalmology residents in both the clinic and operating room. In 2008, Dr. Kloek was selected by Harvard ophthalmology residents to receive the HMS Teacher of the Year Award, reflecting her outstanding mentoring skills and efforts in medical education.

Dr. Kloek’s research activities complement her dedication to teaching and focus on advancing ophthalmology training. In 2009, she served as co-Principal Investigator for a study assessing residency experience for the progressive surgical curriculum, which was presented at the 2011 Annual Educators meeting. For Academic Year 2009-10, she received the HMS Shore Fellowship to support her contributions to developing the innovative Mass. Eye and Ear Cataract Surgery Mentor. She also collaborates with faculty at the Division of Sleep Medicine at Brigham and Women’s Hospital to investigate the effect of sleep deprivation on the learning of surgical skills on a simulator. Recently, she was honored with a prestigious Harvard Medical School Rabin Fellowship in Medical Education to develop a standardized online ophthalmology curriculum designed to enhance the training of U.S. medical school students, and to prepare graduates to move more efficiently in a wide variety of ophthalmic diseases. The case-based program will feature a series of guided interactive modules on topics covered in Basic Ophthalmology, a textbook published by the American Academy of Ophthalmology.

“Virtual Training: The Mass. Eye and Ear Cataract Surgery Mentor offers trainees in 2010 a virtual surgical simulator, which provides a safe and effective means to practice surgery at any time, even fore moving directly to live patients. This program allows residents to practice surgery at any time, even without a teacher or instructor present. It offers a more realistic learning experience while drastically reducing the cost of training on live patients. "We want to make sure that future ophthalmologists can be taught in a safer and more effective manner," says Dr. Henderson. To test the effectiveness of the virtual training tool being developed by Drs. Henderson and Kloek, an investigator from a prospective, multicenter, single-blind, controlled trial using the Mass. Eye and Ear Cataract Surgery Mentor, Drs. Loewenstein, Kloek, and colleagues conducted a study investigating the effectiveness of the computer simulation tool scored significantly higher on post-training tests, and rated the tool more enjoyable to use and more likely to be used repetitively. This study, published in the February 2010 issue of the Journal of Ophthalmology, demonstrates that the Mass. Eye and Ear Cataract Surgery Mentor could be an effective supplement to traditional teaching. "The virtual training tool offers a cost-effective alternative to traditional training programs and practitioners nationwide."

Dr. Kloek assists residency program director, Dr. John Loewenstein, in training programs and practitioners nationwide. The virtual training tool offers a cost-effective alternative to traditional training programs and practitioners nationwide. The virtual training tool offers a cost-effective alternative to traditional training programs and practitioners nationwide. The virtual training tool offers a cost-effective alternative to traditional training programs and practitioners nationwide.
Rajesh Rao, MD

Determined to improve the lives of patients through scientific and clinical innovation, Dr. Rajesh Rao was drawn to the HMS Department of Ophthalmology’s Residency Training Program for a number of reasons: high-caliber programs, broad clinical exposure, and extensive research and educational opportunities—all delivered by a world-class faculty mostly comprised of clinician scientists. Dr. Rao was chosen from an impressive pool of more than 500 applicants to fill one of eight highly competitive residency slots for the Class of 2011.

Dr. Rao graduated this spring, and by his account, the HMS residency program exceeded his expectations—not only in gaining exposure to wide-ranging subspecialty areas and patient populations, but also in opportunities to pursue novel research. In the laboratory of Dong Feng Chen, PhD, an internationally renowned Scheepers researcher, Dr. Rao had a rare opportunity to carry out independent investigations in the burgeoning field of retinal epigenetics. Dr. Chen underwrote the expense of his experiments and provided generously of her time and other resources. Dr. Rao’s original research yielded several presentations and a publication in the December 2010 issue of the journal Investigative Ophthalmology and Visual Science. It also garnered him a Retina Research Foundation Award at the 2011 Association for Research in Vision and Ophthalmology meeting. Dr. Rao’s research has yielded so much promise that Dr. Chen has continued this new direction of investigation in her laboratory.

Dr. Rao considers clinical and surgical mentoring to be one of the great strengths of the HMS residency program. As he progressed in his residency, Dr. Rao was entrusted with gradually increasing roles in clinical care. He also mastered increasingly complex and delicate surgical procedures through the newly implemented surgical training block for second-year residents, complete with state-of-the-art training equipment, including an Eyesi virtual reality simulator. In every facet of training—clinic, classroom, lab, OR, and ED—his mentors provided an exceptional learning environment.

In Dr. Rao’s final year of residency, the line between trainee and ophthalmic professional continued to blur as he fine-tuned his clinical, surgical, and leadership skills. Like his colleagues, he often began his day with an early meeting or Grand Rounds presentation. He gained experience in patient advocacy, ethics in patient practice, and issues with transparency and conflict-of-interest, underscoring the department’s firm commitment to providing a leadership-driven education. At least once a month, he typically presented clinical or research topics at one of several scheduled conferences, rounds or symposia. Despite a brimming schedule, Dr. Rao continued to pursue his sophisticated and productive investigative work at Scheepers.

From the start of residency, he found a supportive and congenial cohort among his fellow HMS trainees. This support network created a sense of community for Dr. Rao and other trainees—many of whom are far from home, family, and friends, and all juggling heavy workloads with rigorous training demands. He credits the support of his peers as one of the most important factors in his success.

“Dr. Rao enjoyed a stellar career at HMS,” notes residency program director, John Loewenstein, MD. “He has a deep-seated appreciation for the challenges and complexities of retinal pathophysiology, and relishes the opportunity to contribute his energy, expertise, and compassion to improve the lives of his patients. I know he will contribute immensely to his chosen field of retinal medicine and science.”

Like nearly all of his residency classmates, Dr. Rao has parlayed his exceptional skills and considerable knowledge into fellowship training so he can delve more deeply into the nuances of ophthalmic retinal diseases. For the next two years, he will be training as a vitreoretinal fellow at Barnes Retina Institute (BRI) at Washington University in St. Louis. Ultimately, he aims to have an academic career that combines clinical practice, teaching, and research—the three-fold mantra of a clinician scientist. In his view, the possibilities are enticing. “The retinal field is poised to benefit from recent pharmacological, regenerative, and surgical innovations that may soon cure retinal disease, not just slow disease progression,” he says.

For Dr. Rao, the promise of HMS’s residency program is all about putting theory into action, working with world-class teachers and mentors, pursuing original research, and utilizing his clinical training to treat a breadth of patients and pathologies. “Doctor typically help one patient at a time,” he notes. “However, as a clinician scientist, you can potentially help thousands more by deciphering the critical mechanisms of a disease.” As a fellow at BRI, Dr. Rao will continue to pursue his passion—refining his skills and knowledge that one day may punctuate a new generation of discoveries.

As a clinician scientist, his journey is just beginning.

“...the retina has long fascinated me. Here, a thin sheet plastered to the back of the eye seethes with millions of bustling, firing neurons that translate light to information we use to understand and interact with the world around us.”

—Dr. Rajesh Rao, HMS Department of Ophthalmology Resident, class of 2011
The Ophthalmology Fellowship Programs of Harvard Medical School are comprised of nine clinical subspecialties that are available at several affiliated hospitals. Together, these individual programs pursue a single goal: to train superb specialists in ophthalmology. These programs not only prepare fellows to evaluate and manage the most difficult clinical cases, but also provide an atmosphere that fosters professional development through teaching and research. This unrivaled breadth of opportunity serves to mold the next generation of educators and leaders in the field of ophthalmology.

### Organization and Facilities

The following clinical fellowship programs are available within the Harvard Medical School Department of Ophthalmology:

- Cornea, Refractive Surgery, and External Disease Fellowship
- Oculoplasty Fellowship
- Neuro-Ophthalmology Fellowship
- Pediatric Ophthalmology and Strabismus Fellowship
- Vitreoretinal Fellowship
- Medical Vitreoretinal Fellowship
- Ophthalmic Pathology Laboratory

All eligible fellowship programs are either currently certified or pending certification by the Association of University Professors of Ophthalmology. Of the 39 clinical fellows enrolled in the Ophthalmology Clinical Fellowship Program for Academic Year 2011-12, 24 are based at Mass. Eye and Ear, three are based at the Children’s Hospital of Boston, and three are based at the Beth Israel Deaconess Medical Center. These fully equipped and state-of-the-art institutions enable fellows to master innovative diagnostic and surgical techniques.

### Exceptional Clinical Experience

During training, fellows will care for patients with a wide variety of complex ocular conditions, advancing their clinical skills for a diverse array of ophthalmic disorders. Fellows participate in all aspects of patient care including routine examinations, patient consultation, emergency and on-call services, and surgery. The devotion to teaching and mentoring of our accomplished faculty members provides a rich academic and clinical experience for fellows.

### Unparalleled Research Opportunities

The HMS Department of Ophthalmology Fellowship Training Program strives to complement its extensive clinical fellowship experience with academic stimulation and research. Abundant and unparalleled opportunities for clinical collaborations exist at several HMS affiliated hospitals and other universities in the Boston area. Ophthalmology clinical fellows who demonstrate strong research potential are given careful consideration for competition for career development grants that offer junior faculty status and protected time for research.

### Excellence in Education

Historically, HMS Ophthalmology fellows have played an active role in the education of residents and medical students. In addition to serving as attending staff in the Emergency Department, fellows organize conference cases, write didactic reviews for ophthalmology test books and journals, and deliver presentations to residents, students, and other fellows. This tradition of educational excellence not only enriches the academic experience of ophthalmology fellows, but is also appreciated and recognized by their trainees. Each year, students and residents honor this tradition of teaching excellence with the Fellow of the Year Award. Fellows are also encouraged to attend and present at national and international meetings, and travel reimbursements and awards are available.

### Clinical Fellowship Opportunities

#### Chair, Fellowship Committee

**Dean M. Cestari, MD**

**Cornea, Refractive Surgery, and External Disease Fellowship**

**Program Director:** Reza Dana, MD, MPH, MSc

Founded in 1958 by Dr. Claes Dohlman, the Cornea, Refractive Surgery, and External Disease Fellowship is an intensive one-year program that equips fellows with advanced diagnostic and surgical skills for the entire spectrum of corneal and external eye disorders. Fellows care for a wide variety of patients with complex disorders in the Cornea Service of Mass. Eye and Ear and at nearby Mass General Hospital. Conferences and teaching activities provide forums for ongoing education and career development. Numerous graduates of this fellowship go on to serve in positions of clinical and academic leadership throughout the world. An optional second year is offered in cornea research.

#### Oculoplastic Fellowship

**Program Director:** Frederick A. Jakobiec, MD, DSc

The Ophthalmic Pathology Fellowship Laboratory at Mass. Eye and Ear is an interdisciplinary educational and research program coordinated between the David G. Cogan Ophthalmic Pathology Laboratory, the Ophthalmic and Orbital Plastic Surgery Service, and the Mass General Hospital Department of Pathology. In the Ophthalmic Pathology portion of the curriculum, fellows receive fellowship training in ophthalmic surgery, histopathology, and ophthalmic pathology. In the Ophthalmic Pathology and Oculoplastic portion, fellows learn to evaluate patients with conditions

#### Clinical Fellowship Programs Offer Unrivaled Opportunities

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of the eyelids, conjunctiva, orbit, and periorbital compartments using advanced techniques. This one-to-
two year program imparts the skills necessary to rapidly and differen-
tially diagnose rare and complex eye disorders. Alternatively, fellows
may choose to complete a one-year program dedicated exclusively to
Ophthalmic Pathology.

**Neuro-Ophthalmology Fellowship**
Program Director: Joseph P. Rizzo, MD, MBA
The Neuro-Ophthalmology Fellowship at Mass. Eye and Ear provides intense training in both ophthalmology and neurology. Fellows learn to evaluate and manage a broad spectrum of neuro-ophthalmic cases, including optic neuritis, ischemic optic neuropathy, various other neurological or neuromuscular conditions that affect the eye, and cases of unexplained vision loss. Working closely with the neurologists and neurosurgeons of Mass General Hospital, fellows provide services for inpatients on a regular basis, and work privately in the Boston area. As experience in basic or applied ophthalmic research. Many graduates go on to serve as professors of ophthalmology, private-practice retina specialists, retina service directors, and academic leaders.

**Medical Retina Fellowship**
*Lloyd Paul Aiello, MD, PhD*
Conducted at the Joslin Diabetes Center, the Medical Retina Fellowship allows exceptional research opportunities along with strong clinical training in the management of diabetic eye diseases. State-of-the-art diagnostic and therapeutic techniques are readily accessible in this full-service diabetes eye treatment and research center, which is located in the heart of Boston’s Longwood Medical Area. Fellows receive excellent training in the history, diagnosis, and treatment of diabetic retinopathy, and interact daily with internationally recognized experts. In addition to attending diabetes and ophthalmology clinics within the local medical community, fellows also have ample opportunities to participate in national and international meetings.

**Vitreoretinal Fellowship**
Program Director: Shizuo Mukai, MD
Established in 1977, the Vitreoretinal Fellowship is offered through Mass. Eye and Ear’s Retina Service, a fully equipped clinical facility with advanced clinical technology. Here, fellows receive comprehensive training in the surgical and medical management of diseases of the retina, vitreous and choroid. The program includes strong components in ocular tumors and pediatric retina. The two-year fellowship provides a uniquely intense clinical experience that allows ample time for academic pursuits. As a result, this program produces vitreoretinal specialists with significant expertise in basic or applied ophthalmic research. Many graduates go on to serve as professors of ophthalmology, private-practice retina specialists, retina service directors, and academic leaders.

**Ocular Immunology and Uveitis Fellowship**
Program Co-Directors: George N. Papadopoulos, MD and Lucia Sobrin, MD, MPH
The Ocular Immunology and Uveitis Fellowship, conducted at multiple clinics within Mass. Eye and Ear and Mass General Hospital, is an intensive one-year program that provides advanced diagnostic, therapeutic, surgical, and research training for ophthalmic disorders. Various assigned clinics provide the necessary skills for delivering high-quality and comprehensive patient care. Through collaborations with the Rheumatology Department of Mass General Hospital, Ocular Immunology and Uveitis fellows may gain clinical experience in the non-ophthalmic effects of inflammatory disorders. Ample research opportunities are also available at Schepens Eye Research Institute, where ongoing research projects are delineating immunological and inflammatory responses within the eye.

**Pediatric Ophthalmology and Strabismus Fellowship**
Program Director: Deborah K. Vanderveen, MD
The Pediatric Ophthalmology and Strabismus Fellowship is a one-year fellowship program conducted at Children’s Hospital Boston. The clinical experience includes broad exposure to every aspect of pediatric ophthalmology, including innovative procedures for pediatric ocularplastic surgeries, cataracts, strabismus, and glaucoma. This fellowship also provides comprehensive training for the clinical management of complex adult strabismus. Fellows have access to advanced diagnostic equipment, as well as the broad research activity and academic stimulation of the Longwood Medical Area. Mandatory research projects are conducted under the guidance of the diverse and internationally respected faculty of Children’s Hospital Boston.

**Community-based clinical fellowships**
Fellows in the Department of Ophthalmology train approximately 150 research fellows who represent a new generation of clinician scientists. Integral to the translational work of the department, our research fellows embody the department’s focus on bench-to-bedside research.

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**Ocular Immunology and Uveitis**
Fellowship: C. Stephen Foster, MD
Preceptors: Mark A. Latina, MD (readership fellowships in ophthalmology, there are also research opportunities along with strong clinical experience in the non-ophthalmic effects of inflammatory disorders. Ample research opportunities are also available at Schepens Eye Research Institute, where ongoing research projects are delineating immunological and inflammatory responses within the eye.

**Retina Fellowships (2):**

*Preceptors: John J. Weiter, MD, PhD, and John E. Huber, MD*

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Research fellows may have far-reaching impact that extends beyond the department. The therapeutic regimes designed by Dr. Danjardi are now used throughout the world in clinical testing and practice; similarly, the information gained from Dr. Cranst’s research has been central to the growing use of corneal imaging worldwide in both laboratory and clinical investigations. Research fellows also serve as liaisons between multiple groups—not only working with primary investigators, but also with patients, other scientists in different fields, and even pharmaceutical companies. Research fellows in the Department of Ophthalmology thus fill a valuable niche in the concept of translational medicine—within our department and beyond.
HIGH-VALUE EDUCATION PROGRAMS

A robust didactic curriculum comprises ophthalmology Grand Rounds, symposia, lectures, workshops, conferences, courses, and special events. This structure offers exceptional breadth and depth of discussion for residents, fellows, and faculty. Program offerings span enduring educational venues such as the Lancaster Course in Ophthalmology—now in its 63rd year—to the department’s new AMD International Symposium, which draws faculty from around the world to discuss emerging trends in AMD research.

International symposia
AMD International Symposium NEW
International Cortnea Conference

Ophthalmology Grand Rounds
(CME credit available)

Visiting Professors and Invited Lectures
Paul A. Chandler Visiting Professorship
Cogan Visiting Professor Lecture Series
Ephraim Friedman Lecture
Murphy/Chylack Lecture
Harvard Visiting Professorship & Residents’ Course
Boston Ophthalmic Pathology Lecture Series
Pediatric Ophthalmology Visiting Professor Lecture Series
Schepens Distinguished Lecture Series

Special Courses, Workshops, Lectures & Seminars
Macula Center Grand Rounds
Mass. Eye and Ear Resident Lecture Series
Pathology Rounds
Dr. Pei Fei Lecture in Ophthalmology NEW
Monthly Cortnea Conference
Neuro-Ophthalmology Fall Festival
Annual Harvard Vitreoretinal Course NEW
Annual Harvard Intensive Cataract Surgical Training Course
Lancaster Conference in Ophthalmology
Weekly VA Journal Club
Weekly VA Surgical Conferences
Molecular Bases of Eye Diseases Course
Cornea Research Seminars and Conferences
AMD Journal Club
Giacone Focus Group NEW
Surgical Retina Conference (twice monthly)
Longwood Medical Area Ophthalmology Conferences (monthly, November–June)
New Frontiers in Corneal Disease NEW
Biennial SportVision Conference

Continuing Medical Education
Presentation of the Red Eye (HMS on-line)
Genetics: Macular Degeneration (HMS on-line) NEW

International
Digital Journal of Ophthalmology

Department of Ophthalmology Annual Meeting & Alumni Reunion
Frederick A. Jakobiec Lecture in Ophthalmology
Marla D. Mead Lecture
Distinguished Alumni Awards and Lectures

HIGHLIGHTS
Ophthalmology Grand Rounds & Visiting Professor Lecture Series at Mass. Eye and Ear, Schepens Eye Research Institute, and Children’s Hospital feature more than two dozen lectures each year, including many named or honorary lectures taught by distinguished HMS Faculty and lecturers from around the world. Grand Rounds presentations at Mass. Eye and Ear are moderated by Simmons Leisell, MD, the Paul A. Chandler Professor of Ophthalmology. The department has also utilized videoconferencing to conduct international Grand Rounds with colleagues at Aravind Eye Hospital, and Shanghai Eye and ENT Hospital at Fudan University. More of these collaborative courses are planned for the future.

Annual Mass. Eye and Ear Vitrectomy Course, co-developed by HMS Ophthalmology Vice Chair for Medical Education, John Lermanstein, MD, and HMS Assistant Professor of Ophthalmology, Demetrios Vavvas, MD, PhD, is designed exclusively for first-year vitreoretinal surgical fellows. This unique and comprehensive one-day workshop course gives beginning fellows a basic but comprehensive introduction to techniques in vitreoretinal surgery and prepares them for fellowship OR experience. Consisting of lectures, wet labs, and “dry labs” using virtual reality simulators, the course is taught by renowned faculty from the U.S. and abroad and features a 2:1 student:teacher ratio. Dean Elliott, MD, is course director.

“The Department’s first AMD International Biennial Conference, launched in 2010, drew a distinguished and diverse group of clinicians and researchers from around the U.S. and abroad to discuss current topics and challenges in AMD research. The interactive format engaged participants in thought-provoking discussion on numerous topics including genetics, inflammation, stem cells and tissue engineering, imaging, animal models, and neurodegenerative disease. Participant feedback spoke to the depth of discussion and meaningful dialogue with colleagues. Plans for the 2012 event are in progress. For more information, visit www.schepens.harvard.edu/amd_symposium.

The Biennial Cortnea Conference, now in its 27th year, explores current basic and laboratory research developments of the cornea and ocular surface, building links between this exciting new information and the numerous disease entities that afflict this portion of the eye. Two days of lectures typically feature some 30 national and international speakers. Session topics include: Ocular Pain and Sensation, Dry Eye and Ocular Surface, Infection, Inflammation and Angiogenesis, Stem Cells and Regenerative Medicine.

The Annual Harvard Intensive Cataract Surgical Training Course is the premier cataract surgery training course for ophthalmology residents in the United States. Founded in 2005 by Bonnie A. Henderson, MD, FACS, the course has been co-directed since 2006 by Dr. Henderson, Sherman Chen, MD, and Roberto Pineda II, MD. The course attracts distinguished faculty from across the country, and offers a complete preparatory program covering all aspects of cataract surgery to more than 100 second-year residents each year. The course is unique in several respects. First, distinguished faculty from around the country are nominated by their respective department chairs as the best representative cataract surgeons in their teaching hospital. The level of instruction is unsurpassed. Additionally, the course consists of lectures and a 20-station wet lab where residents receive focused instruction on each step of cataract surgery while learning varying techniques from preceptors. The course is also foundation-sponsored and free to participating residents.

The Department of Ophthalmology launched a reinvigorated and expanded Annual Meeting & Alumni Reunion in 2010. The 3-day weekend features a new integrated format that combines scientific exchange with networking events and social activities for faculty, alumni and newly graduated residents and fellows. The department’s Annual Meeting—launched in 2004—leads the festivities with a day of featured speakers, including the traditional Mariana D. Mead Lecture, and Distinguished Alumni Awards and Lectures. The inaugural Alumni Reunion was dedicated to ten graduating classes from 1961 to 2006, and featured the observations and career achievements of a representative from each five-year anniversary class. Participants were treated to a celebratory dinner, toured new Mass. Eye and Ear facilities, and capped off their weekend with visits to the Museum of Fine Arts and Fenway Park.

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The Annual Harvard Intensive Cataract Surgical Training Course is the premier cataract surgery training course for ophthalmology residents in the United States. Founded in 2005 by Bonnie A. Henderson, MD, FACS, the course has been co-directed since 2006 by Dr. Henderson, Sherman Chen, MD, and Roberto Pineda II, MD. The course attracts distinguished faculty from across the country, and offers a complete preparatory program covering all aspects of cataract surgery to more than 100 second-year residents each year. The course is unique in several respects. First, distinguished faculty from around the country are nominated by their respective department chairs as the best representative cataract surgeons in their teaching hospital. The level of instruction is unsurpassed.Additionally, the course consists of lectures and a 20-station wet lab where residents receive focused instruction on each step of cataract surgery while learning varying techniques from preceptors. The course is also foundation-sponsored and free to participating residents.

The Department of Ophthalmology launched a reinvigorated and expanded Annual Meeting & Alumni Reunion in 2010. The 3-day weekend features a new integrated format that combines scientific exchange with networking events and social activities for faculty, alumni and newly graduated residents and fellows. The department’s Annual Meeting—launched in 2004—leads the festivities with a day of featured speakers, including the traditional Mariana D. Mead Lecture, and Distinguished Alumni Awards and Lectures. The inaugural Alumni Reunion was dedicated to ten graduating classes from 1961 to 2006, and featured the observations and career achievements of a representative from each five-year anniversary class. Participants were treated to a celebratory dinner, toured new Mass. Eye and Ear facilities, and capped off their weekend with visits to the Museum of Fine Arts and Fenway Park.

The Eye Pathology Service, housed in the David G. Cogan Laboratory of Ophthalmic Pathology, serves as a regional and national diagnostic center, and is an integral part of training physicians and researchers in ophthalmic pathology. The Cogan Laboratory has access to a wide spectrum of ancillary supports, such as flow cytometry, histochemistry and immunoperoxidase staining, and electron microscopy facilities. To provide the best care possible, the Eye Pathology Service utilizes a variety of clinical ophthalmology services to assist in diagnosis and case management. The laboratory can be reached by telephone extensively with the Massachusetts General Hospital Pathology Service to evaluate challenging cases, provide enhanced diagnostic services,

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Dedicated to every facet of their work, faculty receive first-rate and well-deserved support from Department of Ophthalmology executive leaders. Equally requisite support comes from Jeffrey S. Flier, MD, HMS Dean, Faculty of Medicine, and the leadership of HMS affiliate institutions. Since taking the helm in 2003, HMS Ophthalmology Chair Joan Miller, MD, has championed a progressive and rewarding 21st-century workplace environment for HMS faculty. While these actions require a substantial investment of resources and leadership, Dr. Miller anticipates that future returns—in the form of advances in “personalized” patient care, accelerated research and discovery, an increasingly collaborative learning environment, and top-notch faculty recruitment—will be well worth the investment. Some of these newest efforts have led to:

- New funding & mentoring supports
- A streamlined promotion and reappointment track
- Expanded programs for professional development
- A faculty mentorship program
- Establishment of five fully funded HMS professorships in the last two years
- Gender-neutral policies that promote women to leadership roles
- Numerous venues for professional recognition

A few of these efforts are highlighted in the following pages.

HMS Ophthalmology Today

Faculty and Trainees by the numbers
- 235 Faculty
  - 140 Full-Time
  - 94 Assistant Professors
  - 44 Residents
  - 43 Clinical Fellows
  - 100 Research Fellows
  - Postdocs (some overlap with research fellows)
- PhD students, Medical Student Journalists
- 20 percent of full-time HMS Ophthalmology faculty holds the title of Professor

STAYING ON TRACK

Guided by HMS Ophthalmology Vice Chair for Promotions and Reappointments, Dr. David Hunter, the department has made a concerted effort to streamline the promotions and appointment process. Since 2008, 12 faculty members have been honored with promotions to Professor of Ophthalmology or Clinical Professor of Ophthalmology.

- Mark B. Abelson, MD, CM
- Lloyd P. Aiello, MD, PhD
- Larry J. Benowitz, PhD (secondary appointment)
- James Chodosh, MD, MPH
- Robert J. D’Amato, MD, PhD
- Reza Dana, MD, MPH, MSc
- Anne B. Fulton, MD
- David G. Hunter, MD, PhD
- Andruis Katsiavas, PhD
- Deborah P. Langston, MD
- Joseph F. Rizzo III, MD
- Lois M. Smith, MD
MEET OUR SCHOLARS

On average, researchers receive their first RO1 or equivalent award at the age of 41, a statistic that underscores the critical need for intermedary funding between mentored K Awards and independent funding. Scholar funds are a new funding mechanism designed to address this need and maintain momentum in our overall research efforts.

In 2011, six exceptional faculty members were named to fund or scholar positions in retin, cornea and glaucoma. The program is supported primarily through the award and continuing royalties to Mass. Eye and Ear from the department's successful QLT judgment — itself the outcome of successful translational research in the field of wet age-related macular degeneration. Additional multi-purpose funding helps support individual research programs throughout the department, including stem cell studies and other translational research projects in the cornea, glaucoma, and retina services.

Demetrios G. Vavvas, MD, PhD
Joan W. Miller Scholar in Retina Research
Dr. Vavvas is on the full-time faculty of Mass. Eye and Ear's Retina Service. His laboratory research spans neuroprotection, ocular cancer, angiogenesis, and retinopathies of prematurity and diabetes. He is participating in ongoing studies to find safer and less toxic therapies for treating retinoblastoma in infants, and aims to develop therapies that prevent the growth of primary and metastatic tumors in adult malignomas. In collaboration with Dr. Joan Miller, he is also pursuing neuroprotection strategies that can prevent photoreceptor death, and potentially preserve vision in many retinal diseases. Together with Drs. Miller and Kim, he is also developing the first dry AMD primate model.

Ivana K. Kim, MD
Evagelos S. Gragoudas Distinguished Scholar in Retina Research
Director, AMD Unit, Mass. Eye and Ear Dr. Kim joined the full-time faculty of Mass. Eye and Ear's Retina Service in 2003. As a key member of the HMS angiogenesis research group (HMSARG), she has been involved in numerous clinical and translational studies directed toward the development of new therapies for age-related macular degeneration (AMD) and other ocular conditions involving choroidal neovascularization. Her preclinical research utilizes genetic analysis to identify both risk factors and new pathways associated with pathological disease processes investigating both melanoma and macular degeneration. One area of recent focus explores the use of animal models to study the pathophysiology and progression of dry AMD to geographic atrophy and blindness. She is also working with colleagues to test the safety and efficacy of antivascularogenic therapies for various other ocular diseases.

Ula V. Jurkunas, MD
Department of Ophthalmology Scholar
Dr. Jurkunas is a full-time member of Mass. Eye and Ear's Cornea and Refractive Surgery Service and Assistant Scientist at Scheepens Eye Research Institute. Her studies focus on translational research related to corneal dystrophies and stem cell-based therapies for other diseases of the cornea. In 2006, she was one of the first HMS junior clinician scientists to receive a K24 Harvard-Vision Clinical Scientist Development Program award, monies that supported her award-winning research into the pathophysiology of Fuchs' Endothelial Corneal Dystrophy (FECD). In addition, her translational research to bring corneal stem cell therapy into clinical practice has been accepted by the Production Assistance in Cellular Therapies program of the National Heart Lung and Blood Program.

Lucia Sobrin, MD, MPH
Department of Ophthalmology Scholar
K24 Grant Gives HMS Clinician Scientist Time to Grow
Dr. Lucia Sobrin is a full-time clinician scientist with the Retina and Uveitis Services. She completed her ophthalmology residency training at Bascom Palmer Eye Institute in 2003, followed by a medical and surgical retina fellowship at the Mass. Eye and Ear in 2005 and a uveitis and ocular immunology fellowship at the Massachusetts Eye Research and Surgery Institute (MERSIS) in 2004. That year, she joined the Department's Retina and Uveitis Services as one of the Department's first Harvard Vision Clinical Scientist Research Program (K24) recipients, receiving a four-year grant to study the genetics of macular degeneration and diabetic retinopathy under the mentorship of David Altshuler, MD, PhD, Joan Miller, MD, and Johanna Seddon, MD, SM.

One of Dr. Sobrin's primary research interests is elucidating the genetics of diabetic retinopathy in African Americans. She was the first ophthalmologist to be awarded funding under the HMS Catalyst Grant Program, and is principal investigator for a study entitled, “Epidemiology and Genetics of Diabetic Retinopathy in the Jackson Heart Study.” In 2011, she was honored with the ARVO/Alcon Early Career Clinician Scientist Research Award. Here, Dr. Sobrin describes her experience as a K24 recipient.

Has the K24 program enabled you to advance your career as a clinician scientist?
Yes, it gave me protected time so I could learn the field of complex disease genetics. I didn’t have a background in genetics apart from what I learned in medical school. With salary support and protected time to attend seminars and courses in genetics and biostatistics, I was able to gain the skills I needed to do research effectively in this field. It also provided me with time for the job of learning statistical genetics, which is very time consuming. Finally, it provided me with the funds to start the study of diabetic retinopathy in African Americans that I have initiated in the Jackson Heart Study.

How has the K24 support directly benefitted your research efforts?
The K24 funded a study coordinator and photography for the initial year of our diabetic retinopathy study. It also supported my education so I could pursue the research field of complex disease genetics. I didn’t have a background in genetics apart from what I learned in medical school. With salary support and protected time to attend seminars and courses in genetics and biostatistics, I was able to gain the skills I needed to do research effectively in this field. It also provided me with time for the job of learning statistical genetics, which is very time consuming. Finally, it provided me with the funds to start the study of diabetic retinopathy in African Americans that I have initiated in the Jackson Heart Study.

Did the K24 award influence your decision to join the MEE retina and uveitis services in 2006?
It did. I wanted a position that would support me in my initial years of trying to become a clinician scientist. I still needed training in research techniques, specifically biostatistics and genetics, in order to become an effective clinician scientist. The K24 gave me the time and resources to complete this training while allowing me to continue my clinical work.

How does the K24 program meet your expectations?
Definitely. It’s given me the protected time necessary to train in biostatistics and genetics, and under the mentorship of some of the best minds in science – Drs. David Altshuler, Joan Miller, and Johanna Seddon. It has also supported my early stage research and subsequent scientific work that has been the basis for applications for independent funding. I’ve been able to train to become an independent investigator while also continuing to see and treat patients in one of the largest and most prestigious academic medical school environments in the world.

Pedram Hamrah, MD
Henry Allen Cornea Scholar
Dr. Hamrah is a full-time faculty member of Mass. Eye and Ear's Cornea and Refractive Surgery Service. He directs the newly formed Ocular Surface Imaging Center in the Cornea Service, where he is interested in the outcome of successful translational research related to corneal dystrophies and stem cell-based therapies for other diseases of the cornea.
developing live imaging techniques and using in vivo confocal microscopy for image-guided therapy. Dr. Hamrah’s research focuses on immune cell trafficking in immune and infectious diseases of the cornea, including viral and microbial keratitis, corneal transplant tolerance and rejection, neurotrophic keratopathy, and ocular surface disease. From 2008 through May 2010, his research was supported by a K23 Harvard-Visan Clinical Scientist Development Program award. Recent research funding includes Grant-in-Aid award from Fight for Sight, two grant awards from Alcon Research, LTD, and a Research to Prevent Blindness Career Development Award.

SHATTERING THE GLASS CEILING

More than at any other time in the department’s history, HMS women faculty are achieving an unprecedented array of leadership positions in patient-care, teaching, research, and administration. Guided by the vigorous support and gender-neutral policies of department chair, Joan Miller, MD, significant resources have been directed to ensure academic and professional advancement of women faculty, and to redress the inherent balancing act of career and family. This support has come in many forms—administrative policy changes, financial support and scholarship awards, and encouragement and mentorship—to enrich the careers and lives of many outstanding HMS women faculty. Since 2009, the department reached several milestones:

- Established the first short-term disability program for medical leave for professional staff at Mass. Eye and Ear
- Awarded three of six Mass. Eye and Ear Scholar Funds to women faculty
- First women appointed to the following positions at Mass. Eye and Ear:
  - Vice Chair for Basic Research
  - Associate Chair for Clinical Research
  - Associate Director of the Howe Lab
  - Director of the Genetics Diagnostics section of the new Ocular Genomics Institute
- Associate Director of the HMS Ophthalmology Residency Training Program
- Chief Quality Officer in Ophthalmology for Mass. Eye and Ear.

- Promoted two women physicians to full Professor with a third in the pipeline
- Created the first HMS Professorship that will be named for a woman: The Joan Whitten Miller Chair (to be named upon Dr. Miller’s retirement, currently named in honor of her father, Charles Edward Whitten).

HMS ENDOwed CHAIRS

In part through the establishment of endowed chairs, the HMS Department of Ophthalmology attracts and supports the endeavors of world-class clinician scientists and investigators. Endowed chairs offer research and training support to incumbents while giving them the freedom to pursue independent research without the burden of financial risk. These endowments are a wonderful tribute to the past success of their nannies, and serve as a building block for future endeavors. They are also powerful recruiting tools, attracting visionary leaders whose contributions historically have forged many paths in medicine and science. Prior to 2008, just four chairs had been completed; today, that number has shot to 12 thanks to generous department and institutional support, private foundations, and the philanthropy of HMS ophthalmology friends and alumni. These gifts will help ensure that generations of outstanding HMS ophthalmology faculty thrive in perpetuity.

GIFTS PAY TRIBUTE TO EPHRAIM FRIEDMAN, MD (1930-2011)

Dr. Ephraim Friedman, ophthalmologist and past President of the Massachusetts Eye and Ear Infirmary, passed away on June 18, 2011. He was a friend to many within the HMS Ophthalmology community, a loving family man, skilled clinician and retinal surgeon, sculptor, educator, researcher, and administrator. Dr. Friedman was drawn to ophthalmology while serving as a captain in the Air Force, and completed his residency at Harvard Medical School/Mass. Eye and Ear under Dr. David Cogan in 1961. For the next four years, he was a research fellow at the Howe Laboratory of Ophthalmology at Mass. Eye and Ear. The author of 36 scholarly articles focusing on circulation in the eye, Dr. Friedman developed the vascular model for the pathogenesis of age-related macular degeneration (AMD), the leading cause of blindness in the developed world. He served as Dean of the Boston University Medical School (1970-1972) and Dean of the Albert Einstein College of Medicine (1974-1985), before returning to the Mass. Eye and Ear as President (1985-1995). A life-long sculptor, Dr. Friedman retired from administration in 1990 to spend more time with his art, family, research, and the log home he built in Maine.

In 2006, a gift from Friedman Family Foundation initiated the Ephraim Friedman Lecture in honor of Dr. Friedman’s extraordinary teaching, research, and service to the field of ophthalmology and AMD. On the occasion of his 80th birthday in 2011, another family legacy gift was established: the Joan and Libe Friedman Professorship in Ophthalmology at Harvard Medical School. Named for Dr. Friedman’s parents, the professorship was made possible through a very generous gift from the Friedman Family Foundation with contributions from additional donors and the Foundation of Mass. Eye and Ear Infirmary.

“Generations of HMS ophthalmology faculty and trainees will benefit from these gifts as they endure through the 21st century and beyond,” said Dr. Miller. “They commemorate dedication to learning that is a Friedman family hallmark, and create a lasting tribute to a man who gave so much to our institution, our profession and our patients.”

**Endowed Chairs in Ophthalmology**

<table>
<thead>
<tr>
<th>Incumbent 2011</th>
<th>Completed</th>
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<tr>
<td>Henry Willard Williams Professorship</td>
<td>Joan W. Miller, MD</td>
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<tr>
<td>David Glendevring Cogan Professorship</td>
<td>Richard H. Mastland, PhD</td>
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<td>William Frederick Charles Professorship</td>
<td>Elliott L. Benson, MD</td>
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<td>Paul Austin Chandler Professorship</td>
<td>Simmons Lessell, MD</td>
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<td>Charles L. Schepps Professorship</td>
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<td>Sir William Oder Professorship</td>
<td>Michael S. Gilmore, PhD</td>
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<td>Claes Henry Dohlman Professorship</td>
<td>Reza Dana, MD, MPH* MSc</td>
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<td>David Glendevring Cogan Professorship (2)</td>
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<td>David Glendevring Cogan Professorship (3)</td>
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<td>Charles Edward Whitten Professorship</td>
<td>Evangelos S. Gragoudas, MD</td>
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<td>Solomon and Libe Friedman Professorship</td>
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* signifies inaugural incumbent

**The David Glendevring Cogan Professorship was divided into three chairs in 2010 and 2011.**

**Ephraim Friedman Lecture in honor of Dr. Friedman’s extraordinary teaching, research, and service to the field of ophthalmology and AMD.**
“I do have a basic philosophy that the only thing you have left when you die is what you gave away.”
—Norman Knight, Philanthropist
THE GIFT OF SIGHT

The clinical, educational, and scientific endeavors of the HMS Department of Ophthalmology faculty garner support from many sources. Private funds from individuals, families, or foundations, as well as corporate and government grants, all provide for the essential infrastructure that allows faculty to improve the quality of life for countless individuals with vision loss. Today, significant inroads into many areas of ophthalmic medicine and science have set the stage for potential breakthroughs: regenerating optic nerves and repairing damaged retinas with stem cells, providing “personalized” care to patients using an individual’s genetic blueprint, even restoring some sight to the blind with a retinal prosthetic. Once fodder for fiction, the realm of scientific possibility and patient care is widening rapidly, and there is new hope on the horizon for millions of sight-challenged people around the globe.

As these exciting efforts continue to unfold, we would like to highlight the extraordinary support of several of the department’s key foundation partners, alumni, and generous friends. In his quote introducing this section, Mr. Norman Knight, one of the department’s most ardent and loyal supporters, reminds us that the unflagging commitment and generosity of every supporter continues to make the department’s mission possible. Their gifts, large or small, continually change lives in many ways—whether it’s support to accelerate critical areas of vision research, acquire highly specialized equipment for ophthalmic procedures, support the training of promising young ophthalmologists, or perform life-changing surgeries on children.

DONOR PROFILE: NORMAN KNIGHT

A generous friend to all

There is perhaps no greater friend to Mass. Eye and Ear than Norman Knight. A self-made broadcast pioneer and media mogul, this humble man has supported the department’s clinicians, scientists, and nurses with the same vision, drive, and passion that propelled him to the top of his field.

Norman Knight is a man who cares deeply about people and seeks out opportunities to empower individuals to achieve their best. Through scholarships for aspiring nurses, leadership awards for rising clinician scientists, and support for employees faced with personal crises, his impact is broad, personal, and profound. His philanthropy has helped put Mass. Eye and Ear on the forefront of major clinical and research initiatives, including hyperbaric medicine, head and neck cancer research, and nursing excellence. In the HMS Department of Ophthalmology, Mr. Knight endowed The Norman Knight Leadership Development Award, which provides critical seed funding to young ophthalmologists at the start of their academic careers. Recent recipients include Ivana Kim, MD (Retina); Dean Cestari, MD (Neuro-Ophthalmology); and Ula Jankunas, MD (Cornea). “The Norman Knight Award had a great impact on my research career,” says Dr. Jankunas, whose research into stem cell therapy may lead to novel treatments for corneal diseases. “I’m absolutely amazed at his spirit and his willingness to help.”

Mr. Knight’s interests extend to technology as well. In recent years, his generosity has led to the purchase of two anterior segment optical coherence tomography (AS-OCT) scanners (see sidebar) for the Retina and Cornea Services, and a pulse dye laser in the Ophthalmic Plastic and Reconstructive Surgery Service. This equipment is used every day to maximize the care and treatment of patients and further the department’s research efforts. “Over the years, Norman’s selfless spirit has touched so much of what we do at Mass. Eye and Ear, and for that we are truly grateful,” says HMS Department of Ophthalmology Chief and Chair, Dr. Joan Miller. “Thanks to Norman’s many generous endowments, Mass. Eye and Ear and countless patients will continue to benefit from his philanthropy for generations to come.”

When asked to reflect on his own generosity, Mr. Knight characteristically turned the attention back to the hospital. He asked, “What would you do if Mass. Eye and Ear wasn’t here? Where would you get treated for eye diseases that no one else can handle?” Thanks in large part to Mr. Knight’s generosity, that’s a question that may never need an answer.

NIH/NEI funding support

The HMS Department of Ophthalmology leads the country in acquiring support for eye research from the National Institutes of Health (NIH). Numerous grants (R-01, R-08 and K-12 grants, among others) reflect the diversity of our research programs and the significant caliber of our investigators. Total NIH vision research funding in 2008 to HMS Ophthalmology topped $26 million, according to a 2009 ranking by Ophthalmology Times. This is more than twice the level of funding received by any other academic ophthalmology department in the United States.

Harvard Medical School Department of Ophthalmology

$26.3 M

Johns Hopkins University School of Medicine (Wilmot Eye Institute)

$13.5 million

University of Pennsylvania (Scheie Eye Institute)

$12.0 million

Washington University in St. Louis

$11.6 million

University of Wisconsin, Madison

$9.1 million

Patient Care

Assess corneal pathologies

Diagnose and manage corneal infections

Detect corneal melts by measuring monitoring corneal thickness

Immediately evaluate post-surgical success of lamellar transplants in patients with Fuch’s Dystrophy and bullous keratopathy; this capability has enabled fast resolution of complications and significantly improved success rates.

Current Research Trials

Develop an algorithm to differentiate scar tissue from inflammation; this will minimize the use of steroids on patients, which can have harmful side effects.

Analyze the thickness of deadly ocular surface tumors prior to excision; depending on its thickness, a surgical procedure may be eliminated by combining a biopsy of the lymph nodes.
Creating a legacy
Some time ago, visual impairments literally jeopardized the careers of Drs. Philip and Marjorie Gerdine. Dr. Philip Gerdine, an international finance executive, was diagnosed with Fuch’s Dystrophy in 1994; his wife Marjorie, a clinical child psychologist, learned of her age-related macular degeneration (AMD) in 2003. Both sought help from several major medical institutions, and were delighted by the integrated approach offered at Mass. Eye and Ear.

The Gerdines have been quite impressed by the quality of care provided by Joan W. Miller, MD, Chief of Ophthalmology, and a leading expert in treating AMD. Dr. Marjorie Gerdine’s concerns about the disease were considerably allayed once she met Dr. Miller, who explained that she had a mild case of the dry form of AMD, which is less severe and progresses much more slowly than the wet form. Her husband’s care has been guided by Dr. Miller for almost six years and he has progressed to the point where his vision, with help, is almost normal. Both were able to productively continue their professional lives.

In appreciation for their care at Mass. Eye and Ear, they became interested in encouraging young physicians to come to Mass. Eye and Ear to pursue research initiatives in their own specialties, and to take advantage of its rich and diverse urban clinical environment. This led the Gerdines to a decision to leave a bequest of $3.3 million to permanently endow the Marjorie and Philip Gerdine Fellowship in Ophthalmology. “Our care at this institution, which for many years has occupied a pre-eminent role in medical research, education and clinical practice, has proven invaluable,” said Dr. (Philip) Gerdine. “We are grateful for the opportunity to help support the institution’s goals.”

What will your legacy be?
Generous gifts propel our efforts forward and help seed discoveries that provide lasting legacies to society.

Finding Cures
Breakthroughs happen every day. By making a gift to support the research of your physician or a particular subspecialty area, you will help to accelerate the development of new treatments, and make an impact on people all over the world.

Training the Next Generation
The HMS Department of Ophthalmology trains the top medical residents and fellows in the country, helping to ensure that specialty care is available to people wherever they live. When you make a gift to support teaching funds and endowments, you are investing in a healthier future.

Providing Exceptional Care
Maintaining the highest level of patient care depends on continuously upgrading equipment, facilities, and technology. When you make an unrestricted gift, your support is used where it is needed most.

To learn more about gift-giving programs, please contact Melissa Paul, Chief Development Officer for Mass. Eye and Ear, at melissa_paul@hms.harvard.edu or call 617-734-4168.

DONOR PROFILE:
BOB NASER

Generous friend issues challenge for low vision study
“Generous” is the first word that comes to mind when one thinks of Bob Naser. The phrase “A man of action” follows soon after. Mr. Naser wants to make a difference, and wants to help encourage others to do so as well. That’s why after sitting down with Dr. Mary Lou Jackson, Director of the Vision Rehabilitation Center at Mass. Eye and Ear, to learn about the opportunity and promise of research to evaluate patient outcomes after vision rehabilitation services, he couldn’t stay idle.

“How can I help?” he asked. Dr. Jackson explained that the department needed $120,000 to launch a new study that would ultimately impact how vision rehabilitation services are delivered in the future; moreover, the study had the potential to significantly improve the care and quality of life for many thousands of low vision patients. To this, Mr. Naser issued a challenge: he would give half of the funds if Mass. Eye and Ear could raise a matching amount from other patients and friends.

And that is exactly what Dr. Jackson and others did.

“We were very excited about Mr. Naser’s challenge,” he said. “It gave us a wonderful reason to call people who we knew were passionate about vision rehabilitation - and to ask for their help.” Dr. Jackson says, “We were so pleased to be able to meet his challenge, and to exceed it, with $10,000 in additional funds raised. This important project may never have happened without Bob’s inspiration and generosity.”

When asked about his generous gift, he simply said, “I was inspired and I heard the need. I was in a position to help.”

This isn’t the first time that Mr. Naser has issued a challenge to the Mass. Eye and Ear. In 2007, he made his first challenge grant of $55,000 to support the work of Dr. Steven Rauch in his research on balance. Once again, the department exceeded its goal and raised over $30,000. This grant was used to develop an ambulatory vestibular monitoring device.

When asked about his interest in donating, he stated, “I am passionate about vision rehabilitation and have been for many years. I am not a professional in this field, but I have witnessed the impact it has had on patients. I have a vested interest in improving the quality of care for people who have low vision.”

Chair, Massachusetts Eye and Ear Infirmary Board of Directors

Wycliffe Groubeck, MBA, JD

Wycliffe “Wyc” Groubeck was elected Chair of Mass. Eye and Ear’s Board of Directors in January, 2010. Wyc has been devoted to research and educational initiatives relating to vision and the search for cures to blinding conditions that are genetically-based, such as Leber congenital amaurosis, which causes blindness or severe visual impairment at birth or during the first months of life; and retinitis pigmentosa, another genetic condition which leads to progressive vision loss, often in the first decades of life. Wyc’s wife, Corinne, founded and serves as chair of the Trust Board at Perkins School for the Blind, in nearby Watertown, MA. This institution is devoted to educating blind and blind/low vision students worldwide and they are both active in other vision-related causes.

Wyc and Corinne were the innovators behind the successful October 2010 gala “Sense-ation,” for Mass. Eye and Ear’s newly created Mass. Eye and Ear Cure for Kids Fund. The event raised more than one million dollars. The proceeds will fund innovative research in pediatric vision and hearing disease, provide care for needy kids who come to Mass Eye and Ear for treatment, and form a basis for a foundation that will continue to support these efforts into the 21st century and beyond.

A graduate of Princeton University, Wyc received a JD from University of Michigan and an MBA from Stanford. He currently serves as CEO of the Boston Celtics basketball team. Previously he worked in venture capital and was as an investor in many successful healthcare and medical technology companies.

On being elected chair of the Board, Wyc declared, “This institution is at the forefront of preventing and restoring vision and hearing loss, which is a personal mission of mine... I am looking forward to supporting the efforts of the extraordinary vision and hearing researchers, educators, physicians, and patient care professionals of Mass. Eye and Ear.”
A personal experience with vision loss is what drives Charles de Gunzburg when it comes to supporting the work of the Schepens Eye Research. Retinal detachments in both eyes nearly blinded him, but his vision was restored by Dr. Charles Schepens. Since then he has maintained and nurtured a strong, supportive relationship with the Institute.

Mr. de Gunzburg is Chairman of First Spring Corporation, a private New York-based investment company, and a founder of FSG Associates, a leveraged buyout firm. He has a bachelor’s degree from Dartmouth College and a master’s degree in Public Administration from Harvard’s Kennedy School of Government. Mr. de Gunzburg resides with his wife and family in New York City and Concord, MA.

In recent years, Mr. de Gunzburg has focused his energy and generosity on the regenerative medicine component of eye research, believing that for many struck by degenerative diseases, it holds the greatest promise of a cure. Reassured by this belief, he contributed substantial resources to create the Minda de Gunzburg Center for Retinal Transplantation Research. The center, now the Minda de Gunzburg Center for Ocular Regeneration, is dedicated to the development of therapies aimed at regenerating tissues of the eye that have been damaged by disease or trauma. One of the Institute’s most generous benefactors, he has also endowed the de Gunzburg Fund and the Center for Age-related Macular Degeneration Research at Mass. Eye and Ear, Fred and Ines recently extended their commitment to support the Institute and its work and their outstanding generosity.

Fred Yeatts is an engineer who spent his career in the defense industry. Now retired, his passion for science continues ever strong through his interest in medical research. “We know that these are tough problems that will take a long time to solve,” said Fred. “We enjoy hearing about the obstacles and strategies and the victories, and we’re happy that we can play a role in advancing their efforts to find a cure for AMD.”

For Fred and Ines Yeatts, research to develop new treatments for age-related macular degeneration (AMD) is an interesting, exciting, and important means to an end. Long-time friends and supporters of hearing research at Mass. Eye and Ear, Fred and Ines recently extended their philanthropy to include a new partnership with Drs. Joan Miller, HMS Ophthalmology Chair, and Demetrias Vavvas, HMS Assistant Professor of Ophthalmology. Their support has seeded a highly innovative research program in neuroprotection, a burgeoning area of investigation that aims to rescue retinal cells that are at risk of dying, before they die, and potentially preserve vision in many retinal diseases.

“We enjoyed meeting Drs. Miller and Vavvas very much,” said Ines Yeatts. “They made us aware of just how complex and difficult it can be to hit every research milestone in their search for a cure. We were impressed by their energetic pursuit of the problems.”

Research at Mass. Eye and Ear is fueled with the help of thoughtful and generous individuals like the Yeatts. “Neuroprotection offers tremendous promise in many areas of medicine, and especially in preserving vision,” explained Dr. Miller. “This is an area that is very exciting to us and, with the Yeatts’ help, we’ve been able to dive into it and start to make progress in a short time. We could not be more appreciative of their keen interest in our work and their outstanding generosity.”

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“In it is an amazing feeling to support the dedicated people at Schepens Eye Research Institute who have fantastic dreams which, when realized, could change so many lives.”
The opportunity I bring to you, Lions, is this: To foster and support the related scientific and educational foundation for the Blind. Will you not help me raise the day when there shall be no preventable blindness; no little deaf ‘blind child’: no blind man or woman unable? I appeal to you Lions, you who have your sight, your hearing, you who are strong and brave and kind. Will you not constitute yourselves Knights of the blind in this crusade against darkness?"
the disease we now know as retinopathy of prematurity (ROP) was, at that time, afflicting four out of five premature HMs—are weighing four pounds or less. The disease baffled the medical community, which had no dedicated resources for research. Several Lions members mobilized together with Al Hirshberg (Sports Writer for the Boston Post and Chairman of the Foundation for Eye Research) and Dr. Edwin B. Dushney (Chief of Staff at Mass. Eye and Ear). The group produced and mailed a pamphlet telling this story to all Lions in Massachusetts, and to District Governors in the U.S. and Canada. In his accompanying cover letter, Mr. Johnson wrote a passionate call to action: “The attached leaflet tells briefly about the lack of research in the field of blindness,” the letter stated. Mr. Johnson went on to write: “It is unbelievable that so little money is spent on trying to prevent a malady...and I shudder to think that probably a child or grandchild of mine or yours might well be the victim of this.” The condition, which Mr. Johnson called “baby blindness” and noted to strike “rich and poor alike,” drove him to call for the RPB to provide more grants. “It seems that this is a challenge to the Lions of Massachusetts, yes to the country!” he declared.

From 1951 to 2006, Massachusetts Lions raised and donated nearly $60 million to eye research in Massachusetts. Several MS ophthalmology affiliates—including Mass. Eye and Ear, Children’s Hospital Boston, Schepens Eye Research Institute, and Joslin Diabetes Center—have directly benefited from this philanthropy. MLEIF’s funds have provided critical financial support for numerous eye programs, outreach efforts, research initiatives, and technologies that have enabled many medical advances and helped tens of thousands of Massachusetts residents to avoid or mitigate vision loss. Today, Lions support remains steadfast and continues to drive our mission forward.

Research to Prevent Blindness

For half a century, Research to Prevent Blindness (RPB) has cultivated and sustained the careers of thousands of vision researchers whose highly innovative work has, in turn, propelled ophthalmic science forward and transformed millions of lives. Since its founding in 1960, RPB has awarded 5,982 research grants totaling more than $300 million in research support to fund the invention of new technologies, test innovative concepts, and develop potential treatments. In 2010 alone, the organization funded 89 new grants and actively supported more than 151 scientists at 57 departments of ophthalmology at medical schools across the United States. Since 1961, RPB has been a key foundation partner to the HMS Department of Ophthalmology. Funding provided by RPB to date tops $66.7 million. Thanks to this generous and ongoing support, many major developments in eye research and treatment have come to fruition at Harvard Medical School. For example, RPB has consistently invested resources in the evolution of anti-VEGF investigations that have led to the development of intraocular drug treatments. Millions of patients have benefitted from these treatments, which can slow, halt, or sometimes reverse the effects of advanced age-related macular degeneration (AMD).

Throughout this decades-long partnership, RPB support has driven innovative research across a broad range of subspecialty areas and scientific disciplines. RPB individual investigator awards have recognized the efforts of numerous HIMS faculty at every career level; these include the Jules and Doris Stein RPB Professorships, RPB Walt and Lilly Disney Award for Amblyopia Research, RPB Career Development Awards, RPB Senior Scientific Investigator Awards, RPB LeW. Wasserman Merit Awards, RPB Physician Scientist Awards, and RPB Special Scholar Awards.

Along with individual grants, RPB has provided significant unrestricted grant support to the department. During the last several years, this funding has helped to mobilize vigorous new initiatives to expand and enhance the department’s academic programs. The steady influx of RPB unrestricted grants also has enabled the department to pursue new researchers and initiatives and to hone HIMS residency and fellowship programs. Significant funding also has provided for laboratory renovations and the purchase of state-of-the-art equipment.

Seeding a Culture of Excellence

HMS Ophthalmology alumni know first-hand the importance of supporting the vital work of our trainees and faculty. Launched in 2010, the Alumni Giving Society of HMS Ophthalmology at Mass. Eye and Ear shines a light on their philanthropy by recognizing gifts of $1,000 or more to the department within the fiscal year (October 1-September 30). In its first year, over 100 HMS alumni and current or former medical staff signed on; their generous donations totaled more than $100,000. In year two, this generous philanthropy has intensified, with several inspirational gifts celebrated in this section.

The department extends its sincere thanks to all Alumni Society Giving members—past, present and future—for their support. Every contribution matters. We are grateful for your generosity and look forward to recognizing even more alumni. Let us know if you would like to be included in future Alumni Giving Society sections.

Richard J. Simmons and Ruthanne B. Simmons Fellowship Fund

This gift was initiated by Dr. Richard Simmons, a 1975 graduate of Harvard Medical School who completed his ophthalmology residency at Mass. Eye and Ear in 1962. For four decades, Dr. Simmons enjoyed a career as a pre-eminent glaucoma specialist in Boston, first, as student and colleague of Mass. Eye and Ear luminaries, Drs. Paul Chandler and Morton Grant, and later, as the mentor of an entire generation of glaucoma specialists. He was President of the Professional Staff of Massachusetts Eye and Ear Infirmary, President of New England Ophthalmological Society (NEOS), one of the four founders of the American Glaucoma Society, one of the four Founders of the Chandler Grant, Glaucoma Society; author of more than 66 peer-reviewed papers, and author of numerous book chapters on glaucoma. Dr. Simmons is known internationally as a fellowship preceptor and as a frequent guest lecturer nationally and internationally.

Dr. Simmons’ daughter, Ruthanne Simmons, followed in her father’s footsteps. Thirty years after her father, she too, graduated from Harvard Medical School with her MD. Upon completion of her residency and glaucoma fellowship at Duke University Medical Center, Ruthanne joined her father in his ophthalmology practice. Later they practiced together at Ophthalmic Consultants of Boston. She operated at Mass. Eye and Ear and taught in the HIMS Department of Ophthalmology. Like her father, Ruthanne was also active in many professional societies, including the American Academy of Ophthalmology, the American Glaucoma Society, NEOS, and others. She was an active researcher and author.

Tragically, Ruthanne Simmons’ journey was cut short. In 1996, she was diagnosed with breast cancer. She stopped practice for a year to undergo aggressive treatment and successfully returned to active practice for four more years. Sadly, the cancer returned again, and this time, it overcame her. It was a great loss when Ruthanne passed away in 2002.

In honor of his daughter, Dr. Simmons began an effort to raise $50,000 to create a Richard and Ruthanne Simmons Fellowship Fund at Harvard Medical School. He seeded the fund and personally gave $50,000. Mass. Eye and Ear reached out to ask others to join in, and 46 colleagues and friends did just that, making generous gifts to bring the fund to the $100,000 minimum threshold.

From the Simmons Fellowship Fund will provide partial fellowship support to a succession of Simmons Fellows in the Glaucoma Service at Mass. Eye and Ear and help to ensure well-trained specialists for decades to come.

Dr. Richard Simmons with his wife, Anne
Pei-Fei Lee, MD

**Dr. Pei-Fei Lee Lectureship in Ophthalmology**

Paul Lee, MD; JD received his medical degree from the University of Michigan in 1986 and his law degree from Columbia University that same year. He went on to complete his glaucoma fellowship at Mass. Eye and Ear in 1990. Today, he is Professor of Ophthalmology and Vice Chair of Ophthalmology at Duke University School of Medicine. Earlier this year, Dr. Lee honored the memory of his father with a pledge of $50,000 to endow the Pei-Fei Lee Lectureship in Ophthalmology. The lectureship will be held bianually with first preference given to glaucoma-related topics.

Dr. Pei-Fei Lee, who passed away in 2009 at the age of 83, was a dedicated clinician scientist. His son notes that Mass. Eye and Ear held a special place in his father’s heart. Dr. Pei-Fei Lee was Mass. Eye and Ear’s first glaucoma fellow, and was mentored by two Mass. Eye and Ear luminaries, Drs. Paul Chandler and Morton Grant. According to his son, the late Dr. Lee “conveyed not only the thinking but also the importance of the principles and character of both his mentors.” On a personal level, Dr. Lee felt indebted to Mass. Eye and Ear for the outstanding training and education he received during his fellowship. After he retired, the senior Dr. Lee devoted himself to building educational bridges between the U.S. and China. Dr. Paul Lee’s gift not only commemorates his father’s dedication to education, but will continue to advance the education of future ophthalmologists. The gift also holds special significance as the department seeks to build new international bridges—most recently in exploring an academic partnership with Shanghai Eye and Ear, Nose, and Throat Hospital at Fudan University in China.

**The Abelson Family Fellowship in Cornea at Massachusetts Eye and Ear Infirmary**

In 1976, Mark Abelson, MD arrived at HMS’ Department of Ophthalmology to pursue a joint fellowship in corneas and external disease research at Mass. Eye and Ear and Schepens Eye Research Institute. Under the mentorship of Dr. Claes Dohlman, and advisor Dr. Mathew Allansmith, he completed his fellowship two years later and joined Schepens Eye Research Institute in 1978. At Schepens, Dr. Abelson developed a passion for interest in ocular surface inflammation and allergy response—areas where little research was being done and funding from sponsoring industry and government agencies was scarce. With Dr. Dohlman’s encouragement, Dr. Abelson set out to build a clinical practice and a clinical research organization to develop therapies for allergy and ocular surface disease. He was extremely successful in both activities. The research organisation, Ophthalmic Research Associates (Ora), has been involved in the development of over one-third of the world’s currently marketed ophthalmic pharmaceutical products. Throughout his career, Dr. Abelson has maintained his connection and support of Schepens, where he is currently a Senior Clinical Scientist and Trustee. In recent years, he has joined in HMS departmental activities more broadly—editing a section on pharmacology and contributing chapters for all three editions of Albert & Jacobson’s Principles and Practice of Ophthalmology. In addition, Dr. Abelson lectures at department meetings, and teaches HMS students. In 2011, he was promoted to Clinical Professor of Ophthalmology at Harvard Medical School.

The Abelson family—including Dr. Abelson and his wife Annalene, their son Stuart (who now heads Ora and is a Trustee of Mass. Eye and Ear) and wife Kathryn, their son Richard and wife Mariana, and other Abelson family members—wanted to give back to Mass. Eye and Ear, they partnered with his mentor, Dr. Dohlman, to establish a fellowship fund at Mass. Eye and Ear. The Abelson family has pledged $600,000, matched with $600,000 from Mass. Eye and Ear from the proceeds of the Boston Keratoprosthesis, to create the Abelson Family Fellowship in Cornea at Massachusetts Eye and Ear Infirmary. “This gift from the Abelson family is extraordinary on many levels,” says Dr. Joan Miller, Chief Chair of the HMS Department of Ophthalmology. “Dr. Abelson is a shining example of an HMS Ophthalmology fellow who has gone on to establish a prominent career in bench-to-bedside research. Not only is Dr. Abelson a quintessential clinician scientist, but his family has also perpetuated his far-reaching impact with their ongoing work. We are extremely proud of Dr. Abelson’s achievements, and truly honored to carry on his legacy with the Abelson Family Fellowship in Cornea.”

—Joan W. Miller, MD
“Massachusetts Charitable Eye Infirmary partly originated in the fact that one of its founders had the happiness of restoring a beloved father to sight by the operation for cataract. The tender relation in this case of surgeon and patient, becoming extensively known among the small population then composing our community, brought to his observation, a large number of Ophthalmic patients....The great majority of all these cases belongs to the humbler ranks of society; and have their prolific parentage in the various privations and sorrows unavoidably consequent upon poverty.”
— Edward Reynolds, MD, in his address at the dedication of the Massachusetts Charitable Eye and Ear Infirmary, 1850

Founded on the principle of caring for the community and inviting “the poor, afflicted with diseases of the eye to come there for gratuitous aid,” the Massachusetts Charitable Eye Infirmary was established in 1824 by Edward Reynolds, MD, and John Jeffries, MD. It would eventually grow into the Massachusetts Eye and Ear Infirmary and form the nucleus of the HMS Department of Ophthalmology. In 1824, Drs. Reynolds and Jeffries were at the cusp of great changes in medical education, including enormous advances in the diagnosis and treatment of eye diseases. By the 1870’s, HMS established subspecialty departments (including a Department of Ophthalmology), reflecting the enormous growth in medical knowledge and the increasing trend toward medical specialization. Today, the HMS Department of Ophthalmology comprises over 300 faculty and trainees who provide care to thousands in need—around the corner and around the globe.
The adage “charity begins at home” forms the cornerstone of the department’s community outreach mission. Every year, HMS physicians, fellows, and residents provide free care, information, and screenings to thousands of area residents. Collaboration is key to these efforts, and the department joins with numerous organizations to target populations in need of eye care but otherwise may not have access to ophthalmic services.

Since 1995, Mass. Eye and Ear and Children’s Hospital Ophthalmology Fellowship (CHOF) staff have provided pediatric vision screenings to the Neighborhood Charter School in Dorchester, which is home to 400 children of diverse backgrounds. For the last two years, HMS staff members have provided vision screenings at Camp Harbor View, a summer camp held on Boston Harbor’s Long Island, for 600 at-risk, low-income youth. HMS staff also collaborates with Massachusetts Vision Coalition to provide eye exams to children at the West End House Boys and Girls Club in Allston, MA, as well as vision screenings to young adults in the Year Up Boston program, which prepares young urban adults for successful careers. Those in need of eyeglasses have received free pairs courtesy of Vision Coalition Massachusetts and the Mass. Eye and Ear Optical Shop. Each year, CHOF, Mass. Eye and Ear, and other affiliates join with the Massachusetts Lions Clubs to collect used eyeglasses for refurbishing and distribution in underserved or impoverished areas. CHOF staff also has provided free eye exams at the Children’s Museum Boston during Child Life Week, and visits local Girl Scout groups for informational presentations on eye health. Mass. Eye and Ear staff participate in adult eye screenings at numerous community centers, such as the Harriet Tubman House in Boston’s South End, the Center for Adult Learning Experiences in Somerville, and the Blackstone Senior House in Boston. Businesses such as the Boston Omni Parker House Hotel have also arranged eye screenings for employees. HMS ophthalmologists give informational presentations at Massachusetts Lions Club meetings throughout the state, and participate in many of their mobile screening van programs. Vision screenings and “ask a doctor” sessions target regional health fairs such as Partners Health Expo and Runners Health Expo. HMS faculty members regularly provide free public lectures and presentations on topics such as glaucoma, age-related macular degeneration (AMD), and pediatric glaucoma. Open forums for the community feature a range of topics, such as “Update on AMD.”

Each year, as participants in the World Health Organization’s World Sight Day, Schepens Eye Research Institute and Mass. Eye and Ear provide screenings and raise awareness of gender inequalities in vision loss. This international day of awareness, held annually in October, focuses on the global issue of avoidable blindness and visual impairment. Schepens also invites the public to its annual Eye & Vision Research Symposium, which highlight the Institute’s latest research and current clinical advancements. These symposia series are designed to empower patients and their families by providing the latest information about vision research and interventions for vision loss. A display of low vision aids is also provided. Events are held in Boston, Cape Cod, and in several Florida locations.

**Joslin Vision Network reducing barriers to eye care**

The Joslin Vision Network (JVN), a national telemedicine program targeting diabetic retinopathy, was pioneered by Lloyd M. Aiello, MD at the Joslin Diabetes Center. Dr. Aiello sought to mitigate the terrible consequences of diabetic retinopathy, in which abnormal blood vessels proliferate, bleed, and detach in the retina, leading to cell death and blindness.

In the 1990s, Dr. Aiello worked with Dr. William F. Beetham to develop the pan-retinal laser treatment for diabetic retinopathy, and oversaw the clinical trials that showed the technique to have a 66 percent success rate in patients. Despite their success, however, diabetic retinopathy continued to be the leading cause of blindness in the United States, mostly due to a shortage of skilled diabetic eye care in many areas of the country. Dr. Aiello teamed with colleague Sven-Erik Bursell, PhD, who used video technology in his research laboratory at Joslin. The two developed a plan for a diagnostic system composed of a specialized camera to take retinal photographs, and a video transmission system to send the images to Joslin’s highly skilled clinicians for reading and interpretation.

Today, the JVN utilizes custom software and a unique digital retinal-imaging device to screen and evaluate diabetes patients. The JVN systems are set up in central areas, such as medical center pharmacies, to optimize patient access. Imaging takes 15 minutes, and requires no pupil dilation. The brief encounter also permits patient education staff to reinforce the importance of medications, monitoring, and life-style modifications. The non-dilated diabetic eye evaluation (considered the gold standard of imaging), coupled with broad access to the JVN service and 48-hour turnaround for results and...
of blindness to less than two percent in patients diagnosed with diabetic retinopathy. The treatment of diabetic proliferating retinopathy, which is the leading cause of blindness among working-age Americans, has dramatically increased compliance with early stage retinopathy treatment, which is often asymptomatic. For thousands of patients, early detection and treatment has prevented devastating vision loss. In recent years, the JVN has expanded its reach across Massachusetts and to borders beyond.

Local: In an ongoing collaboration with Massachusetts Lions Clubs, Joslin staff provides diagnostic support and evaluation of retinal images acquired by the Massachusetts Lions EyeMobile service. The EyeMobile has logged more than 30,000 miles throughout western Massachusetts—traveling to over 150 Lions’ events and serving some 4,500 residents and visitors.

National: The Indian Health Service-JVN Teleophthalmology Program is leading the way to improve early identification of American Indians and Alaska Natives at risk of vision loss due to diabetic retinopathy. These populations often live far from health care centers that provide nationally accepted standards of eye care, including eye exams that can diagnose high-risk candidates for diabetes-related blindness. The HIS-JVN Program addresses this health care gap by using telemedicine technology to reduce the incidence and severity of diabetes-related vision loss; to date, the program has imaged more than 24,000 patients.

Global: The JVN-Venezuela program was established in Caracas in 2006 through the Foundation M.M.G with the support of Morella Mendoza Grossman, Joslin Diabetes Center Trustee, and Dr. Lloyd M. Aiello, JVN founder. The program is an American Telemedicine Association, category 3 ocular telehealth program, and has provided high-level diabetes-eye care to more than 83 children. More recently, the program was expanded to include pregnant women and adult patients. The program serves as a model for the international eye care initiatives of the JVN, enabling extensive retinal image analysis in pediatric populations to identify novel retinal lesions. By potentially predicting future severe retinal diseases, this program may allow earlier interventions that protect against vision loss.

Teleretinal imaging program captures high risk patients

In 2008, Mass. Eye and Ear and Massachusetts General Hospital (MGH) collaborated to establish the Ocular Telemedicine Program at MGH’s Chelsea Health Center to screen high-risk diabetic patients for diabetic retinopathy. The center serves an urban, indigent, and predominantly Hispanic population. As an ethnic group, Hispanics are far less likely to get regular annual screenings than other ethnic groups and also have an increased prevalence and more rapid progression of diabetic retinopathy. On-site retina photographs are sent electronically to Mass. Eye and Ear for diabetic retinopathy or other pathologies. Findings are posted securely to Borders beyond.

All 235 images reviewed by trained telemedicine readers who referred patients to ophthalmology.

Lloyd M. Aiello, MD

Clinical Professor of Ophthalmology, Harvard Medical School

Founding Director, Beetham Eye Institute at Joslin Diabetes Center

Dr. Lloyd M. Aiello received his medical degree from Boston University, and completed postgraduate work at HMS and Mass. Eye and Ear. In 1997, he was appointed Director of Joslin’s Beetham Eye Institute, and in 2003 he was named Founding Director. From 1990 to 2001, Dr. Aiello headed the Section on Eye Research, which is now led by his son, Lloyd Paul Aiello, MD, PhD. Dr. Aiello is the second of three generations of Joslin ophthalmologists. Working with his father-in-law, William P. Beetham, MD, Dr. Aiello revolutionized the diagnosis and treatment of diabetic retinopathy. Prior to the pioneering work of Drs. Aiello and Beetham, there was a 75% to 80% risk of blindness for patients with diabetic retinopathy. In 1967, Aiello and Beetham developed a pan-retinal laser technique that reduced the risk of blindness to less than two percent in patients diagnosed and treated early in addition to careful follow-up. The landmark paper, “Ruby Laser Photocoagulation in Treatment of Diabetic Proliferating Retinopathy,” was published in 1969. For the next 25 years, Dr. Aiello would lead clinical trials and studies that set the standard of care for diabetic retinopathy, and save the sight of millions of people. Dr. Aiello has authored more than 90 original articles and 37 book chapters and review articles. He has served as a Trustee of Joslin Diabetes Center, a member of the Executive Committee of the HMS Department of Ophthalmology, and President of the New England Ophthalmological Society. Dr. Aiello’s numerous honors include the Warren Alpert Foundation Prize, the David Rumbough Scientific Award of the Juvenile Diabetes Foundation International, the Lighthouse Pictor Vision Award, the Leo B. Breitman Excellence in Research Award from the Juvenile Diabetes Foundation Massachusetts Affiliate, the Massachusetts Society of Eye Physicians and Surgeons Man of the Year, the American Diabetes Association Outstanding Physician Clinician in Diabetes Award. In 2003, Dr. Aiello received the American Telemedicine Association President’s Award (for his contributions to the development of telemedicine and its advancement worldwide), and the Gertrude D. Pyron Award for Outstanding Achievement in Retina Research, recognizing his lifelong contribution to the understanding and treatment of diabetic retinopathy.

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“When we preserve a woman’s sight, we improve the lives of her children, spouse, and community. We want women to know that they can take steps to optimize their eye health.”

—Irene K. Gipson, PhD, Chair, Women’s Eye Health.org

More than ever before, the interconnected global community is bringing the plight of eye disease into sharp focus. The statistics are sobering, according to the World Health Organization: 3.4 million people suffer from visual impairment, and 4 million of them are blind. Nearly nine out of 10 people who suffer from blindness or visual impairment live in developing countries that have minimal or no access to quality, affordable healthcare.

States and abroad to form Women’sEyeHealth.org (WEH.org), an online education and advocacy group that raises public awareness about women’s eye health, and supports blindness prevention research and programs. The group’s core mission is to alert women to their increased and disproportionate risk of eye disease; the organization also encourages lifestyle changes and actions that optimize eye health, such as having regular eye exams and not smoking. The group promotes its message through their website (www.womenseyehealth.org) as well as a variety of outreach venues including health fairs, lectures, and literature campaigns.

Dr. Pineda, director of Refractive Surgery at Mass. Eye and Ear clinician scientists, including Drs. Ula Jurkunas and Claes Dohlman, Dr. Pineda is also developing treatments with other ophthalmologists. He notes that his involvement in establishing a keratoprosthesis clinic in Ethiopia came about as a direct result of his experience with ORBIS.

In November 2010, as a guest speaker at an ORBIS fundraiser in New York City, Dr. Pineda lauded the organization’s broad social impact on global health. “ORBIS volunteers and staff work hand-in-hand with the unique requirements and customs of governments around the world,” he says. “In doing so, they pull together all the elements needed to establish a working and sustainable health care infrastructure in developing communities. In this way, ORBIS heightens awareness of eye disease globally and at every level of government. I’m proud to be part of an effort that effects real and positive change around the world.”

Women'sEyeHealth.org envisions a better future for women Earlier this decade, an analysis of 70 epidemiological studies revealed that two out of three people who are blind or visually impaired in the world are women. Reasons vary as to why women bear a greater burden of blindness or visual impairment in the world. Here are some of their stories.

Women’s health: women bear the burden

A report published in 2004 established in many U.S cities and in nations around the world. This report, authored by the World Health Organization, points to the role of social and economic factors in impeding a woman’s access to health care.

As visiting volunteer faculty, my role is both clinician and teacher,” says Dr. Pineda. “I’m screening patients, doing surgical demonstrations, giving lectures, and teaching—even fixing equipment! Missions typically last just for a week, but my contributions have a high impact.” There is continuity as well; local doctors can continue to communicate and consult with Dr. Pineda once he returns to Mass. Eye and Ear through an on-site, web-based interface that allows them to share information and images.

As Director of the Refractive Surgery Service at Mass. Eye and Ear, Roberto Pineda II, MD, regularly performs refractive surgeries and serves as co-investigator in eximer laser FDA clinical trials while also developing tools used in managing LASIK complications. His clinical interests also include complex corneal transplantation procedures, such as Descemet’s stripping endothelial keratoplasty for toxic anterior segment syndrome. In collaboration with other Mass. Eye and Ear clinician scientists, including Drs. Ula Jurkunas and Claes Dohlman, Dr. Pineda is also developing treatments for reducing complications after various corneal procedures—including LASIK, PRK, and Boston KPro.

Many HMS Department of Ophthalmology physicians, optometrists, and support staff are determined to change these statistics by joining volunteer medical missions that serve communities across the far reaches of the globe. Missions are wide-ranging and include: providing eye exams, performing sight-saving surgery, conducting vital skills-based training for local medical staff, and establishing self-sustaining ophthalmology clinics and programs. HMS faculty and staff have joined medical missions to El Salvador, Guatemala, Nicaragua, Cambodia, and in many other locations throughout the world. Here are some of their stories.

HMS ophthalmologists on a mission to advance global health

HMS Assistant Professor Aaron M. Fay, MD, and Roberto Pineda II, MD, have made a commitment to improving global eye health as medical volunteers for ORBIS International. ORBIS was founded nearly three decades ago as a non-profit organization dedicated to saving sight and eliminating avoidable blindness worldwide. In 1982, its now-iconic Flying Eye Hospital—at the time a converted DC-8 outfitted as an ophthalmic teaching hospital and surgical center—flew its first mission to Panama. Seventy-five countries and hundreds of flying missions later, ORBIS’s unique and highly lauded program has evolved into a broad-based, “capacity building” effort that is dedicated to helping developing countries create sustainable, accessible, and affordable eye health care within their communities.

Central to the ORBIS mission are the services of a core group of 500 volunteer faculty members. Drs. Fay, Pineda and other ophthalmology experts provide high-level, hands-on surgical and clinical training to local staff. Dr. Fay, of Mass. Eye and Ear’s Ophthalmic Plastic and Reconstructive Surgery Service, traveled with ORBIS to India to teach oculoplastic techniques. Dr. Pineda, director of Refractive Surgery at Mass. Eye and Ear, is a 12-year veteran of ORBIS. Since 1998, he has traveled on ten missions to remote communities in Ethiopia, Uzbekistan, Burma [Myanmar], India, China, Cuba and, most recently, Indonesia [Java]. He has trained hundreds of local physicians in the techniques of cornea surgery [including corneal transplants], cataract surgery, and other anterior segment surgeries. ORBIS’s strong focus on educating and training a complete medical “core” of personnel—from doctors to nurses and OR staff—is a philosophy that appeals to academic clinicians like Dr. Pineda. “The ORBIS program is unique in that it’s very comprehensive and very structured. As visiting volunteer faculty, my role is both clinician and teacher,” says Dr. Pineda. “I’m screening patients, doing surgical demonstrations, giving lectures, and teaching—even fixing equipment! Missions typically last just for a week, but my contributions have a high impact.” There is continuity as well; local doctors can continue to communicate and consult with Dr. Pineda once he returns to Mass. Eye and Ear through an on-site, web-based interface that allows them to share information and images.

Tapping the expertise of highly skilled clinicians like Drs. Pineda and Fay has multiple benefits. Pineda notes, for example, that lack of funds, government restrictions, and political strife may prevent most local doctors in these developing countries from traveling overseas for specialised training opportunities. “Our involvement fills a training gap by helping local doctors broaden their skill sets,” he said. Dr. Pineda’s commitment to ORBIS also has been a conduit for striking up new collaborations with other ophthalmologists. He notes that his involvement in establishing a keratoprosthesis clinic in Ethiopia came about as a direct result of his experience with ORBIS.

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“These...simple interventions can have a huge, life-changing impact for a child who has a blinding eye disease but is otherwise healthy.”
— Danielle Ledoux, MD

Dr. Ledoux (far right) surgery, back to camera) coaches a local Guatemalan ophthalmologist through a cataract surgery. Surgeons are at side by side in the same OR to maximize resources and streamline a medical procedure forbidden in Guatemala.

HMS ophthalmologist gives hope—and sight—to children around the world.

Long before she became a pediatric ophthalmologist, Danielle Ledoux, MD, had a strong desire to serve children in underprivileged communities, which helped shape her future medical career. “I chose ophthalmology because I knew it would allow me to do the international work I wanted to do,” says Dr. Ledoux, whose busy pediatric ophthalmology practice at Children’s Hospital Boston is focused on cataract and strabismus surgery.

Her desire to be involved in global outreach was fueled during her pediatric fellowship at the Medical University of South Carolina (MUSC). She was mentored by M. Edward Wilson, MD, Chair of the Department of Ophthalmology at MUSC, who is well known in the international medical community for his longstanding outreach work in developing countries. Through Dr. Wilson’s collaboration with a private family foundation, Danielle had the perfect venue to put her skills—and her heart—to work. The U.S.-based foundation, which funds several global outreach programs, established one of its most successful endeavors in Guatemala: a pediatric cataract surgery program at Hermano Pedro Hospital in Antigua.

For the last five years, she has traveled to the hospital as part of a weeklong mission to perform cataract and, more recently, strabismus surgery on children from impoverished areas of that region. “These are relatively straightforward and simple interventions, but can have a huge, life-changing impact for a child who has a blinding disease but is otherwise healthy,” remarks Dr. Ledoux. “This is especially true of children from poor, remote villages whose life circumstances are already challenging.”

According to Dr. Ledoux, young patients are screened ahead of time by a local ophthalmology team to determine if they are candidates for surgery. The program’s original focus was cataract surgery, but has been expanded to include strabismus surgery. The cost for surgery, room and board, and short-term follow-up care, is fully funded through the foundation, which also subsidizes the travel expenses of families who accompany patients. Dr. Ledoux is one of a team of three pediatric surgeons (including Dr. Wilson) who perform a total of about 50 surgeries during their weeklong stay.

“The work is not without its challenges. Although Hermano Pedro hospital is clean and well run, it is not a full-service hospital; not only does it have limited patient facilities, but it also lacks the medical staff, as well as the entire orthopedic oncology, vascular, plastic surgery.”

Lack of resources, staff, and technology that other hospitals in wealthier countries have readily at hand, Dr. Ledoux says she has to consider the implications of each surgery she performs knowing that the hospital has limited resources, and that most patients will return to a remote village with little or no access to long-term medical care. “Depending on the individual needs of each patient, my approach and methods may vary in order to ensure the best outcome possible,” she says.

Dr. Ledoux notes that the program also has helped cross a cultural divide. In past years, patients and their families have been reticent to seek treatment or follow-up care because of the stigma attached to diseases. “This is slowly changing,” she explains, as the program builds momentum through education and word-of-mouth. “I’ve noticed more and more patients are willing to return for follow-up care and families of potential patients are seeking out our help,” says Dr. Ledoux. “It’s gratifying to see how the program is creating this continuity of care which, ultimately, will enable us to help more young patients.”

In February 2021, Dr. Ledoux put her experience and talent to work on a month-long mission at the Nepal Eye Hospital in Tripureshwor, Kathmandu. There, she worked with a local pediatric ophthalmologist who has established a pediatric ophthalmology department and training program. She credits her outreach opportunities to the strong web of support she receives from the International Health Services Program at Children’s Hospital Boston—particularly to David Hunter, MD, PhD, the hospital’s Ophthalmology-in-Chief. “I have received incredible support from the hospital, especially from Dr. Hunter, who has encouraged my outreach efforts from the beginning,” says Dr. Ledoux. These experiences have helped me grow personally and professionally. It’s simply an amazing feeling to have such a real and lasting impact on the health of children around the world.”

Vision on the go: global demand increases for Boston keratoprosthesis

An estimated eight million people in the world are blind from corneal disease, and the majority of patients live in developing countries. For some patients, conventional corneal transplantation offers a successful and life-changing solution. But sometimes transplants fail, while other patients suffer from conditions that make them poor candidates for traditional transplantation. HMS Emeritus Professor of Ophthalmology, Claes H. Dohlman, MD, PhD, has devoted much of his life’s work to solving this problem. Dr. Dohlman, founder of the cornea specialty, invented the Boston Keratoprosthesis (KPro), which combines a corneal prosthesis with a synthetic supporting structure that sometimes can be used as a successful alternative to conventional corneal transplants. Approved by the FDA nearly two decades ago, the KPro is now used in 150 centers in the United States and around the world, offering sight to thousands of people who would otherwise remain blind.

Pilot programs in developing nations around the globe are bringing KPro’s sight-saving benefits to these populations. Programs exist in India, China, Thailand, Sudan, Central and South America, Africa, and, most recently, Ethiopia. Cornea experts James Chodosh, MD, and Robert Pineda II, MD, have also worked to broaden the availability of the Boston KPro worldwide. Dr. Chodosh has performed and assisted with artificial cornea implantation surgery in India, Italy, England, and Israel. Recently, he began a project to develop a KPro keratoprosthesis for use in underdeveloped countries.

In 2008, Dr. Pineda led the effort to establish the first KPro center in Africa. His team traveled to Addis Ababa, Ethiopia to teach surgical implantation techniques to ophthalmologists and medical support staff. Dr. Pineda’s team also offers training on the follow-up care needed for successful outcomes. Establishing self-sustaining, long-term KPro centers in poorer demographic areas like Addis Ababa is not without challenges. Scarcity of medications and advanced microbiology labs, along with maintaining rigorous patient protocols, can make an already-challenging task even more difficult. Dr. Pineda notes that careful up-front planning helped the process run smoothly. Today, the clinic is self-sustaining. Back in Boston, the KPro team is in the third year of a five-year longitudinal study to study the viability of the Boston KPro in underdeveloping countries and hone the program as needed.
“What the developing world needs is a safe, long-term and inexpensive corneal prosthesis. Our goal with the KPro is simple: get it out there so it is doing some good and helping as many people as possible.” — Dr. Claes Dohlman

How does someone approach the formidable task of creating a new ophthalmic subspecialty?

You have to have a somewhat fanatical interest and focus. It’s not a part-time undertaking, not something you do now and then. You have to stick with it because it’s so time-consuming. It’s not only a career but rather a life you live.

What were some of the challenges?

When I first came to the U.S. in 1978, there was no formal Cornea Service; it was just me for many years and that was the biggest challenge. I was fortunate in that, once I established the Cornea Service and a structured fellowship program, we were able to attract many students who had academic ambitions. Drs. Swiebe, Boruchoff, Martola and Wiedman were important early faculty and laboratory leaders. Over the years, the faculty has trained more than 200 clinical fellows. Eighty of those individuals have become full professors and more than 40 have become department chairs. We were very lucky to get great people who have gone on to become pioneering researchers and leaders in the field.

And what happened?

When I retired from my administrative duties in 1999, I decided to concentrate on something practical – the KPro – and the prosthesis has been the centerpiece of my work for the last twenty years. I’m glad I did because developing an artificial cornea has been very exciting. It has been a lesson in patience and perseverance - not just time consuming but fraught with complex and difficult challenges. As I said, it was years before we realized some promising outcomes.

You use the term “we.” Absolutely. The clinical success of the KPro has required a great collaborative effort among Harvard’s ophthalmic research community and close research partners at MIT. Turning the KPro into a viable, clinical reality for patients has required multi-disciplinary expertise not only in surgery but in biomaterials, bioengineering, optics, inflammation, bacteriology, glaucoma, retinal detachment, plastics and contact lenses. None of these disciplines are my areas of expertise so, over the years, I have enlisted the collaboration of numerous HMS faculty as well as partners like MIT.

Who are some key members of the KPro team?

Presently Dr. James Chodosh – who is an astute researcher on a professorial level – is addressing autoimmune issues; Drs. Ilene Gipson and Eli Peli from Schepens, are foremost experts in enzymes and optics respectively. Dr. Kathryn Colby is refining surgical development techniques; Dr. Irurgard Helbush, an infectious disease expert at Mass. Eye and Ear, examines bacteriology issues; Dr. Joseph Golino has developed a drug releasing contact lens in collaboration with several researchers from Professor Robert Langer’s laboratory at MIT, supervised by Dr. Daniel Khobane who now runs his own lab at MIT. Dr. Roberto Pineda is our ambassador abroad and has established KPro clinics in some of the poorest nations. Dr. Samir Melki is developing telemetric techniques for measuring the intracoracrical pressure. I also have seven international research fellows working on KPro improvements. Of course, there are many other individuals here and abroad who have provided key guidance and expertise in helping us to develop the KPro and to spread the word.

What have some of the KPro milestones?

There have been two primary ones in recent years. Historically, post-operative bacterial infections caused some disastrous failures, especially in patients with autoimmune diseases. In the early part of this decade, Dr. Marlene Durand (Director of Infectious Disease at Mass. Eye and Ear) suggested vancomycin prophylactically, which dramatically lowered infection rates. It was a revolutionary improvement in treatment. A second challenge we’ve addressed is tissue melt around the cornea. In 2000, we redesigned the KPro and added holes in the back plate of the dillar button shaped prosthesis; this improves nutrition to the holding graft. We also started to use a soft contact lens to protect against dehydration. Both advances have mitigated tissue melt by almost 100 percent in non-autoimmune eyes.

What are the challenges that lay ahead?

Despite recent successes in improving clinical outcomes with the KPro, I temper my enthusiasm with the caveat that we are only half way to the train station – we still have some significant challenges to overcome. Autoimmune disease and chemical burns remain problematic because they lead to tissue disintegration. We’re working on several fronts to address these issues. An other troubling KPro outcome is that it can trigger glaucoma, a complication that can be particularly vicious in patients with chemical burns. We have worked closely with Mass. Eye and Ear’s glaucoma service, specifically Drs. Cynthia Grosskreutz and Lucy Shen who have helped us to develop new procedures, while one of my fellows at MIT is working on a new type of shunt.

You and your team have made a significant effort to promote the Boston KPro to some of the world’s poorest nations. Why?

Most of the world’s 8 million people with corneal blindness live in the developing world and they need a safe and inexpensive prosthesis. Our goal with the KPro is simple: get it out there so it is doing some good and helping as many people as possible. That’s why we’ve established self-sustaining KPro clinics in some of the poorest nations, most recently in Sudan and Ethiopia. Logistically, these efforts have gone remarkably well thanks to Dr. Pineda. Cost, unfortunately, still remains an issue.

Can you elaborate?

For many developing countries, the cost of the KPro procedure is prohibitively expensive. Even if the device were provided free of charge, there are additional costs associated with physician time, long-term medication, contact lenses, follow-up care, etc. We’ve mitigated this situation somewhat by providing the KPro to some countries at a substantially reduced cost – in some cases for free – in order to make it affordable and available to those who need it. Even so, it remains out of reach for many people.

You’ve inspired thousands of fellows, students and colleagues throughout the years. Who inspired you?

As a fellow at the Wilmer Institute (Johns Hopkins) in the early 1970s, I had the good fortune to study under Dr. Jonas Friedenwald who, at the time, was one of the country’s premier eye researchers. Another inspiration was Dr. Charles Schepens, renowned for his work on retinal detachment and for building the Schepens Eye Research Institute into a foremost eye research facility. He had an enormous talent for focusing on a single problem, and then building up an organization, research, and fellowship training around it. His advice was invaluable to me after I arrived in Boston (1978) and began to build a cornea specialty and structured cornea fellowship program.

Now in your ninth decade, you remain an active member of the Cornea Service. How do you spend your time?

I teach and mentor, run a small, specialized KPro patient clinic and direct a program of clinical R&D. I also like to keep up with my colleagues and other eye researchers, find my advice so make an effort to answer my correspondence. I stopped operating in the spring (2010) – I’m 88 so I have a good excuse. I’m still having fun, though, and especially enjoy teaming up fellows with the right expertise to tackle the remaining KPro issues. Even though we’ve made a lot of progress there is still so much to accomplish. I am convinced that, if we future, we will have the most talented cornea team in the world, headed by Dr. Rena Dana, to carry on at Harvard when I eventually retire.

You’ve made indelible contributions to ophthalmic science and research. How do you want people to remember you? Your work?

I don’t know. I have been very lucky in my work and I have always been happy doing it – never bored. I would like to pay tribute to my wonderful family who has been extraordinarily supportive. My great wife has done so much to support my career. I have a lot to be grateful for!
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