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NECROLOGY

In Memorium

BERNARD BECKER, MD, ELECTED 1960

MELVIN L. RUBIN, MD, ELECTED 1975

RONALD E. SMITH, MD, ELECTED 1982

FRED M. WILSON II, MD, ELECTED 1983

Bernard Becker, MD

By *Paul L. Kaufman, MD*



Dr. Bernard Becker, one of the leaders of 20th century ophthalmology research and education, passed away on August 28, 2013, at the age of 93 years.

Bernie Becker excelled in many arenas and had a vast array of interests both professionally and personally. His range of scholarship was legendary. He read journals in all branches of science and medicine in the Washington University Medical Library (which would eventually bear his name and house his world-renowned ophthalmic historical book collection). He was a talented physician, an outstanding researcher as well as an exceptional speaker on an almost limitless variety of topics. His organizational mastery led to founding and/or leadership roles in RPB, AUPO, NEI, ARVO and many other key organizations, all in a very quiet way, yet with passion. Bernie became Chair of Ophthalmology at Washington University School of Medicine-Barnes Hospital in 1958 essentially directly from chief residency at Johns Hopkins/Wilmer Institute of Ophthalmology. The Department of Ophthalmology rose to great national and international prominence under his leadership.

Bernie felt that research held the key to the future. He was the first to realize and to clinically apply the role of carbonic anhydrase in aqueous humor formation, introducing carbonic anhydrase inhibitor drugs for the treatment of glaucoma. He was among the first to appreciate and characterize the IOP-elevating effect of glucocorticosteroids, its relationship to primary open angle glaucoma (POAG) and diabetes, and the heritability of all three. He promoted research at every turn and encouraged his residents towards careers encompassing discovery. For a young resident it was an incredible program; interactions with some of the best minds in the field, guidance, encouragement and an unfailingly supportive environment. He would get to know you, your particular skills and abilities and work to optimize a path forward, opening doors to collaboration, fellowship training and faculty placement. He certainly did this for me.

Beyond the research and organizational advances, one of his great legacies was effective, gentle career-long mentorship for his trainees. He and Janet hosted elegant yet informal dinners for the residents at his home, and he had a keen memory for all of us. My wife and I visited Bernie and Janet over the years whenever we returned to St. Louis for meetings, events, or to see old friends, and we immensely enjoyed a just-the-four-of-us dinner during a meeting in Santa Fe in 2000, shortly after his 80th birthday and a meeting at their home just two years ago. His scientific and personal intellects were as keen as ever. He was, as always, supportive and genuinely interested in our lives. It was that attitude towards his "other children", always ready to listen and to offer impeccable but never intrusive advice or assistance whenever he could, that I and many others appreciated through the years and have tried to emulate. Many of his trainees went on to distinguished academic careers and leadership roles, continuing his focus on mentorship and nurturing a follow-on generation of leaders. Thus, Bernie became a professional as well as a personal grandfather. We still think of him lovingly and try to make him proud. We will miss him.

Melvin Lynne Rubin, MD, MSc

By *Peter R. Laibson, MD*



Melvin Lynne Rubin, MD, MSc, died at his home in Gainesville, Florida on February 23, 2014 from lung cancer, which he had fought heroically for over two years. He was 81 years of age.

Mel was born in San Francisco in 1932 and attended high school there. On his graduation in 1953 from the University of California, Berkeley with top honors in optometry, he was awarded "The Most Promising Clinician Award" from the School of Optometry. He was soon directed toward medical school by William Spencer, MD, his lifelong friend and mentor. In 1957 Mel graduated from the University of California Medical School in San Francisco, attaining the highest scholastic standing.

One can already see a pattern of excellence forming in Mel's life. His residency was at the University of Iowa, where he also completed a Master's degree in visual physiology in 1961. While in Iowa City, Mel acquired special retinal surgery skills with Robert Watzke, MD. Following his residency, he spent two years at the NIH in Bethesda, serving as executive secretary of the Ophthalmology Training Grants Committee.

In 1963 Mel was certified by the American Board of Ophthalmology and also became a fellow of the American Academy of Ophthalmology. In both organizations he rose to top leadership roles, as president of the AAO and chairman of the ABO. In addition, he became president of the Association for Research in Vision and Ophthalmology (ARVO) and chairman of the Council of the American Ophthalmological Society.

With his special interest in retina- vitreous diseases, Mel joined the full-time faculty at the University of Florida College of Medicine in Gainesville in 1963, soon after Herbert Kaufman, MD was appointed chairman there. By 1967 he was a full professor and became chairman in 1978, when Dr. Kaufman moved to Louisiana State University.

Mel's expertise in retinal-vitreous diseases is widely known and resulted in over 100 publications and numerous named lectures and books throughout his ophthalmic career. His reputation, however, has been especially burnished by his teachings and textbooks on optics, including the book he wrote with Benjamin Milder, MD entitled "The Fine Art of Prescribing Glasses Without Making a Spectacle of Yourself."

As an educator, Mel was a founding member of the American Academy of Ophthalmology's Committee on Continuing Education and is recognized as the principal originator, the "father" of the national Ophthalmic Knowledge Assessment Program (OKAP). He also served as Secretary for Instruction and chairman of the AAO Foundation. In honor of his contributions to education and his leadership role in the AAO, he was awarded the Academy's Special Recognition Award in 2010.

During their many years in Gainesville, Mel and his wife Lorna contributed significantly to the community through their love for and identification with the arts. In the early 1980's Mel began collecting photography seriously. By 2005 he and Lorna had amassed a formidable collection that included most of the pillars of 20th century photographic history such as Strand, Stieglitz, Steichen, Weston and Ansel Adams, as well as other Bay area photographers of the Group f/64. Mel and Lorna were fully cognizant of the educational opportunities that such a comprehensive collection offered. The Harn Museum of the University of Florida, Gainesville was the ideal recipient for photographic gifts from Mel and Lorna, and many selections from the Rubin collection were displayed there in several exhibitions.

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Mel was particularly proud of the UCSF Medical School's naming him Alumnus of the Year in 2012. Although already very ill, he was able to fly to San Francisco with Lorna, his partner of 60 years, to receive this honor. Mel's proudest achievements certainly were his three children, Gabrielle, Danny and Michael, along with his five grandchildren. Danny is best known for authoring, with Harold Ramis, the script for the cult movie "Groundhog Day." Michael, a Droidmaker, has worked with George Lucas, and Gabrielle is a clinical psychologist. For many summers, the entire family spent two weeks together for study and fun at the Chautauqua Institution in New York state.

It is clear that the international ophthalmic community has lost an immensely talented and innovative clinician, teacher and mentor. Those who have been privileged to know Mel personally will miss a remarkably warm and giving individual, a fun loving friend and a devoted colleague. His legacy will be forever remembered.

Ronald E. Smith, MD

By *Alfredo A. Sadun, MD, PhD*



It is with great sadness that I report that Ronald Smith died May 17, 2014. He was my mentor, my role model and my big brother. He died from an aggressive form of bladder cancer that advanced very quickly. His loss shocked us, especially coming so soon after the death of his close companion, Steve Ryan.

Ron was very proud of his early years in Walkersville, MD. He played baseball and basketball and led his high school to a championship. This led to his hobby of collecting sports awards, trophies and newspaper tributes that covered the walls and surfaces of his office.

From Walkersville he went to Washington College in Maryland and then attended Johns Hopkins University and then Johns Hopkins School of Medicine (in 3 years!). His residency in ophthalmology at Wilmer was where he forged many of the lifetime friendships that became a social core for the AOS and other ophthalmological societies. Following his fellowship in Uveitis and Cornea at the Proctor Foundation, he returned to Wilmer as Chief Resident. Two years with the U.S. Public Health Service removed him to the wilds of Alaska. He came to Doheny Eye Institute in Los Angeles, as Steve Ryan's first recruit. Together, they built Doheny into the world renowned program we are all familiar with. Ron was the soul of Doheny for almost 40 years, the last 20 as Department Chair. Ron brought grace and intelligence to a leadership style that was inspirational and deft.

His humility belied his great international acclaim and accomplishments. He was a person of pronounced compassion, impeccable integrity and profound honor. Ron's accomplishments included President of the AAO, 10 years on the Academy Board of Trustees, and Chair and Board member of the ABO. He was also past Vice-Chairman for ARVO. Ron was a member of many honorary societies in addition to the AOS, such as Academia Ophthalmologica Internationalis, and the Johns Hopkins Society of Scholars. He was awarded the Gold Medal of the International Uveitis Society and the Castroviejo Medal of the Cornea Society. He received the Lifetime Achievement Award by the AAO.

He was able to do so much for so many societies and American ophthalmology because of the quality of his personal relationships that were based on his generosity of spirit, his sincerity and his willingness to trust, even as he proved himself to be completely trustworthy. I admired this approach and so I turned to Ron for his sage advice, for his friendship and for his goodness.

Ron was an eminent scholar and scientist as well. He published about 320 articles, co-edited 2 books and many chapters. He was a popular speaker at congresses throughout the world.

Ron was beloved by many, in many circles. His residents and fellows adored him and stayed in close contact with him long after their training. His faculty, his co-chairs at USC, his co-chairs in ophthalmology across the country and his academic colleagues, also loved him. So too did his patients, his neighbors and many others who came to know Ron as a simple and unassuming man. For Ron

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was a Mensch, meaning that he took personal responsibility for treating each person with kindness and with respect. Ron graciously connected with everyone, notwithstanding his stature as a giant in ophthalmology. Ron's friends turned into my friends and they became the best part of academic ophthalmology.

He is survived by his wife of 34 years, Suzette, his previous wife, Sara Watt; his daughter, Kelly Parker and husband, John, and his son, Matt Smith and wife Tirza, as well as by four grandchildren and his brother, Dick and wife, Ann.

Fred Mattison Wilson II, MD

By *Paul R. Lichter, MD*



Fred Mattison Wilson, II, age 72 died surrounded by his family on August 23, 2013. He faced his cancer diagnosis with courage and his usual understated manner. When he was first diagnosed he was retired from active clinical practice but was staffing a cornea clinic with our residents at the Roudebush VA Medical Center in Indianapolis. At that time he was wearing a surgical hat since he had lost his hair related to his therapy and did not want to disturb the residents or cause them any anxiety. This was typical of Dr. Wilson. He continued staffing with the residents until he was no longer able.

Fred grew up in Indianapolis, Indiana graduating from a local high school, Indiana University, and the Indiana University School of Medicine. He was a Heed Fellow in cornea and external ocular diseases and a National Eye Institute Fellow at UC San Francisco. Fred was a dedicated surgeon, educator and researcher. Perhaps, more than anything, Fred thoroughly enjoyed working with students and serving as a mentor. I was fortunate to have him as one of my mentors during residency along with Merrill Grayson, MD with whom he worked closely in the department of ophthalmology at Indiana University for many years. He was the author of several books and publications. He created a manual for the beginning ophthalmology resident which continues to be a popular publication of the American Academy of Ophthalmology and is now in its 6th edition. He was dedicated to the American Board of Ophthalmology as a Board Director and served as the Chair of the Committee for the Oral Examination.

Fred had several loves outside of his work. He loved the outdoors, music, and was devoted to his family. He enjoyed camping, hiking, bird watching and photography. In his younger years, he would spend extended periods of time with friends in remote camping environments. He was engaged with the Boy Scouts of American and was an Eagle Scout and member of the National Eagle Scout Association. He enjoyed music and playing the guitar and piano.

Fred married Toni Pemberton in August of 1964. Together they created a wonderful family with three children and six grandchildren when he passed away.

In 2012, he authored a necrology of his father for the Transactions of the American Ophthalmological Society. It was a touching tribute and he was proud to be a member of the profession to which his father also dedicated his professional career.

MINUTES OF THE PROCEEDINGS

One Hundred and Fiftieth Annual Meeting

May 15-18, 2014

The ONE HUNDRED AND FIFTIETH ANNUAL MEETING of the American Ophthalmological Society (AOS) was held at The Ritz-Carlton, New York, Battery Park, New York

On May 16, 2014, Friday, President Hans Grossniklaus, MD called the opening session to order. The program began with the following AOS-Knapp symposium:

SYMPOSIUM: OCULAR GENE THERAPY

1. Introduction by David J. Wilson, MD
2. Verhoeff Lecture: "The Rocky Road to Successful Human Gene Therapy": Timothy Stout, MD
3. Introduction of AOS-Knapp Symposium – Edward G. Buckley, MD
4. Brief History of the Knapps: Froncie A. Gutman, MD
5. Introduction of Genetic Eye Disease: Edwin M. Stone, MD
6. Gene Replacement Therapy: Albert M. Maguire, MD
7. Pharmacologic Delivery with Gene Therapy: Peter A. Campochiarot, MD
8. Gene Therapy vs. Stem Cell Therapy: Marco A. Zarbin, MD
9. Risks of Gene Therapy: Paul A. Sieving, MD
10. Ethical Considerations in Gene Therapy: Alex V. Levin, MD

EXECUTIVE SESSION, SATURDAY, MAY 17, 2014

Hans Grossniklaus, MD: Good morning everyone I'd like to call the order of this Executive Session of the 150th Meeting of the American Ophthalmological Society.

The Executive Vice President, Dr. Tom Liesegang will now give his report:

REPORT OF THE EXECUTIVE VICE-PRESIDENT 2014

THOMAS J. LIESEGANG MD: The investments of the Society have prospered nicely over the past several years and presently stand at a historic high. The Society remains in a strong financial condition. The Council is actively engaged with the Society's financial managers at Vanguard, including direct dialog during the Council meetings. The AOS has an investment committee and an audit committee to monitor the financial activities of the Society; these committees are pleased with the present financial status of the AOS. There was a clean audit report for 2012 and the 2013 audit will be completed and reviewed shortly. The AOS Council recommends no increase in dues next year.

The three sources of income for the AOS are membership dues, annual meeting registration fees, and investment income that is derived from 3 Funds – The AOS Fund, the Charitable, Educational and Scientific Trust Fund, and the Knapp Fund. The investment income from the 3 Funds continues to subsidize the meeting, the Transactions, and the membership activities, in accordance with the bylaws of each Fund. The Knapp symposium held during the Annual Meeting is supported by the Knapp Fund. The Council is careful to use the bequeathed funds following the legal guidelines for their use. The Council carefully monitors all the expenses in an attempt to maximize the AOS holdings.

There are now 217 active members and 144 emeritus members with the bylaws permitting up to 275 active members. New members that have been accepted for membership last year were featured in the spotlight session during the Annual Meeting on the Thursday afternoon and are introduced at the Saturday banquet. The AOS website continues to be refreshed each year with information on new members, Council and Officers, as well as past and present members. There is information about the history of the Society, of the Charitable, Educational and Scientific Trust Fund, of the Herman Knapp Testimonial Fund, of the Howe Medal; a listing of all past members and prior meeting sites; membership requirements, a calendar of activities for the year and there is a history of all the athletic trophies and their winners over the years, along with a photo of the trophy. There is linkage to the full text of each article in each Transactions volume since 1864. All members are encouraged to submit a biosketch and photo for the website. Recent changes by the Council include hastening the review of theses and permitting a provisional status if a candidate has a thesis accepted midyear, the invitation to ophthalmology tabloid reporters to attend the meeting, and participation with an AOS Symposium at the World Congress of Ophthalmology Tokyo April 2014, under the encouragement of Marilyn Miller. Dan Albert has just completed an addition of the past 25 yrs to the history of the AOS, along with photographs provided by Ralph Eagle. This is available at the AOS website.

This year the AOS Council formed a task force to evaluate the interaction of the AOS and the Funding sources for the AOS, namely the CES and the Knapp Fund, seeking to confirm the purpose and use of investment income to support AOS activities and other activities that are consistent with the AOS mission. The summary of that report is presented on the website.

The AOS continues to record the scientific program with audio and video for web presentation. This will assist in extending and prolonging the effect of the Annual Meeting, especially for those unable to attend.

The AOS Council publishes a Newsletter twice a year over the past 7 years, highlighting AOS activities, announcements, and encouragement of participation in leadership positions and the annual meeting.

The AOS is preparing for the 151st meeting in Newport Rhode Island next year.



2014 AOS PRESIDENT HANS E. GROSSNIKLAUS, MD

REPORT FROM THE COUNCIL CHAIR

DAVID WILSON, MD: In 2013 to 2014, the Council has consisted of myself, Jay Erie, Ed Wilson, Anne Coleman, and Woody Van Meter. The Council's duty is to supervise the day to day operations of the AOS and oversee the financial status of the AOS funds. The Council met on May 15, 2014 and at that time received and accepted a clean audit of the AOS fund; the Charitable, Educational, and Scientific Trust fund, and the Herman Knapp Testimonial fund.

My main message for you today is to encourage you to attend and participate in the 151st Annual Meeting of the AOS to be held in Newport, Rhode Island. The 151st Annual Meeting will return to the traditional format, and will include free paper and poster presentations by the members. The meeting will also provide CME credit, so it is essential that members submitting papers include the appropriate information with their abstract submission. This year's Knapp Symposium will be on "Innovations in Medical Education" and the Saturday Symposium will be on "Healthcare Reform". A new addition to the 151st meeting will be the inaugural Frederick Blodi lecture to be given by Tim Olsen. The meeting should prove to be outstanding, and will also feature the return of the much beloved athletic events.

It has been a great privilege and honor to serve the AOS these past five years. Its leadership next year is in the very capable hands of Jay Erie M.D.

REPORT OF THE AOS AUDIT COMMITTEE

JOHN CLARKSON, MD: John Clarkson is the Chair of the AOS Audit Committee this year with additional members David Wilson (Council Chair) and Thomas Liesegang (EVP). The Audit committee met on June 23, 2014 with additional guests including Neil Erickson and Daniel Figueredo of Burr, Pilger, and Mayer Accountants and Alice Paw as Finance Manager, American Academy of Ophthalmology. AOS Management staff included, Lisa Brown and Timothy Losch.

The Committee reviewed the Fiscal Year 2013 Audited Financial Statements and Ms. Paw provided an overview. Ms. Paw noted that there were no significant changes to the presentation of the footnotes. Ms. Paw reported that the total net assets increased from the prior year primarily as a result of an increase in investments due to unfavorable market conditions. Dr. Liesegang noted that the 2014 Trans Am Ophthalmol Soc / 112 / 2014

financials will likely show a significant shortfall due to the increased expenses of the 2014 Annual Meeting in New York City celebrating the 150th anniversary.

Dr. Clarkson convened an Executive session with no irregularities reported.

REPORT OF THE COMMITTEE ON THESES

Thomas Gardner, MD: Chair and reporting member, Committee Members include: John D Gottsch, MD and John Thompson, MD: The AOS Thesis Committee reviewed 16 thesis submissions in 2014. This included one second revision, 5 first revisions and 10 new theses. There were 4 international candidates with 3 women and 13 men. Five were private practitioners while 11 were full time academic practitioners. Of the 16 theses, one was rejected, one was accepted, while 9 were minor revisions, meaning likely acceptance this year and five were major revisions.

In total, of the 16 submissions this year, 1 was accepted, 9 required only minor revision, and 5 were returned for major revision and 1 was rejected. Those requiring minor revisions were all eventually accepted and 2 of the major revisions also were revised to be “provisional” members for the coming year.



2014 AOS PRESIDENT HANS E. GROSSNIKLAUS, MD AND HIS WIFE DAURICE

REPORT OF THE EDITOR

EMILY Y. CHEW, MD: The 2013 111th volume of the *Transactions* of the American Ophthalmological Society (TAOS) was published online. All previous publications in the *TAOS* are easily accessible through PubMed Central at pubmedcentral.org Trans Am Ophthalmol Soc / 112 / 2014

<http://www.ncbi.nlm.nih.gov/pmc/journals/308/>. In addition to the full text of the 14 theses, the contents included the proceedings of the Executive Session, reports from the Society to other organizations, Necrology, Banquet, abstracts of the 18 oral and 12 poster presentation of the 2013 Annual Meeting, and presentation of the Howe Medal.

The scientific community continues to access articles from this original source of important information. The data from the National Library of Medicine (NLM)/NCBI showed that we had 411 hits on our website during the last year.

It is worthwhile to reiterate the issue of duplicate publication. It has been brought to our attention recently by Committee on Publication Ethics (COPE) and other groups that monitor ethical publishing that 26 articles published in *Transactions* of the American Ophthalmological Society had been duplicate publications within PubMed. These were indeed articles that were originally published as AOS thesis. The AOS no longer encourages authors to publish their theses in other journals. The AOS has repeatedly been criticized by ethical societies and by promotion boards for permitting this duplicate publication which is considered plagiarism. If two articles are published, they appear next to each other in PubMed and this is not ethically correct even though they might be somewhat different. When papers are peer-reviewed by 2 separate journals, they will be somewhat different, but the main theme will be still conveyed. Going forward, we request that the AOS theses be published only in the *TAOS* to avoid duplicate publications and the potential violation of plagiarism rules.

As noted last year, we have changed the publication procedures to accelerate the publication of all the theses. This is a welcomed change by all. We believe we have fulfilled a number of criteria for obtaining an impact factor for the Transactions of the American Ophthalmological Society. We have submitted the paperwork and we will keep you posted on any progress. I appreciate this opportunity to serve the society.

REPORT OF THE COMMITTEE ON PROGRAMS

Carol L. Shields, M.D.: The 150th AOS anniversary meeting in New York City is a celebration of our rich heritage. The program was specially designed to review accomplishments in science in general and specifically to review the developments in each subspecialty of ophthalmology. The program committee includes Edward Buckley, Jerry Sebag, David Tse, and Carol Shields with guidance from Thomas Liesegang (Executive Vice President) and David Wilson (Council President). The full program is listed on the AOS website. The program is divided into 4 parts including:

- Herman Knapp symposium with invited speakers
- Ophthalmic subspecialty symposium with invited speakers
- History of the American Ophthalmological Society with invited speakers
- Posters with abstracts submitted

Friday May 16, 2014 is the Herman Knapp Symposium, focused on “Ocular Gene Therapy” with the following invited speakers:

Timothy Stout MD	Verhoeff lecture: The Rocky Road to Successful Human Gene Therapy
Edwin Stone MD	Introduction to genetic eye disease
Albert Maguire MD	Gene replacement therapy
Peter Campochiaro MD	Pharmacologic delivery with genetic therapy
Marco Zarbin MD	Gene therapy vs stem cell therapy
Paul Sieving MD	Risks of gene therapy
Alex Levin MD	Ethical considerations of gene therapy

Saturday May 17, 2014 and Sunday May 18, 2014 is the Subspecialty Symposium, designed to review the development of each ophthalmic subspecialty and provide a historical account of the accomplishments within each. Historical video clips from previous meetings will be provided by Dr. Jay Erie and Dr. George Bartley. The invited speakers are all members of the AOS and included:

George Spaeth MD	Glaucoma
Lee Jampol MD	Retina
Alfredo Sadun MD	Neuro-ophthalmology
George Bartley MD	Plastics
Carol Shields MD	Ocular oncology
Hans Grossniklaus MD	Ophthalmic pathology
Marilyn Miller MD	Pediatric ophthalmology and strabismus
Ivan Schwab MD	Cornea
Doug Koch MD	Cataract and refractive surgery

Minutes of the Proceedings

Saturday May 17, 2014 is the *The History of the AOS Symposium*, provided in lecture and pictorial format by the following AOS members:

Dan Albert MD	150 th Anniversary Lecture: History of the American Ophthalmological Society
Ralph Eagle MD	Pictorial History of the American Ophthalmological Society

Posters will be presented by AOS members during the 3 days of the meeting.

REPORT OF THE COMMITTEE ON MEMBERSHIP

MARIAN MACSAI, MD: The Committee consisted of Marian Macsai, Joel Schuman, William Mieler and Mary Elizabeth Hartnett. We met in August 2014 with Tom Liesgang (ex officio). We reviewed 18 applications 14 males, and 4 females ranging in age from 40-69. The group consisted of 5 Professors and chairs, 3 professors and vice chairs, 8 professors and 2 associate professors. 15 national and 3 international candidates, 4 MD PhD, and 14 MD. The range of peer reviewed publications was from 3-250. Each Candidate was discussed in detail and presented to the Board of the AOS for review on Sept 13 2014 in Rochester, Minnesota.

The individual candidates were presented to the Board using the following format

- Name
- National/International
- Rank
- Specialty
- Sponsors
- # per reviewed publications
- Ability to write thesis
- Boards or Directorships
- Comments
- Recommendations

It was noted that the AOS board found the format of presentation to be useful for deliberation and review of each candidate

REPORT OF THE ARCHIVIST PHOTOGRAPHER

RALPH C. EAGLE JR MD: I took nearly 1400 digital photographs at the one hundred forty-ninth annual meeting of the American Ophthalmological Society held at The Lodge at Torrey Pines, La Jolla, California on May 16-19, 2013. The photos were taken using a Nikon D800E digital camera. Six photos were included as color illustrations in the 2013 on-line volume of the TRANSACTIONS OF THE AMERICAN OPHTHALMOLOGICAL SOCIETY. These included photos of 2013 AOS President Richard K. Parrish, II, MD, President Parrish and his wife Marianne, and group photos of The Council and the New Members. Also included were a photo of 2013 Lucien Howe Medalist Dan B. Jones, MD receiving his medal from John Clarkson, MD, and another photo of Dr. Jones with his wife Marilyn Jones. A show comprising more than 240 selected digital images in PDF format from the 2013 meeting can be downloaded from the meeting photos section of the *Members-Only* section of the AOS website. Photo shows from the 1996 through 2013 meetings currently can be online, as well as a number of historical photos from 1940's through the 1960's entitled "Images from the Past". In preparation for 2014 meeting I scanned more than 1000 slides from the 1990-1995 meetings and enhanced the images with Adobe® Photoshop® software. Additional photo shows are being prepared from scanned photos and will be placed on the website soon.

The digital archives of the AOS now comprise more than 8400 high-resolution digital photographs and 1400 digital images prepared from scanned transparencies.

Additional slides will be scanned in the future. The images are stored on redundant digital hard drives and on CD and DVD's in some instances. A backup hard drive containing all the images will be stored in the AOS office in San Francisco.

REPORT OF THE COMMITTEE ON EMERITI

FRONCIE GUTMAN, MD: Since our AOS Meeting in 2013, the following deaths have been reported to the Secretary:

<u>NAME</u>	<u>YEAR INDUCTED</u>	<u>RESIDENCE</u>
Bernard Becker, MD	1960	St. Louis, MO
Melvin Rubin, MD	1975	Gainesville, FL
Ronald E. Smith, MD	1982	Los Angeles, CA
Fred M. Wilson, II, MD	1983	Carmel, IN

May I ask for the membership to stand for a moment of silence to respect the memory of these friends and colleagues.

The following members have applied for Emeritus membership:

<u>NAME</u>	<u>YEAR INDUCTED</u>	<u>QUALIFICATION</u>
Gerhard W. Cibis	1994	70+ years of age, member for 10+ years
Paul R. Lichter	1976	Member for 25+ years
Narsing A. Rao	1990	70+ years of age, member for 10+ years

COUNCIL APPOINTMENTS

DAVID WILSON, MD: After taking into consideration all member names submitted to the Council for potential leadership positions for 2014-15 the Council put forward the following individuals for consideration:

AOS Council – **Marco Zarbin**

AOS President – **Richard Mills**

Executive Vice President – **Thomas Liesegang** to continue

Editor – **Emily Chew** to continue

Member, Committee on Theses – **Joan Miller** to join John Thompson and Thomas Gardner

Member, Committee on Programs – **Eduardo Alfonso** to join Edward Buckley, J. Sebag and David Tse

Member, Committee on Membership – **Mary Hartnett** to join Marian Macsai, Joel Schuman, and William Mieler

Chair, Committee on New Members – **Evelyn Paysse & David Coats** to continue

Member, Committee on Prizes – **Hans Grossniklaus** to join George Bartley and Lee Jampol

Chair, Committee on Emeriti – **Froncie Gutman** to continue

Committee on Athletics – **Rick Fraunfelder**

Audit Committee – **David Wilson and Richard Parrish III** to join Thomas Liesegang Clarkson

Investment Committee – **Richard Mills and Jay Erie** to join Thomas Liesegang

Archivist/Photographer – **Ralph Eagle** to continue

Representative to AAO Council – **Marco Zarbin**, alternate **Richard Mills**

Representative to the International Council of Ophthalmology – **Marilyn Miller** to continue

Representative to the American College of Surgeons – **Ed Raab** to continue; alternate **George Speath** to continue

Representative to the Pan American Association of Ophthalmology – **Eduardo Alfonso** to continue

Representatives to the American Orthoptic Council:

James Reynolds to join alternates **Edward Raab and David Weakley** to continue

Representative to JCAHPO – **William Mieler**

Parliamentarian – **Edward Raab**

All were contacted and agreed to serve.

REPORT OF THE REPRESENTATIVE TO THE COUNCIL OF THE AMERICAN ACADEMY OF OPHTHALMOLOGY

THOMAS J LIESEGANG MD: The Council of the American Academy of Ophthalmology (AAO) continues to meet in formal session twice yearly, first during the annual American Academy of Ophthalmology Annual meeting in the fall and then jointly with the AAO Board and State and Subspecialty Leadership at the Mid-Year Forum (MYF) in Washington in April. The Council was established to provide liaison between the AAO Board of Trustees and the numerous member societies involved with socioeconomic, governmental and public service issues. The current Council consists of voting representatives of all fifty states and includes Puerto Rico and the District of Columbia. Twenty-four Sub-Specialty societies have equal representation; however, the five “Special Interest Societies” which include the AOS, Association for Research in Vision and Ophthalmology (ARVO), American Board of Ophthalmology (ABO), Eye Bank Association of America (EBAA) and the Canadian Ophthalmological Society have Associate Non-voting Councilors because of the way we are incorporated or because of our membership eligibility. Each representative, including the AOS representative, provides a semi-annual report to the AAO Council each year summarizing the activities of the individual states and societies.

Since its founding in 1864 the objective of the AOS has been “the advancement of ophthalmic Science and art”, and its activities are primarily for the academic, educational and collegial benefit of its members. Although the AOS maintains no political or economic agenda, participation in the Council reflects its broad support for the Academy’s mission.

As in previous years, the AAO has sponsored and promoted a Congressional Advocacy Day at the Mid-Year Forum during which a significant number of Councilors or alternates were briefed on the Academy’s top legislative priorities and counseled on relationship building with their congressional representatives before proceeding to Capitol Hill and the offices of their personal representatives in the House and Senate. Issues highlighted this year included Medicare Physician Pay, Support for the Electronic Health Records Improvement, Truth in Healthcare Marketing, Support for the National Institutes of Health, and Support of the Department of Defense Vision Trauma Research Program.

During the Mid-Year Forum and Council meeting, several recurring problems continue to take precedence. Hearings this year included the following symposia: Finding Balance in a Changing Reimbursement Landscape, Where is the RUC and CMMI headed, Trans Am Ophthalmol Soc / 112 / 2014

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Physician Profiling, A Value Based Payment System, Managing the Risks of the Electronic Health Records, The Promises and Perils of Healthcare Integration, The AAO Biennial Member Survey, and The AAO role in the Wide World of Ophthalmology.

There are additional meetings held at the MYF, including meetings of different regions of the USA, meetings of state society representatives, and meetings of Subspecialty



AOS COUNCIL FROM LEFT: JAY C. ERIE, MD, WOODFORD S VAN METER, EMILY Y. CHEW, MD, M EDWARD WILSON, HANS E GROSSNIKLAUS, MD, DAVID J. WILSON, MD, ANNE L. COLEMAN, MD, THOMAS J. LIESEGANG, MD

REPORT OF THE REPRESENTATIVE TO THE AMERICAN COLLEGE OF SURGEONS

EDWARD L. RAAB, MD: Dr. Edward L. Raab continues as our Society's representative to the American College of Surgeons, and serves on the ACS Board of Governors and the Ophthalmic Advisory Council. These meet in conjunction with the ACS annual Clinical Congress, at the interim Spring Meeting and Leadership Summit, and by teleconference at various times. An ACS Governor acts as liaison between the organization represented by the Governor and the Board of Regents of the College. Governors represent either specialty societies across the range of surgical fields or geographic regions of the United States and Canada and a number of other countries.

The College has reorganized the structure of the Board of Governors in an effort to increase Governor involvement in membership committees and to improve communication with the Board of Regents. Governors receive frequent updating on issues to be shared with their constituents, by means informational webinars and the circulation of weekly "NewsScopes". Governors are assigned according to 5 major headings or "pillars": Member Services, Education, Advocacy and Health Policy, Quality Research and Patient Care, and Communication. Dr. Raab is assigned as Vice-Chair of the Education Pillar and a member of the Patient Education Committee. During the past year, a Patient Education Workgroup has been developing a survey, to be sent to all ACS members, regarding their need for patient educational materials of various kinds, their present resources, and what they would like the College to develop in support of this effort. Dr. Raab assisted in the formulation of appropriate survey questions and in the editing toward a document that would encourage a high response rate.

During the past 3 years, Advocacy Summits have been held in preparation for participants to visit Capitol Hill to express member concerns to federal legislators. Increased funding for emergency medical services to trauma victims remain prominent in the College's advocacy efforts.

The Ophthalmic Advisory Council is an important component of the College in conveying the particular concerns of ophthalmologists to the ACS Board of Regents. Dr. Raab is 1 of 2 representatives of the Board of Governors on this body, which also includes representatives from the American Academy of Ophthalmology, the Association of University Professors of Ophthalmology, the American Board of Ophthalmology, and Young Surgeons and Residents representatives. This year the Council is fortunate in including a Board of Regents representative who is an ophthalmologist and Immediate Past Chair of the Advisory Council, improving

ophthalmology's voice to the Board of Regents.

A situation affecting our specialty and therefore our Society is the marginal presence of ophthalmologists at the membership and governance levels of the ACS. Possibilities for an ophthalmology program at the Annual Clinical Meeting of the College are handicapped by the necessity of identifying a topic of general interest to surgeons in all specialty areas and by a confining policy on speaker expenses. Dr. Raab has agreed to develop a program offering for the 2015 Annual Meeting.

Among other action items considered by the Advisory Council at its recent meeting were an expression of concern to the Regents over the publication of a position paper discouraging the use of ambulatory surgical centers for surgery on children, the work of a group whose membership and processes were not known to the Advisory Council prior to this publication. This concern was expressed across the surgical specialties comprising the College. The Council also discussed a proposed Statement on Peak Performance and the Management of Fatigue, a subject of current importance to the College.

Other items under continued general scrutiny include preparation for practice of graduating surgery residents because of the decrease in opportunities for progressive assumption of responsibility for decision making, and a trend among surgeons to seek full time in-hospital employment.



2014 AOS NEW MEMBER LUNCHEON

REPORT OF THE REPRESENTATIVES TO THE AMERICAN ORTHOPTIC COUNCIL

EDWARD L. RAAB, MD: The American Orthoptic Council [AOC] establishes requirements for and accredits orthoptic teaching programs; examines candidates for certification; determines standards for continuing education of certified orthoptists; and promotes and oversees the knowledgeable and ethical practice of orthoptics. Currently there are 13 Orthoptic Teaching Programs approved by the AOC. The Council consists of ophthalmologists specializing in pediatric ophthalmology and strabismus, and of certified orthoptists. Our Society's representatives to the Council during the past year have been Drs. Thomas France, Edward Raab, and David Weakley. All are Past Presidents of the Council.

Dr. France has now retired from the Council after many years of outstanding service. He most recently served as Chair of the Accreditation and International Affairs Committees, Representative to the Canadian Orthoptic Council, and member of the Editorial, Nominating, Program, and Finance Committees.

Dr. Raab served as Chair of the Bylaws Committee and a member of the Program, Ethics, International Affairs, and Program Support Committees.

Dr. Weakley served on the Executive Committee as Immediate Past President; as Chair of the Nominating Committee; and

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member of the Accreditation, International Affairs, Editorial, and Long Range Planning Committees.

The American Orthoptic Council has revised its structure so that the number of Certified Orthoptist members will be equal to that of the ophthalmologist members. The Council has also added ophthalmologists representing the Section of Ophthalmology of the American Academy of Pediatrics, in order to extend the awareness of orthoptics and its practitioners to a large constituency of physicians interested in eye care of children. AOS member Dr. James Reynolds, the Editor of the American Orthoptic Journal, served last year *ex officio* as a non-voting member, and now rejoins the Council as a full-voting representative.

The Council's Annual Meeting and certifying examinations were held in Nashville in October, 2013. Fourteen candidates were certified. The 2014 examinations of 15 candidates will be conducted in September in Houston. Candidates must initially pass a prior written examination, now given in electronic form.

Members of the Council and the American Association of Certified Orthoptists continue to be active in national and international professional meetings. The AOC and the AACO join each year with the American Academy of Ophthalmology to present the traditional Sunday Symposium at the AAO Annual Meeting, and offer a workshop at the Annual Meeting of the American Association for Pediatric Ophthalmology and Strabismus. The 2013 workshop, "DVD: A Conceptual, Clinical, and Surgical Overview" co-moderated by Dr. Raab, became an invited submission to the Journal of AAPOS, and has been accepted for publication. The traditional Sunday Symposium, co-sponsored by the Academy, the Council, and the AACO and titled "Mythbusters: Examining the Orthoptic and Surgical Management of the Most Puzzling Childhood Syndromes", was a feature of the Academy's 2013 Annual Meeting in New Orleans and will be published in the American Orthoptic Journal. For 2014, The AAPOS meeting offering will concern visual discomfort in adult patients with strabismus, and the AAO Sunday Symposium will deal with ocular torsion.

The American Orthoptic Journal continues to investigate re-establishing an arrangement with AAPOS in which receiving the Journal is reinstated as an AAPOS member benefit. The recently achieved Medline recognition is an important enhancement to the worth of this excellent peer-reviewed publication, and is an important element to the recognition of orthoptics as a profession.

Other action items that have come before the Council during the past year include the following:

- Changes to financial reporting to better track allocation of income and expenses;
- Further realignment of the Council to integrate its increased membership and our sponsoring organizations;
- Refinements in the content and conducting of the certifying examinations;
- Further development of a Policy and Procedure handbook to supplement the overall provisions of the bylaws.

These and other items were discussed at the Council's Midyear Meeting in April of this year.

Your Representatives strongly encourage continued support of the American Orthoptic Council and the profession of orthoptics.



NEW MEMBER JUDY E. KIM, MD SIGNING MEMBERSHIP BOOK

REPORT OF REPRESENTATIVE TO THE INTERNATIONAL COUNCIL OF OPHTHALMOLOGY

Marilyn Miller, MD: AOS Symposium at ICO in Japan, 2014

BACKGROUND

There has been considerable discussion in the past at the AOS Council meetings as to the desirability of an AOS sponsored symposiums at ophthalmologic meetings and it was decided to accept the invitation to organize a symposium for the 2014 ICO meeting. Dr. Thomas Liesegang's assistance and support was invaluable throughout the process of developing and monitoring a symposium. Topics were solicited for presentation from the AOS membership and a symposium was developed that involved subjects from a wide variety of ophthalmologic conditions. Seven presentations were selected for the 90 minute period and the title of symposium was "New Challenges in Ophthalmology". There were a few more submissions than could be included but the names of the members whose topics were not accepted were given to the ICO organizers and may have had the opportunity to participate in other ICO symposiums.

Unfortunately, I was unable to attend due to a conflict with the AAPOS meeting where I had a commitment but Tom was a participant at the meeting and arranged for moderators for the symposium. I have heard that the symposium went without any problems.

After the meeting, Tom sent out a questionnaire to the AOS members of the symposium and I will summarize the responses (5 responded):

Question #1: Did you enjoy the experience and found it worthwhile? -- Most (3-4) responded positively but it was pointed out that the audience was small and it is disappointing to have a well prepared presentation and not have a receptive audience.

Question #2: Would you suggest that the AOS continue to participate in an international venue? -- More responded yes although one speaker felt it would not be worthwhile unless the event became an integral part of the program. Another observation was that since many AOS members often go to international meetings so identifying potential speakers would probably not be difficult.

Question #3: Would you be willing to participate again? -- Most said yes

Question #4: Do you think the location should influence AOS participation? -- Divided responses with "no" winning by one

Question #5: Did you see AOS members at the meeting for other reasons? -- yes

Question #6: Should the AOS accept invitations to speak at other venues domestic and international if offered? -- The answers are generally yes, but with selectivity.

My personal observation about symposiums sponsored by ophthalmic organizations (based on my AAPOS experience) is that the organization is generally pleased if the expectations are not too high. I have never been able to predict attendance as often the subject matter of competing symposiums offered at the same time influences the attendance. The organizers of the meeting obviously benefit from the increased attendance of individuals who might not have gone without their speaking commitment but the organization giving the symposium and its speakers also get recognition. One benefit is the informal conversations with the speakers and the introduction of the symposium. These opportunities assist in educating the audience about the organization. The AOS is committed to education and it is helpful to have a forum to show our commitment. The downside is there is a significant time commitment for those organizing the symposium (as I am sure Tom will agree). Without support from Tom and the AOS staff it would have been very difficult to develop a symposium.

As the Council knows I am a supporter of the AOS sponsoring some symposiums but I do believe the decision should be selective and involve more AOS members in the organizing steps.

Recommendation: The AOS accept some invitations to organize future symposiums, but that a committee of the AOS be established to 1) Draw up guidelines to present to the Council about the types of meetings in which that the AOS will consider participation and 2) The organizing process be shared by the members of the committee and AOS staff.

REPORT OF THE REPRESENTATIVE TO THE PAN AMERICAN ASSOCIATION OF OPHTHALMOLOGY

EDUARDO ALFONSO, MD:

1. PAN-AMERICAN COUNCIL OF UNIVERSITY PROFESSORS (PACUPO)

Eduardo Mayorga MD (Argentina) chairs *PACUPO*. The purpose of this program is to unite and standardize university training programs throughout Latin American through exchange programs and other means. Dr. Mayorga is also chairing the growing E-Learning Initiative where the Pan-American plans to organize several webinars a year.

2. FELLOWSHIPS COMMITTEE.

Paulo Augusto Arruda de Mello MD (Brazil) chairs the *Fellowships Committee*. Scholarships are funded from a variety of sources. Over \$150,000 in scholarships and other awards were given out in 2012.

In addition to using its Pan-American Foundation unrestricted resources, funding for these programs is provided by personal donations to the Pan-American Foundation, from donations from industry partners and private or family foundations, such as the Trans Am Ophthalmol Soc / 112 / 2014

Retina Research Foundation, the Tim & Judith Sear Foundation and the David and Julianne Pyott Foundation.

3. VISITING PROFESSORS COMMITTEE

José Antonio Roca MD (Peru) chairs the *Visiting Professors Committee*. The Visiting Professors Program sends Visiting Professors to the majority of the countries in Latin America.

4. 2013 MEETINGS & EDUCATIONAL ACTIVITIES

Mark J. Mannis, MD, PAAO President, has broadened its scope of educational activities to include a PAAO symposium during the Cuban Congress in 2013.

- **10th Leadership Development Course “Curso de Liderazgo”**

Jointly with the American Academy of Ophthalmology (AAO) & the European Ophthalmological Society (SOE)

January 11-13, 2013

San Francisco, California

- **XXI Pan-American Regional Course**

Jointly with the Spanish Society of Ophthalmology

April 25-27, 2013

Santiago de Compostela, Spain

- **2013 Pan-American Research Day (one day before the ARVO meeting)**

May 4, 2012

Seattle, Washington

- **PAAO Symposium at the 7th International Congress of Ophthalmology at the 15th Cuban Congress of Ophthalmology**

May 29-31, 2013

Havana, Cuba

- **30th Pan-American Congress of Ophthalmology jointly with the 37th Brazilian Congress of Ophthalmology**

August 7-10, 2013

Rio de Janeiro, Brazil

- **XXVI Lo Mejor de la AAO en Español**

November 20, 2013

New Orleans, Louisiana

5. MAJOR INITIATIVES FOR THE YEAR

- Expand PAAO educational courses to virtually all countries in the Western Hemisphere.
- Expand the PAAO's online educational programs.
- Endorse guest speakers at national meetings, resident exchange, newsletter features; consultant visits, shared executive expertise and shared advocacy experience



2014 VERHOEFF LECTURE TIMOTHY STOUT, MD

REPORT OF THE REPRESENTATIVE TO THE JCAPO

William F. Mieler, MD: The mission of the Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO) is to enhance the quality and availability of ophthalmic patient care by promoting the value of qualified allied health personnel and by providing certification and education. JCAHPO has a membership of 20 ophthalmology and allied health organizations, and has 35 representatives who are JCAHPO Commissioners. I was recently appointed as the AOS representative to JCAHPO, and I have voting privileges as one of the Commissioners.

JCAHPO continues to have ongoing, active initiatives in certification, education, E-learning, international relationships, career development, and in communication. As I become more involved in the JCAHPO organization, I will report much more detail in future reports, regarding the current activities in these specific areas. With virtually every national ophthalmology meeting, there is an accompanying JCAHPO program. This past year, at the JCAHPO meeting at the AAO in Chicago, there were 1749 attendees, the average attendee participated in 14 courses, and the most popular courses were on imaging, anterior segment surgery, and office management.

The involvement of the AOS with JCAHPO continues to promote a positive relationship between the two organizations. I recommend that the AOS and its members continue to actively support and endorse JCAHPO's certification and continuing education programs. I have actively participated in a variety of JCAHPO educational programs over the past eight to nine years, and I encourage all of you to become involved when asked to do so. This will only serve to strengthen the quality of our ophthalmic technical staff.

SCIENTIFIC SESSION, SATURDAY, MAY 17, 2014

THE HISTORY & EVOLUTION OF OPHTHALMIC SUBSPECIALTIES: PAST, PRESENT & FUTURE

SATURDAY EVENING BANQUET, MAY 17, 2014

REPORT FROM THE COMMITTEE FOR NEW MEMBERS

EVELYN A. PAYSSE, MD and DAVID K COATS, MD: The New Members Committee welcomed 18 new members at the 150th annual meeting of the American Ophthalmological Society, including 2 members who joined in 2013, but were unable to attend last year's meeting. The new members are Anthony Arnold, MD, Sophie Bakri, MD, Michael Chiang, MD, Christina Flaxel, MD, Peter Francis, MD, PhD, Karl Golnik, MD, David Haung, MD, L. Jay Katz, MD, Judy Kim, MD (2013), Shigeru Kinoshita, MD, PhD (2013), Alex Levin, MD, MHSc, FRCSC, Steve Mansberger, MD, MPH, Timothy McCulley, MD, Cameron Parsa, MD, Luis Pasquale, MD, FARVO, Jonathon Sears, MD, David Stagers, Jr., MD, FACS, FAAP, and Joshua Stein, MD, MS.

A brief background summary for each new member follows:

Anthony Arnold, MD

- Professor of Chief, Neuro-Ophthalmology Division
- UCLA Jules Stein Eye Institute
- Neuro-ophthalmology
- Thesis studied the spectrum of optic disc ischemia in patients less than 50 years of age

Sophie Bakri, MD

- Professor of Ophthalmology
- The Mayo Clinic
- Vitreoretinal Diseases
- Hobbies include travel, family, and she is a concert-level pianist

Michael Chiang, MD

- Professor of Ophthalmology
- Casey Eye Institute at Oregon Health & Science University
- Pediatric Ophthalmology and Strabismus
- Special interest and expertise in health informatics

Christina Flaxel, MD

- Professor of Ophthalmology
- Casey Eye Institute at Oregon Health & Science University
- Vitreoretinal diseases
- Hobbies include long distance running and travel

Peter Francis, MD, PhD

- Oregon Eye Physicians and Surgeons
- Vitreoretinal diseases
- Hobbies including marathon running and duathlons

Karl Golnik, MD

- Professor of Ophthalmology, Neurology, and Neurosurgery
- University of Cincinnati and The Cincinnati Eye Institute
- Neuro-ophthalmology
- Hobbies include competitive cycling

David Huang, MD

- Casey Eye Institute at Oregon Health & Science University
- Cornea and external disease
- Co-founded a Gobiqity Mobile Health, which produces mobile diagnostic products

L. Jay Katz, MD

- Professor of Ophthalmology
- The Wills Eye Hospital
- Glaucoma
- Enjoys hiking and travel

Judy Kim, MD

- Professor of Ophthalmology
- Medical College of Wisconsin
- Vitreoretinal Diseases
- Hobbies include photography, traveling, gardening, and swimming. Claims to have a black belt in shopping.

Shigeru Kinoshita, MD, PhD

- Professor and Chair of Ophthalmology
- Kyoto Prefectural University of Medicine
- Cornea and external diseases
- Hobbies include music and art appreciation

Alex Levin, MD, MHSc, FRCSC

- Chief of Pediatric Ophthalmology and Ocular Genetics
- Wills Eye Hospital
- Pediatric Ophthalmology
- Hobbies include gold and collecting pre-1930 flat top Schaeffer pens

Steve Mansberger, MD, MPH

- Vice Chair and Director of Glaucoma Services and Fellowship
- Legacy Devers Eye Institute
- Glaucoma
- Hobbies include biking, hiking, triathlons

Timothy McCulley, MD

- Associate Professor of Ophthalmology
- The Wilmer Eye Institute, Johns Hopkins School of Medicine
- Ophthalmic Plastic and Reconstructive Surgery
- Hobbies include travel and family

Cameron Parsa, MD

- Associate Professor of Ophthalmology
- UPMC, Sorbonne University, Paris, France
- Neuro-ophthalmology
- Hobbies include international travel, photography, and swimming

Luis Pasquale, MD, FARVO

- Director of Glaucoma and Telemedicine
- Mass Eye and Ear Infirmary
- Glaucoma
- Hobbies include running and tennis

Jonathon Sears, MD

- Cole Eye Institute
- Vitreoretinal Diseases
- Hobbies include gardening and bluegrass banjo

David Stagers, Jr., MD, FACS, FAAP

- Clinical Associate Professor, UT Southwestern
- Pediatric Ophthalmology and Strabismus
- Hobbies include cycling and travel. Co-founded One World One Vision

Joshua Stein, MD, MS

- Associate Professor of Ophthalmology
- University of Michigan Kellogg Eye Center
- Glaucoma
- Hobbies include softball and family

REPORT FROM THE ATHLETIC COMMITTEE:

RICK FRAUNFELDER, MD: Athletic events at the 2014 meeting at the Ritz Carlton Battery Park in New York City are not being offered, however, there will be private parties that are playing golf at some of the surrounding courses. If interested, contact me at fraunfelderf@health.missouri.edu and foursomes can be arranged. Looking forward to robust athletic opportunities in 2015.

REPORT FROM THE COMMITTEE ON PRIZES

MARILYN MILLER, MD: The established criteria for the Howe Medal Award are as follows (should have one or more)

- Significant contributions as an ophthalmic educator
- Meritorious and remarkable service to ophthalmology
- Outstanding original investigation in the field of ophthalmology
- Discoveries so notable as suddenly to advance the progress of ophthalmology in all parts of the world

The process taken by the 2014 Committee on Prizes included:

- Review the AOS Membership list for possible candidates
- Seek nominations from membership
- Select top candidates
- Make a final selection of one candidate



2014 LUCIEN HOWE MEDALIST MORTON F. GOLDBERG, MD

Morton F. Goldberg, MD, was selected to be the 2014 Awardee of the Howe Medal based on his professional career of outstanding leadership and contributions in education. Dr. Goldberg was a Magna Cum Laude and Phi Beta Kappa graduate of Harvard College. He received a Cum Laude Degree from Harvard Medical School where he was a member of the AOA. After an internship at Peter

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Bent Brigham he did his residency at Wilmer Ophthalmological Institute of the Johns Hopkins University and a Post-doctoral NIH fellowship in Medical Genetics.

Dr. Goldberg was recruited to the University of Illinois Eye and Ear Infirmary to be the first full time chairman of the ophthalmology department. Over the next years he established an excellent residency program, built strong research activity, developed the ophthalmic subspecialty units and added a Lions of Illinois Research Institute.

He returned to Wilmer in 1989 as Director of Ophthalmology and continued his strong leadership in education and research with personal involvement in over 500 journal articles and 50 book chapters. Dr. Goldberg also was the editor of the Archives of Ophthalmology for 10 years in addition to being involved with other editorial boards. He has received honorary degrees from the F.R.A.C.O. Royal Australian College of Ophthalmology and the U. of Coimbra in Portugal. He also has had a great number of invited lectures and many visiting professorships.

Morton Goldberg is married to Myrna Davidov and has two children and a grandchild.

The 2014 Committee consisted of Drs. George Bartley, Lee Jampol and Marilyn Miller

The committee report was presented by Dr. Marilyn Miller, 2014 Chair of the Committee on Prizes. Dr. Goldberg was escorted to the podium by Drs. Lee Jampol and George B. Bartley.



2014 LUCIEN HOWE MEDALIST MORTON F. GOLDBERG, MD AND WIFE MYRNA



WEDNESDAY, MAY 18, 2014

SCIENTIFIC SESSION, SUNDAY, MAY 18, 2014

THE HISTORY & EVOLUTION OF OPHTHALMIC SUBSPECIALTIES: PAST, PRESENT & FUTURE

Members registered for the 2014 meeting. XXX professional guests are at the end of the list. Members

Abbott	Richard	Active Member	Francis	Peter	Active Member
Adelman	Ron	Active Member	Fraunfelder	Frederick	Emeritus Member
Albert	Daniel	Emeritus Member	Fraunfelder	Frederick	Active Member
Alfonso	Eduardo	Active Member	Friedman	Alan	Active Member
Archer	Steven	Active Member	Gardner	Thomas	Active Member
Arnold	Anthony	Active Member	Godfrey	William	Emeritus Member
Asbell	Penny	Active Member	Goldbaum	Michael	Active Member
Augsburger	James	Active Member	Goldberg	Morton	Emeritus Member
Bakri	Sophie	Active Member	Golnik	Karl	Active Member
Bartley	George	Active Member	Gottsch	John	Active Member
Bateman	J. Bronwyn	Active Member	Gragoudas	Evangelos	Active Member
Baudouin	Christophe	Active Member	Gross	Ronald	Active Member
Baum	Jules	Emeritus Member	Grossniklaus	Hans	Active Member
Berler	David	Emeritus Member	Gutman	Froncie	Emeritus Member
Biglan	Albert	Emeritus Member	Haik	Barrett	Active Member
Black	Bradley	Active Member	Haller	Julia	Active Member
Blair	Norman	Active Member	Han	Dennis	Active Member
Bobrow	James	Active Member	Harris	Gerald	Active Member
Brodsky	Michael	Active Member	Hartnett	Mary	Active Member
Brown	Gary	Active Member	Hersh	Peter	Active Member
Browning	David	Active Member	Holz	Eric	Active Member
Buckley	Edward	Active Member	Huang	Andrew	Active Member
Budenz	Donald	Active Member	Huang	David	Active Member
Bullock	John	Emeritus Member	Ing	Malcolm	Active Member
Cantor	Louis	Active Member	Jabs	Douglas	Active Member
Caprioli	Joseph	Active Member	Jaeger	Edward	Emeritus Member
Chan	Chi-Chao	Active Member	Jampol	Henry	Active Member
Chen	Teresa	Active Member	Jampol	Lee	Emeritus Member
Chew	Emily	Active Member	Jarrett	William	Emeritus Member
Chiang	Michael	Active Member	Johnson	Mark	Active Member
Chodosh	James	Active Member	Johnson	David	Active Member
Chow	Alan	Active Member	Jones	Dan	Emeritus Member
Cibis	Gerhard	Emeritus Member	Katz	L. Jay	Active Member
Cioffi	George	Active Member	Kerr	Natalie	Active Member
Clarkson	John	Active Member	Kim	Judy	Active Member
Coats	David	Active Member	Kinoshita	Shigeru	Active Member
Cohen	Elisabeth	Active Member	Kinyoun	James	Active Member
Coleman	Anne	Active Member	Koch	Douglas	Active Member
Coleman	D. Jackson	Emeritus Member	Laibson	Peter	Emeritus Member
Crawford	J. Brooks	Emeritus Member	Lakhanpal	Vinod	Active Member
Day	Susan	Active Member	Laties	Alan	Emeritus Member
Durrie	Daniel	Active Member	Levin	Leonard	Active Member
Eagle	Ralph	Active Member	Levin	Alex	Active Member
Edward	Deepak	Active Member	Lewis	Richard	Active Member
Elman	Michael	Active Member	Lichter	Paul	Emeritus Member
Erie	Jay	Active Member	Liesegang	Thomas	Active Member
Esmaeli	Bitia	Active Member	Ludwig	Irene	Active Member
Farris	R. Linsy	Emeritus Member	Lueder	Gregg	Active Member
Feldon	Steven	Active Member	Macasai	Marian	Active Member
Feman	Stephen	Emeritus Member	Manche	Edward	Active Member
Fish	Gary	Active Member	Mansberger	Steven	Active Member
Flach	Allan	Active Member	Maumenee	Irene	Emeritus Member
Flaxel	Christina	Active Member	Mazow	Malcolm	Emeritus Member
Forster	Richard	Emeritus Member	McCulley	James	Active Member
France	Thomas	Emeritus Member	McCulley	Timothy	Active Member
			McDonald	Marguerite	Active Member
			McLeod	Stephen	Active Member
			Merriam	John	Active Member
			Mets	Marilyn	Active Member

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Miller	Marilyn	Active Member	Wilkinson	Charles	Active Member
Miller	Joan	Active Member	Wilson	R. Sloan	Emeritus Member
Miller	Joseph	Active Member	Wilson	M. Edward	Active Member
Mills	Richard	Active Member	Wilson	David	Active Member
Mitchell	Paul	Active Member	Wood	Thomas	Emeritus Member
Netland	Peter	Active Member	Wright	Kenneth	Active Member
Newman	Steve	Active Member	Yannuzzi	Lawrence	Active Member
Nirankari	Verinder	Active Member	Yeatts	R. Patrick	Active Member
Olsen	Timothy	Active Member	Younge	Brian	Emeritus Member
Packer	Samuel	Active Member	Zarbin	Marco	Active Member
Parrish	Richard	Active Member			
Parsa	Cameron	Active Member			
Pasquale	Louis	Active Member	Professional Guests		
Payne	John	Emeritus Member	Bauereiss	Paul	Professional Guest
Pepose	Jay	Active Member	Del Priore	Lucian	Professional Guest
Pulido	Jose	Active Member	Felch	William	Professional Guest
Puro	Donald	Active Member	Francis	Beth	Professional Guest
Raab	Edward	Active Member	Galst	Jay	Professional Guest
Rapuano	Christopher	Active Member	Huh	Sara	Professional Guest
Ravin	James	Active Member	Jager	Martine	Professional Guest
Reynolds	James	Active Member	Jonas	Jost	Professional Guest
Ritch	Robert	Active Member	Lang	Gabriele	Professional Guest
Runge	Paul	Active Member	Lang	Gerhard	Professional Guest
Sadun	Alfredo	Active Member	Liebmann	Jeffrey	Professional Guest
Schaefer	Daniel	Active Member	Little	Josh	Resident/Fellow
Schein	Oliver	Active Member	Luntz	Maurice	Professional Guest
Schocket	Stanley	Emeritus Member	Marsiglia	Marcela	Professional Guest
Schubert	Hermann	Active Member	Merlau	Daniel	Professional Guest
Schuman	Joel	Active Member	Nouri-Mahdavi	Kouros	Professional Guest
Schwab	Ivan	Active Member	Pennesi	Mark	Professional Guest
Sears	Jonathan	Active Member	Rosen	Richard	Professional Guest
Sebag	Jerry	Active Member	Russell	Steven	Professional Guest
Sergott	Robert	Active Member	Stahl	Erin	Professional Guest
Sherwood	Mark	Active Member	Stem	Maxwell	Professional Guest
Shields	Jerry	Active Member	Stout	Ann	Professional Guest
Shields	Carol	Active Member	Vajaranant	Tahasarat	Professional Guest
Siatkowski	R. Michael	Active Member			
Sieving	Paul	Active Member			
Simon	John	Active Member			
Sommer	Alfred	Active Member			
Spaeth	George	Active Member			
Spivey	Bruce	Emeritus Member			
Stager, Sr.	David	Active Member			
Stager, Jr.	David	Active Member			
Stamper	Robert	Active Member			
Stark	Walter	Emeritus Member			
Stein	Joshua	Active Member			
Stone	Edwin	Active Member			
Stout	Tim	Active Member			
Straatsma	Bradley	Emeritus Member			
Sugar	Alan	Active Member			
Summers	C. Gail	Active Member			
Tasman	William	Emeritus Member			
Taylor	Hugh	Active Member			
Terry	Mark	Active Member			
Thompson	John	Active Member			
Traboulsi	Elias	Active Member			
Truhlsen	Stanley	Emeritus Member			
Tsai	James	Active Member			
Tse	David	Active Member			
Van Meter	Woodford	Active Member			
Wallace	David	Active Member			
Waring	George	Emeritus Member			
Weiss	Jayne	Active Member			
Wilensky	Jacob	Active Member			

HISTORY OF THE AMERICAN OPHTHALMOLOGICAL SOCIETY: THE SESQUICENTENNIAL OF THE AMERICAN OPHTHALMOLOGICAL SOCIETY—OUR MISSION CONTINUES

By Daniel M. Albert, MD, MS

It was a privilege to be asked to join the ranks of American Ophthalmological Society (AOS) “historians,” which began with Alvin A. Hubbell in 1908 (Figure 1). As with previous histories of the AOS, my focus has been primarily on names and dates, committee members, and details picked from minutes of annual meetings—it is history through a telephoto lens. But for this account, I would like to take a broader view through a wide-angle lens and capture the Society’s history as it demonstrates and expresses our country’s history and culture and the evolution of American medicine. To accomplish this in the space allotted, I will take what pathologists call “step sections” and review this story at 50-year intervals, highlighting one of the outstanding ophthalmologists as a representative for each of these eras.

1864: THE FOUNDING OF THE AOS

On Tuesday, June 7, 1864, 18 physicians met at the New York Eye and Ear Infirmary to form the American Ophthalmological Society (Figure 2). This was a time when the United States was consumed by the Civil War. In June 1864, Lincoln came to believe that he would be defeated in his bid for reelection that November.¹ Despite Union victories at Gettysburg and Vicksburg a year earlier, the Confederate armies had come back with a vengeance and Union casualties approached 200,000 killed, wounded, or missing in action. It was not until Sherman captured Atlanta in early September that public opinion again favored Lincoln.¹ Many of the Society’s early members were serving as surgeons in the army (Figure 3). For example, William Fisher Norris, who would become the Society’s fifth president in 1885, had operated, mainly amputating limbs, for 36 consecutive hours at Gettysburg² (Figure 4). Tragically, more than 70% of soldiers with battlefield amputations died of sepsis.³ Now, at age 25, he was in charge of the eye wounds at the 300-bed Douglas Hospital in Washington, DC. Many younger, future members were fighting as soldiers in the war.



FIGURE 1

Alvin A. Hubbell was the first to document the history of the American Ophthalmological Society in 1908.



EYE AND EAR INFIRMARY.

Corner Second Avenue and Thirteenth Street.

FIGURE 2

On Tuesday, June 7, 1864, 18 physicians met at the New York Eye and Ear Infirmary to form the American Ophthalmological Society.

Civil War soldiers were not used to subordinating themselves to large organizations, and discipline was loose. Nonetheless, the letters they sent to their loved ones rang with expressions of “patriotism, idealism, concepts of duty, honor, manhood and community.”⁴



FIGURE 3

Surgery being performed on the battlefield as depicted in a drawing by Winslow Homer.



FIGURE 4

William Fisher Norris, who became the Society's fifth president in 1885, had operated, mainly amputating limbs, for 36 consecutive hours at Gettysburg.

In 1864, Norris and the other army surgeons were “regular” or orthodox physicians, but medicine was still in an early stage, and the harsh treatments employed, involving bleeding, sweating, blistering, vomiting, laxatives, and diuretics, were not effective against the epidemics and contagious diseases of the time.⁵ The Jacksonian concept of “every man his own doctor” was prevalent. Indeed, more money was spent advertising patent medicines than advertising any other item, and eye remedies of the patent medicine variety were numerous among these.⁶ Outright quacks were also abundant. Alternative or irregular medicine boomed with proponents advocating homeopathy, chiropractic, osteopathy, wild herbs, botanics, electrotherapy, cold baths, hypnotism, and more (Figure 5).

Formal medical education was limited to those practicing regular medicine (Figure 6). Many of these physicians never attended medical school, studying instead for 3 years as apprentices under practicing physicians. Those who did receive a formal medical education in the United States suffered from medical schools' low educational standards and the lack of clinical facilities, anatomical specimens, or medical libraries.⁶ The few who could afford it trained in the far superior schools and hospitals in Europe.⁷ 1864 saw the growing professionalization of medical practice and the emergence of specialties and establishment of specialty hospitals in obstetrics, pediatrics, orthopedics, and neurology.⁶ Recognition of ophthalmology as a specialty in the United States, however, met with strong resistance for two major reasons^{8(p68)}:

1. The general surgeons refused to relinquish the practice of ophthalmology as part of general surgery.
2. The ranks of “oculists” in the United States contained many incompetent practitioners and quacks.

With the introduction of Helmholtz's ophthalmoscope a decade earlier, views toward ophthalmology in the United States began to change. The degree of training, patience, and skill required to master the effective use of the early preelectric ophthalmoscope, reflecting the light of a candle or gas lamp, exceeded the ability of most practicing physicians. At the same time, cataract extraction supplanted couching as the operation of choice for cataracts and called for a degree of knowledge and skill that general surgery training did not provide. This, then, was the setting in January 1864, when the founders of the AOS decided to form a special ophthalmological society. Their major challenge was the limited number of well-trained, competent ophthalmologists. As it was, the AOS had only 19 members at its onset.

Importantly, as Wheeler^{9(p27)} and Newell^{10(p64,65)} point out, the constitution, minutes, and bylaws of the Society from its initial meeting clearly show that the purpose—the Society's mission—was to establish a body of practitioners whose main concern was the welfare of the patient (Figure 7). This concern expressed itself in a series of amendments to the bylaws (and subsequent actions the Society took) “to ensure that the members of the Society met the highest standards of medical practice.”^{10(p407)} This constituted a “golden thread” that has continued to exist through the Society's 150 years.

The members who took a leading role in organizing the Society had much in common. They all were young (average age, 29 years); all had studied in Europe, where ophthalmology had been an accepted surgical specialty for nearly a century, and had been inspired by what they had seen and heard abroad; and most had limited their practice to the eye, the eye and ear, or “double ENT” (EENT).

During its first 50 years, the Society was dominated by three leaders: Edward Delafield, the first President; Henry Noyes, the first recording secretary; and John Green, Chair of the Society's membership committee.^{10(p47-56)} I will highlight Delafield's career:

Edward Delafield was the most senior, respected, and influential of the Society's founders (Figure 8). At age 70, he was still in active practice. Together with his schoolmate John Kearney Rodgers, he had founded the New York Eye and Ear Infirmary. He accepted the presidency of the AOS in 1864, and during his 4 years in office, he played an active role in the management of the Society. Through his leadership, and because he was also a highly regarded general surgeon, he did much to establish ophthalmology as an accepted, independent branch of medicine.



FIGURE 5

An over-the-counter eye remedy popular in the mid-to late 19th century.



FIGURE 6

The medical school of the University of Pennsylvania—the first American medical school to provide formal medical education to those practicing “regular” medicine.

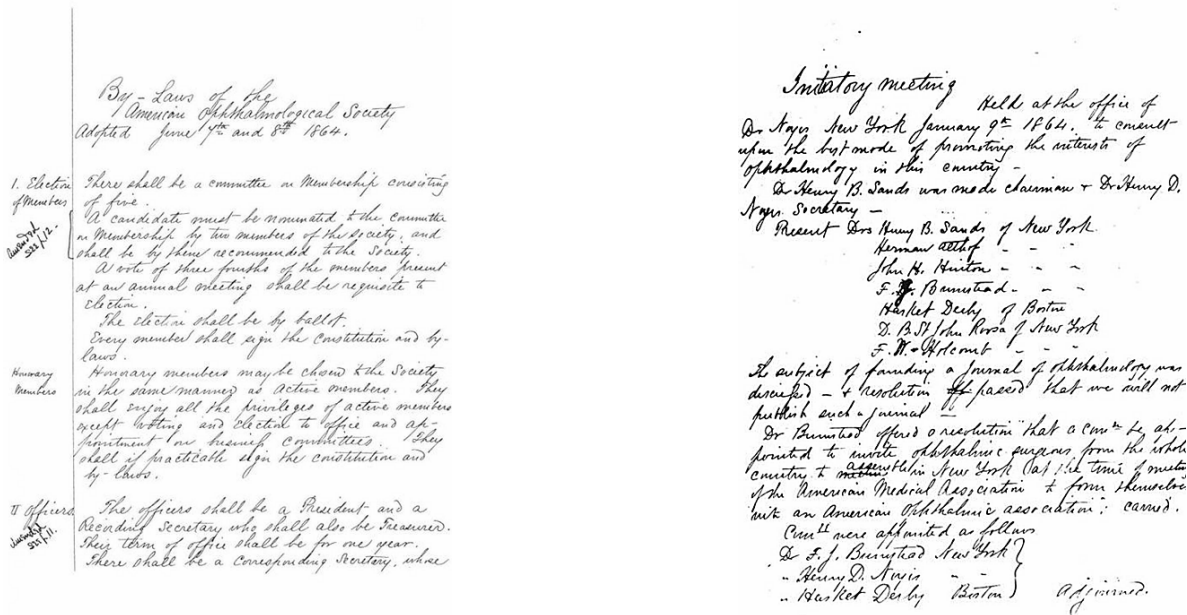


FIGURE 7

The constitution, minutes, and bylaws of the American Ophthalmological Society from its initial meeting clearly show that the purpose—the Society's mission—was to establish a body of practitioners whose main concern was the welfare of the patient.

The impact of the AOS on the development of ophthalmology and on effectively treating eye disease was profound. Ophthalmologists were sent consults by general doctors for an expert fundus examination. In addition, Lister's antisepsis and sterile operating room technique was gradually adopted in ophthalmology and resulted in a marked decline in infection following ocular surgery. Ether and chloroform general anesthesia were found unsuitable for intraocular surgery. With the introduction of cocaine

topical anesthesia by Carl Koller in 1884¹¹ (AOS member 1889-1944, and the AOS's first Howe medalist, 1922), painless ocular surgery became a reality (Figure 9). The surgical armamentarium of the ophthalmologist now included cataract extraction, strabismus procedures, trephining for glaucoma, iridectomy, and creation of an artificial pupil.

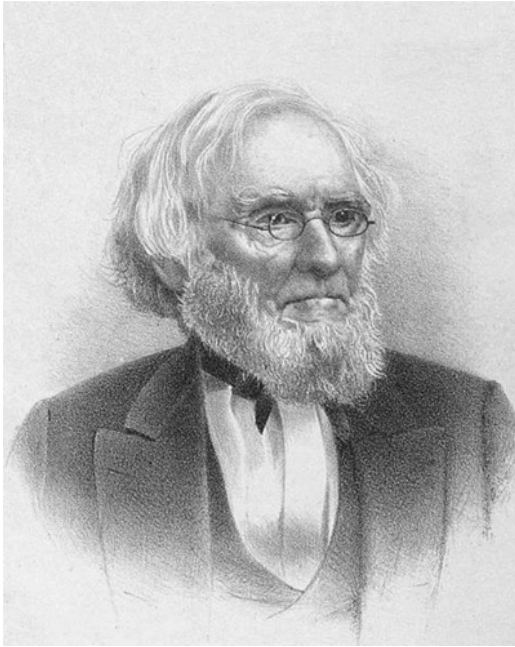


FIGURE 8

Edward Delafield was the most senior, respected, and influential of the Society's founders.



FIGURE 9

Carl Koller (AOS member 1889-1944, and the AOS's first Howe medalist, 1922) made painless ocular surgery a reality with his introduction of cocaine topical anesthesia in 1884.

1914: THE AOS AT 50

Again the nation was preoccupied with war. In August 1914, German troops invaded neutral Belgium, and Britain declared war on Germany for this violation of Belgian neutrality. President Wilson proclaimed US neutrality. Public opinion until early 1917 strongly favored the United States staying out of the war.¹²

In 1914, and in the 4 years preceding it, medicine was making startling advances. Allopathic (orthodox or regular) medicine represented by the American Medical Association (AMA) had triumphed over its competitors. The 1910 Flexner report¹³ for the Carnegie Foundation revealed that many American medical schools—including all of the proprietary ones—were unsatisfactory. Medical education in the United States was undergoing reform, with the new Johns Hopkins Medical School setting the “gold standard,” and the quality was dramatically improving.

By 1914, the introduction of the “germ theory” and the work of Pasteur and Koch had brought understanding to the treatment of the external infectious diseases, and the concept of bactericidal agents was introduced for the eye and other organs. Microbiology continued to lead the basic sciences in its contributions to medical science. A profusion of new infectious agents and diseases were discovered— including diphtheria and the rickettsial diseases. The antibacterial agent Salvarsan was heralded as a hopeful cure for syphilis.¹⁴ Peyton Rous discovered that tumors could be induced by viruses.¹⁵ The *Journal of the American Medical Association* (JAMA) in 1912 reported the first proven diagnosis of death by myocardial infarction, and pathologists were explaining how “hardening of the arteries” affected the heart and the fatty nature of atheromatous plaques.¹⁶

By 1914, the AOS had grown from its original 19 members to an organization of 165 members. The AMA, founded in 1847, had established a Section on Ophthalmology, Otology and Laryngology (1878) with Herman Knapp as chairman. The American Academy of Ophthalmology and Otolaryngology had been organized in 1869. American ophthalmology had matured sufficiently to successfully host the Fifth International Congress of Ophthalmology in New York City in 1896, with AOS members playing a major role. Of the 165 members in 1914, the names of more than half are still recognizable 100 years later for their contributions. These include Alexander Duane, Harry Friedenwald, Lucien Howe, Edward Jackson, B. Joy Jeffries, Arnold Knapp, Carl Koller, George de Schweinitz, Frederick Verhoeff, and William Holland Wilmer (Figure 10).

The practice of ophthalmology had progressed since 1864 and included tonography, slit-lamp examination, perimetry, the electric ophthalmoscope, and the fundus camera.

Two founding members were still active: William H. Carmalt of New Haven, who remained active in the Society for 65 years until

his death at age 90 in 1929 (Figure 11), and B. Joy Jeffries of Boston, son of one of the founders of the Massachusetts Eye and Ear Infirmary (Figure 12). Jeffries combined the specialties of ophthalmology and dermatology in his practice. 1929 also saw the induction of the first female ophthalmologist into the society: Maud Carvill of Boston, who was on the staff of the Massachusetts Eye and Ear Infirmary and the faculty of Tufts Medical School.^{9(p35)}

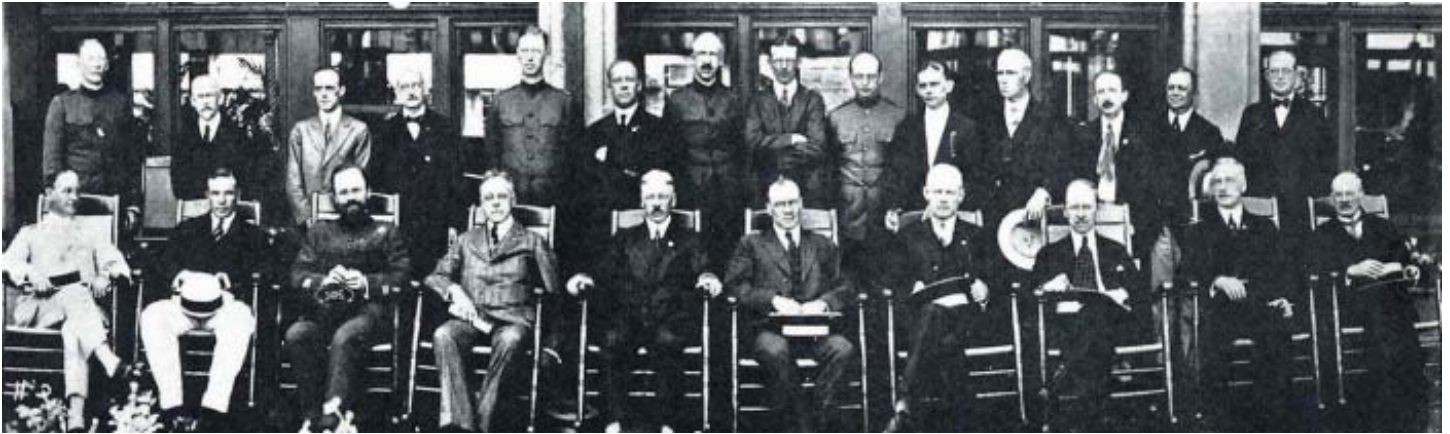


FIGURE 10

The AOS members in 1914. These included Alexander Duane, Harry Friedenwald, Lucien Howe, Edward Jackson, B. Joy Jeffries, Arnold Knapp, Carl Koller, George de Schweinitz, Frederick Verhoeff, and William Holland Wilmer.

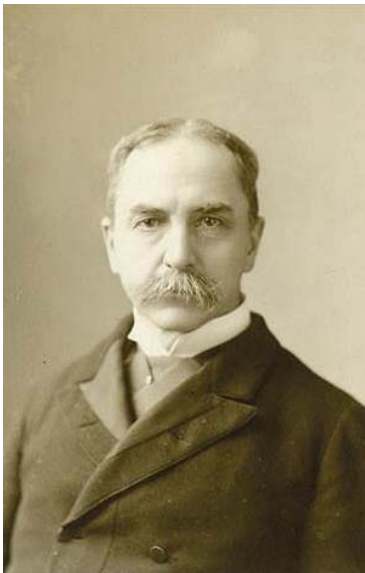


FIGURE 11

William H. Carmalt, of New Haven, Connecticut, who remained active in the Society for 65 years until his death at age 90 in 1929.

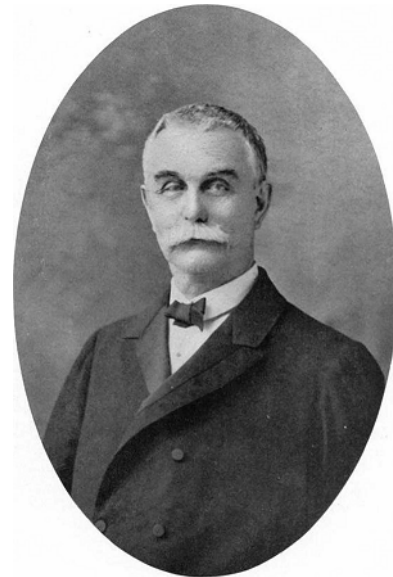


FIGURE 12

AOS founding member, B. Joy Jeffries of Boston, the son of one of the founders of the Massachusetts Eye and Ear Infirmary.

The most celebrated and influential of this august group was George Edmund de Schweinitz (Figure 13), and he would play a key role in the final act that established ophthalmology as a legitimate and respected medical specialty in the United States—the establishment of the American Board of Ophthalmology.^{9(p74)} He was able to accomplish this largely because of the esteem in which he was held. This is typified by the following quotation from Frederick Verhoeff, an ophthalmologist generally sparing in his praise of others. Verhoeff wrote: “de Schweinitz was lavishly endowed both physically and mentally. He had an imposing, yet charming, personality and was the handsomest ophthalmologist I have ever known. He was the most fluent speaker I have ever heard and at the same time one of the clearest.”¹⁷

De Schweinitz, in 1914, was Chair of Ophthalmology at the University of Pennsylvania. De Schweinitz, who was a Brigadier General in the army reserves and ophthalmologist to Woodrow Wilson, had responsibility for ensuring that when the United States entered WWI, our troops would have quality ophthalmic care, and he realized that a major problem existed. There were three paths that led to a career in ophthalmology. As was the case in earlier years, those who could afford it took their graduate training in Europe, particularly Berlin and Vienna, and to a lesser extent Paris and London. The path that most young medical graduates followed was to preceptorships with established US ophthalmologists, working as their assistants, and serving in indigent eye clinics of major hospitals. De Schweinitz himself had spent 10 years in such a role.

Beginning in the 1870s, a third pathway to a career in ophthalmology became popular. Major medical centers in New York, Philadelphia, Chicago, and other large cities established graduate hospitals, or “polyclinics,” where medical graduates could receive instruction in one or more of the specialties they had not been taught while medical students, and which they now desired to include in their practice. Courses were usually 6 weeks in duration. Increasingly, worn-out general practitioners enrolled in these short courses for the purpose of becoming a specialist in diseases of the eye. Their training, needless to say, was badly deficient.

De Schweinitz’s close colleague, Edward Jackson (Figure 14), summed up the situation as follows: “Today there are more than 2000 specialists in eye, ear, nose and throat within the borders of our country. Sending medical graduates out to adopt what line of practice they please, and qualify themselves for it as best they can is disastrous. There is great and pressing need that stable, conservative institutions of learning should offer formal [training] fitting their graduates for ophthalmic practice.”^{8(p334)}



FIGURE 13

George Edmund de Schweinitz, the 20th president of the AOS.

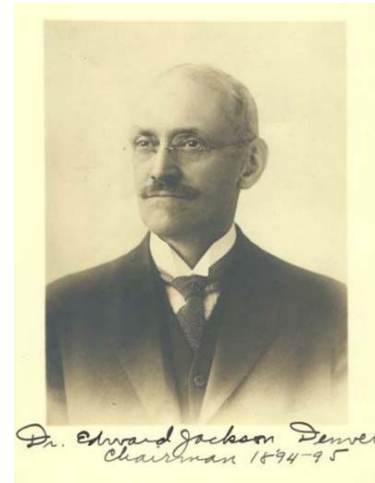


FIGURE 14

Edward Jackson, who with others established the American Board of Ophthalmology.

Initially, de Schweinitz, Jackson, and others worked through the AOS to promote a Doctor of Ophthalmology graduate degree that would ensure adequate training.^{10(p149)} Finally, in 1914, a combined committee representing the AOS, the AMA, and the American Academy of Ophthalmology set to work, under the leadership of de Schweinitz and Jackson, to determine the training required for competent ophthalmic practice. This culminated, in 1915, in the formation of the American Board of Ophthalmic Examination, the first of the medical specialty examining boards, and the first examination was held in Memphis in 1916.

When the United States became a combatant in the war in April 1917, more than 50% of the ophthalmologists entering the military service were found unqualified to practice their specialty.¹⁸ De Schweinitz helped to establish the Army School of Ophthalmology at Fort Oglethorpe, Georgia, where ophthalmologists were given additional training. De Schweinitz, himself, spent the war years in the European theater treating eye injuries among the 4,000,000 American troops, 110,000 of whom were killed.

World War I changed ophthalmology, changed America, and changed the world. After the carnage of the war, Hemingway wrote that abstract words like “honor,” “glory,” and “courage” often seem obscene and pretentious.¹⁹

1964: THE HUNDREDTH ANNIVERSARY

In 1964, the United States was still numbed by and preoccupied with the assassination of John F. Kennedy the previous November. Shortly before midnight on August 4, 1964, President Lyndon Johnson made a speech by radio in which he described an attack by North Vietnamese vessels on two US Navy warships in international waters in the Gulf of Tonkin. Congress promptly passed the Gulf of Tonkin resolution. The number of American military personnel in Vietnam increased dramatically from 16,000 advisors/soldiers to 550,000 combat troops. As US casualties soared and the war showed no signs of ending, all levels of American society were affected and the social fabric itself began to fray—as had occurred with the Civil War a century before.

Physicians entering medical practice by the late 1950s and early 1960s were told by their older colleagues that it was the “golden age” of medicine. J.J. Marr, a retired Hopkins academic physician, recalls the days as follows: “The physician was priest and seer; his opinions were respected, given great credence, and sought in areas outside of medicine. He was a scholar in the broad, liberal arts

sense of the term. He was the alchemist who understood science, and he knew the workings of the human body and psyche as well. He was a shaman at the end of the age of shamans. It was like that.”²⁰

As Dr Marr describes, doctors were almost totally responsible for the management and delivery of health care, but there was an awareness that care was unevenly distributed and closely related to the ability to pay. Doctors practiced singly or in small groups, and medicine was a stable “cottage industry” with little incentive to change. Although the medical staff had authority to run the hospitals, they believed they should stick to patient care and hired accountants and “business types” for the actual management and administration. Computers were still an interesting novelty in medicine.²⁰

The threat of Medicare and Medicaid in the 1960s caused great concern in organized medicine because it raised the specter of government intrusion into medicine with consequent socialized medicine. When Medicare and Medicaid became law in 1965, the initial outrage was replaced with acceptance as doctors realized that the medical care they had been providing gratis would now be reimbursed by the government.²⁰

The AOS in 1964 had grown to 215 members (Figure 15). Many members were veterans of World War II who, like most other veterans, dedicated themselves to work and self-discipline. They had a basic faith in large organizations—big armies, corporations, and professional societies where they could enjoy the warming embrace of solidarity and companionship.²¹ The Society now had five women members, including Dame Ida Mann, the first Professor of Ophthalmology at Oxford and subsequently a brilliant researcher in Australia studying the relation of culture, race, and climate to eye disease (Figure 16). She was made an honorary member in 1945 and received the Howe Medal in 1958. Georgianna Dvorak Theobald, distinguished pathologist to the Illinois Eye and Ear Infirmary for 30 years, was an AOS member from 1934 until her death in 1971 (Figure 17). She was awarded the Howe Medal in 1957. The Society had attracted a number of ophthalmologists who were physician-scientists, were outstanding clinicians, and possessed strong leadership ability. A number were the chairs of departments and the heads of eye hospitals, and prominent among them was its 66th president, Francis Heed Adler, an outstanding example of multitalented ophthalmologists of that era^{10(p230,231)} (Figure 18). In addition to his clinical career, Adler was a gifted scientist, teacher, musician, and scholar—eminent in each of these activities. Adler was one of the pioneers in initiating a modern ophthalmology residency program. He directed the American Board of Ophthalmology as its secretary-treasurer for 35 years, introducing modern standardized examinations. Adler remained active in the AOS from his induction in 1930 until his death at age 90 in 1987, his 57 years approaching the record of 65 years held by the founding member William Carmalt.



FIGURE 15

The AOS in 1964 had grown to 215 members.



FIGURE 16

Dame Ida Mann, the first Professor of Ophthalmology at Oxford and subsequently a brilliant researcher in Australia studying the relation of culture, race, and climate to eye disease. She was made an honorary member in 1945 and received the Howe Medal in 1958.



FIGURE 17

Georgianna Dvorak Theobold, distinguished pathologist to the Illinois Eye and Ear Infirmary for 30 years, was an AOS member from 1934 until her death in 1971. She was awarded the Howe Medal in 1957.



FIGURE 18

The AOS's 66th president, Francis Heed Adler, was an outstanding example of multitalented ophthalmologists of that era.

A number of advances in ophthalmic practice occurred in 1964, or in the 3 years immediately preceding. Retinal detachment surgery became increasingly effective. The surgical microscope and fine nylon sutures were introduced for intraocular surgery. Lasers were introduced, and fluorescein angiography burst upon the scene. Cryoextraction was employed in cataract extraction, and the Binkhorst 2-loop iridocapsular intraocular lens arrived from the Netherlands. The Goldmann perimeter became the standard for visual fields. Society members lent their names to various entities, including Hollenhorst plaques, Ascher aqueous veins, and Scheie syndrome.

And then there was the birthday party—the centenary celebration presided over by Maynard Wheeler (Figure 19) and featuring *The AOS: The First Hundred Years*, the magnificent history he had written for the occasion.⁹ Wheeler had served as secretary-treasurer of the Society from 1940 to 1960.

In 1989, at the 125th anniversary meeting, Frank Newell (Figure 20) contributed his 560-page book, *A Continuation of Wheeler's First Hundred Years*,¹⁰ in which he mentioned “the honors, positions, and contributions to medical literature of members between 1964 and 1989.” He dedicated the book to Wheeler “and all the others who served the Society as secretary-treasurer, editor (of the

Transactions), or both, without whom the Society would have no recorded history.”¹⁰

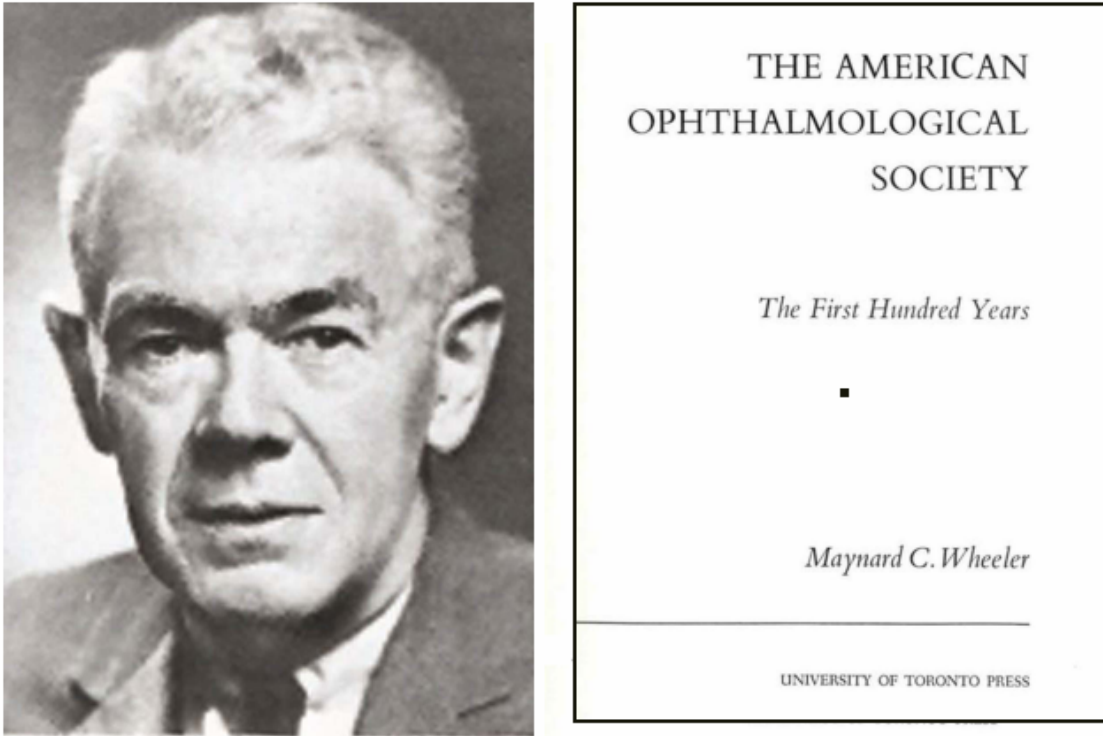


FIGURE 19

The centenary celebration was presided over by Maynard Wheeler and featured *The AOS: The First Hundred Years*.

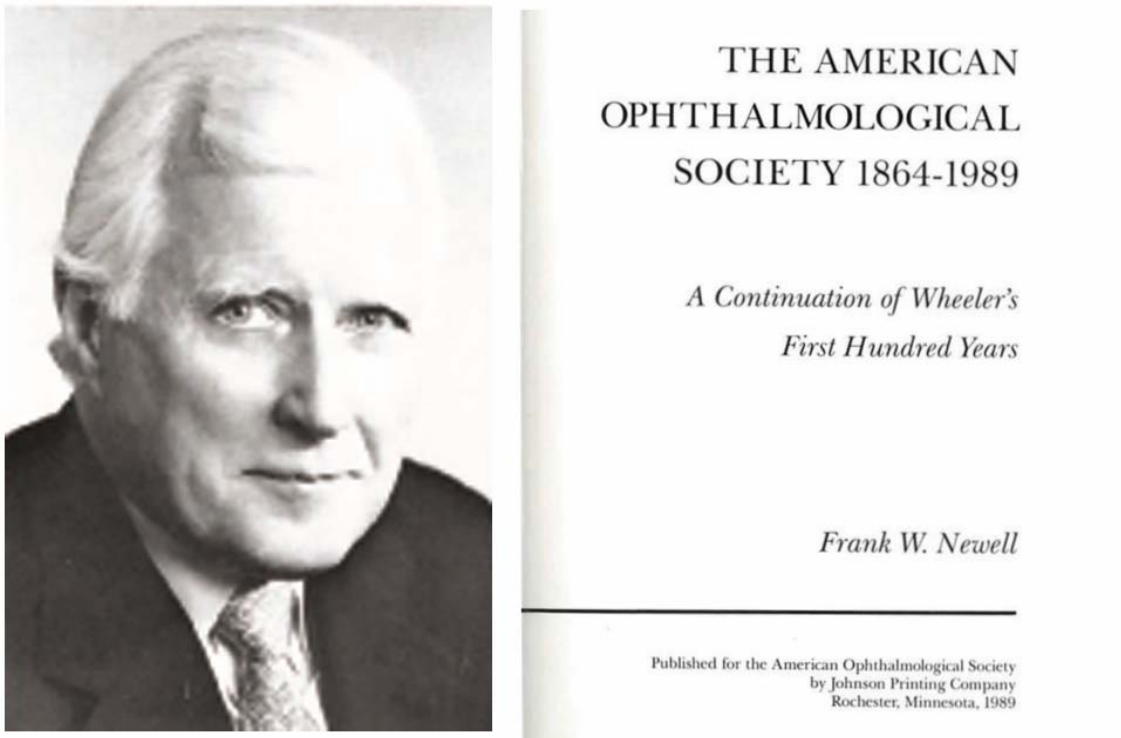


FIGURE 20

In 1989, at the 125th anniversary meeting, Frank Newell contributed his 560-page book, *A Continuation of Wheeler's First Hundred Years*.

2014: THE PRESENT

There is no need to discuss what is happening in the United States or the world in 2014; you've already read about it in your morning papers or online.

Presently, there are six living generations that compose the American population. Taking center stage is the "Millennium Generation"—those born between 1981 and 2000 (aged 14 to 33). The "Millennium Generation" (also known as "Generation Y" or "9/11 Generation")²² can be characterized as follows:

- Grew up in the digital environment, have digital literacy
- Do not "live to work" and desire relaxed work environment
- Prefer to work in teams
- Schedule everything
- Respect authority

From the 1970s on, a revolution in health care has occurred. On balance, it improved patient care and improved the efficiency with which health care is delivered. At the same time, it diluted the physician's role and altered the doctor-patient relationship.

Many forces—most interrelated—acted to cause this change:

- On a philosophical basis, good health care became viewed as an entitlement and not as a commodity purchased by the patient.
- Enormous progress was made in biotechnology, bioengineering, and drug development.
- The introduction of Medicare and Medicaid led to a massive increase in the demand for health care and a marked expansion in the medical care system.
- As the cost of health care soared, and DRGs and managed care were introduced, the focus of medical care shifted from patient care to patient care at the lowest possible cost to caregiver organizations and payers.
- A complex variety of providers arrayed in increasingly larger group practices appeared.
- The operational chain of physician, nurse, and patient was replaced at many levels by "physician extenders" of various sorts.
- Business management people became involved for the purpose of instituting efficient business practices, and quarterly earnings became an increasingly important factor.
- The Affordable Care Act appears to have gained general acceptance and will provide care to people who cannot now afford it.

What is the result of these changes? Doctors still play an important—even essential—role. However, this role has been diminished from being "doctors" in the traditional sense to "health care providers": skilled labor employees in an increasingly impersonal, mechanized health care delivery system.²⁰

The same factors that so profoundly revolutionized medical care during the past quarter century radically altered ophthalmology as well. There is indeed improved quality of eye care today delivered more efficiently than in previous years, but in quite a different form.

The AOS today consists of 361 members: 217 regular and 144 emeritus. The scientific and intellectual demands needed to stay current and monitored by Maintenance of Certification requirements are greater than ever. The AOS scientific sessions and symposia have remained an outstanding source of authoritative instruction during the past 25 years. Leading topics—based on citations following their publication—are listed here:

1. Retinal diseases, particularly macular degeneration, retinal dystrophies, and vascular disorders—their pathogenesis, diagnosis, and treatment
2. Ocular manifestations of HIV and its treatment
3. Ocular surface diseases, particularly dry eye
4. Visual disorders and their impact on quality of life

The cornucopia of information offered, of course, also includes glaucoma, pediatric ophthalmology, uveitis, neuro-ophthalmology, oncology, and ocular plastics.

The two individuals I would like to recognize as "representative" members during the past 25 years are ophthalmologists whose steadfast leadership as secretary-treasurer—now upgraded to the title executive vice president—have kept the AOS on course, abreast of the times, and still retaining its most important traditions: Charles "Pat" Wilkinson (Figure 21) and Thomas Liesegang (Figure 22).

Pat, a member since 1981, is Hopkins and Wilmer trained with a vitreoretinal fellowship at Bascom Palmer. He is Chair of the Greater Baltimore Medical Center and Professor of Ophthalmology at Johns Hopkins. He was secretary-treasurer of the AOS from 1999 to 2006 and its president in 2009 and 2010.

Tom Liesegang is a graduate of the NYU School of Medicine and had his postgraduate training at Duke, Bascom Palmer, and Baylor. Tom has been an AOS member since 1988, succeeded Pat as Secretary Treasurer in 2006, and was editor of the *Transactions* of the AOS from 2002 to 2006.



FIGURE 21

Pat Wilkinson, a member since 1981, was secretary-treasurer of the AOS from 1999 to 2006 and president in 2009 and 2010.



FIGURE 22

Tom Liesegang, an AOS member since 1988, succeeded Pat Wilkinson as secretary-treasurer in 2006 and was editor of the *Transactions of the AOS* from 2002 to 2006.

CONCLUSION

We take pride in the fact that the AOS is the oldest medical specialty society in the United States. We take greater pride in the fact that it continues to thrive and contribute significantly 150 years after its founding. I believe there are six major components to its success:

1. The AOS fills important needs for knowledge combined with collegiality and recreation.
2. The AOS attracts and selects major leaders and contributors to “Ophthalmic Science and Art.”
3. The AOS has represented in its ranks the entire world of ophthalmology, with all its divisions and diversity.
4. The AOS has changed with the times and tries to anticipate the cultural, ethical, and economic future.
5. The AOS has stayed true to its mission—its golden thread—to establish and maintain a body of ophthalmic practitioners whose main concern is the welfare of the patient.
6. The AOS does not have commercial ties.

What will the practice of ophthalmology be like 25 years from now? There will be an ever better level of scientific medicine. Evidence-based ophthalmology and telemedicine will be key components. Ophthalmologists will increasingly use genomics in treatment and in managing probabilities of disease. Regenerative medicine will provide new tissues for the eye. Ophthalmologists will utilize robotic surgery in their work. Society will be demanding that ophthalmologists—together with other physicians—do more, do it better, and likely do it with fewer resources.²⁰ And I expect the AOS will be there to support their efforts and benefit their patients.

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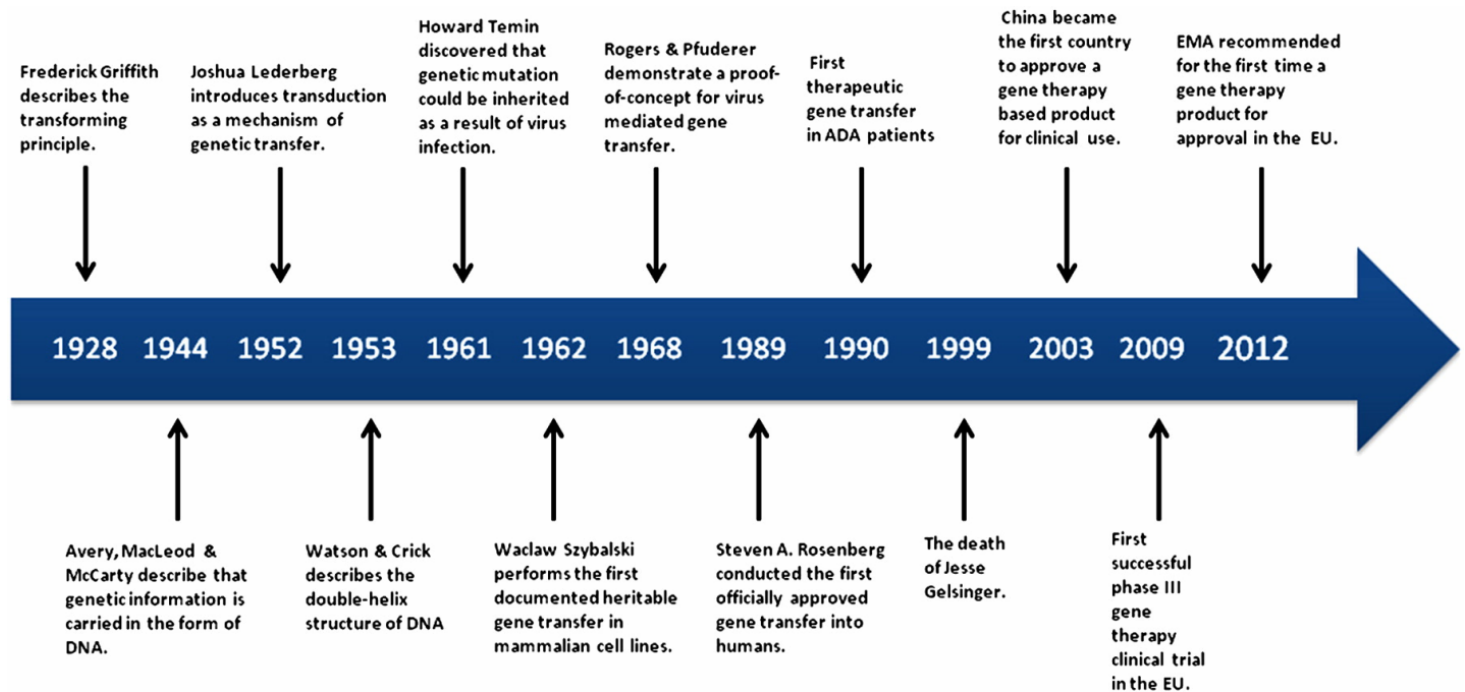
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THE ROCKY ROAD TO SUCCESSFUL HUMAN GENE THERAPY (2014 VERHOEFF LECTURE)

By Timothy Stout, MD

In 1972 Ted Friedmann, a pioneer in gene transfer research, made the following comment: “The ability to transfer DNA into diseased tissue will revolutionize medicine over the next decade.” Francis Crick, thirty years later said, “Gene therapy has nearly completely failed to live up to its promise.” So what happened?

All the basic building blocks were in place. At the close of World War II, Avery had described the fact that the “transformative chemical” was DNA. Watson and Crick accurately described the structure of DNA in 1953. Rogers demonstrated that you can use viruses to shuttle DNA from outside of a cell to inside of a cell and use it as a “transforming” agent. So “all” of the elements were there for moving DNA into cells – or so we believed. Why did it take another thirty years for the first gene therapy drug to be approved in the by the European Medicines Agency (EMA) of the European Union (EU)?



As is almost always the case in biomedical research, progress is slowed by some combination of biology, politics, hubris, money, and the control of expectations. How did these alter the progress of human gene therapy?

The first legitimate gene therapy trial was performed in 1975 in Germany. Investigator Dr. H Terheggen treated three siblings who had arginase deficiency, an inborn error in the urea cycle which leads to hyperammonemia. Rabbit data suggested that when rabbits were infected with the Shope virus, arginine levels in the blood decreased as arginase levels increased. This led to a clinical trial in which three siblings were intravenously infected with wild-type Shope virus. The results were conclusive - there was neither therapeutic benefit nor harm. It was later shown that the Shope virus did not actually contain the arginase gene, so perhaps the first lesson in the study of gene therapy is to make sure that you have the ability to deliver the right gene.

What was the outcome and reaction to this trial? Practically nothing. The authors wrote it up. They said it was a good idea, but it failed—no harm no foul—and that was the end to it. We should recall that gene therapy experimentation was in its infancy and was largely invisible to the general public. Recombinant DNA Advisory Committees were forming and Institutional Review Boards and Biosafety Committees were starting to notice, but it was a time when a negative experiment was largely a quiet event. This is the last time that there would be such a distance between public scrutiny and failed gene therapy experiments.

The first human recombinant DNA therapy experiment was performed in Los Angeles in 1990. Martin Klein, MD employed recombinant beta-globin DNA to treat patients with beta-thalassemia. He attempted to transduce bone marrow cells with naked DNA without a viral vector. DNA was incubated with the cells, and the cells were re-infused into the host patients. While this had little biologic effect, it had a resounding societal effect.

Klein’s study required approval of the newly formed Recombinant DNA Committee and an Institutional Review Board. There was confusion about regulatory jurisdiction and authorization requirements, so Dr Klein proceeded without authorization. The experiment neither helped nor hurt these patients, but Klein’s decision to disregard the regulatory bodies was newsworthy. The public’s response to this was rapid, robust, and negative. A presidential commission was formed and Klein was ultimately required to step down as chair and was forbidden from conducting research for the next three years.

A few years later, the first, what I’m going to call “successful”, human recombinant gene therapy experiment was performed at the NIH and involved treating patients with adenosine deaminase (ADA) deficiency. ADA deficiency results in an early-onset, severe, T-cell based immunodeficiency. Without treatment, death typically occurs within the first five years of life. Patients can be treated with an intravenously delivered recombinant ADA that has been complexed with polyethylene glycol (PEG-ADA). Michael Blaese, MD,

French Anderson, MD, and Kenneth Culver, MD isolated peripheral T cells from an ADA-deficient patient and transduced those terminally differentiated T cells *ex vivo* with a retrovirus that contained a normal ADA gene. The transduced T cells were re-infused into each patient. Since these T cells were already terminally differentiated, they had a lifespan of less than three months; as a result, the patient had to be periodically re-treated. Despite the need for retreatment, functioning copies of the ADA gene were present in this patient and the requirement for PEG-ADA was reduced. Two years later, these investigators modified the protocol to treat stem cells, rather than terminally differentiated T cells. This treatment proved efficacious. By 1995, the immune function in both patients was considered nearly restored, allowing them to enroll in school and live normal lives, despite a need for low-dose enzyme replacement therapy. Both children are still alive and are almost immune-competent - a remarkable success. Unfortunately, for a variety of reasons the product was not developed commercially.

The first fatal complication for gene therapy occurred a few years later. Ornithine transcarbamylase (OTC) is an urea cycle disorder with a spectrum of pathology. Some OTC deficient patients are remarkably sick with hyperammonemia within first few months of life and have a shortened lifespan. At the other end of the spectrum, there are patients whose hyperammonemia can be controlled with a low protein diet. Jesse Gelsinger was a patient who had partial OTC deficiency and was able to control his ammonia levels with a low-protein diet. In 1999, Jesse was dosed via hepatic artery with adenoviral vector containing the OTC gene. Four days later he developed a severe immune reaction and died from multiple organ failure. The outcome from this was quite negative. There were allegations of undisclosed financial conflicts of interest, misleading information on the recruiting website and a failure to disclose prior adverse events. The Food and Drug Administration (FDA) came down very hard in this situation: they suspended the study and a number of other studies; they held sanctions against the PI, the institution, the investigators, other investigators; legislation was introduced for a tighter oversight; and ultimately there was a financial settlement with the Gelsinger family. A black episode in the history of gene therapy.

The second fatal human recombinant gene therapy complication occurred during the treatment of X-linked severe combined immunodeficiency (X-SCID). X-SCID is caused by a mutation in the interleukin-2 receptor gamma chain gene. Two trials were set up in Europe, one in England and one in France, in which CD34+ cells were isolated from the bone marrow, were transduced *ex vivo* with a retrovirus that contained the receptor gamma chain gene, then those cells were put back into the patients. In 2002 and 2003, four patients in the French trial developed leukemia. These patients developed leukemia because of a process called insertional mutagenesis. When these retroviral vectors infected cells, the genetic information integrated into the recipient's cell host genome. The vast majority of the time, these vectors integrated into a benign genomic location. Vary rarely, they would integrate into a site proximal to an oncogene. Since the control elements in these viruses could "turn on" flanking DNA sequences, the rare, but consequential turning on of other genes (in this case the LMO and CCND oncogenes) gave these cells a growth advantage and led to unchecked cell division. These patients, because of insertional mutagenesis, developed leukemia; three were successfully treated; one patient died.

The adverse effects of this treatment prompted both the FDA and the European agencies to halt further trials with these vector types. The silver lining in this was that it prompted scientists to go back to the drawing board and come up with new vectors - now referred to as "self-inactivating" vectors. These vectors carry in the genetic information, integrate, but they are unable to turn on flanking genes. Unfortunately, because of the consequences of this trial and death, only recently has the concept of gene therapy for X-SCID been re-considered.

What about the eye? From a strategic perspective, a number of potential therapeutic scenarios come to the ophthalmologist's mind. First, you might replace missing or inadequate genes - especially in the case of autosomal recessive disease. Second, you might consider silencing disease causing genes - perhaps as a way of treating autosomal-dominant disease. You can target dividing cells for death - in the treatment of neoplastic or neovascular disease. In addition, one could consider gene therapy as a method to immunize against infectious disease, modulate the immune system, promote the growth of new tissue or prevent the death of at risk issue. These are all conceptual approaches through which the control of genetic information might be useful.

To a gene therapist, the eye presents a remarkably attractive organ to study the potential for gene therapy. First, we have remarkably easy access. We can literally see what is going on inside. We have exquisite noninvasive functional and anatomic testing. It's a relatively immune-privileged area and finally, it is a relatively small organ.

The first human ocular recombinant gene therapy experiment involved retinoblastoma. Investigators at Baylor College of Medicine in Houston, Texas, treated eight patients with retinoblastoma with vitreous seeds. These patients were destined for enucleation; but prior to enucleation, they were treated with an adenoviral vector that contained the herpes thymidine kinase gene. The herpes thymidine kinase gene allows for "suicide gene therapy". Cells that that express herpes thymidine kinase (HSVtk) are killed by ganciclovir. Usually, human cells do not express herpes thymidine kinase and so are resistant to ganciclovir. If one were to employ a vector able to transduce only dividing cells, you can introduce the HSVtk gene into those dividing cells, and subsequently expose all cells to ganciclovir. The cells that weren't transduced (the normal non-dividing retinal cells) will remain resistant, however those cells that were dividing rapidly (the dividing retinoblastoma cells), are killed by the ganciclovir.

The therapy was safe and elicited no adverse reactions aside from some low to moderate inflammation. There was clearly no tumor spread outside of the eye. At high doses, the vitreous seeds seemed to resolve. While this was deemed a success as an adjunct to current treatment; it was not thought to be a stand-alone treatment and no commercial partner was found to continue development.

The second gene therapy trial in the eye, championed by Peter Campochiaro, MD, involved age-related macular degeneration. Many years ago, pigment epithelial derived factor (PEDF) was noted to have anti-angiogenic and neuroprotective qualities. Preclinical evidence suggested that PEDF up-regulation blunted the development of retinal neovascularization in mice. A trial was designed to test the ability of a single intravitreal injection of an adenoviral vector, harboring the human PEDF gene, to decrease leakage as a

consequence of choroidal neovascularization in patients with AMD. The trial treated 28 patients. This phase one study was focused on safety and revealed no adverse reactions aside from low to moderate inflammation. Patients that received the high vector dose showed more improvement or stabilization than patients who received a low dose. At high doses, 93 percent of the eyes at three months and 71 percent of the eyes at six months had lesions that were stabilized or improved. Unfortunately, since adenoviral vector expression is time-limited, the effect was felt to be transient and, despite these encouraging results, the commercial partner shifted focus, and the project was not developed further.

What about gene-replacement therapy? The first gene therapy trial for a recessively inherited retinopathy involved Leber Congenital Amaurosis (LCA). LCA is an inherited retinal dystrophy caused by mutations in at least 13 different genes; 10 percent of people in United States with LCA carry mutations in their RPE65 genes. LCA presents as blindness of birth or a rapid loss of vision in the teenage years. Patients have a nondetectable electroretinogram despite a relatively preserved photoreceptor structure and an intact visual cortex. When Jean Bennett, MD, PhD and Al Maguire, MD started the original trial, there were no therapeutic options. They employed an adeno-associated virus which contained the human RPE65 gene. This is a non-replicating virus - a one-way shuttle system for delivering genes into cells. RPE65 is an isomerase able to convert all-trans retinal to all cis-retinal for use in the visual cycle. Without RPE65, all-trans retinal accumulates, and the cycle is aborted.

This trial introduced an adeno-associated vector containing the human RPE65 gene beneath the retina (into the subretinal space), to transduce retinal pigment epithelium and reestablish this cycle. Very elegant preclinical studies had shown this feasible in the Briard dog model. The first phase of this trial demonstrated the concept to be safe. All patients, between 8 and 44 years of age, showed sustained subjective and objective improvement. Often improvements were noted in studies of dark adaptometry, pupillometry, electroretinography, nystagmus, and ambulatory behavior. The greatest improvement was noted in children, all of which who gained ambulatory vision. The public response to this trial was swift, robust, and incredibly positive. This elicited tremendous interest by the legislature, the NIH, philanthropic foundations, the public, and, importantly, sources of commercial interest. It also increased the number of other diseases that could be targeted by this type of approach.

Our trial at Oregon Health & Science University (OHSU) involved the treatment of twelve LCA patients. We treated patients who were six years of age or older with two different doses. The vector was delivered following a vitrectomy which included a peeling of the posterior hyaloid. Following the vitrectomy, 450 microliters of virus-containing solution was injected into the subretinal space through a 41-gauge needle. We observed no drug-related adverse events. One of twelve patients lost vision; this was likely due to a friability and disruption of the RPE as the material was being injected into the subretinal space. There were no serologic abnormalities or inflammatory sequelae noted in any of these patients.

The first patient we treated had bilateral central scotomas preoperatively, and now three years later, has lost the central scotoma in her treated eye and retains the central scotoma in her untreated eye. This patients reports much improved ambulation. When we analyzed visual acuities for both the low-dose group as well as the high dose group, there was no improvement in the untreated eye, but there are a number of patients who had improvement in their visual acuity in the treated eyes. When we asked these patients or their parents, was their quality of life improved, the answer was usually yes. We believe our trial demonstrated safety and efficacy. We observed that the best acuity response was associated with the younger age, vision loss was associated with older patients in which the material was delivered beneath the fovea, and there was a trend towards improved visual function on quality of life assays.

The next ocular gene therapy trial involved Stargardt disease. Stargardt disease is a common form of inherited juvenile macular generation. It's generally autosomal recessive, and most people that have Stargardt disease have mutations of the ABCA4 gene.

Investigators at Columbia University demonstrated that lentiviral vectors, harboring the ABCA4 gene, were able to transduce photoreceptors in mice. Lentiviral vectors are RNA-based viruses. Since much of the wild-type viral genome can be excised and still result in a normally packaged virus, it is a vector with a large carrying capacity. The ABCA4 gene is a relatively large gene that would not fit into an adeno-associated vector - the lentiviral vector is perfect for the situation. These investigators were able to show that this vector was able to reverse the phenotype in ABCA4 knockout mice. Abnormal A2E levels are associated with Stargardt disease in humans, and in the knockout mouse, were normalized in treated mice. This evidence allowed the FDA to give the go-ahead to Oxford BioMedica for a Phase I/IIa dose escalation study of subretinally injected ABCA4 containing lentivirus in patients with Stargardt disease.

This trial involves a single administration of an ABCA4 lentiviral vector into the subretinal space of Stargardt disease patients. The trial commenced with a relatively low dose of drug in patients who are older and have poor vision. As no dose-limiting toxicities were observed, the trial proceeded to a higher dose of drug - again, in patients who have poor vision. If no dose-limiting toxicities are observed with this cohort, the trial will proceed to the highest dose. Should no toxicities be observed, the highest dose is determined to be the "maximum tolerated dose". At this time, younger, better-sighted patients are able to be enrolled. This is the first FDA-approved trial to treat patients with Stargardt disease. We've treated ten patients so far. Again, we've had no drug-related adverse events, no vision loss. We've seen no retinal tears, no serologic abnormalities or inflammatory sequelae, and efficacy data are being collected.

Recently, similar trials have commenced for Usher Syndrome. Usher Syndrome is form of retinitis pigmentosa and deafness. There are three types. The most common genotypic abnormality in Type 1 involves a defect in the MYO7A gene. These patients are deaf at birth. They suffer from early vestibular disease, and they begin to lose vision in their teen years. Investigators in California showed that a lentiviral vector containing the MYO7A gene could be used to treat the abnormal melanosome migration phenotype in MYO7A-deficient mice. These data convinced the FDA to permit Oxford BioMedica to go forward with a Phase I/IIa study looking at the safety and efficacy of a lentiviral vector containing MYO7A in patients with Usher syndrome. Same algorithm and mentioned earlier - poorly sighted older patients, low-dose, then medium dose, then high-dose, and if that proves safe then we will treat younger

patients who have preserved vision. This is the first trial approved by the FDA to treat Usher syndrome. So far six patients have been treated; again, no drug-related adverse events, the subretinal fluid all goes away, we've not seen any complications, and we're collecting efficacy data now.

We have reviewed gene therapy for autosomal recessive disease, but what about neovascular disease? Can you employ a viral vector, able to be expressed over a long period of time, and can deliver antiangiogenic genes to the retina? Will that result in a sustained antiangiogenic effect? To address these questions, we injected beneath the right retina in non-human primates, a lentivirus that contained either a marker gene or two antiangiogenic genes - endostatin and angiostatin. We then applied CNV-inducing laser to both eyes and quantitated the development of subretinal vascularization between the two eyes. Control animals exhibited no differences between the right and left eyes in terms of the proclivity for developing subretinal neovascularization. But in animals that received either 1X or 10X of an antiangiogenic vector, there was a remarkable inhibition of neovascularization in the right eye. This suggested that this approach was effective for treating the neovascularization, but was this effect sustained? We allowed these animals to rest for 10 months and then re-lasered them. Laser was performed in a foveolar-sparing fashion, so these animals remained well-sighted. As we applied new spots, our subsequent examinations quantitated the development of CNV at these spots only. It was clear the effect persisted – control animals evidenced no difference between the left eye and the right eye in terms of development of subretinal neovascularization. But there was a persistent long-lived effect in terms of the inhibition of the neovascularization in the right eye. As you may remember this was actually the basis of my AOS thesis six or seven years ago.

Vascular endothelial growth factor (VEGF) blockade for exudative AMD is effective, but it's cumbersome. We have a number of antiangiogenic genes that might provide therapeutic effect, and we've demonstrated the long-term inhibition of subretinal neovascularization is possible using a lentivirus. This proved to be the basis of the development of a drug called RetinoStat under clinical investigation now, again spearheaded by Peter Campochiaro, MD with Oxford BioMedica. There are other gene therapy trials for AMD underway. Trials being conducted by Genzyme and by Avalanche employ an adeno-associated virus harboring the sFLT gene which encodes a soluble form of the VEGF receptor.

To summarize, I believe the eye provides a unique opportunity to study gene transfer, the delivery systems are safe, long-term expression is possible and there are positive therapeutic effects. Our goal is new treatments for diseases that we've never been able to treat—Leber, Usher, Stargardt diseases—and sustained treatments for diseases that we have treatments for now, but those treatments are relatively cumbersome.

So what have we learned since the prophetic comment by Ted Friedmann about how medicine is going to be changed in ten years? First, biology is oftentimes more complicated than we expect. Vector design, how vectors work, how cells respond to transgenes and the vector, the consequences of expression – all of these are difficult to accurately predict. The process is iterative, educative and sometimes surprising; we should never underestimate our ignorance. Second, we should take the regulatory process seriously and be transparent with all of our trials. The third thing is that drug development does not happen without partners. We discussed number of examples today of gene therapy experiments that worked, but no commercial partner was found or developed and so a good idea died.

Thank you for the opportunity to discuss the past, present and a possible future for gene therapy at this, the 150th meeting of the American Ophthalmological Society. I think the future is indeed bright and I agree with Ted Friedmann...I think he just got the timing wrong.