Historical Perspectives on the Management of Macular Degeneration, Diabetic Retinopathy, and Retinal Detachment

Personal Reminiscences

Stuart L. Fine, MD,1 Morton F. Goldberg, MD,2 William Tasman, MD3

We were challenged and delighted when Dr. Sharon Solomon, guest editor of this Retina Supplement, invited us to reminisce about caring for patients with common retinal disorders before there was access to the diagnostic and therapeutic tools that are readily available today. We agreed to confine our remarks to 3 common, but serious, conditions: age-related macular degeneration (Dr. Fine), diabetic retinopathy (Dr. Goldberg), and retinal detachment (Dr. Tasman). Each of us completed our ophthalmology training about half a century ago. At that time, a patient who received any 1 of the 3 diagnoses was at considerable risk of severe and irreversible loss of vision. Most readers today will have little if any experience in evaluating and treating such patients without access to a plethora of diagnostic and therapeutic technologies, including intravenous fluorescein angiography, laser photocoagulation, optical coherence tomography, ophthalmic ultrasound, angioinhibitory drugs, vitrectomy, intraocular gases, and many others. We are both pleased and privileged that each of us has practiced our profession long enough to enjoy what the enormous technological developments of the past half century, as described in this article, have meant for our patients.


Age-Related Macular Degeneration: A 48-Year Perspective

Stuart L. Fine, MD

In March 1968, I received an offer letter for a residency in ophthalmology at the University of Florida in Gainesville. I accepted the offer promptly. (Obviously this notification occurred before the beginning of the ophthalmology match.) One week later, I received a letter from Dr. Raymond Sever, a junior attending on the Retina Service, describing the large volume of patients and wide variety of pathologic features seen in each and every retina clinic. “Every day, we see two or three patients with senile macular degeneration,” Sever wrote. Since I had not taken an ophthalmology elective in medical school, I had to look up “senile macular degeneration.” Thus, there was a name for the condition, but nothing could be done to ameliorate the problem. So Kuhnt-Junius or senile disciform macular degeneration was what we called it. Only 2 years earlier, in 1967, Gass had reported that fundus fluorescein angiography (FA) could document the presence of subretinal neovascularization as the immediate underlying cause of the exudative macular detachment. However, FA was not used routinely at that time to evaluate patients with exudative maculopathies. The most frequent indication for FA was in postoperative cataract patients; the purpose was to identify the presence of cystoid macular edema, or what then was called Irvine-Gass syndrome, as a possible explanation for impaired postoperative acuity. Photocoagulation had not yet entered the therapeutic armamentarium to treat leakage in patients with exudative maculopathy, the one exception being central serous chorioretinopathy with focal leakage outside the fovea when the submacular fluid had not resolved spontaneously by the end of 3 months.

For the patients with senile disciform macular degeneration, or what we now call neovascular age-related macular degeneration (AMD), we counseled the patient that no

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effective treatment was available, reassured the patient that the condition would not lead to complete loss of vision, and referred the patient whose second eye was involved for a low-vision consultation, which typically meant a prescription for magnifying glasses. When it was the first eye that was involved, we discussed the possibility of second eye involvement, but it would be nearly a decade before the measurable risk factors for second eye involvement would be quantified and reported.

By the time I arrived at Johns Hopkins for a medical retina fellowship with Arnall Patz, MD, just over 3 years later, in September 1972, the evaluation of patients with exudative maculopathy had changed immensely. During that 3-year interval, argon laser photocoagulators had become commercially available, facilitating the slit-lamp delivery of coherent laser light to tiny areas of focal leakage in the posterior pole. As a consequence, FA was performed routinely in patients with recent vision loss resulting from exudative maculopathy (and macular edema) in an effort to determine whether potentially treatable focal leakage was present.

As is common whenever new medical technology becomes available, many investigators began performing and evaluating the outcomes of laser photocoagulation in patients with SMD and other exudative maculopathies whenever the FA disclosed an area of focal leakage outside the fovea.10-12 (It would be several years before ophthalmologists abandoned the term senile in favor of AMD.) Laser courses in Baltimore, New York, and Palo Alto, California, were popular among retinal specialists and other ophthalmologists who wanted to learn about the indications for and the techniques of applying argon laser photocoagulation.

In addition to the paucity of information about treatment of AMD, there was astonishingly little information about its cause. After the Framingham Eye Study (FES) identified SMD (AMD) as the major cause of severe irreversible vision loss in the United States, interest developed in learning more about the condition. In 1978, Harold Kahn, a biostatistician who worked on the FES while at the Office of Biometry and Epidemiology at the National Eye Institute and who was a visiting faculty member at the Johns Hopkins School of Hygiene and Public Health (now the Johns Hopkins Bloomberg School of Public Health), suggested to Leslie Hyman, a PhD student, that she select the epidemiology of SMD as her thesis topic. Hyman’s case-control study identified a number of risk factors for the development of SMD, including older age, family history, cigarette smoking, hypertension, and reduced hand-grip strength.10,11 During that same interval, Neil and Susan Bressler, medical students working with me during an elective rotation, followed up on SMD patients with choroidal neovascularization (CNV) within the foveal avascular zone. They reported the natural history of these lesions and also described the ocular risk factors for the development of CNV in the fellow eye.12 When they presented their findings at a research forum for medical students, a presentation that resulted in their receiving the Paul Ehrlich Award for best clinical research by Johns Hopkins medical students, the Hopkins Chief of Medicine and world-renowned geneticist, Victor McKusick, expressed astonishment that so little was known about the most prevalent cause of severe vision loss in the United States and the developed world!

After the initial report from the Diabetic Retinopathy Study (DRS) in April 1976, there was widespread recognition throughout the ophthalmic community that the randomized clinical trial was the gold standard for evaluating new treatments for major public health problems. Indeed, this recognition was almost as important as the principal finding from the DRS that pan-retinal photocoagulation had reduced by more than 50% the frequency of severe vision loss in treated versus untreated eyes with high-risk proliferative diabetic retinopathy.13 Without question, publication of the DRS results facilitated the ophthalmic community’s acceptance of many trials that would be initiated over the next several years.

Inspired by the impact of results from the DRS, I collaborated with Argye Hillis, PhD, a biostatistician, to prepare 2 proposals to assess argon laser photocoagulation in patients with extrafoveal CNV secondary to either SMD or ocular histoplasmosis (Fig 2). Eventually, these 2 proposals were merged into a single study—the Macular Photocoagulation Study—although eligibility criteria and other aspects of the protocol differed for each substudy.

Funded by the National Eye Institute in 1979, 224 patients at 12 clinical centers enrolled in the SMD portion of the Macular Photocoagulation Study over the next 3 years. In 1982, the data and safety monitoring committee recommended stopping the trial early because, after only 6 months of follow up, 60% of untreated eyes compared with 25% of laser-treated eyes had demonstrated 6 lines or more of vision loss. This outcome was reported in an expedited publication and also at a nationally attended press conference at the National Institutes of Health.14 Unfortunately, this initial report about the benefit of argon laser treatment was to be disappointing for 2 reasons: (1) only a small proportion of SMD patients with exudative maculopathy had well-defined, extrafoveal CNV lesions and (2) there was a high

Figure 1. Fluorescein angiogram showing extrafoveal choroidal neovascularization in the left eye. Courtesy of Daniel F. Martin, MD.
rate of recurrent (and typically untreatable) subfoveal CNV after what initially had seemed to be successful obliteration of the new vessels (Fig 3). Nonetheless, from 1982 through 1999, when the first report of photodynamic therapy with verteporfin was published, laser photocoagulation remained the only treatment whose benefit, albeit temporary, had been established by means of a randomized clinical trial.15

Of more than casual interest is the following anecdote. In March 1982, I telephoned each of the 12 Macular Photocoagulation Study principal investigators to inform them that our data and safety monitoring committee had recommended stopping the trial early because of a significant difference in vision outcomes between laser-treated and untreated eyes. I then asked them to opine whether the difference was in favor of treatment or no treatment. Eleven of the 12 principal investigators, all highly respected retina specialists, opined that laser treatment probably was of no benefit. Does one need a more compelling example to document the benefit of a randomized clinical trial?!

Recognizing that AMD was a major public health problem and that existing treatment options were of limited benefit provided a substantial impetus for industry to invest resources into addressing the problem of neovascular AMD treatment. The discovery and purification of vascular endothelial growth factor (VEGF) were enormous advances and led to the development of the anti-VEGF drugs that now are used around the world for the benefit of AMD patients with neovascular maculopathy.16–19 Ongoing research undoubtedly will result in anti-VEGF drugs and other drugs that are equally or more effective than existing treatments and that will require less frequent interventions.

Remarkably, in the span of less than 50 years, my lifetime in ophthalmology, our profession has progressed from having nothing but counseling and low-vision aids for patients with vision-threatening neovascular maculopathy to having available a variety of highly effective pharmacologic interventions that not only stabilize, but often improve, visual acuity. And it will only get better!

Before closing, it’s worth noting that the late Professor Isaac C. Michaelson postulated in the 1940s that some factor, which he called “factor X,” must be elaborated by ischemic retina to stimulate the development of neovascularization in the retina and in the anterior segment as well.20 His disciples called it the “Michaelson factor.” It remained for Napolean Ferrara at Genentech to identify and purify the “Michaelson factor,” and the rest, as they say, is history.21

Innovations in Treating Diabetic Retinopathy over the Last 5 Decades: A Personal Perspective

Morton F. Goldberg, MD

Acquisition of new knowledge and development of innovative technologies periodically have punctuated the progress of therapies for diabetic retinopathy. My own observations of this evolution now extend for more than half a century. They include several pivotal events leading to dramatic improvements in visual outcomes for this previously misunderstood, initially untreatable, and increasingly prevalent cause of visual loss.

Somewhat fortuitously, I have been able to interact with several of the pioneers responsible for improving the status of diabetic retinopathy patients. My personally selected (and very incomplete) list of these discoveries and the responsible trailblazers include the following: the identification and mechanisms of the blood–retinal barrier (Jose Cunha-Vaz, Mark Tso22; Fig 4); the pathogenesis of the diabetic microaneurysm (David G. Cogan); the technique of fluorescein angiography and the identification in diabetic retinopathy of both nonperfusion and leakage (A.E. Maumenee et al); a standardized nomenclature, classification, and photographic technique for diabetic retinopathy (Stuart Fine, Matthew Davis, Airlie House Symposium participants, et al23; Fig 4);
Figure 4. Covers of 4 important books in the history of diabetic retinopathy and its treatment.22
retinal photocoagulation (Gerd Meyer-Schwickerath; Fig 4; Francis l’Esperance, Arnall Patz, et al); the methodologies of randomized clinical trials (Barbara Hawkins, Frederick Ferris, et al); surgical vitrectomy (Gholam Peyman, Robert Machemer, et al); so-called tight metabolic control (Frederick Ferris, Matthew Davis, et al); intravitreal injections (Gholam Peyman et al); anti-VEGFs (Isaac Michaelson; Fig 4; Lloyd Paul Aiello, Quan Nguyen, and the Diabetic Retinopathy Clinical Research Network, including Neil Bressler, Lee Jampol, et al); and optical coherence tomography (Carmen Puliafito, Gabriel Coscas, Richard Spaide, et al). Re
demments regarding many of these topics are continuing.

The following comments on 4 of the therapeutic innovations (photocoagulation, vitrectomy, metabolic control of diabetes, and anti-VEGFs) represent my admittedly biased memories of their origins. Limitations in space preclude detailed descriptions of the latter 2 subjects.

Photocoagulation. Therapeutic photocoagulation was invented by one man, Professor Gerd Meyer-Schwickerath, in Germany, and can be assigned to a specific day in history. Meyer-Schwickerath personally observed “a number of patients with macular damage following the eclipse of the sun on July 10, 1945.”24 He underwent an epiphany and realized that he could focus the sun’s rays (onto his patients’ retinas) on the roof of his eye clinic and thereupon achieve therapeutic coagulation of retinal holes and other fundus diseases. It was a fortunate stroke of serendipity, but, as Louis Pasteur famously said, “Chance favors the prepared mind.” Included among Meyer-Schwickerath’s patients were 5 with diabetic retinopathy, 1 of whom had microaneurysms and exudates. These abnormalities partially resolved after he was treated with photocoagulation.

When the English translation of Meyer-Schwickerath’s book (Fig 4)25 appeared in 1960, its effect on ophthalmology was like a meteorite exploding onto the earth, and the world of retinal diseases changed forever. If Meyer-Schwickerath had lived a few years longer, he almost certainly would have received a Nobel Prize, as his earth-shattering discovery eventually benefitted innumerable patients with a wide array of maladies, not just in ophthalmology, but also in dermatology, in the management of endoscopically treated diseases, and in others. Meyer-Schwickerath was an attractive, gracious, and chatty person, with no evidence of egocentricity despite the magnitude of his discovery. Years ago, I sat next to him for several pleasurable hours during a trip from Tokyo to Kyoto on the Shinkansen Bullet Train (Fig 5), and I still treasure the memory of our delightful conversation.

Shortly after Meyer-Schwickerath’s discovery, the Zeiss corporation (Carl Zeiss Meditec, Jena, Germany) manufactured a xenon arc photocoagulator for commercial distribution. I used this device frequently during residency and found it to be reliable and valuable. However, it was bulky and unwieldy (Fig 6), and it reminded me of a military jeep (It was ugly, but it always started!). This instrument used a pinhole direct ophthalmoscope as its delivery system and was very awkward in clinical practice (Fig 7). It emitted noncoherent and overly intense white light, and its excessive energy created wide and deep chorioretinal scars that were unsuitable for precise, modulated intramacular coagulations. It did not use a laser and eventually was supplanted by more clinically useful photocoagulators that did, including the newly invented ruby laser and, especially, the argon laser in the late 1960s. I found the 2 laser-based photocoagulators to be technically sophisticated and very useful.

The clinical adaptation of nonophthalmic engineering discoveries to therapeutically beneficial devices occurred remarkably quickly after the invention of, first, the microwave amplification by stimulated emission of radiation...
By 1967, when I finished my chief residency at the Wilmer Eye Institute, the available—but nonvalidated—therapies for diabetic retinopathy included the following: the xenon arc photocoagulator, several laser photocoagulators, improved (i.e., tighter) metabolic control, and amazingly, surgical hypophysectomy. There was no invavitrreal therapy of any kind. When asked by a recent medical school graduate named Stuart Fine, “What is the most effective treatment for diabetic retinopathy?” I had to admit that no one knew for sure. Even the distinctions between nonproliferative and proliferative retinopathy were not appreciated, and the natural history was largely unknown. Neither a standard nomenclature for describing fundus features nor a standard classification system existed. More than 1200 pituitary ablations and more than 1600 photocoagulations had been performed for diabetic retinopathy in the previous 10 years and were still being performed, but their relative benefits and complications were not known.

In 1967, by sheer coincidence, Stuart Fine and I had begun our 2 years of required military duty together in the United States Public Health Service, where we were assigned to the same office space. Stuart had not yet chosen ophthalmology for his career, but he was not pleased with the paucity of clinically useful information on diabetic retinopathy and determined to correct this deficiency. We therefore applied for, and received, an internal grant from the United States Public Health Service and convened an international meeting of more than 50 ophthalmologic, neurosurgical, and diabeticologic experts in 1968. The meeting was held at the Airlie House Conference Center in Warrenton, Virginia. It was an intense 3-day experience. All available knowledge was studied and evaluated by the attendees. We edited a book, The Airlie House Symposium on the Treatment of Diabetic Retinopathy (Fig. 4), with more than 900 pages filled with valuable information. Among many other items of advice, the performance of randomized controlled trials (RCTs) for treatment of diabetic retinopathy was recommended by the participants. These clinical studies would use the Airlie House symposium’s new system of nomenclature, its easily replicated method of fundus photography, and importantly, its standardized classification of diabetic retinopathy (the Airlie House classification, or modified versions thereof).

There was widespread acceptance of the terminology along with the photographic procedures and classification systems, making it possible for the first time to pool clinical data from several institutions. This resulted in collaboration of numerous investigators in different locations. Statistically valid sample sizes of patients then could be amassed. Despite understandable forebodings about coagulating normal portions of the retina via the panretinal photocoagulation technique, the Diabetic Retinopathy Study (DRS) of proliferative retinopathy was completed successfully. It was the first major randomized clinical trial in the history of ophthalmology, after a more limited trial for retinopathy of prematurity by Arvall Patz and colleagues. Armed with this successful undertaking, collaborating investigators then began and successfully completed the Early Treatment Diabetic Retinopathy Study of nonproliferative retinopathy. These 2 large clinical experiments paved the way for subsequent RCTs.

During my residency training in the mid 1960s, so little was known about the treatment of any form of diabetic retinopathy that my customary, though regretful, response to patients with this disease was, “I am really sorry, but there is no acceptable treatment.” That deplorable, depressing situation changed rapidly when the favorable results of panretinal photocoagulation were reported in 1976 by the DRS. Remarkably, the rate of severe visual loss was reduced by as much as 50% to 60%. Initially, so-called background or nonproliferative retinopathy (now termed diabetic macular edema) was not recognized as a major cause of visual morbidity, but in 1985, the Early Treatment Diabetic Retinopathy Study established the benefit of focal intramacular laser photocoagulation in this disease as well.

When the beneficial results of the DRS and Early Treatment Diabetic Retinopathy Study became known, hypophysectomy, with its induced panhypopituitarism and its devastating systemic side effects, was quickly abandoned.
Diabetic retinopathy.

Photocoagulation became the worldwide standard of treatment for both the proliferative and nonproliferative forms of diabetic retinopathy.

**Vitrectomy.** Despite appropriately performed pan-retinal or focal photocoagulation, some diabetic patients retained or went on to demonstrate visually disabling vitreous hemorrhage or tractional retinal detachment. Therefore, in the early 1970s, purposeful vitrectomy through the pars plana was contemplated as a new, but extremely radical and potentially dangerous, therapy. Heretofore, instrumentation of the vitreous was tantamount to surgical malpractice. Every textbook and every surgical preceptor said so. During cataract surgery, for example, loss of vitreous through the limbus was considered a catastrophe, and as soon as vitreous gel herniated outside the eyeball, further intravitreal manipulation typically was not recommended. Furthermore, 2 relatively common complications of diabetic retinopathy, intravitreal hemorrhages and tractional retinal detachments, were considered to be untreatable.

At that time, daring and revolutionary surgical approaches for vitrectomy through the pars plana were being developed for the first time, primarily by Gholam Peyman at the University of Illinois in Chicago, where I was Chair of the Department of Ophthalmology, and by Robert Machemer at the Bascom Palmer Eye Institute in Miami. They published their startling ideas independently and simultaneously in 1971.29,30 I had recruited Peyman to his first faculty appointment because of his unique experimental approaches to previously untreatable vitreoretinal diseases. He was one of the few surgical pioneers in the world who was brave enough and ingenious enough to invade the then terra incognita of the intravitreal space. The Chairman of the Bascom Palmer Institute, Edward W. D. Norton (Fig 5), told me that Machemer’s discoveries were so comprehensive and important that it would take him a lifetime to exploit them fully (he was correct!). Machemer often has been called the “father of vitrectomy” by his numerous, outstanding surgical trainees. Both Peyman and Machemer received their basic ophthalmic training in Europe and then saw their surgical dreams and innovations come to fruition in the facilitative environment of American academia.

Peyman was (and remains) a technical virtuoso in the operating room and an inventive genius in the laboratory. He holds a very large number of patents related to vitrectomy instruments, surgical microscopes, endolaser photocoagulation, intravitreal delivery techniques, and even LASIK. By developing the vitreous-related innovations, he and others destroyed the taboo that surgeons should not invade this part of the eye. Peyman also led the way for intravitreal injection of many drugs, physical agents, and biologics, such as antibiotics, steroids, silicon oils, gases, and anti-VEGFs. In 2012, President Obama awarded him the National Medal of Technology and Innovation during an impressive White House ceremony, which I had the honor of attending (Fig 8).

Initially, the surgical technology of pars plana vitrectomy lagged far behind its theoretical concepts. For example, in the early 1970s, our existing surgical microscopes were exclusively manual and clumsy, because there was no motorized capability for focusing, zooming, or x–y movements. Foot pedals were not widely available. Moreover, the initial pars plana vitrectomy instruments were fully functional and, therefore, rather large; that is, the single intravitreal instrument tip contained all of the hardware components that were needed in a vitrectomy procedure, such as suction, cutting, and infusion, and thereafter, intravitreal illumination, as well. It is not surprising, therefore, that initial results were sometimes suboptimal. In fact, they could be extremely distressing for both patients and physicians. Serious complications could and did occur. Many of my residents who had been psychologically shaken by such events, actually refused to assist in these early surgeries. After all, their textbooks and surgical preceptors advised avoidance of the vitreous altogether, and some of the initial results were intensely disappointing. A large group of these residents came to me en masse and insisted that pars plana vitrectomy was unethical, and therefore, they would not participate in the care of our patients (think of that!). Within about 6 months, however, through the dogged persistence and ingenuity of Peyman and many others, the instrumentation, techniques, and results improved so impressively that many of the same residents did an about face and asked me whether they could remain as vitrectomy fellows after completion of their residency training. By 1976, we published the results of our first 100 consecutive operations with the new vitrectomy procedure,31 and in that year also published our results in 125 eyes specifically affected with diabetic vitreous hemorrhage.32 In 1978, we reported 400 first-time vitrectomy procedures using Peyman’s Vitrophage, demonstrating that the benefits of visual improvement far outweighed the risks of the surgery.33 The revolution in intraocular, intravitreal microsurgery had begun in earnest.

To evaluate the pros and cons of pars plana vitrectomies in diabetic eyes more formally, a third major RCT, the...
Diabetic Retinopathy: Vitrectomy Study, was initiated throughout the country. Results were reported first in 1985 and again in 1990; they demonstrated vitrectomy’s usefulness in nonclearing vitreous hemorrhage, especially when performed relatively early in the eyes of patients with type 1 diabetes.34

Tight Metabolic Control. Whether tighter metabolic control could affect the development or course of diabetic retinopathy was debated at the Airlie House symposium. This issue was not resolved fully until results of a fourth RCT, the Diabetes Control and Complications Trial, were published between 1983 and 1993.35 It clearly showed that keeping blood glucose levels as close to normal as possible slowed the onset and progression of retinal (as well as renal and peripheral nerve) disease. Ophthalmologists are now mindful of these results when counseling their diabetic patients. Space constraints limit the description of this landmark trial with its important therapeutic implications, readers are referred to its important principal publication.35

Anti-Vascular Endothelial Growth Factor Pharmacologic Treatment. After profoundly successful use of anti-VEGFs in the treatment of neovascular AMD, similar intravitreal injections were evaluated in both diabetic macular edema and proliferative diabetic retinopathy. Aiello et al36 demonstrated that high concentrations of VEGFs were present in diabetic patients’ intraocular fluids, so perhaps it was not altogether surprising that RCTs by several groups, including the Diabetic Retinopathy Clinical Research Network, confirmed the benefit of anti-VEGFs for both macular edema and proliferative retinopathy.37 Again, limitations in space prevent a full description of these highly useful discoveries.37

Now, for the first time in the last half century, traditional laser photocoagulation is being supplanted in some carefully selected diabetic patients by these pharmacologic therapies.37 It remains to be seen whether this current trend will withstand the test of time. A recent publication38 of anti-VEGFs raises the possibility of increased risks for death and potentially for cerebrovascular accidents. This important and fascinating story is not yet finished.

Conclusions. The following instruments and techniques were not in widespread use or did not exist at all during my residency training from 1963 through 1967: motorized surgical microscopes, paras plana vitrectomy, intravitreal injections (with drugs, gases, and other agents), and the methodology of RCTs. If nothing else, this incomplete list underscores the necessity for lifelong learning and, in particular, continuing medical education. Personal participation in evolving technologies and RCTs also is extremely useful.

Almost 50 years after The Airlie House Symposium on the Treatment of Diabetic Retinopathy, was published, laser photocoagulation, surgical vitrectomy, improved metabolic control, and intravitreal administration of anti-VEGFs have been proven to have substantial value in treating diabetic retinopathy, an increasingly common, potentially blinding disease. These valuable advances occurred because of many courageous innovators, their brilliant discoveries (only a few of which could be described here), and importantly, the results of randomized, collaborative, controlled clinical trials. It is no longer common for a diabetic patient to be told that “there is no acceptable treatment for your retinopathy.” What extraordinary achievements these discoveries have been for diabetic patients and for the entire world of modern medicine!

History of Retinal Detachment: Diagnosis and Repair

William S. Tasman, MD

Blindness is something that everyone fears. Descriptions of vision loss have been around since the beginning of time and are even well documented in the Bible. Jesus is well known for healing the blind, as exemplified in Matthew 10:27–31. In the Old Testament, there are numerous accounts of individuals who lived long lives, with Methuselah holding the record at 969 years of age. Methuselah had a son, Lamech, who was blind. Also described in the Old Testament is Eli (1 Samuel 3:2), a priest for 40 years who began to lose his sight as he grew older. By age 98, he had trouble seeing, and when he died, Eli was blind.

It should not be surprising that it is approximately 100 times more likely that one can go blind after the age of 65 than at a younger age.40 Most commonly, the cause is cataract, but open-angle glaucoma, AMD, and diabetes also have to be considered. Missing from this list is retinal detachment, because this usually occurs in 1 eye; in a small number of cases the second eye is affected later.

Until 1851 with the development of the ophthalmoscope, there was no known way to view the ocular fundus adequately.41 Despite that, the great French ophthalmologist Mâitre-Jan42 noted a retinal detachment in a deceased cow’s eye, which also harbored a dislocated lens. Retinal detachment symptoms were described by de St. Ives in 1722.43 He reported a shadow in the visual field that corresponded to the area of detachment. In 1766, Morgagni44 noted a retinal detachment with retracted retina in a case of intraocular tumor. Other signs of retinal detachment were noted by Sichel45 in 1841 and Desmarres46 in 1847.

In 1704, Méry47 was involved in research that used cats. While drowning a cat during a research project, Méry noticed the cat’s pupils dilated, thus allowing him to see the fundus perfectly. Five years later, in 1709, that phenomenon was explained by de la Hire,48 who realized that the corneal refraction was neutralized by the flat surface of the water to allow a view of the fundus. With the advent of Helmholtz’s description of the direct ophthalmoscope in 1851 and Ruete’s description of the indirect ophthalmoscope in 1852, it became possible to examine the retina. Ophthalmologists began to learn about holes in the retina, starting with Coccius50 in 1853.

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With that background, let’s take a look at the history of retinal detachment before contemporary times. Factors such as age, gender, heredity, trauma, and myopia were noted to be associated with retinal detachment. Morax59 in 1913 attempted to drain subretinal fluid as described and illustrated in a textbook he wrote (Fig 9). In 1911, the Swedish ophthalmologist Gullstrand won the Nobel Prize
for medicine. Many think he received this prestigious award because of his development of the slit lamp, which also provided a view of the interior of the eye; however, he actually received the Nobel Prize for developing a mathematical model of the eye. It finally fell to Gonin to identify retinal breaks as the cause of retinal detachment. Gonin lived in Lausanne, Switzerland, and worked with Marc Dufour. Noëlle Chomé-Bercioux, a student who helped him review a large number of postmortem retinal detachment eyes, was indispensable. It was examination of those eyes that led to confirmation of retinal breaks as the cause of retinal detachment. This was to be reported by Gonin in 1929 at the World Congress of Ophthalmology in Amsterdam. His assistant, Chomé-Bercioux, actually gave the presentation at the meeting because Gonin was suffering from exhaustion.11–13 His book on retinal detachment, Le Décollement de la Rétine, was published in 1934 (Figs 10 and 11). In 2015, Albert et al54 wrote an article on Jules Gonin in Ophthalmology. In the article, they described how Gonin had worked in 1904 with Marc Dufour. The 2 had looked for tears in their reviews of retinal detachments and depended on a modified indirect ophthalmoscope to accomplish the task. By this time, pathologic features were more and more appreciated because of the revelations that were provided regarding the disease processes.

Schepens55 contribution of binocular indirect ophthalmoscopy, which he reported at the 1947 American Academy of Ophthalmology meeting, made finding retinal breaks easier. However, many senior staff members whose professional lives had been devoted to direct ophthalmoscopy had difficulties learning indirect ophthalmoscopy. I can remember being asked as a resident to take a Schweigert perimeter to the patient’s beside, where I was instructed to map out the meridians in which retinal breaks had been noted so that the surgeon could localize them more readily in the operating room. (You can imagine how well that worked!) These were often full-thickness scleral resections. As more time passed, scleral resections were adopted in the United States by Dr. Dohrmann Pischel in San Francisco and by Dr. Peter Kronfeld in Chicago. In the 1950s and 1960s, Schepens refined scleral buckling by performing lamellar scleral resections, a so-called trap door, with diathermy precisely placed in the scleral bed and most frequently a silicone rubber implant to go into the bed and an encircling silicone rubber band 360° around the globe.

The first significant scleral buckling procedure was performed by Ernst Custodis in 1949. He used an episcleral exoplant (i.e., polyviol), which was sutured to the sclera beneath the retinal breaks. Made by combining polyvinyl alcohol with Congo red, the exoplant was quite irritating to the sclera, but it nevertheless produced successful results in many patients. Custodis also advocated a nondrainage procedure, but this was not readily accepted in the United States. Some surgeons, such as Benjamin Steinert and Richard typed in Figure 10. Cover of Gonin’s book from 1934.
States, where drainage was common. Once again, Schepens and his colleagues led the way in developing scleral buckling procedures in the United States. This work began in 1951 and continued through the early to mid 1960s.

In 1967, Harvey Lincoff resurrected external buckles in conjunction with cryotherapy (and often nondrainage) of the detachment with considerable success. Clearly, Schepens and Lincoff had taken a major step forward; eyes operated on for retinal detachments no longer looked like a fried egg left in the frying pan too long, as had been the case with diathermy on the surface of the sclera.

As mentioned earlier, scleral resections were attempted first in 1903, but cures nonetheless remained rare. A survey conducted in 1912 by Dr. Derrick Vail Sr. queried ophthalmologists in the United States about the number of successful operations they had performed. Of 281 ophthalmologists who responded to the survey, only 20 successfully treated cases were documented adequately; from this information, Vail extrapolated that the incidence of successful treatment was approximately 1 in 1000 cases. However, Gonin’s series had a 53% cure rate. Today, vitrectomy, with adjuvants such as sulfur hexafluoride, fluorocarbon liquids, and even silicone....

**Figure 11.** One of 38 plates in Gonin’s book showing (top) preoperative and (bottom) postoperative retinal repair. Most of the figures were executed by Gonin.
oil, has led to successful results more than 90% of the time. Sulfur hexafluoride was introduced in retinal detachment repair by Ed Norton in 1973. The perfluorocarbon liquids were introduced by Stanley Chang. Silicone oil was introduced by John Scott in England. Pneumoretinopexy was introduced in retinal detachment repair by the late George Hilton, Paul Tomambe, and Sandy Grizzard. Although this article covers the history of retinal detachment repair before the mid-twentieth century, acknowledgement should be made of Machemer et al’s revolutionary development of vitrectomy.

One other person who should be mentioned is Paul Cibis. During World War II, he survived 2 years on the Russian front and afterward came to the United States, where he practiced in St. Louis. He was one of the best and most creative surgeons I have seen, and I firmly believe if he had not died prematurely of a heart attack at age 54, he might have been the first one to get into the vitreous. At the time of his death, he had already developed forceps that could be frozen to membranes to help in their removal.

One thing not yet discussed was care of the patient before and after surgery. Bedrest, with both eyes patched, to see whether the retina would settle down was used frequently. However, there were those who thought the retina had a better chance to settle if, for example, they told the patient with a temporal detachment in the left eye to lie on the right side. Perhaps they believed that the subretinal fluid would exit through the breaks into the vitreous cavity. However, most instructed the patient to lie on the same side as the retinal breaks, so bed rest before surgery was used sometimes for 2 to 3 days before surgery. Today, of course, retinal detachment has moved from 1 to 2 weeks in the hospital to, for most patients, outpatient surgery.

In preparing this article, I have had some speculative thoughts about well-known people who might have had detached retinas before modern techniques were available. One of these was the twenty-sixth President of the United States, Theodore Roosevelt, who was highly myopic and as an adult would engage in strenuous physical activity and exercise, including boxing. On one occasion in 1904 while boxing with an aide, Captain Daniel Moore, Roosevelt was struck in the left eye. He described seeing spots and never told Moore that the blow had caused any problem. As a matter of fact, there were only a very few people who knew Roosevelt’s eye had been injured. One of these was Dr. William Holland Wilmer, who at the time was practicing in Washington, DC, and who had examined Roosevelt. In an unpublished biography of Wilmer, the author, Donald Bartlett, said that Wilmer noted that Roosevelt’s retina was not detached in the left eye but that there was hemorrhage present. As if that were not enough, there was an assassination attempt in 1912 in Milwaukee where Roosevelt, who was dissatisfied with William Howard Taft, was campaigning. A 38-caliber bullet from an assassin’s gun was blunted by Roosevelt’s eye glasses case and a copy of his speech, which were in his coat pocket. The bullet lodged in the fourth rib but penetrated no vital organs, so Roosevelt went on and delivered his speech (Fig 12). Fast forward to
1918, when Wilmer was going overseas during World War I. He stopped by Oyster Bay to see the former President. Wilmer could see that there was a mature cataract in Roosevelt’s left eye, but we certainly do not know whether he had a detached retina in that eye.

One of Roosevelt’s great nieces, Virginia Roosevelt Armentrout (now deceased), was a good friend of my wife, Alice Lea, and she and her husband lived near us. We saw them frequently. One night during dinner at their house, Virginia, who bred dogs, said that she had sold one of them to a family who accused her of selling a blind dog. The dog previously had been hit by a car. My reaction was to say, “Virginia, dogs get hit by cars all the time,” but I made the mistake of asking what kind of dogs she was breeding. “Collies,” she answered. At that point I told her that collies can get detached retinas. Virginia asked me to examine her dogs, and interestingly enough, there was one who had a detachment of the retina. So, the bottom line is that although we don’t know whether Teddy Roosevelt had a detached retina in his left eye, we have confirmed retinal detachment in the canine side of the family (Figs 13 and 14).

Conclusions

We three authors, having participated in retinal diagnosis and treatment over the past half century, are enormously impressed with the technological advances that have resulted in better outcomes for our patients with AMD, diabetic retinopathy, and retinal detachment. For many of these advances, RCTs documented the benefits beyond any doubt.

Is it possible that we can do better? Will the next decade bring about greater advances that will lead to even better outcomes for our patients? Lest anyone think that we are approaching an asymptote with respect to technological breakthroughs, we invite you to consider that a mere decade ago, the following did not exist: Netflix, Twitter, Instagram, the Tea Party, ISIL, smart phones, Facebook, Snapchat, live streaming, crowd funding, and many others. Have these developments changed our lives? One needs little imagination to conclude that the next decade is likely to witness substantial improvements in diagnosis and treatment for the conditions discussed in this article and for many others as well. How fortunate are we, the authors; our readers, who are our colleagues; and our patients to be participants in the unrelenting, beneficial advance of science and medicine!

References


Footnotes and Financial Disclosures

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Abbreviations and Acronyms:
CNV = choroidal neovascularization; DRS = Diabetic Retinopathy Study; FA = fluorescein angiography; RCT = randomized controlled trial; SMD = senile macular degeneration; VEGF = vascular endothelial growth factor.

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