II. Jonas S. Friedenwald, Man of Science

Arnall Patz

Jonas Stein Friedenwald was born in Baltimore on June 1, 1897. Jonas was named after his great-grandfather who came to this country in 1824. Jonas inherited a great tradition of leadership in ophthalmology, starting with his grandfather, Aaron Friedenwald, one of the first ophthalmologists in Baltimore and one of the early American ophthalmologists to study in Europe. There he worked in the clinics of Von Graefe in Berlin and Arlt in Vienna. Aaron Friedenwald returned to Baltimore in 1862 where he combined ophthalmology with the general practice of medicine.

Jonas' father, Dr. Harry Friedenwald, was born in Baltimore in 1864 and became a distinguished ophthalmologist, scholar, and historian. Harry Friedenwald had studied ophthalmology under Hirschberg in Berlin and returned to Baltimore to practice ophthalmology and otology in 1890. He made numerous contributions to clinical ophthalmology, especially in the ocular manifestations of general diseases such as arteriosclerosis and diabetes (Fig. 1).

Early years*

Jonas and the class bully. Dr. Friedenwald's skill in handling the most meticulous research program in his adult years was already apparent in his early childhood. A striking example was the precise and scientific manner through which he confronted a personal challenge that developed with a classmate at Friends School in Baltimore at age 13.

It was the class bully who provoked a physical confrontation with Jonas that resulted in an almost-lost Friedenwald front tooth. Jonas recovered the traumatically extracted tooth from the ground and ran to the neighborhood dentist. Although the dentist was able to reinsert the tooth, with time it became discolored. As a result, Jonas wore with pride for the rest of his life a blackened front tooth. In this episode, typical of the way he would address scientific challenges in his future years, Jonas confronted the problem head-on. He immediately purchased a punching bag and started boxing lessons along with a rigorous physical fitness program. Within a few months Jonas was in trim physical shape and as a result had no further encounters with the class bully or, indeed, challenges from anyone else while he was in school.

Jonas' sojourn in the Baltimore city jail. When Jonas was 14 years of age, a heavy January snowfall covered Baltimore. Four of his friends, but not Jonas, were doing what most 14-year-old boys do after a heavy snowstorm—namely, having a royal snowball fight. The battle took place at the corner of the 2300 block of Eutaw Place and Whitelock Street. The snow was of a wet consistency and packed into a marvelous missile. Unfortunately, the aim of the combatants was not perfect, and one of the hard-packed snowballs crashed through the first floor window of the corner house. One of Jonas' friends responsible for the accident, it happens, is now my father-in-law, Lester Levy (pictured in Fig. 2 with Jonas at a later age). When the combatants heard the window crash, the four dispersed in all directions. The broken win-
Fig. 1. Physicians of the Friedenwald family in waiting room of the 1212 Eutaw Place office. Left to right: Jonas Friedenwald; Jonas' uncle Edgar Friedenwald (pediatrician); Jonas' father, Harry Friedenwald (ophthalmologist); Jonas' uncle Julius Friedenwald (gastroenterologist). Portrait in background is of Jonas' grandfather, Aaron Friedenwald (ophthalmologist).

dow prompted an immediate call to the police by the owner.

By quirk of fate, Jonas and a friend, who were three blocks away, started walking up Eutaw Place. They arrived at the corner of Whitelock Street just as the police arrived, whereupon the gentleman who had called the police shouted: "Those are the boys that broke my window." Innocent bystanders though they were, Jonas and the other lad were promptly hauled off to the city jail where they spent several hours challenging their arrest—but to no avail—until Dr. Harry Friedenwald arrived to secure their release.

Fig. 2. Jonas Friedenwald (left) with schoolmate, Lester S. Levy, during Jonas' second year at The Johns Hopkins University.

A career in medicine

Jonas was a brilliant mathematician and considered making mathematics his career, according to Dr. Robert A. Moses, who stated in his article As I remember—Jonas Stein Friedenwald: "I think that Dr. Friedenwald was shy. I know he told me that in his college days he intended to become a mathematician but then realizing his tendency to be ingrown, he thought that being in an office by himself might encourage him to be still more withdrawn. To counteract this tendency he went into medicine so that he'd have to be with people."

Following graduation from Hopkins Medical School in 1920, Dr. Friedenwald spent a year interning on the medical service of the Hopkins Hospital. During his internship he met and later married a Hopkins nurse, Mary Louise Sherwin. His charming wife was a
most gracious person who completely devoted her life to Jonas and his career. Recognizing the constraints on his limited time by his involvement in a large clinical ophthalmic practice combined with an extremely productive research career, she always saw to it that his free moments were not encroached upon by people in whom he had no deep interest.

Jonas moved to Boston after internship to spend a year of study in ophthalmic pathology under Dr. Frederick Verhoeff. He was granted a Master of Arts degree from Harvard for his brilliant studies. His second year of training in ophthalmology consisted of a clinical preceptorship in Philadelphia under Dr. George de Schweinitz. The late Dr. Alan C. Woods, who was Director of the Wilmer Institute during much of Dr. Friedenwald’s career, commented in a memorial service for Jonas:

This was Jonas’ formal training in ophthalmology—just two years’ preceptor training, but both under distinguished tutors. It is notable that he had no formal training in any special ophthalmic hospitals of that era. In the light of the present minimum requirements laid down by today’s specialty boards, this was indeed scant preparation either for practice or for a scientific career. But when one considers that Jonas had been trained in ophthalmology in his home from his first days in medicine, that he undoubtedly learned more in one year than the average student could assimilate in three, that he utilized to the limit every educational facility available to him, this training was more than enough. With the possible exception of ophthalmic surgery, in which he later perfected himself under the guidance of his father, Jonas Friedenwald returned to Baltimore in 1923 a remarkably well-trained man.

He then began practice with his father in a house on 1212 Eutaw Place (Fig. 3). At that time he received an appointment to work in ophthalmic pathology in the Department of Pathology at Hopkins under the late Dr. William G. MacCallum. This began his career at Hopkins, where he continued to serve without interruption until his untimely death 32 years later in 1955.

When the Wilmer Institute was founded in 1925, Jonas was appointed as Director of the Pathology Laboratory and rapidly rose in academic rank to his final appointment as Associate Professor. Dr. Alan Woods further commented in the memorial service:

Due to the fixed distribution of academic titles in The John Hopkins University School of Medicine, the title of full Professor was denied him.
Nevertheless, there never was a member of this faculty who more richly deserved the title. To all intents and purposes, in the last fifteen years of his life Jonas was the revered but uncrowned Professor of Ophthalmic Pathology. He likewise was in charge of and directed the lion's share of the research activities in the Wilmer Institute.

Dr. Friedenwald's first scientific paper was written in collaboration with Dr. Verhoff on the interesting topic of Injury to Cornea and Conjunctiva due to Fish Bile. Jonas wrote the following introduction, which is an example of the eloquent style and sharp wit that would appear in many of his future publications.

The road of science is a tortuous one, that twists and turns and not infrequently crosses some of the most ancient footpaths. We were, therefore, much interested to discover, when we had completed the studies that are the subject of this paper, that our ideas had been anticipated by an ancient observer some two thousand years ago. In the Book of Tobit (II, 9 and 10), the story is told how Tobias, the father, became blind thru getting some bird droppings in his eyes, and his eyes were covered with white films. But his son obtained some bile from a fish of the Tigris river and he (Book of Tobit XI, 10-13) "ran unto him, and took hold of his father; and he strake the gall on his father's eyes, saying, Be of good cheer, my father. But when his eyes began to smart, he rubbed them; and the white films scaled away from the corners of his eyes and he saw his son, and fell upward on his neck." In modern medical literature, however, we have found no record of such a procedure. We wish, therefore, to report the following case, together with some experiments on animals.

During his years on the Wilmer Institute staff, Jonas Friedenwald probably inspired or trained more young scientists in basic research related to ophthalmology than any other investigator in this country. Because of the broad diversity of his knowledge and expertise, he was eagerly sought out for consultation by medical students at Hopkins, basic science investigators, and all members of the Wilmer Institute staff. It was unique that a clinical ophthalmologist was at home and a leading authority in so many areas of basic science. His initial training and interest involved pathology, yet he kept abreast of new developments in chemistry, mathematics, and physics.

Scientific contributions

Glaucoma. Friedenwald's presentation at the 13th International Congress of Ophthalmology in Amsterdam in 1929, entitled The Pathogenesis of Acute Glaucoma, was a classic paper and was a major milestone in the development of his scientific career. The presentation brought him immediate international recognition as a distinguished ophthalmic investigator. This series of studies was later followed by his brilliant investigation of the mechanism of aqueous humor secretion and circulation and the permeability of the ciliary body, along with the dynamic factors involved in the aqueous secretion. He pursued these studies with the most fundamental evaluation of enzymatic oxidations, examining factors such as ascorbic acid, epinephrine, cytochrome c, and cholinesterase to determine their role in the passage of fluid across the ciliary body–aqueous humor barrier. Later in his career he delivered the first Proctor Award Lecture in 1949 with a paper entitled The Formation of Intracocular Fluid. His studies on the role of bicarbonate formation in the aqueous humor played a major role in the understanding of the chemistry of aqueous humor secretion and the subsequent development of carbonic anhydrase inhibitors. In the Proctor Lecture, he suggested that the ciliary processes used oxidative energy to separate protons and electrons at boundaries within the cells. Thus an accumulation of hydrogen ions occurred at one boundary and hydroxyl at the other. With the buffering of hydroxyl ions by carbon dioxide, bicarbonate was formed, which was balanced by sodium at the boundary which Friedenwald identified as the secretory or epithelial boundary. Some of these ideas had already been postulated by other investigators, but Friedenwald synthesized them along with his own observations into the broader perspective for the mechanism of aqueous humor secretion. This was an extremely important new direction of research in glaucoma, since until that time the ophthalmic community accepted the concept that the aqueous humor was a neutral secretion. As in many areas of fundamental research investigation, the magnitude of his contribution was not im-
mediately appreciated, but over the years his contribution to our knowledge of aqueous humor formation and the ultimate treatment of glaucoma represented a major step in the attack on this important ophthalmic disorder. His brilliant studies on tonometry and standardization of tonometers provided concepts for the development of tonography.

Cornea. In 1943 Friedenwald joined the war effort in studying wound healing and the effects of war gasses on the corneal epithelium. His specific studies involved the mitotic activity during cell division and regeneration of the corneal epithelium following trauma. Virtually all his research activities and facilities were devoted to the study of war gasses in view of their known and specific deleterious effect on the eye. Those who knew Friedenwald at that time knew the frustration that this type of study involved in view of his great humanitarian philosophy, but he and his staff made numerous contributions in this field. Indeed, 17 of the studies were published in a single volume after they were declassified at the end of World War II. Fortunately, war gasses were not used during World War II, but the knowledge learned from these studies directed by Friedenwald have provided important findings clarifying the metabolism of the cornea and providing a basis for further studies on wound healing.

Histochemistry. From the post–World War II era until his untimely death in 1955, Jonas became more involved in the study of enzymes and specifically the development of techniques in enzyme histochemistry. Indeed, having mastered the technique of enzyme histochemistry, he became one of the world authorities in this field. One of the departmental chairmen in the basic sciences at Hopkins commented: "This is a most phenomenal spectacle—an ophthalmologist is our foremost authority and most distinguished scholar in the field of histochemistry." Numerous papers in the field of enzyme chemistry attest to his leadership role, and the contributions in collaboration with George B. Koelle on the histochemical localization of cholinesterase in the ocular tissues were widely recognized.

Dr. Bernard Becker, who came to Wilmer to work with Dr. Friedenwald in the field of enzyme histochemistry, joined him in the studies on aqueous secretion, and these studies led to the development of the clinically useful carbonic anhydrase inhibitors for the treatment of glaucoma.

Jonas' initial move into the field of histochemistry was interesting. The technique of enzyme histochemistry was in the process of development in many tissues throughout the body, most noteworthy by Dr. Wislocki and his colleagues at Harvard. The technique had not been applied to the eye, and Friedenwald chose as his first study of ocular histochemistry the demonstration of "fixed carbohydrate" that had been recently refined by Hotchkiss and McManus. The internal limiting membrane of the retina and the basement membrane of the retinal vessels were structures staining strongly with this technique. Dr. Friedenwald and Dr. Becker applied this method to flat preparations of the retina to study many retinal vascular abnormalities, particularly the retinal changes of diabetic retinopathy, associating their findings with the lesions observed in the kidney.

Ophthalmic pathology. Dr. Friedenwald's 1 year of fellowship in the pathology laboratory of Dr. Frederick Verhoeff at Harvard provided a solid background in ophthalmic pathology that led him to become the nation's leading authority in this special field of ophthalmology. His textbook The Pathology of the Eye, published in 1929, was a classic and, indeed, represented the most authoritative reference source on ocular pathology for approximately two decades. Later, he served as the principal editor in developing the Atlas of Ophthalmic Pathology, which was published by the American Academy of Ophthalmology and Otolaryngology through material largely assimilated at the Armed Forces Institute of Pathology. He served as an active consultant to the ophthalmic pathology program there, and it is of considerable interest that the illustrations in his original Pathology of the Eye textbook were prepared by Helena Campbell. Helena Campbell subsequently married, and her new name, Helena Campbell Wilder, was soon to become one of the
most distinguished names in ophthalmic pathology, well known to all ophthalmologists. It was of interest that Mrs. Wilder had only a high school degree, but her brilliant and creative ability, nurtured by her training with Dr. Friedenwald, led her to achieve unparalleled recognition in the field of ophthalmic pathology.

Optics. Jonas' flair for mathematics and the application of the basic principles to physiological and geometrical optics enabled him to develop early in his career a modification of the standard astigmatic dial for measurement of astigmatism.

His recognition of the limitations of standard ophthalmoscopy led him to develop the "Friedenwald ophthalmoscope." This device enabled the examiner to direct a slit beam on the retina so that elevation of the retinal structures could be appreciated. By incorporating a yellow-green filter, he was able to utilize monochromatic light to visualize the retinal vessels and provide much sharper contrast of these structures than with standard illumination then in use. The Friedenwald ophthalmoscope, indeed, anticipated the later techniques developed to study macular diseases (Fig. 4).

Jonas applied his solid background in mathematics and geometrical optics to elucidate the portrayal of depth in painting. He delivered the sixth Brodel Memorial Lecture before the annual convention of the Association of Medical Illustrators in 1953. His paper Knowledge of Space Perception and the Portrayal of Depth in Painting, published by the Association, is a fascinating discussion of this topic. He eloquently discussed the role of monocular and binocular perspective as he traced the development of perspective drawing from the early Renaissance through the contemporary masters.

There is almost no field of ophthalmology in which Dr. Friedenwald did not contribute to our basic knowledge on the subject. His contributions to diseases of the retina are a prime example. He elucidated the pathogenesis of diabetic retinopathy, retrolental fibroplasia, and retinal arteriosclerosis. It is of interest that some of Friedenwald's earlier scientific publications concerned retinal diseases, and he highlighted his years of study in this field in 1949 with the Jackson Memorial...
Fig. 5A. Letter to Dr. Harry Friedenwald mailed by his patient during her travels in Europe in 1899. Medical notes are recorded on envelope.

Fig. 5B. Reverse side of envelope in Fig. 5A. The notes continue through 1906 and include a sketch of a fundus abnormality.
Lecture A New Approach to Some Problems of Retinal Vascular Disease.

Clinical practice

Jonas started private practice of ophthalmology with his father in 1923. Their office address was 1212 Eutaw Place, next door to the Baltimore Eye, Ear, Nose and Throat Infirmary, where both Harry and Jonas performed most of their surgery (Fig. 3). Jonas examined a large number of patients each morning except on the mornings assigned to surgery. His father always "dismissed" Jonas promptly at 1:00 P.M. from the office responsibilities, enabling Jonas to travel across town to his laboratories at Wilmer.

Under his father's tutelage, Jonas became a skilled ophthalmic surgeon and developed an active medical and surgical practice. His brilliant background in mathematics and optics made refraction quite easy. His reputation as the most capable refractionist in Baltimore was quickly established.

Dr. Ernst Bodenheimer, who received his ophthalmology training in Germany, emigrated to the United States to join the Friedenwalds in the mid-1930s. Dr. Harry Friedenwald retired from active practice in 1945. From 1945 until his death 10 years later, Jonas relied heavily on Dr. Bodenheimer to share the responsibility of managing a large clinical practice. This association enabled Jonas to continue dividing his time between the research laboratory and the care of his patients.

After Dr. Jonas Friedenwald's death in 1955, I was invited by Dr. Bodenheimer to join him in practice in the 1212 Eutaw Place office. This led to a close and warm professional relationship. One special dividend for me was the privilege to examine some of the Friedenwalds' former patients.

It was a fascinating experience to review records on patients dating back to the turn of the century. They had been followed initially by Harry, then by Jonas. Most of their patients' examination results were handwritten. Harry's notes were frequently written on any pieces of paper available, then inserted into a protective jacket for filing. An interesting example was the record on a patient who had written to Dr. Harry Friedenwald from Europe in 1899. Using both sides of the envelope addressed to him, Harry entered his examination notes for the next 7 years (Figs. 5A and 5B). Jonas used a loose-leaf notebook for most of his records. For patients originally followed by his father, he continued Harry's system.

Being keenly aware of Jonas' reputation as an expert refractionist, I was always reluctant to change the glasses he had prescribed. It was astounding to see the precision in his refraction records. A typical example was the record on a patient examined when Jonas was in his early thirties. Here he changed the
recorded axis of a 2.25 cylinder by 1 degree, indeed a very precise refraction (Fig. 6).

The research laboratory
Jonas maintained a close personal relationship with many of his staff, especially the technicians and assistants in his research laboratory. Sylvia Sigelman Weinberg, who worked as a research technician from 1931 until Dr. Friedenwald's untimely death in 1955, graciously permitted me to include one of the letters she received from him. This letter written in 1932 typifies Jonas' warmth and keen sense of humor in dealing with his staff (Fig. 7).

According to Sylvia, Dr. Friedenwald was a handyman and master craftsman in the laboratory. He constructed numerous devices from small-animal holders to modifications for special equipment. I was fortunate to locate recently a cigar box containing the tools Jonas used to adjust and repair the laboratory microtomes (Fig. 8, A and B).

Honors
During his lifetime, Jonas Friedenwald received numerous prestigious honors. These included the Research Medal of the American Medical Association in 1935, the first Proctor Award of this organization (then known as the Association for Research in Ophthalmology) in 1949, the Howe Medal of the American Ophthalmological Society in 1951, along with a host of other special honors in this country. He received the prestigious Donders Medal of the Dutch Ophthalmological Society in 1952. Although recognized widely in ophthalmological research circles, he was also elected to the American Society for Clinical Investigation, an honor awarded to very few in the field of ophthalmology. He served on the Editorial Board of the Archives of Ophthalmology and also the Journal of Histochemistry and Cytochemistry.

Memorial service for Jonas Friedenwald
Jonas Stein Friedenwald died Nov. 5, 1955, at the age of 58. On Feb. 10, 1956, a memorial service was held for Dr. Friedenwald in the Great Hall of the Welsh Library at Hopkins. The speakers were introduced by Dr. A. Edward Maumenee, the new Director of the Wilmer Institute. They were Dr. Alan C. Woods, past Director at Wilmer; Dr. Abel Wolman, Professor of Sanitary Engineering of The Johns Hopkins University; and Honorable Justice Felix Frankfurter, Judge of the Supreme Court of the United States. Dr. Woods spoke on Dr. Friedenwald's contributions to the Wilmer Institute and his scientific contributions. Dr. Abel Wolman spoke about Dr. Friedenwald's contributions to the development of the Hadassah Medical School and Hospital in Jerusalem. He indicated that over a period of approximately 25 years, Dr. Friedenwald had served as a member of the Board of Governors of the Hebrew University and on the Development Committee and Medical Advisory Board of the Medical School. Justice
Fig. 8. A, “Tool box” used by Dr. Friedenwald to store his tools used for repair of the microtomes in the pathology laboratory. B, Wrenches and other tools from the cigar-box container.

Frankfurter spoke about his personal recollections of Jonas, whom he had come to know while Dr. Friedenwald was in fellowship with Dr. Verhoeff at Harvard. The relationship which started between Justice Frankfurter and Dr. Friedenwald in the early 1920s continued until Jonas’ death. At the memorial service, Justice Frankfurter reminisced about their relationship.

Very soon I began to realize that Jonas’ interests far exceeded the boundaries, however far-stretched, of the medical sciences. He wanted to know, and this was characteristic of him, about the basic ideas of law and jurisprudence. “What can I read?” We had some talk, a good deal of talk, on and off. He wanted something more than fugitive talk, and so I bethought myself and told him to read Holmes’ Common Law. That’s not an easy book I can assure you, and the lawyers and judges here will hear me out that Holmes’ Common Law is indeed tough going. It is not a book for freshmen. And so I gave him Holmes’ Common Law to read, and he read it. I do not mean he passed the eye over the page. He read it thoughtfully. And I remember well saying at the time to a friend of mine, “This young doctor has asked me more embarrassing questions about some of Holmes’ chapters than ever I was asked in discussion about the book by colleagues of mine on the Harvard Law School faculty.” And that is not a denigrating remark about the members of the Harvard Law School faculty.

In another area Justice Frankfurter commented:

I wrote a friend of both of us of a talk I had with Jonas in which he told me a story that sheds light on his relaxed temper of mind. Jonas’ motto seemed to have been “ohne Hast, ohne Rast,” without haste, without rest. Serenity it is, serenity, which, I think, is hard to attain unless the good Lord deposited something of what we call humor. I had occasion to repeat to Jonas the cynicism of a friend of mine about the medical profession. Jonas said that it reminded him of a minister who came to see him recently who was suffering from eczema. Jonas stated “The minister had your friend’s cynicism about the medical profession and said to me ‘After all these years of medical re-
search I do not see why your profession has not found the cause of my eczema. I offered to bet the minister ten to one that we would find the cause of eczema before he found why the righteous suffered.

Summary

Jonas S. Friedenwald, a quiet and modest person, was one of the most distinguished research scientists of his era. As a brilliant mathematician, physicist and chemist he applied these basic disciplines to his research studies in ophthalmology. His contributions encompassed the entire field of ophthalmic investigation ranging from his classic textbook on ophthalmic pathology to the development of the Friedenwald ophthalmoscope. His pioneer studies on the pathogenesis of glaucoma, the standardization of tonometers, enzyme chemistry, corneal wound healing, and diseases of the retina laid the groundwork for future generations of investigators.

REFERENCES