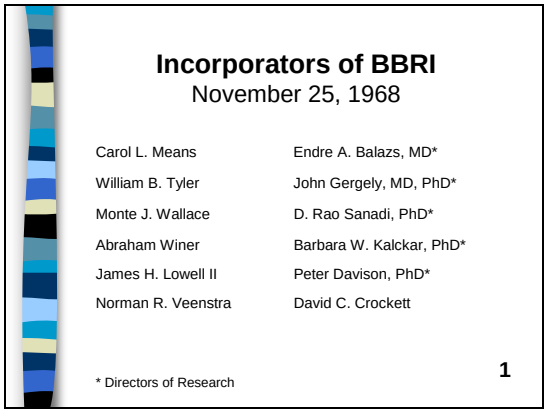
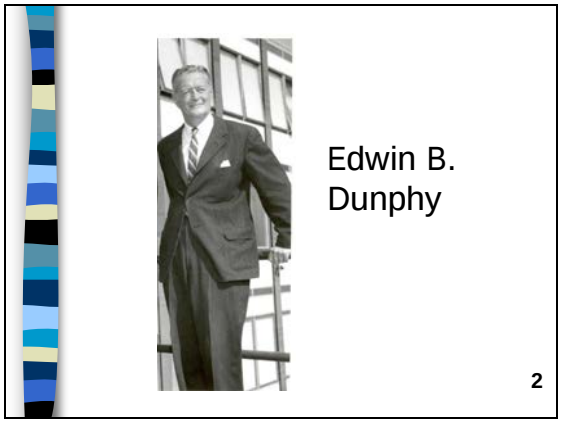
Endre A. Balazs speech at the meeting to celebrate the 40th anniversary of BBRI's incorporation
(date speech given: November 13, 2008)

Twelve days from today – November 25 – will mark the 40th anniversary of the incorporation (1968) of the Boston Biomedical Research Institute as a charitable research and educational corporation. It was not a new birth, but rather a reincarnation (SLIDE 1).

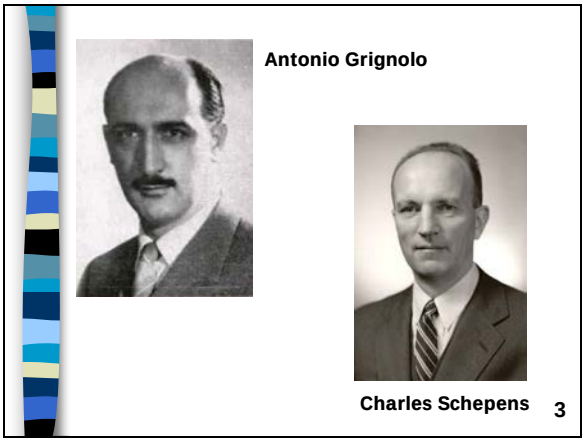


As you can see, five of the twelve incorporators were the research directors of the five basic research departments.

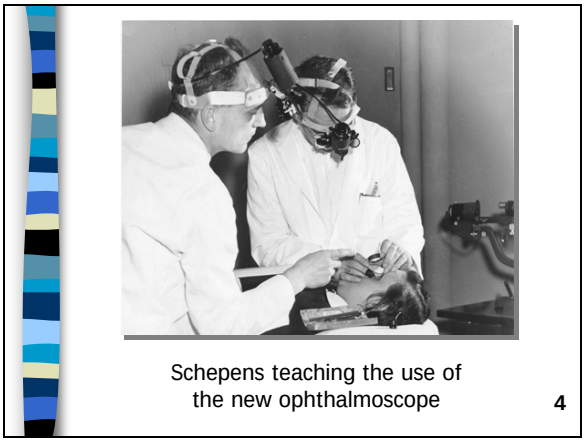
The parent organization, the Retina Foundation, had been organized 18 years earlier in April 1950 - 58 years ago - as a charitable trust and a new basic research unit of Massachusetts Eye and Ear Infirmary under the supervision of Edwin Dunphy, Professor of Ophthalmology at Harvard Medial School and Chief of Eye Service at Mass Eye & Ear Infirmary (SLIDE 2).



The organizational initiative (SLIDE 3) came from Charles Schepens and Antonio Grignolo, both eye surgeons who specialized in vitreo-retinal diseases, and who also were recent emigrants from Belgium and Italy. Charles Schepens became the Director of the Foundation.



He was already involved in the development of a new diagnostic tool for retinal detachment (SLIDE 4): the binocular ophthalmoscope, which was later named after him.



Antonio Grignolo was involved in studies of the vitreous fibers (SLIDE 5) with the new electron microscope.

The first electron microscopic picture of collagen fibers in the vitreus

Matoltsy, Gross and Grignolo (Retina Foundation 1951)

5

I arrived, at the invitation of Edwin Dunphy, in December 1950 from Stockholm and joined Schepens and Grignolo - as a third emigrant, to establish and administer the research laboratories of the Foundation and to teach the structure and function of connective tissues of the eye at a postgraduate course at Harvard Medical School.

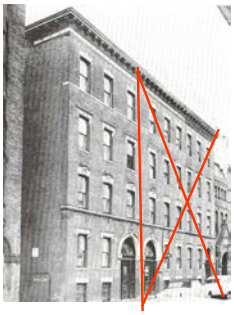
In Stockholm, I had been working at the Karolinska Institute — the medical school of Stockholm — on polysaccharides and on the structure and function of the "intercellular substance". I was planning in the future to focus my research on the simplest and largest intercellular substance in the vertebrate body – the vitreus of the eye.

The reason I was happy to accept Dunphy's invitation was that eye surgeons specializing on vitreo-retinal diseases were convinced that pathological changes in the vitreus were the cause of retinal detachment.

Chambers Street

6

To my surprise, the building (SLIDE 6) in which I was supposed to install the basic research laboratories was in the oldest Italian section, the West End of Boston: at 30 Chambers Street. It was a very old, five-story tenement (SLIDE 7), without an elevator. A breath-taking contrast to the recently completed modern laboratory building I worked at in Stockholm. I was also astonished that the Retina Foundation was not a real foundation. It had no money to pay my first year's salary!



30 Chambers Street

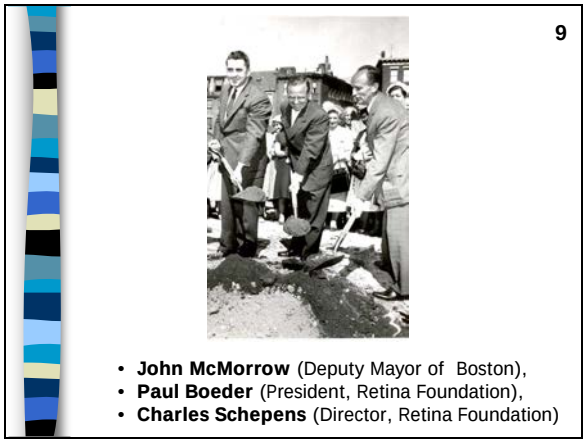
7

But the Foundation had an advisory board with three very important members: (SLIDE 8) Ralph Lowell, then President of the Boston Safe Deposit Corporation and Chairman of the Board of Overseers of Harvard University.

Ralph Lowell

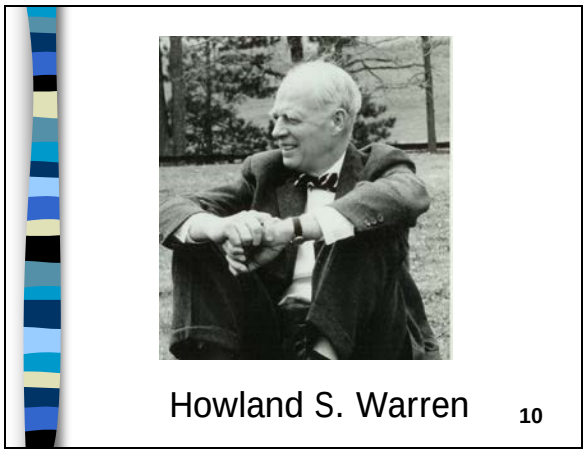
8

The second (SLIDE 9), Paul Boeder, was Director of the Bureau of Visual Sciences at the American Optical Company and a highly respected teacher of physiological optics at Harvard Medical school and many universities throughout the country.



This picture was taken at the groundbreaking ceremony of the new building in 1960. Paul Boeder is in the center with Charles Schepens and the Deputy Mayor of Boston.

The third important member of the advisory board (SLIDE 10) was Howland Warren from the famous family of physicians who founded Harvard Medical School in the 19th century.

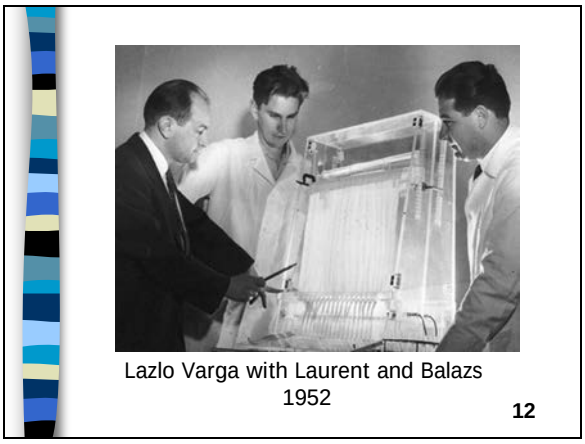


Warren also became the first Treasurer of the Foundation. With their and Dunphy's help, we raised enough money that, by the end of 1951, I could establish three thousand six hundred square feet of new laboratory space in the old tenement house. I also received my first NIH grant in September 1951. During the next few years we raised over $200,000, which in today's value corresponds to two million dollars. From this we could purchase the most modern equipment to start research in biochemistry, cytology, physical chemistry, and fine structure.

Most importantly, with the new equipment in place and with funds available I could convince established investigators and experts in various fields of research to work with me as full-time associates or part-time consultants.

The first of these experts was (SLIDE 11) Marie Jakus who worked at MIT using the new electron microscope. The first electron microscope in Boston was installed for her use in the basement of our old tenement house in September 1951.

The second (SLIDE 12), Laszlo Varga, a physicochemist from MIT helped me, as a consultant, to separate large molecules in the vitreus of the eye.



John Gergely, the third established investigator, came to the Retina Foundation as a consultant from Massachusetts General Hospital (SLIDE 13). He was an old friend of mine from high school days and later a colleague from medical school in Budapest. His expertise on the molecular structure of muscle

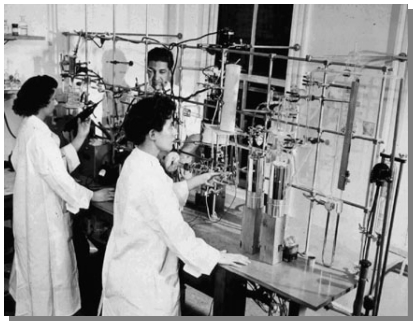
proteins helped us to understand the structure of the largest polysaccharide in our body, and the one on which I have worked all my life — hyaluronan.

John Gergely with Laurent and Balazs
1953 **13**

In this picture he is explaining to me and Torvard Laurent the intricacies of the light scattering method for the determination of the mass of molecules. Torvard Laurent was at that time a medical student at the Karolinska Institute in Stockholm and also working on his doctoral degree in biochemistry and physical chemistry. He was my first doctoral student and he followed me to Boston to the Retina Foundation where he completed his doctoral thesis and returned to Sweden.

Analytical Ultracentrifuge for
measuring properties of molecule **14**

(SLIDE 14) We also installed an analytical ultracentrifuge in the old tenement house, as well as a free electrophoresis apparatus (SLIDE 15) and a carbon fourteen combustion train to study the metabolism of hyaluronan, before the modern-day scintillation counters were discovered.

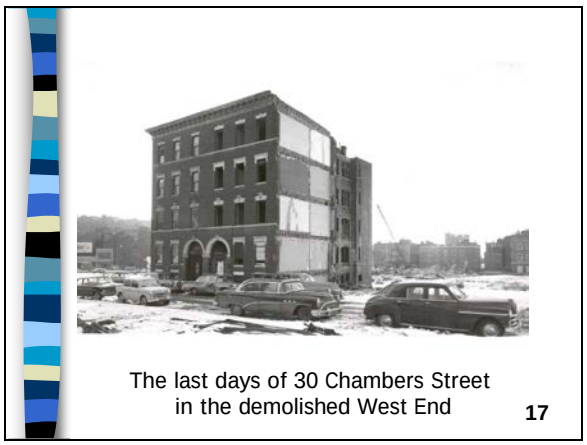


^{14}C Combustion Train
Collecting Radioactive-Labeled Carbon **15**

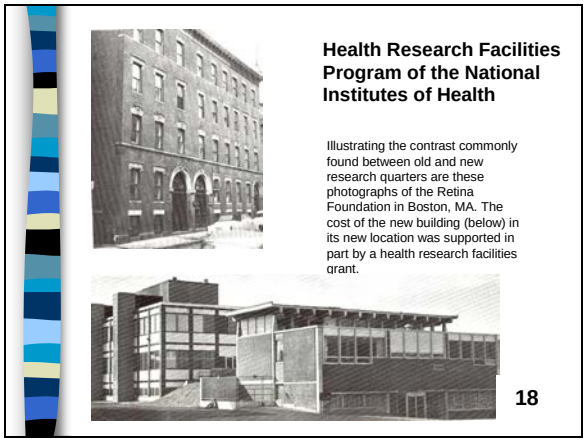
Later with John Gergely (SLIDE 16) we purchased a nuclear and electron magnetic resonance spectroscopic instrument to determine the structure of water around large polymeric molecules such as nucleic acids and hyaluronan.

Balazs and Gergely using
Nuclear and Electron Magnetic Resonance
Spectroscopy Instruments **16**

All this success demonstrated that one does not need the most modern laboratory building to install the latest and most sophisticated research equipment and recruit top scientists. As one of our visitors remarked: This proves that it is not the cage, but the singing of the canaries in it, that is important!!



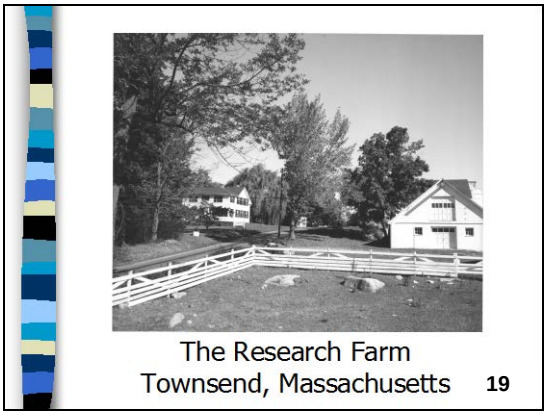
(SLIDE 17) In the late 1950s, the houses around us were demolished to make space for the first urban development project in the country. Ralph Lowell and his friends arranged for us to receive land in the demolished area to build a new research building (SLIDE 18).



We received a grant from NIH to cover more than half of the cost of the building, and the rest we received from public and private charitable foundations, as well as donations of the patients of Charles Schepens and his Retina Associates.

Obtaining financial help for the building project from both the Federal Government and from charitable foundations required a broader scientific program and a name change. The new modern research building was named the Institute of Biological and Medical Sciences of the Retina Foundation and contained 50,000 square feet of laboratory and support space at a cost of 2 million dollars—which in today's dollar value is 14 million. We moved into the building in 1962, and soon realized that we needed more research space. By design, we had already planned an extension to the building, which was then started and completed by 1967.

(SLIDE 19) We also purchased a research farm in Townsend, Massachusetts to house our monkey colony and horses for the study of the therapeutic use of hyaluronan in the eyes and joints.



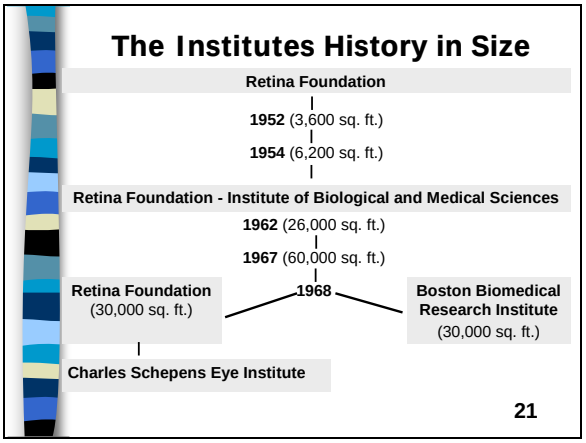
(SLIDE 20) In the new building the Retina Foundation management was reorganized to accommodate the broader research objectives and the greatly expanded staff. The five Research Directors and their research staff represented a multidisciplinary biomedical research faculty of both basic and clinical researchers with a close cooperation of these two disciplines. This research included specific projects on the retina and cornea of the eye, as well as general research projects on muscle, connective tissue and bioenergetics.

When I accepted the associate directorship of the Retina Foundation, I did so under the condition that I would study only the vitreus, because I was not interested in other parts of the eye.
From the beginning, it was our concept to create a research institute that integrated the research of clinical scientists and basic scientists. Remember that this was half a century ago, when biomedical research was not the major objective of medical schools. When I started working with Schepens, I realized the advantages of cooperating with a clinical scientist who could explain the difference between the function of healthy and pathological tissues. I became a strong believer that integrating these two research disciplines made biomedical sciences more effective and shortened the time between basic discoveries and the development of new diagnostic tools and therapeutics.

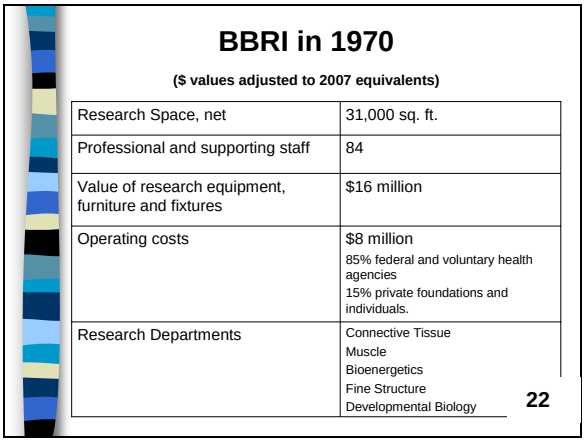
Schepens and I were in complete agreement that the new organization should have a broad program of scientific research, and that we would start with muscle tissues and invite John Gergely to run the department. Why, a few years later, did we have to separate the two institutes? Both Schepens and I realized then that his long-term plan was to organize and control an eye research institute, while I wanted to organize an institute to study more than just the pathology of the eye.

Consequently, we believed it would be best to separate the two Institutes, the Retina Foundation – later named the Charles Schepens Eye Institute and the Institute of Biological and Medical Sciences - later named the Boston Biomedical Research Institute).

(SLIDE 21) The next slide shows the development of these two Institutes during the 1950s and 60s.



By 1970, the separation was complete (SLIDE 22) and BBRI continued its function uninterrupted in the same space with the same staff and the same financial support, but without the donations from the Retina patients.



(SLIDE 23) I have said much about the cage, but nothing about the songs of the canaries. This slide summarizes some of the major accomplishments of the research staff before the two institutes separated. As you can see, the results cover clinical and basic sciences in the eye and other tissues, as well as establishing an international eye research journal and a society.

This is the story of the first two decades of a successful research institute.

Contributions of the Research Staff of the Retina Foundation and the Institute of Biological and Medical Sciences

- Construction and introduction of the binocular indirect ophthalmoscope.
- "Scleral buckling" surgery for retinal detachment.
- Instruments for vitreo-retinal surgery.
- Structure and composition of the vitreus during development and aging.
- Fine structure of the cornea
- Molecular structure and metabolism of hyaluronan in the vitreus, joint and skin.
- Development of highly purified hyaluronan and the discovery of its therapeutic use in eye surgery, for the treatment of joint pain and as connective tissue filler.
- The interaction of actin and myosin and its regulation by calcium ions. A variety of myosins.
- The founding and editing of Experimental Eye Research, first International Journal in this field.
- The organization of the International Society for Eye Research.

23

The endeavor was carried out with the energy, the naiveté, and even the audacity of recent emigrants from Europe who believed that America was the land of unlimited opportunities and never doubted success. I always wondered how in greater Boston, in the land of medical schools and science, we succeeded.
One day I asked Ralph Lowell why he supported us from the beginning and for more than two decades, including the time of separation. His answer was: "In this old city, it is sometimes good to open the window to get some fresh air."

(SLIDE 24) I want to show you the picture of Charles Schepens, John Gergely and myself. This picture was taken in front of the conference hall in Ipswich where Charles organized a meeting of clinicians and basic scientists. It is this continuing combination of medical and basic scientific focus that has shaped the path of both Institutes and made them what they are today.

Balazs, Gergely and Schepens
Ipswich 1958

24

Charles spent his entire life as clinical scientist, working at these Institutes. John spent more than 50 years helping to create and working in them. I spent only 25 years here. I had an exciting and rewarding time, an, unquestionably, the most challenging of my career
.
My sincere thanks and gratitude to my fellow emigrants and all the others from this country and from around the world who helped us in this endeavor. I am grateful to you for this invitation and for the opportunity to talk about those decades. I congratulate you, and wish BBRI continuing success.

Thank you.

25