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Editorial

Neglected but Precious; The Grant Perfusion System

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The Golden Era of glaucoma research took off with the development of the stainless steel Grant Perfusion System, and landed with the loss of a truly bona-fide leader in the field of glaucoma research, Dr. David L. Epstein, MD. Dr. Epstein was a distinguished physician and scientist and served as the Joseph A.C. Wadsworth clinical professor and chair of Ophthalmology at Duke University Eye Center, North Carolina, USA. I was fortunate enough to have the opportunity to learn about glaucoma research under his guidance, and always felt honored to participate in his favorite brain-storming sessions.

The eye is an essential, vital organ in gaining knowledge, and let's face it, life would be pretty bland if we human beings were unable to see. Eyes are not only attractive to behold, but hold great challenges for physicians, surgeons, physicists, biomedical engineers, and neuro- biologists for deeper study. Though technology is quite advanced, a vast array of issues regarding the eyes remain unresolved and untouched. There is much more to do, yet sorely lack in expertise in the field.

In truth, eye research has garnered little attention – with involvement from only a fraction of scientific groups worldwide. Thus, very little progress has been made, and as Dr. Epstein explained to me when I first joined his group, eye research is at least twenty to thirty years behind as compared to other areas of science. The challenges are enormous and technology has not yet caught up enough to address far too many unanswered questions.

My expertise lies in the field of cell biology, earned largely from working in the internationally renowned laboratory of Professor Michael Sheetz, a Lasker award winner. It was then that the complex nature of glaucoma research was clearly outlined to me by Dr. Epstein. He provided me with a self-authored book on glaucoma as shown in figure A, and in response to my inquiries into glaucoma research he said, "the study of glaucoma can be both clinically satisfying and intellectually stimulating. Yet it is also the most humbling of disciplines, both because of our clinical failures, but even more, our lack of real understanding. There are multiple types of glaucoma and multiple schools of thought contribute to fuzzy thinking".

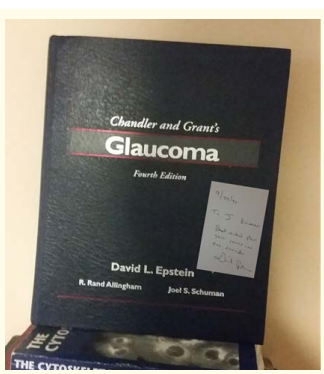

Figure A: *This book was presented to Dr. Kumar at his first official meeting and brain storming session with Dr. Epstein. This is dedicated in the memory of Dr. David L. Epstein, who taught us not only how to proceed in glaucoma research, but to be inquisitive and remain concerned about the inadequacy of our knowledge about glaucoma.*

Glaucoma is a progressive optic neuropathy, which is generally associated with elevated intraocular pressure (IOP) and therefore, an increased IOP is considered to be major risk factor for glaucomatous nerve damage. IOP is the result of the balance between the rate of aqueous humor formation and the outflow that includes conventional aqueous humor outflow (trabecular meshwork/Schlemm's canal), uveoscleral outflow and episcleral pressure. By using tonography, it has been suggested that measuring the ratio between the pressure and aqueous humor outflow facility followed by a standard nomogram is useful in clinical detection of glaucoma. The contribution of transcellular pore formations or paracellular pathways to fluid flow across the inner wall of SC is not clear. Thus, it is obvious that understanding the regulation of aqueous humor outflow and/or fluid dynamics still holds a major challenge in understanding glaucoma.

Even though Dr. Epstein always had a busy schedule, during our first meeting, he took me on a tour of his laboratory himself instead of allocating the task to a subordinate. He showed me the two perfusion systems to measure aqueous humor outflow facility in eyes, ex-vivo. The first perfusion system he showed to me was his favorite – the Grant perfusion system – that uses whole porcine eyes freshly obtained from abattoir, and the other perfusion system was the organ culture system that uses the half globe from human cadavers' eyes. As shown in figure B, Dr. Epstein explained that the Grant perfusion system was designed and reproduced by his mentor Prof. W.M. Grant in 1955, and he carried it over to Duke University. This perfusion system has not only generated a plethora of published scientific articles, but patents for glaucoma therapy, and has resolved issues in the regulation of outflow at molecular level.

Figure B: *The Grant Perfusion System developed by W. Morton Grant (1955) at MEEI, Harvard University Medical School, Boston. The picture was taken with the permission of Dr. Epstein, DUMC, NC.*

As a cell biologist, eagerly observing the Grant Perfusion System with my own eyes, I have often felt that even though the system is old, using this system is more logical, meaningful, and promotes a high level of confidence in evaluating outflow facility. In the immortal words of John F. Kennedy, "A man may die, nations may rise and fall, but the idea lives on." The main principle of the Grant perfusion system is that the measurement of the outflow is directly proportional to the loss of water from the reservoir placed on the pan of the measuring balance; i.e. 1.0 µL outflow of water is equal to 1.0 mg loss of water from the reservoir, and the sensors display data on the chart recorder quite accurately. In a revival of ideas, a Real Time Perfusion System was designed and reassembled at Tufts University in the laboratory of Professor Noorjahan Panjwani, which I presented at ARVO, Fort Lauderdale, in 2006. As shown in figure C, the Real Time Perfusion System is an advanced form of the Grant Perfusion System equipped with updated technology and sensitive instruments such as Mettler Balances and a computer equipped with the Balance Talk XL program. Of special significance, the Real Time Perfusion System can be disassembled and reassembled with ease in glaucoma research facilities worldwide, and it is our assertion this system provides a much better understanding of fluid dynamics of aqueous humor outflow and that its unique features can measure the outflow facility precisely – even up to nl/sec /mmHg. Such a feature will allow us to understand more in depth about the osmotic pressure of aqueous humor in the anterior

chamber of the eyes, and whether the flow is continuous or pulsatile. Hence, we suggest that determining these physical parameters may play a key role in understanding the regulation of aqueous humor outflow facility.

Figure C: *A real time perfusion system developed at Tufts University, Boston department of ophthalmology, and presented by Janardan Kumar at ARVO, 2006.*

And none of this would have come about or even been possible without the passion and brilliance of Dr. David Epstein. He was a truly remarkable, wonderful man – both in and out of the laboratory. I am proud that he was a mentor, teacher, colleague, and friend to me. He is sorely missed.

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