

Michael A. Kass, MD

Dr. Kass shares his thoughts on glaucoma research and how to improve patients' compliance with treatment.



1. Having participated in trials focused on the efficacy of treatment for ocular hypertension prior to the Ocular Hypertension Treatment Study (OHTS), were you surprised by any results from OHTS?

In OHTS, treatment reduced the onset of open-angle glaucoma (OAG) by more than 50%. I was pleased by how clear the results were, because many previous studies¹⁻³ examined this question but, as a group, yielded inconclusive results. Although ophthalmologists knew that central corneal thickness affected IOP measurements, I was surprised at how powerful a predictor it was of who developed OAG in the OHTS study group. I was also somewhat surprised by how well tolerated medication was overall. When my co-investigators and I compared the treatment and observation groups for quality of life and adverse events, we found little difference between them in terms of death and hospitalization rates or the development of new medical conditions. This similarity suggests that physicians are able to select well-tolerated, safe medications for their patients from the wide variety of agents currently available.

2. What research questions do you personally hope to answer during the next 10 years?

When first seeing an individual with elevated IOP, a physician may elect to begin or delay treatment after discussing these options with the patient. The fundamental question in this situation is whether delaying treatment initiates a process of optic nerve degeneration (either of the connective tissue or the cellular components) that is less responsive to later treatment. We are attempting to address this question in the current phase of OHTS by treating subjects in the previous medication and the previous observation groups. Over

the course of OHTS, I would also like to develop a better risk model of who is likely to develop OAG. The genetics of this issue are of particular interest. How does a patient's having an IOP of 26 mm Hg and allele A instead of allele B or C affect his chances of developing glaucoma? Finally, I would like to help define better what constitutes early glaucomatous damage to the visual fields, optic disc, or nerve fiber layer. This information would enable us to improve the sensitivity and specificity of diagnostic tests.

3. How can physicians help patients comply with treatment?

The better the rapport and higher the level of trust patients have with their physicians, the more receptive they will be to their doctors' treatment suggestions. Additionally, it is necessary to educate patients and their families about why treatment is important, what medication accomplishes, and the course of glaucoma. Conversations are best supplemented by written materials, to which patients can later refer. They can really benefit from written instructions on how many times to take each medication. It is also worthwhile teaching the proper instillation technique, including eyelid clo-

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FAST FACTS

- Professor of Ophthalmology and Chairman of the Department of Ophthalmology and Visual Sciences at the Washington University School of Medicine in St. Louis
- Director of The Heed Ophthalmic Foundation, 2002 to present
- Recipient of the AAO Senior Honor Award, 1991
- Principal Investigator, the Ocular Hypertension Treatment Study, supported by the National Eye Institute of the National Institutes of Health, 1992 to present
- Recipient of The New York Academy of Medicine's Lewis Rudin Glaucoma Prize, 2003

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sure or nasolacrimal occlusion, to patients or the people who administer their drops.

Physicians need to work to understand their patients' lives. Do they have a social support system? A spouse or family member can help remind a patient to use his glaucoma medication. Unfortunately, many elderly individuals lack a social support system. A patient who lives alone and does not drive may need assistance arranging for medications to arrive by mail. Additionally, many people find it difficult to remember to take their medications unless that act is keyed to another event. By finding out about a patient's life, a practitioner may be able to suggest that he administer his drops at the same time he takes his vitamin and heart pill, for example.

Prescribing the fewest agents and the smallest number of doses per day to achieve the desired therapeutic effect enhances compliance. Moreover, directly asking patients about the side effects and cost of medications can be revelatory. Patients may irregularly instill their eye drops rather than announce that an agent is bothering them. They also often will not inform their physicians that they are unable to afford both their medications and food. By making inquiries, doctors may realize that they need to alter what they have prescribed or that they should pursue an alternate strategy such as laser therapy or surgery.

4. How does an investigator balance corporate sponsorship and the ideal pursuit of scientific knowledge?

Medical school curricula, ethics committees, and a whole series of regulations for the pharmaceutical industry have sought to address this timely, important issue. It is possible, but not easy, to balance corporate sponsorship and scientific investigation. The first step is for researchers to recognize that a potential conflict of interest always exists, even if it is simply their subconscious desire that their ideas bear fruit.

The second step is to take the necessary measures to address the potential conflict of interest. Investigators should report the potential conflict to fellow scientists, departments, institutions, granting agencies, institutional review boards, journals, and audiences for any talks given. Colleagues and patients should be able to consider the potential conflict when judging the information presented.

In addition, investigators must ensure that corporate sponsorship does not unduly influence the research. Is the question being asked posed in a way to elicit the maximum scientific return? Is the data analysis scientifically and clinically relevant as well as free from bias? Can the investigators present and publish the data without

any constraints? Is the data collection masked to prevent bias? Investigators need to set ground rules for a study at its outset so that their enthusiasm or financial interest does not affect the results. If the study cannot be masked, then perhaps a disinterested party should make the measurements, or the data should be replicated at another institution where the person does not have a potential conflict of interest. Investigators must exercise forethought and discipline.

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5. What should the next glaucoma studies address?

Until now, the treatment of glaucoma has been limited to lowering IOP. I think all practitioners hope for the development of an agent that protects ganglion cells by another mechanism. In addition to neuroprotection, the field would benefit from a study of the effect of genetic mutations on the type of glaucoma that patients develop as well as their prognosis and response to treatment. Also of interest would be a determination of the degree of glaucomatous visual loss that a person must suffer before becoming visually disabled (eg, develops difficulty with driving or reading, experiences an increased incidence of falls). It would be important to relate this information to quality-of-life questionnaires and everyday living. Although the level may be variable, knowing generally when people develop real visual dysfunction would reveal the level of damage that practitioners wish to prevent. Finally, I hope to see a study delineate the tradeoffs (eg, amount of therapy, side effects, costs) for various amounts of IOP reduction. Although it might be nice to reduce every patient's IOP by 40%, it would be useful for physicians to know the long-term implications of doing so. For example, how many patients would require surgery or develop cataracts, endophthalmitis, or blebitis? □

1. Heijl A, Bengtsson B. Long-term effects of timolol therapy in ocular hypertension: a double-masked, randomized trial. *Graefes Arch Clin Exp Ophthalmol*. 2000;238:877-883.
2. Kass MA, Gordon MO, Hoff MR, et al. Topical timolol administration reduces the incidence of glaucomatous damage in ocular hypertensive individuals: a randomized, double-masked, long-term clinical trial. *Arch Ophthalmol*. 1989;107:1590-1598.
3. Epstein DL, Krug JH Jr, Hertzmark E, et al. A long-term clinical trial of timolol therapy versus no treatment in the management of glaucoma suspects. *Ophthalmology*. 1989;96:1460-1467.