5 QUESTIONS

Peng T. Khaw, MD, PhD

Dr. Khaw reveals the driving forces behind his research and his approach to caring for patients.

What caused you to focus on modulating the wound-healing response in glaucoma?

As a new resident at Moorfields Eye Hospital in London, I saw a child who had undergone more than 50 anesthetics and multiple operations, all of which had failed due to scarring. Her mother would ask me, "Isn't there any treatment better than this?" I didn't have any answers for her, and that focused my attention on both wound healing and pediatric glaucoma.

As a junior resident, while passing through Miami, I took a chance and called the department of glaucoma at Bascom Palmer Eye Institute. Paul Palmberg, MD, PhD, invited me to visit during his lunch break. He gave me a copy of his meta-analysis of several studies showing that, the lower the average IOP, the lower the rate of glaucomatous progression. I was already convinced of the role of IOP in glaucoma based on my reading and my observations of changes in the optic nerve. I was convinced that controlling wound healing and getting the IOP in the low teens would slow or stop the majority of glaucomatous progression.

When I finished my ophthalmology training, I decided to pursue a doctoral degree and returned to the laboratory for 3 years. During that time, I worked with Ian Grierson, PhD; Greg Schultz, PhD; and Mark Sherwood, MD, and I discovered that very short applications of antifibrotic agents could arrest fibroblastic growth for a prolonged period.[1] When we began using mitomycin C (MMC), we found that the blebs were thin and cystic, and they often developed complications. I began to think about why these blebs leaked and became infected. It seemed to me that they all shared two characteristics: (1) a ring of scar tissue, which my colleagues and I called the *ring of steel*, and (2) an area of drainage that was anterior at the limbus.

What drove me to change my approach to trabeculectomy surgery was a young child who was blind in one eye after multiple failed glaucoma operations. When he was referred for surgery on his second eye, I performed a traditional trabeculectomy with MMC, which produced a cystic bleb. Three years later, he returned with endophthalmitis. After we treated the infection and administered intensive topical and intravitreal antibiotics, the eye improved. Within 1 week, however, the child had developed proliferative vitreoretinopathy. In the OR with a vitreoretinal specialist, I watched as the patient's retina disintegrated, and I then had to inform his mother that her child was blind. I decided at that moment that I had to improve our surgical technique to prevent the occurrence of cystic blebs. Based on my clinical observations and the understanding of what was happening in the bleb from our laboratory studies, we showed that making the surface area larger produced dramatically healthier blebs. Even though my colleagues and I used the same concentration of MMC, the blebs were diffuse. Our rate of complications in the high-risk group of children and young adults decreased from approximately 20% to 0.5%.[2-7]

It took 5 years to convince my colleagues to adopt the technique. I began presenting my findings at meetings in 1997, but I realized that talking about my results was not effective. I began showing a video I created in which a photograph of a cystic bleb from the right eye of a child I had treated with a traditional trabeculectomy using MMC morphed into the diffuse bleb of the child's left eye, on which I had performed

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FAST FACTS

- Director of the UK National Institutes for Health Research, Biomedical Research Centre at Moorfields Eye Hospital and the UCL Institute of Ophthalmology in London, 2007 to present
- Professor of Glaucoma Studies and Ocular Healing & Consultant Surgeon, Institute of Ophthalmology, 1998 to present
- Described the hypothesis for the evolution of cystic blebs (ring of steel and anterior aqueous drainage) and the principle of applying antimetabolites over a large surface area, which has markedly reduced the incidence of thin, cystic blebs and blebitis, particularly with mitomycin C
- First to describe the ability of antimetabolites to arrest the long-term growth of fibroblasts after short treatments with 5-fluorouracil, beta radiation, and mitomycin C,[1,8,9] leading to the first use of a single application of 5-fluorouracil on a sponge[10]
- Designed laboratory studies leading to the first successful clinical trial of a treatment regimen that reduced proliferative vitreoretinopathy[11]
- Primary inventor of new methods for the prevention of cell-mediated collagen contraction and scarring and new methods of drug delivery

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trabeculectomy with a larger surface area and MMC. This really helped to persuade colleagues it was worth changing.

Interestingly, one of the people who were most instrumental in popularizing the technique in the US was Dr. Palmberg. After seeing my video, he began using a larger surface area in his trabeculectomies, and he noticed a dramatic decrease in bleb-related complications within weeks. He became a strong advocate for the surgery internationally. At a later meeting, he came up and hugged me. He said he always hugged people who made a difference for his patients. I told him, years ago, you gave up your lunchtime to meet with a resident you didn't know. That was me, and that meeting was one of the reasons I began researching wound healing, which led to the improved technique.

How do you expect the surgical treatment of glaucoma to change during the next 10 years?

I am optimistic. My colleagues and I have just completed a long-term study and follow-up of trabeculectomy with and without an antiscarring agent in which we followed patients for nearly a decade. Not one patient whose IOP never exceeded 14 mm Hg twice (approximately 20% to 30%) experienced visual field or optic nerve progression. We are currently working on the next generation of antiscarring agents. Our experimental data suggest that trabeculectomy with these antifibrotics may achieve that sort of IOP control in 70% to 80% of patients—with fewer problems, one hopes, than MMC.[12-15] Obviously, one never knows what will be found in clinical trials, but I am hopeful.

In the future, with advances in microtechnology, I hope that our control of aqueous microflow will be precise enough to allow us to set each patient's IOP. Combined with effective control of scarring for several decades, we could halt glaucomatous progression in the majority of our patients with a procedure under topical anesthesia that one hopes would be carried out in minutes. On a separate note, some of the exciting advances in stem cell biology I have seen in the laboratory lead me to believe that it may be possible to improve nervous function in glaucoma.[16]

How do you manage patients' expectations?

It is important to ensure that patients' expectations are realistic. I specifically ask them what their expectations are of me and the team looking after them, and I address these issues. I describe to them the pros and cons of the different options of treatment and of no treatment. Essentially, I walk them down each road. By talking to each other, we figure out the right course of management for them and build a relationship that endures even in difficult times.

What is the most important lesson you have learned from treating patients with glaucoma?

I teach my residents to ask patients what worries them. No matter how good your knowledge, research, and surgery, you cannot look after people if you do not understand them as human beings.

Specifically, if you do not know patients' fears, you cannot address them. Their worries are often very different than what you would think. Asking patients what worries them also demonstrates that you care about them as people, which they value.

What has working with pediatric glaucoma taught you?

Dealing with young children and their families has taught me perspective, among other things. Because the unit here at Moorfields has been running for more than 5 decades, I learn from the long-term results of my two predecessors. I have learned to consider the long term, even when making short-term decisions, and the patients and their families appreciate this. My work with children has taught me when to intervene aggressively and when doing so will not really be of benefit to the patient or family unit. It is important to look after patients and their families and not just the eyeball. ❑

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