No. 3

THE CAMBRIDGE GLAUCOMA LETTER

published by THE CAMBRIDGE GLAUCOMA FOUNDATION, INC.

THE FIRST LETTER FROM ABROAD

I like to travel abroad, down narrow country roads lined with fruit trees, bounded by fields of grain swaying gently in the breezes of the late summer. I am especially fond of the small university towns with their half-timbered houses clustered around the medieval marketplace. Visits to such places become somewhat more affordable when I can combine them with a professional purpose; I can then list my travel expenses on my Federal Income Tax return, and I have consequently made it a habit to stop to visit the local optometrists and ophthalmologists. I talk with them about glaucoma, the only thing I know to talk about. Thus I obtain some idea of how eye problems are dealt with in other parts of the world, and sometimes, it pleases me, they want to know how we diagnose and treat glaucoma in Cambridge. Of course one meets many different personalities on such junkets, which are made all the more interesting by their unpredictability. One such imaginary encounter, which stands out in my memory, is the subject of this month's Glaucoma Letter.

On this occasion, I found myself in a German-speaking district. I was particularly eager to meet with an oculist, because several days had gone by since the last such encounter, and I knew that my expenses might well be disallowed unless such a meeting took place soon. I had been directed to what in our country would be an old apartment building, built perhaps a hundred years ago. Its outside was covered with a rather monotonous brown stucco, and impatient students had cut a path across the narrow ribbon of lawn that bordered it. Upstairs were apartments or dormitory rooms obviously occupied by students. The windows were open, and one could hear that within a not unaccomplished oboist was practicing his scales. The downstairs rooms had been converted into offices, one of which belonged to a professor of ophthalmology at the local medical school with whom I had made an appointment. The door to the professor's office was open. The waiting room was furnished with simple maroon-covered armchairs which were empty. The secretary, a tall lady with graying hair and a pleasantly modulated voice turned at her desk to welcome me.

"Guten Morgen", she said, "You are no doubt the gentleman from the Cambridge Glaucoma Foundation who wishes to speak with Professor K. He is waiting for you. Please go straight down the hall. You will find him in the last room on your left."

I did as I was told. I knocked on the designated door, and a voice from within bade me enter. "Guten Tag, setzen Sie sich nur, dort in den Untersuchungsstuhl," and he added with a smile, "Und ich verspreche auch Ihre Augen nicht zu untersuchen."

"I am sorry, Herr Professor," I began, "my German is not that good. I must ask you to repeat what you were saying."

"Oh, my apologies, we can speak English, I was merely inviting you to sit down in my examining chair and I promised not to examine your eyes. Tell me what brings your here."

I said that I was traveling abroad, visiting various optometrists and ophthalmologists, interested in confirming the similarities and understanding the differences between the way that glaucoma is diagnosed and treated in our respective cities. "Ein sehr interessantes Unternehmen," he began, and then he quickly corrected himself. "A fascinating project. But tell me first, where are you from?"

"I come from Cambridge, Massachusetts," I began. He looked perplexed. "That is not in England?"

"In the United States, near Boston," I explained. His look of perplexity persisted.

"Is it anywhere near St. Louis?" he asked. I shook my head.

"The optic disc," he said. "What a puzzle! Do you understand how the excavation occurs?"

"I wish I did," I said.

"I suspect we often skip over the details of what we observe, because we assume that we all agree, and sometimes because we are afraid to reveal our ig-

norance."

"Have you ever observed glaucomatous excavation to regress?" I began.

"Yes, I think I have. In infants whose congenital glaucoma is relieved by goniotomy, a deep excavation may disappear, and the disc will then actually appear quite normal."

"What about optic excavation in the adult, do you think that can disappear."

"It surely does not occur very often, but once every few years I see a patient where I think that is just what must have taken place. As the patient's glaucoma progresses, the excavation becomes more and more severe, and we become more and more concerned that he might lose field. We then use increasingly strong miotics; the pupil becomes very small; the disc impossible to see. Often cataract develops, and, in spite of our best efforts, field loss supervenes."

"But surely under those circumstances you do not expect the disc excavation to regress."

"No not just then; such a patient may then require filtering surgery, it is performed, the pressure becomes very low, the cataract progresses. Some months or perhaps years later the cataract may be removed, usually by means of a cataract extraction from below, and then when the wound has healed and the media have become clear when one looks in one may be surprised, it is the exception, I repeat, and not the rule, to find that the disc is not so badly cupped after all, indeed that it is quite flat."

"What about its color?"

"I should have mentioned that. The color is pale. The disc is atrophic."

"And the field?"

"The field is usually badly damaged, so we are sure that there is something amiss with the eye, but we wonder if it was really glaucoma?"

"Rather than what?"

"Oh, some vascular problem, something like anterior ischemic neuropathy, for example. We do not really know. Since the pupil was miotic all the while that the excavation was progressing, we had no chance to photograph it, and without a photograph, we wonder if we might not have made a mistake in our description."

"I make mistakes all the time," I said.

"Isn't it strange how our preconception of what we will find affects our thinking, if not indeed our observation. If the disc had indeed been cupped, we would have thought nothing of it, but when our observations conflict with our preconceptions, we would sooner deny what we see than modify what we believe. Perhaps that is one way in which we perpetuate errors from year to year and from generation to generation."

"I take it then that in your experience the disc damaged by elevated intraocular pressure never recovers to become normal."

"I think not."

"Does it always get worse?"

"If the pressure remains elevated, given time, these discs always deteriorate until there is total cupping."

"And if the pressure is normal?"

"The concept of a normal pressure isn't strictly applicable in these cases. A pressure which would be statistically normal and tolerated indefinitely by a healthy disc can still cause progression of the cupping and lead to field loss where the disc has once been damaged."

"But if one lowers the pressure sufficiently . . . ."

"It is hard ever to be certain whether the pressure is low enough. As a practical matter, we get the pressure as low as possible with medication, or with surgery if it is appropriate, and hope for the best."

"Can you give me some idea of how rapidly excavation of the nerve head develops?"

"That depends on the pressure. The higher the pressure, the faster the progression. I like to think of it in mathematical terms. The rate of excavation is a function of the pressure and also a function of the time. It seems, however, not to be a linear function."

"What do you mean 'a linear function?'"

"Actually two things, first of all, if the rate of excavation were linear with pressure, a disc with a pressure of 36, for example, would deteriorate one and a half times as fast as a disc under a pressure of 24, but this is not the case. The rate of excavation at 36 mm. Hg. is not one and one-half but perhaps seven times as great as the rate of excavation at 24 mm. Hg. Second, if the rate of excavation were linear with time, then a disc subjected to a pressure of 36 for two years would sustain just twice as much excavation as a disc subjected to such a pressure for one year. This also is not the case. The rate of excavation accelerates, and after the second year, the damage is significantly greater than twice the damage that might have been observed after the first year."

"I conceive of the relationship between pressure and the rate of excavation of the disc as a geometric curve. It is a curve which I believe rises very rapidly, exponentially, in fact. I have no reason to think that it is not everywhere continuous. I believe it has a derivative at every point."

I didn't know what to say. I groped

for an appropriate reply.

"It is a fascinating disease," I began, "provided you don't have it yourself," Professor K. completed my sentence.

"Incidentally, I have a tentative explanation of the factors that affect the rate of excavation. Would you like to hear it?"

"Very much so, "I said, "if I am not taking too much of your time."

"It is not the time that concerns me," he said solemnly. "It is the potential misunderstanding. Please remember that I said my explanation was very much tentative."

"I would still like to hear it," I said.

"Before I continue, tell me whether my account of the relationship of time and pressure to the rate of disc excavation corresponds to what doctors in your country understand of glaucoma."

"I myself agree," I said. "I would rather not speak for the others." "You are very cautious," Professor K. said.

All the while we were speaking, a large green spider had been making its way along a strip of molding high above his head. Now the spider appeared to have reached its destination, for it paused, and began to lower itself, at first slowly, and then ever faster by means of a thread which it was spinning as it descended. Professor K. must have noticed my distracted gaze. He turned, and when he saw the spider, nodded to it, as if it were a not unwelcome friend. "He is much better at this sort of thing than I am," he said. Then he paused for a few moments, while we watched the spider begin to build its web. "That web will be complete long before mine, and much more craftsmanlike." There ensued another long pause.

"I have a mathematical model for the process of glaucomatous excavation of the optic disc," began Professor K. diffidently, as if he were revealing some clandestine illicit undertaking. "Please tell me about it," I asked. "But first," he replied deliberately, "I must extract from you a promise. Will you give it to me?" "Tell me what I must promise." "Promise me that you will never treat a patient by my mathematical formula." "I promise," I said, but as I spoke the absurdity of the promise came home to me. Either the man was a fool, or he was making a fool of me. Perhaps, I mused, he is exercising a peculiar sense of humor. But Professor K. accepted my promise solemnly. His features betrayed no trace of a smile.

"You asked how rapidly excavation of the nerve develops. To begin with, remember that all the figures that we are able to cite have only statistical validity. Consider that subject to the same intraocular pressure, one eye may deteriorate to a given level of visual loss in five years, another eye in four, or six, or seven. Not only will any "average" value that we hypothesize reflect intuitive judgment rather than empirical measurements, but even if the measurements were feasible, the averages calculated from them would give us only limited information about any given eye. For example, the economists are fond of talking about the average annual personal income in a given region. If we are told that in a city of 1000 persons, the average annual personal income is 2500 Mark, this might mean that each of the 1000 inhabitants had an income of just 2500 Mark. But it might also mean that of the 1000 inhabitants one had an income of 2.5 million Mark and 999 had no income at all. Nonetheless the statistical values are useful, provided we interpret them properly. If I said that at a pressure of 36 an eye deteriorates seven times as fast as it would at a pressure of 24, you must interpret that figure to be but an average value, inferred from the model. I suspect that the actual values are widely scattered, which is the reason why the course of glaucomatous cupping is so relatively unpredictable and why the effects of therapy, for example, are so difficult to assess. And yet, if we undertake to deal rationally with the problems of glaucoma diagnosis and therapy, we have no alternative but to try to understand the distribution of values with reference to their mean."

"The mathematical model of which I speak relies on two fundamental assumptions. Let me articulate them for you, and you may decide whether they are sufficiently plausible to make the modeling process worthwhile. The first of these assumptions is that the optic disc may be considered a segment of a thin-walled sphere, and that excavation of the disc is a consequence of the mechanical stresses induced in that sphere by the intraocular pressure."

I said nothing.

"It seems to me to be not only a plausible, but perhaps an unavoidable assumption," he continued, "since only a solid structure can contain the intraocular pressure. Therefore the forces induced in the disc may properly be treated as stresses."

"You remember then the formula for stresses induced in a thin-walled sphere is S=p*r/(2*w). 'r' is the radius of the globe. 'p' is the intraocular pressure. 'w' is the thickness of the disc, and 'S', of course, is the induced stress. If, therefore, over a period of time an elevated intraocular pressure 'p' brings

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2 Sacramento Street
Cambridge, Mass. 02138

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Dr. and Mrs. Heinz Meyer
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about a thinning of the disc, it will bring about a decrease in the value of 'w' and a corresponding increase in the stress 'S'. If now we adhere to our assumption that the destructive effects of the intraocular pressure are brought about by the stress which that pressure induces in the disc, then for any given pressure acting over a period of time, as the disc becomes attenuated, the destructive effect of that pressure will continuously increase. Accordingly, and this is the second assumption, the model specifies that there is a rate of excavation equal to some multiple of the pressure, but that this rate is continuously compounded. Mathematically this entails the assumption of some very slow, fundamental rate of attenuation of the optic disc, R0, which is multiplied by the exponentiated pressure, exp(p*k). Thus we write simply: R1=R0*exp(p*k), where R0 is some constant to be experimentally determined which corresponds to the "natural" rate of excavation in the absence of all intraocular pressure, and 'k' is a second constant which corrects the scale and the dimension of the pressure. 'R1' is the rate of excavation which we wish to find. 'p' is the intraocular pressure which we assume to remain constant. Finally, if we are interested also in the effect of differences of disc thickness and globe diameter on the process of excavation, we may, in the above equation, replace 'p' with 'S': R1=R0*exp(S*k), or R1=R0*exp(p*k*r/(2*w)) if we substitute for 'S'. This is our model."

"I don't understand it," I said.

"I think I can explain it to you, if you cared to spend the time," Professor K. said apologetically. "It is late now. Perhaps you would like to come back tomorrow or the day after." My head had started to ache. I dreaded the thought of coming back. I glanced at the spider who was making progress with the construction of his web. As yet he had caught no fly. It seemed obvious that Professor K. was eager to tell someone about his mathematical model. Perhaps he could get no one else to listen. I made an effort to be polite. "Thank you," I said as I rose from the examining chair. "I will come back if it is at all possible. I wish I were a more competent mathematician."

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