No. 4

THE CAMBRIDGE GLAUCOMA LETTER

published by THE CAMBRIDGE GLAUCOMA FOUNDATION, INC.

THE SECOND LETTER FROM ABROAD

In the last letter that I wrote to you from abroad, I told about my visit to Professor K. with whom I had sought an interview in order that the expenses for my vacation in this quaint, historic valley might become deductible on my Federal Income Tax return. The interview with the professor had begun auspiciously enough. He had seated me in the examining chair in his office, and, in the company of a spider busily weaving its web, we had chatted amiably about possible regression and progression of optic disc excavation in glaucoma. The pleasure of that conference had, however begun to fade, for me at least, when the professor began to regale me with the details of a mathematical model, that I infer to be his brainchild, describing the manner in which elevated intraocular pressure brings about excavation of the optic disc. I have never been much of a mathematician. Indeed it was, aside from a love for humanity and for an affluent lifestyle, a distinct disinclination from the intellectual rigors of mathematics that led me to dedicate myself to medicine. I had listened politely enough to the professor's exposition, but I made no pretence of being able to understand it. Time was my ally and released me, but not before I had contracted a pounding headache in the left temporal-parietal region, which did not cease tormenting me until I had quenched it with the third glass of Moselbluemchen in the Wirtshaus later that evening. At that time I had made the firm resolve to eschew further biophysics instruction and to leave the mathematical modeling of nerve excavations to more cerebral ophthalmologists than myself.

My mind has changed. I am reluctant to leave this quaint little city, all the more so since Lotte, the young lady who cashes my travelers checks for me at the Hotel, has agreed to be my guide and companion on a hike, Sunday next, to the ruins of the old Königswarte, where the Emperor Frederick II is said to have stayed overnight just before setting out on his third expedition to Lombardy. To make a long story short, it is impossible for me to leave at this time, and, given the intransigence of the Internal Revenue Service familiar to me from previous audits, I had no choice but to place a telephone call, almost a week after my original meeting with him, to Professor K's office. The secretary, whose mellifluous voice immediately recalled to my memory the entire scene, oboist, professor, spider, exponential equation and all, was obviously pleased to hear from me.

"Of course, I remember your visit. We have been expecting your call. How would you like to come this afternoon at three o'clock."

I had not expected so early an appointment. I was taken by surprise. Did he have nothing to do other than teach me mathematics? The excuse which I thought of later did not find its way to my tongue in time. At three o'clock, therefore, I found myself, without further introductory ceremonies, seated once more in the examining chair in the innermost room of Professor K's office. The spider's web, I noted, had disappeared. "Guten Nachmittag, Herr Kollege", the professor's buoyant baritone greeted me. He seemed much less somber than at our last meeting, and I was reminded how exuberant I had felt as a child, when my friends came to play with me and one of my model trains. "How charming it is of you to come here all the way from St. Louis."

"From Cambridge," I corrected him.

"A suburb of St. Louis," he chuckled ingratiatingly. I let it pass, and thought to myself, I hope his mathematics is better than his geography.

"When we ran out of time last week," he began, "if I remember correctly, I had just finished describing to you the mathematical model of the excavation of the optic disc."

"I couldn't understand it, Herr Professor, and I had a very bad headache."

"Is your headache better now?" he asked solicitously.

"Oh yes, much better, it went away that same evening."

"That is good," he said, "then we can start from the beginning."

A twitch of anguish must have contorted my face. What will not a man endure for the sake of a tax deduction, I

thought, or for the opportunity to be shown by a pretty young woman where the Emperor Frederick II spent the night before his third expedition to Lombardy.

My facial expression may have given Professor K. pause to think. There was a moment of silence. Then he said: "It is not really necessary for you to be able to derive the model. Let us be practical. Let us begin at the end and end at the beginning. I will show you how it works."

With that he turned in his chair to a computer terminal that stood on the further side of his desk and upon the click of a switch, the room resonated to the dull monotone of a 50 cycle per second power supply. "In our hospital," the professor began, his voice rising above the hum, "we have glaucoma conferences every Wednesday morning at 8 a.m. At last week's conference, one of our assistants presented a twenty-six year old patient with previously healthy eyes who sustained a corneal laceration, with presumably flat anterior chamber, which he neglected to have treated. He comes to us with 75% of his angle closed, and with an intraocular pressure fixed at 30 mm. Hg. How long, the assistant asked me, do I think that this pressure can be sustained until total cupping of the disc supervenes. What is your estimate?"

"I can only guess," I said.

"None of us can do any more."

"I tell my patients that I am only a doctor, I am not a prophet, I am not even a professor."

"Well said," Professor K. nodded, "And yet, if he were perfectly healthy with a life expectancy of sixty years, you would presumably treat him, while if you knew that he had leukemia and only a year or two to live, you might well spare him the rigors even of medical therapy."

"I will will bet on ten years," I said, but don't hold me to it, because I don't know. Professor K. ignored my disclaimer and proceeded, "And what if the pressure were 36."

"Then I would give him four years to total cupping if his disc was previously healthy," I said recklessly. "Does your model require such shots in the dark?"

Professor K. was obviously hurt. "You are reluctant to commit yourself to specific values," Professor K. continued, "because you wish to preserve the appearance that you know what you are doing. You do not wish to be wrong. I fault you for seeking to avoid error by such evasion. Implicit in the clinical decisions that you make day after day are numerous judgments of this sort, and there is some virtue in making them explicit. Of course you cannot know how long this particular disc will sustain a pressure of 30 or of 36, but it is your duty to have some idea of the average survival time of a disc in these circumstances. On what other grounds can you give your patient advice?"

"I am sorry," I said.

"I happen to agree with your ballpark estimates. Let us see what the model thinks of them."

With these words, Professor K. lifted the receiver of the telephone on his desk from its cradle and inverted it into a small electronic device nearby. He dialed a number. The terminal consulted briefly with its superior in the hierarchy of machines. Then it began to importune its operator with questions. "Pressure #1," it demanded, and Professor K. dutifully typed:"30". "Estimated survival time #1,""10" the exchange continued, "Pressure #2,""36" "Estimated Survival time #2,""4" That was all. After its questions had been answered, the terminal paused, as if to swallow the newly acquired information, and then with relentless rhythm, it disgorged the tables which I have reproduced below. Professor K. leaned back in his chair with evident satisfaction. The performance of the machine seemed to compensate him for my sceptical recalcitrance. The spider that we had watched the week before or another one just like it, had reappeared on the molding, and having anchored its thread to the woodwork, prepared for another descent.

Equations

$$R1 = R0*\exp(S*k)$$

$$(u1-u0)/t = R1$$

$$S = p*r/(2*(w-u0))$$

$$(u1-u0)/t = R0*(\exp(p*r*k/(2*(w-u0))))$$

Variables

p = intraocular pressure
r = radius of globe = 11 mm
R1 = rate of excavation
S = tangential stress in disc
t = survival time
u0 = prior excavation = 0 mm
u1 = depth of excavation = .9 mm
w = thickness of disc = 1 mm

Assumed Data

At 30 mm Hg survival time = 10 yrs.
At 36 mm Hg survival time = 4 yrs.

Calculated Constants

R0 = .9216e-3
k = .277664e-1

Predicted Survival Time of Normal Disc

tension	time	tension	time
11 mm	182.03 yr	41 mm	1.86 yr
12 mm	156.25 yr	42 mm	1.60 yr
13 mm	134.12 yr	43 mm	1.37 yr
14 mm	115.13 yr	44 mm	1.18 yr
15 mm	98.82 yr	45 mm	1.01 yr
16 mm	84.83 yr	46 mm	317.04 da
17 mm	72.81 yr	47 mm	272.14 da
18 mm	62.50 yr	48 mm	233.60 da
19 mm	53.65 yr	49 mm	200.52 da
20 mm	46.05 yr	50 mm	172.12 da
21 mm	39.53 yr	51 mm	147.74 da
22 mm	33.93 yr	52 mm	126.82 da
23 mm	29.12 yr	53 mm	108.86 da
24 mm	25.00 yr	54 mm	93.44 da
25 mm	21.46 yr	55 mm	80.21 da
26 mm	18.42 yr	56 mm	68.85 da
27 mm	15.81 yr	57 mm	59.10 da
28 mm	13.57 yr	58 mm	50.73 da
29 mm	11.65 yr	59 mm	43.54 da
30 mm	10.00 yr	60 mm	37.38 da
31 mm	8.58 yr	61 mm	32.08 da
32 mm	7.37 yr	62 mm	27.54 da
33 mm	6.32 yr	63 mm	23.64 da
34 mm	5.43 yr	64 mm	20.29 da
35 mm	4.66 yr	65 mm	17.42 da
36 mm	4.00 yr	66 mm	14.95 da
37 mm	3.43 yr	67 mm	12.83 da
38 mm	2.95 yr	68 mm	11.02 da
39 mm	2.53 yr	69 mm	9.46 da
40 mm	2.17 yr	70 mm	8.12 da

"Please explain to me what all this means," I demanded impatiently. "182.03 years seems a rather protracted life span. In Cambridge, the patients don't live that long."

"Very good," Professor K. answered. "You have already learned the most important lesson that the model has to teach."

"What is that?"

"Not to take it too seriously: to be sceptical."

"But to learn to be sceptical, one doesn't need an elaborate model, just common sense," I retorted.

Professor K. was annoyed. "It is true, that the model makes no provision for the span of human life, and is prepared to calculate survival times for the optic disc far beyond any possible survival of the human body. At the other end of the pressure range, the model is also patently deficient, inasmuch as it describes total cupping, for example, produced by a pressure of 70 mm Hg as occuring over a period of only 8.12 days. Since we would always operate in such a situation, we have only rare occasion to observe the development of cupping at such very high pressures, but it is my impression that a healthy disc does not develop total cupping in less than several weeks, perhaps even a few months. The eye, of course, usually goes blind much sooner, from optic atrophy, apparently caused by a different pathophysiologic mechanism."

"But what about the other 'survival times' as you call them?"

"The term 'survival time' refers to the period required for a given pressure to produce a given amount of cupping. The table above is calculated on the assumption that 90% of disc thickness is eroded by a pressure of 30 mm Hg in 10 years and by a pressure of 36 mm Hg in 4 years. These assumptions determine the other values in the table. The calculations also assume a radius of the globe of 11 mm and an initial thickness of the disc of 1 mm. These last assumptions are not at all critical, so long as the values are the same for the survival times that one chooses to calculate. The model can also be used to study the effect of variation of the radius as in axial refractive errors. For example:

Ametropia and Survival Time
Tension = 30 mm. Hg.

refrctve error	survival time	refrctve error	survival time
-18 D	3.59 yr	-2 D	8.92 yr
-16 D	4.02 yr	0 D	10.00 yr
-14 D	4.51 yr	2 D	11.21 yr
-12 D	5.05 yr	4 D	12.56 yr
-10 D	5.66 yr	6 D	14.07 yr
-8 D	6.34 yr	8 D	15.76 yr
-6 D	7.11 yr	10 D	17.66 yr
-4 D	7.96 yr	12 D	19.79 yr

Thus the model appears to corroborate what has long been suspected, that the myopic disc is relatively more sensitive and the hyperopic disc relatively more resistant to the destructive effects of elevated intraocular pressure."

"It is interesting also to look at the effect on the survival time of prior excavation of the disc:"

Prior Excavation and Survival Time
Tension = 18 mm. Hg.

prior cup	survival time	prior cup	survival time
0 mm	62.50 yr	.40 mm	5.56 yr
.10 mm	40.93 yr	.50 mm	1.78 yr
.20 mm	24.45 yr	.60 mm	123.12 da
.30 mm	12.83 yr	.70 mm	8.31 da

"This table illustrates two important clinical impressions. It makes explicit how prior excavation increases the susceptibility of the disc to yet further excavation. Specifically, a disc without prior excavation might tolerate a pressure of 18 for 62.5 years. But a disc already excavated to .4 mm would survive a pressure of 18 for only 5.56 years. Hence a tension adequate to preserve vision in a healthy eye might be entirely inadequate

The Cambridge Glaucoma Letter
2 Sacramento Street
Cambridge, Mass. 02138

BULK RATE
U.S. POSTAGE
PAID
BELMONT, MASS.
PERMIT NO. 58290

Dr. and Mrs. Heinz Meyer
Route #2
Damascus, Va. 24236

to protect from further destruction a disc already diseased. It is also apparent from this table that for any given pressure the rate of disc excavation is initially very small and then becomes ever greater as the excavation deepens. This characteristic of optic nerve cupping, which I believe the model exaggerates, explains the origin of the disagreement about the nosology of glaucoma. Those optometrists and ophthalmologists who believe that ocular hypertension can be distinguished from glaucoma look at the early part of the curve, where disc excavation is so slight as to be imperceptible.

* * * * *

The Cambridge Glaucoma Foundation, Inc. is planning a series of Round Table Discussions on Glaucoma at times and places convenient to prospective participants. There is no charge either for the conferences or for the Glaucoma Letter. If you are interested, please write to us or check the coupon below and mail it to

The Cambridge Glaucoma Letter
2 Sacramento Street
Cambridge, Mass. 02138

(Telephone: 617-868-9307)

Place me on your mailing list for:

__ The Cambridge Glaucoma Letter

__ Glaucoma Discussion Groups

_____
name

_____
street

_____
city, state, ZIP

Those, on the other hand, who believe all ocular hypertension should be considered glaucomatous look to the end of the process, no matter how remote, where excavation and consequent field loss must always be expected."

"If I understand you correctly, all the figures in the tables you have shown me have been extrapolated from my two guesses," I said.

"You guessed well."

"But I do not really believe that a disc under a pressure of 30 mm Hg will survive for just 10 years, or that under a pressure of 36 it would survive for just four. Besides, no patient maintains a constant pressure for four years, not to speak of ten."

"But that is not what we said. We said only that if the pressure remained constant the average survival might be 10 and 4 years respectively. Nothing was said about the scatter of values about these hypothetical means. Perhaps the scatter is so great that the means are relatively meaningless."

"We agree that we cannot, with any certainty, predict the course of glaucomatous excavation in a given patient. Nonetheless we advise him, on the basis of pressure measurements, to take medication or to undergo surgery. I can't reconcile these facts unless I assume that we have some notion of the average rate of disc destruction induced by any given pressure."

"Exactly. That is what makes the model compelling. This model may not be optimal. It is certainly not the only possible model. One can immediately suggest important emendations. The point is that there must be a model of some kind to guide our judgment."

"Just as we must have in mind some model of the anatomy before we begin a surgical operation."

"Yes. The anatomic drawing which guides us is always more or less schematic. It does not include all variations. It shows us our problem in only one of many possible perspectives."