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SHOULD WE START TREATMENT ?

"When does one start treatment ?" is one of the most common and persistent questions asked at conferences and symposia about glaucoma. The experts are always pleased to oblige with advice. You start treatment for glaucoma, they tell us, when the intraocular pressure reaches a level of 30, plus or minus 4 mm. Hg., provided that the disc appears healthy. If the disc is damaged, treatment should be started at a lower pressure. The advice is simple and obvious. We have heard it often and yet the answer does not dispose of the question. Confronted with a patient who has early glaucoma, one frequently asks oneself in perplexity, "Should I start treatment?" If the question is to be considered once more, perhaps one should seek not to provide yet another answer, but to try to understand what is wrong with the conventional answer, and perhaps also, what is wrong with the conventional question.

The conventional question "When should you begin treatment for glaucoma?" fails, in the first place, to acknowledge that glaucoma is not one but many diseases. Although it is seldom phrased explicitly, I have always assumed that the conventional question addressed itself, if to a real disease at all, then only to primary open angle glaucoma, leaving a set of cognate questions concerning the optimal time for initiating treatment of other glaucomas not only unanswered but also unasked. In view of the diversity of these other kinds of glaucoma, the question about open angle glaucoma represents only the small fragment of a much broader issue; and if notwithstanding this arbitrary limitation the narrower issue does not appear soluble, perhaps reviewing it in a broader frame of reference might be of help.

To the extent that the conventional question "When do you start treatment for glaucoma?" addresses itself to an actual disease rather than an abstract conception, it ignores the fact that primary open angle glaucoma can often not be unequivocally identified. The diagnosis of open angle glaucoma is in large measure a diagnosis of exclusion. We refer to it as primary because examination of the eye, and particularly of the angle, shows nothing that might explain its origin. Yet primary open angle glaucoma differs among patients in many ways. One patient develops primary open angle glaucoma against the background of a strong family history; another is the first in his family to acquire the disease. In some patients, the disease appears to be unmasked by corticosteroids, while others are demonstrably unaffected by this class of drugs. In some patients, the disease develops and progresses at relatively low intraocular pressures, while yet other patients are able to tolerate markedly elevated tensions for many years before the discs finally show the characteristic stigmata of glaucomatous excavation. Then there are eyes that have been subjected to blunt trauma that develop a disease indistinguishable from open angle glaucoma without showing any disruption of the trabecular meshwork, while other patients with significant angle recession seem to have normal pressures, normal outflows, and no evidence of progressive disc excavation. There are relatively many patients in whom open angle glaucoma and angle closure glaucoma appear to coexist, where tension elevation at one stage of the disease is attributable to the open angle component, at another stage to reversible angle closure, and at yet a third stage to the formation of permanent anterior peripheral synechia. There are, furthermore, the well-identified patterns of pigment dispersion syndrome and pseudoexfoliation of the lens which are sometimes accompanied by glaucoma and sometimes not. In all of these situations, where open angle glaucoma coexists with other pathology, the indications for therapy will be correspondingly different, and the conventional answer may be inapposite.

It is remarkable, in view of the diversity of the glaucomas and in view also of the frequent difficulty of identifying primary open angle glaucoma as such, that the question "When do we start treatment of glaucoma?" is nonetheless asked - and answered - in so general a form. And if those who ask and those who answer the

question agree that it is meaningful that may be because at its root there is an assumption about glaucoma which should be made explicit. This assumption is that although there are many kinds of glaucoma and many different causes of elevated pressure and even though it may be possible to recognize subspecies even of open angle glaucoma, yet one may meaningfully speak of the glaucomas as a group because of the process that they have in common, namely the excavation of the optic nerve and the ensuing field loss brought about by an intraocular pressure of which, over a period of time, the eye proves intolerant. In this perspective the question is logical, for if tension elevation is the unique mechanism by which nerve excavation and field loss are brought about, then the modality by which that pressure is elevated to intolerable levels is irrelevant to its destructive effects.

Thus it appears that the conventional question "When do we institute treatment for glaucoma?" addresses itself not to an actual disease, but to a schematic representation of that disease, in other words, to a model. If the conventional answer to the question is unsatisfactory that may be because it is not models of disease that we are constrained to treat, but actual pathologic processes in unique human beings. This conundrum about the proper time to begin the treatment of glaucoma illustrates the hazard of uncritical reliance on an abstraction. The model is a generalization that disregards the mechanism by which the pressure is elevated. It disregards also the particular circumstances surrounding the disease, the patient's age, sex, race. It disregards the history of glaucoma in his family. It ignores the concomitant existence of other pathology. It ignores the patient's acceptance or rejection of treatment. It ignores the severity or mildness of any side effects that the patient might experience from the therapy, and finally it ignores the relative effectiveness or ineffectiveness of the treatment in actually lowering the pressure. It addresses itself solely to the phenomenon that a given intraocular pressure may over a period of time cause excavation of the optic disc and ensuing field loss, that increasing the pressure will accelerate, and diminishing the pressure, will retard this process. From this model one infers intuitively that when, in an eye with a normal disc, the intraocular pressure reaches some stated value such as 30 mm Hg, treatment to lower the pressure should be begun. Implicit in this conclusion is the assumption that for pressures under the threshold value, the probability of field loss within a forseeable period of time is relatively small, and perhaps also, although it is never made explicit, the assumption that the elevated pressure might subside spontaneously before it had caused any damage to the field. For values above the threshold pressure, on the other hand, the probability that the patient will develop field loss in a forseeable span of time is deemed to be substantial and the possibility that the pressure would remit spontaneously, relatively remote.

It is useful to make explicit the reasoning by which such conclusions are reached. By definition, a healthy disc subjected to a normal pressure should not deteriorate. It is also a matter, unfortunately, of common experience that a disc subjected to a pressure of 45 mm Hg usually begins in a matter of months to show evidence of excavation, which, if the pressure is unrelieved, will soon progress to field loss and then to blindness. For intraocular pressures less that 45, for pressures of 42, 39, 36, 33, 30, for example, the rate of disc deterioration will become progressively slower until at at pressure of 15 it will have ceased altogether. Between 45 and 15 there must be some value of the pressure at which the rate of disc deterioration has become sufficiently retarded that although disc damage progresses, the rate is so slow that the patient will experience no functional disability during his lifetime. When the experts postulate a tension of under 30 as requiring no treatment, that is what they have in mind. Nor is it unconditionally necessary that the loss of vision be postponed for the whole of the patient's life. As a practical matter, if loss of vision is delayed for perhaps a matter of five or ten years, the advice to withold treatment may, rightly or otherwise, appear to have been correct. If the patient is followed carefully, excavation of the disc would be detected before it had advanced too far; treatment could then be instituted before field loss supervened, although it is necessary to point out in this context that under those circumstances where excavation has already occurred, a much lower pressure level appears to be required if the progression of excavation is to be stopped.

The observation that the conventional answer refers not to an actual patient but to a model of a disease is borne out by its implicit assumption of an elevated intraocular pressure fixed at a specified level. The pressure may indeed be 30 today; it may have been 42 yesterday and it may be 22 tomorrow. The examiner who measures the patient's intraocular pressure is after all, only sampling that pressure in the statistical sense. And it would be rare indeed for an examiner to obtain only a single pressure measurement on a suspected glaucoma patient. More likely, there would be a series of measurements over a period of weeks or months.

Under these circumstances, linking the decision to start treatment to a single tension reading is clearly erroneous. It is a set of numbers which we must interpret. It is faulty to extract from this set at random, or even worse, with some ill-defined preconceptions of its significance, a number that strikes our fancy, and interpret it as being of decisive value. A statistician could suggest a better approach.

A statistician would wish to know, in order to obtain a clearer impression of pressure behavior of the eye, how many measurements had been taken, and over what period of time. He would calculate the intervals between tonometric readings, and the more closely they were spaced, the more confidently he would interpret them. He might calculate also the arithmetic mean of the pressures and the standard deviation from that mean. He might also determine whether the pressures tended to rise or fall by fitting individual measurements to a curve by the least squares approximation, and thereby project values for the tension to any arbitrary point in the future. Such mathematical techniques would aid the interpretation of tonometry and would make decisions based on tonometric data more rational and more persuasive. The present methods of interpreting tonometric values in the treatment of glaucoma are adumbrated with the aura of number magic. Perhaps as computers become less expensive we will become accustomed to more rigorous analyses of the tonometric data on which the decision to begin treatment is based.

More difficult and less accessible to rationalization than tonometry is the interpretation of the disc. The rules of thumb that we have been taught are qualified with the provision: "If the disc appears normal ..." but it is often very difficult to identify a normal disc. Consequently we classify the discs that we observe into three groups. The first of these groups consists of those discs which are obviously pathologically excavated, and in the presence of elevated tension one has no choice but to attribute such excavation to the elevated intraocular pressure. The second group consists of those discs which appear to be normal. Of such discs once cannot with certainty say that they have not been damaged by tension elevation. All that one can say is that such glaucomatous damage, if any, is not visible through the ophthalmoscope. The third group, and it is by no means small, contains all the rest, all those discs of which one cannot say with certainty whether or not the morphology of the disc has been altered by elevated intraocular pressure. To be sure, for the experienced examiner that number will be smaller than for the novice, and with experience ones uncertainty in this judgment diminishes. But there are many discs about which not even the most experienced of examiners can say whether or not they exhibit glaucomatous damage. In a surprisingly large number of patients who develop no other signs of glaucoma the discs show some measure of excavation, or some degree of asymmetry, some pallor and/or some nasal displacement of the retinal vessels which though far from diagnostic for glaucomatous change would not be incompatible with such damage in its early stages. When one measures an elevated pressure in an eye that has a disc of this third class, then the simple rule that one should begin to treat patients when the pressure is over 30 is potentially very misleading.

Now we know why the question "When do we start treating glaucoma?" is asked over and over again, and why the answers to that question, however elegantly they may be presented, do not seem to help us very much when we are faced with practical problems. At the heart of the conventional answer there is a model of glaucoma, but it is not a very useful model because it is not articulated logically or mathematically, and its features therefore necessarily remain subjective to the expert.

The best way that I know of to broach the question of whether or not we should institute treatment is to outline for ourselves as best we can the answers to the questions: what will happen to him if we treat the patient, and, on the other hand, what will happen to him if we withhold treatment. And if, at any given juncture, we must admit to ourselves that we do not really know, then it is important to take that uncertainty into account when we make plans for our patient. That we must take action in the face of uncertainty is integral to our responsibility. To acknowledge that uncertainty will give to our decisions a measure of humility and a measure of dignity to our mistakes. It will discourage us from presuming to know the future, and it will leave us with a mind open to new observations. Perhaps the best answer to the question, when do we start treatment, is that it is not the time at which but the manner in which treatment is instituted or withheld which is critical. Whether the decision is for treatment or against it, the fact that the issue ripened to the point of decision means that we must thereafter follow our patient faithfully, on the lookout for new evidence that might compel us to reverse whichever course we had taken.

Here are two illustrations of the pitfalls of treating patients by rule rather than by observation:

A physician sees a patient in his

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early thirties and notes an intraocular pressure of 28. The disc appears normal. He tells his patient that he has ocular hypertension and instructs him to return in half a year. The next morning at 6 a.m. however, unbeknownst to the physician, the pressure is 39, the following afternoon it is 18, and so it fluctuates from day to day and from week to week. At the time of the six months' examination, the physician still finds no disc changes and records a pressure of 20. He tells his patient that there is nothing wrong with him and tells him that no further examinations are required. By the time the patient returns, he is almost blind.

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Consider, on the other hand, a patient with large and somewhat asymmetric central excavations who was found by his physician to have a tension of 31. He was immediately given medication and subsequent pressure readings ranged between 15 and 19. It was assumed that he had glaucoma, that the excavations were the result of tension elevation, and that the medication had brought the tension to a safe range which prevented further damage. The patient is told that he must take medication for the rest of his life.

What the physician did not know was that perhaps because of transient extraocular muscle tension, or for some other ill-defined reason, this patient's tension elevation was not reproduceable. Subsequent tonometries, even without medication would have given values in the mid to high teens. If the physician had obtained a few more pressure readings at intervals of perhaps six days, no need to wait six months, he would have found the tensions much lower. It was only when the patient switched physicians and was taken off all medications to assess the effect of the drops that he was receiving, that it was found that his pressures remained normal even without medication, in fact that he "no longer" had glaucoma.

Both of these errors could have been avoided. The first one, if the patient with a tension of 28 had been seen for at least a few times at one month's rather than at six months' intervals, and if he had not been dismissed on the basis of only a single "normal" tonometry. The second error might have been avoided if the physician had waited a few days before instituting therapy while additional pressure measurements were obtained, or at least if, after six or twelve months of presumably essential therapy, he had taken his patient off medication for a few days to determine what the pressures would be without treatment.

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