INTRODUCTION

THE PROBLEM OF GLAUCOMA

By

SIR STEWART DUKE-ELDER

SINCE it was first established as a disease-entity, primary glaucoma has always excited controversy and discussion, and during the last decade this has intensified. The reason for this revival of interest is the recent elaboration of new techniques and methods of investigation – a renewal of research on the problem of the origin and circulation of the aqueous humour, the suggestions that alterations in secretion as determined by adrenalin, ascorbic acid and inhibitors of carbonic anhydrase may cause changes in the intra-ocular pressure, the discovery of the aqueous veins, the development of new methods of assessing the flow of aqueous, the mine of new information derived from gonioscopy – all these have had an impact upon our previous theories and conceptions. There is a danger, however, that new knowledge may be given a disproportionate importance by the generation which is thrilled by it, and it is often some time before it sinks into its proper perspective in the mass of the old knowledge gathered by previous generations. There is a danger that those actively engaged upon a problem may be mesmerized by new techniques with their exciting possibilities – that the biochemist, for example, will see the whole answer to the problem in his laboratory studies, or that the gonioscopist will believe that the whole of glaucoma lies in the territory of the angle of the anterior chamber. They may be right; and it is the purpose of this symposium to find out. We have gathered together a physiologist, a biochemist, a pharmacologist, a pathologist, a gonioscopist, all of whom have a right to be heard by reason of the excellence of their researches, and we have introduced them to a number of experienced clinicians drawn from all over the world who themselves have thought much about this problem; it is up to us to decide – if that is possible –

how all this new knowledge fits in and how far it is leading to the solution of our fundamental problem – the aetiology of primary glaucoma.

For this reason I do not think we should concern ourselves more than is necessary in our discussions with the historical development of our problem; nor do I think we should worry overmuch over incidental details that do not contribute to its solution. I think our thoughts should always be directed towards the fundamental things that are unknown. How much does this new observation, we should ask ourselves, how much does this new relationship contribute to our understanding of the aetiology of primary glaucoma?

The Two Types of Glaucoma

I think, in the first place, that it will clarify matters if we accept the fact, well recognized for over three-quarters of a century, that there are two distinct clinical entities called primary glaucoma. They are characterized by the common sign of raised ocular tension, or, as I would prefer to say, *unstable or raised* ocular tension; they may both end up presenting much the same clinical picture of absolute glaucoma; but in their initial and developing stages they are so dissimilar in their symptomatology, in their clinical evolution and in their pathology that I, personally, regret that they have not entirely different names.

Let us define them.

The first type is characterized by episodic subacute attacks of raised tension, the most notable features of which are halos and diminution of vision, and between which the tension is normal. From the less severe of these attacks the eye recovers, but subsequent attacks tend to involve a permanent rise of tension, or a severe acute attack may abolish vision; field defects and cupping of the disc are late phenomena. It occurs typically in persons, usually women, in the fifth or sixth decade of life, who are of an excitable habit with an unstable vasomotor system. And it occurs in eyes which are usually but not invariably hypermetropic, with a shallow anterior chamber, and almost exclusively in those with a narrow chamber angle.

The second type is not characterized by premonitory symptoms and a turbulent course; on the contrary, it is insidious in origin and

slowly progressive, showing a triad of symptoms – field defects, cupping of the disc from a relatively early stage, and a rise of tension which, although phasic, eventually tends to be permanent but nevertheless is sometimes insignificant and even absent. It occurs equally in either sex a decade later than the first type, affecting persons of no typical psychological pattern. And it occurs in eyes of any type, of any refractive error, the width of whose angles varies from wide to narrow as do those of the general population.

That, I hope we can take as established.

Terminology

The primary task before us is to clarify so far as we can the aetiology of these two types – or rather, of these two diseases. And this raises the question of terminology. Some of us prefer the old terminology – *acute* or *congestive glaucoma* and *simple glaucoma*. The term 'congestive glaucoma' is used because the attacks of raised tension and halos were held to be associated with oedema and congestion of the inner eye – not necessarily of the outer eye. 'Simple glaucoma' is a very suitable and innocuous contrasting term, established by long usage. Barkan, in 1938, however, introduced an anatomical method of nomenclature and used the terms *narrow-angle* and *wide-angle glaucoma*, which were adopted with enthusiasm throughout America and elsewhere. This terminology is not ideal since the first type of glaucoma can occur in an eye the angle of which is normally – that is, between attacks – of considerable width; and wide-angle glaucoma occurs indiscriminately in eyes with an angle of any width, broad or narrow. The later terms, *closed-* and *open-angle glaucoma*, have been much more happily chosen since they do indicate the occurrence of an event (closure of the angle) in the first type which certainly is an immediate cause of the rise of pressure, and its absence in the second. If, as Barkan believes, the intra-ocular congestion is wholly a result of the closure of the angle, this terminology seems to me to be appropriate; but this is a problem which requires discussion. If the types of glaucoma are to be defined by a nomenclature depending on the configuration of the chamber angle, I hope, at least, that we can agree to discard the terms 'wide-' and 'narrow-angle', and adopt in their place 'open-' and 'closed-angle'. But this again

is a question about which I hope we shall have some argument.[1] Terminology, however, is of relatively little importance so long as we know what we mean by the terms we use.

The Fundamental Problem

This brings us to the crux of the matter and to the primary problem of this symposium – the aetiology and the fundamental nature of primary glaucoma. As I have already said, about this there are wide divergences of opinion.

Let us take the most extreme views on either side of the controversy, remembering at the same time that neither may contain all the truth, for, as in other things in life, this often lies somewhere midway between the most divergent opinions.

On the one hand, there are those who think that closed-angle glaucoma is determined primarily and entirely by mechanical events in the angle of the anterior chamber. The corneal diameter is usually small, the lens usually disproportionately large, the axial depth of the anterior chamber usually shallow so that the lens-iris diaphragm lies well forward; and whether or not this occurs the angle is always narrow. Owing to the anatomical arrangements, the iris in a particular stage of dilatation presses itself closely against the protruding lens and can at the same time relax, a functional seclusion of the pupil occurs resulting in an iris bombé, the root of the iris comes against the cornea, the angle is blocked, drainage of aqueous ceases or at any rate is hindered, the tension rises and consequently the eye becomes congested. In this view, so far as I understand it, the primary cause of the disease is the anatomy of the anterior chamber; other changes in the eye are secondary; and it follows that if the anatomy is altered, the sequence of events is broken. Thus by equalizing the pressures in the posterior and anterior chambers by a peripheral iridectomy or even by an iridotomy, the condition is cured and, *ipso facto*, the disease ceases to exist.

On the other hand, there are those who think that in closed-angle glaucoma, while the same sequence of events may determine the eventual rise in ocular tension, the initial cause often lies deeper. It is admitted that simple blockage of the angle can cause

[1] At the end of the symposium (p. 315) it was agreed that the terms *closed-angle glaucoma* and *simple glaucoma* should be adopted meantime. These terms are therefore used throughout this report.

a rise in tension and subsequent congestion of the eye, a sequence seen, for example in mydriatic glaucoma and perhaps in the dark-room test. But it has been suggested that in ordinary life this may not be the primary event; for the initial cause may be a vasomotor instability which leads to a localized rise in the pressure of the small blood-vessels of the anterior segment of the uveal tract so that an excess of fluid is poured out into the posterior chamber and anterior vitreous; in certain circumstances this may lead to widespread congestion and oedema of the ciliary body. In an eye in which the drainage channels are free and the angle is wide, nothing untoward happens; the safety-valve provided by the canal of Schlemm is effective. But in an eye in which the angle is narrow, the bellying forward of the iris causes the mechanical blockage we have already described. The occurrence, therefore, of an acute attack of tension in this view, although not caused primarily by the anatomical configuration of the angle, can be realized only if the angle is sufficiently narrow.

In both views the existence of a narrow angle is therefore a necessity, and in both the therapeutic effect of an iridectomy is admitted. But the essential difference between the two views is that in the first the primary cause is structural, in the second functional. The most important consideration is that in the first view, that is the structural view, the patient himself is normal and his chamber angle only is abnormal; in the second view, the patient himself is abnormal, and although the rises of tension characteristic of the disease can be eliminated by an operation which relieves structural difficulties, the fundamental vasomotor instability still persists even although it is rendered innocuous in so far as it does not cause a rise of tension. The iridectomy does not cure the patient but puts him in the safe position of a similarly constituted person with a wide angle.

If the mechanical view is correct, we have to explain why every person with this peculiar anatomical configuration of the chamber angle does not get glaucoma. We have to explain why it occurs particularly in persons of an excitable temperament with vaso-motor instability. We have to explain why it tends so often to occur in conditions of strain or excitement. We have to explain why the pupil behaves in this peculiar way so often in people of this habit, and practically only in people of this habit, when they

are exposed to anxieties, or business or family worries. We have to explain why, after the disease has progressed for some time but while the angle is still normally open, it often closes periodically in a regular rhythm, for example, every morning or every evening, without regard to light or darkness or movements of the pupil. Finally, we have to explain why, if the disturbance is sufficiently severe, such as is caused by an acute attack or an operation on one eye, an attack so frequently follows in the other even although the pupil is controlled – or at any rate largely controlled – by miotics.

We will now turn to simple glaucoma. On the one hand, there are those who think that the condition is due primarily and perhaps solely to a local impediment in the drainage of the aqueous humour; whether the impediment is in the trabeculae[1] or whether it affects the drainage channels distal to Schlemm's canal is a question of great importance and interest which we will discuss at length at a later stage; but in either event, the cause of glaucoma is said to be essentially a localized obstructive process in this important region of the eye. The increase in the phasic variations of tension is claimed to represent the normal variation intensified by drainage difficulties or perhaps (in a more recent view) by a periodic increase in the secretion of aqueous. The condition of glaucoma without demonstrably raised tension in this view has to be explained by the presence of a weak lamina cribrosa which cannot withstand a normal intraocular pressure. The proof of these assumptions we will have to examine.

On the other hand, there are those who think that the ultimate cause of the condition is more fundamental and is again essentially a vascular disturbance. There is, for example, the view which I myself elaborated some years ago that the increase of phasic variations in tension characteristic of the earlier stages of the disease was due to a periodic sympatheticotonia involving constriction of the small blood-vessels, and that eventually, as this periodic functional change progresses to become a permanent

[1] The word *trabeculum* frequently appears in the literature but is etymologically incorrect. The term is derived from the Latin *trabecula*, the diminutive of a bean or bar. One piece of the lattice-work could correctly be called a *trabecula*, the whole circumferential structure of lattice-work, the *trabeculae*.

organic constriction, a gradual condition of tissue-sclerosis due to a lack of adequate blood supply spreads over the eye. The obliteration of the small vessels in the posterior segment of the eye and in the optic nerve is said to lead to an atrophy of the nervous elements which is clinically manifested as cupping of the disc and defects in the visual field; a similar process at the angle of the anterior chamber to sclerotic impediments to the drainage of the aqueous humour. This last change would lead to a rise of tension owing to drainage difficulties, and if a raised tension were added to the sclerotic process in the posterior segment, the cupping of the disc and the effects upon vision would be greater. But if the sclerotic changes affecting the drainage channels were absent or small in degree, the condition classically known as lacunar atrophy would result wherein a cupped disc and field loss could occur in the absence of a pathological rise in tension. Glaucoma without raised tension would thus be essentially a condition of sclerotic optic atrophy and would occur provided the sclerotic process remained localized to the posterior segment of the eye and the drainage channels remained open. Indeed, I have gone so far as to suggest that simple glaucoma should not necessarily be defined as a disease wherein the ocular tension is raised, but also as a condition wherein the diurnal phasic variation of the eye is greater than 5 mm. Hg as measured on the Schiötz tonometer, even although this variation constantly lies within normal limits. And this condition, I think, often occurs.

If the pathology of simple glaucoma is essentially a sequel of raised pressure in the eye due only to defects in drainage, we have to explain why excavation and pallor of the disc with their associated defects in the visual field sometimes show so little correlation with the tension, particularly in the early stages of the disease – a stage when raised tension may be completely absent and the progress of the scotomata most rapid. We have to explain why, after a drainage operation which has been technically and clinically successful in relieving the tension, the visual fields often continue to deteriorate. We have to explain why the loss of nervous tissue in the optic nerve, which pathologically forms the picture of lacunar atrophy, commonly occurs far up the trunk of the nerve where the intra-ocular pressure cannot exert a direct influence on the tissues. We have to explain, also, why cases of

secondary glaucoma which have no associated arterial disease may show normal fields and a normal disc even although the tension of the eye has been very high (90 mm. Hg or over) for some considerable time. We also have to explain why in so many cases the bilaterally symmetrical scotomata typical of glaucoma so frequently bear the characteristics of a vascular lesion in the nerve at a site proximal to the globe. The answers to these questions seem difficult if the essential pathology is localized to the angle of the anterior chamber; indeed, so far as simple glaucoma is concerned, I should have little hesitation in saying that the secret lies not in this region but in the posterior segment of the globe and in the optic nerve.

The essential difference between the two views is that in the first the pathology is localized, while the second insists that in simple glaucoma, as in closed-angle glaucoma, there is a sick eye in a sick body. In the mechanical view, the damage is due primarily to raised tension; in the vascular view, to vascular disease usually but not invariably associated with raised tension. If the disturbance is a localized obstruction, a drainage operation which effectively reduces the tension should stay the progress of the disease; it often does, but all too frequently it does not; for we have all met cases wherein the tension has been pathologically but not markedly high before operation in which the loss of vision and pallor of the disc have progressed even although the tension has been rendered permanently subnormal by one or several drainage operations. In the mechanical view, operative treatment to relieve the impediment at the chamber angle is certainly more logical treatment than miotics, for it is difficult to see how miotics can relieve a trabecular obstruction when the angle is wide and open. In the vascular view, on the other hand, miotics are legitimate treatment – actually the most logical treatment – provided they reduce the tension to normal limits; for these drugs undoubtedly counter the vasoconstriction by dilating the small vessels and opening out new capillary systems which are normally intermittently closed. There is no doubt, of course, that if, despite miotics, the tension rises either intermittently or permanently, both views demand that free drainage must be established by surgery; but in the second view the continuation of miotics after surgery is logical because of their vasomotor effect. We have

thus a direct antithesis here, a divergence of opinion which is not of theoretical but of extreme practical importance.

This, to my mind, is the essential question, to solve which we should direct our efforts, and in the light of which we should orientate our discussions.