THE
ULSTER MEDICAL JOURNAL

PUBLISHED ON BEHALF OF THE ULSTER MEDICAL SOCIETY

Vol. XXII 1st MAY, 1953 No. 1

Primary Glaucoma as a Vascular Disease

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The James A. Craig Prize Lecture, Queen's University, Belfast

As a rule in commencing a lecture of this type one starts by extolling the great figure by whom the lecture is founded or to whom it is dedicated, and as a general rule his fame is gradually being enveloped in the mists of the past: the lectureship thus acts after the manner of infra-red or radar emanations, as it were, to re-establish contact with the retreating figure. This can be a delightful and profitable enterprise, but my privilege to-day is much more exciting; for the founder of this lecture is here among us, apparent by the ordinary visible part of the spectrum, looking hale and hearty, and appearing younger than I am myself.

This puts me in a little difficulty as to what to say. The formula for the receding figure in the mist was easy—de mortuis nil nisi bonum. When the subject of your esteem is sitting in front of you, is the opposite applicable? I hope not; for it would indeed be difficult to find.

And since you know him much better than I do, I will confine myself to saying that his characteristic and delightful gesture of founding this Prize and Lecture is typical of the tradition of medicine wherein service has always had its complement in generosity. Of service he has given much to this University, to medicine, and in particular to ophthalmology; and a lectureship of this kind is of more than ordinary value. It is of material benefit in so far as it will serve as a focal point in perpetuity, so that new thoughts and new advances in our science of ophthalmology can be integrated. And it is also of spiritual value in so far as it interweaves the factual basis of our science with the interest and warmth of human affection, and thereby transforms our conception of it.

And it is surely fitting that a lectureship of this type should be inaugurated in Belfast; for here ophthalmology is taught and respected in a unique way among our Universities. For this, of course, James Craig has been largely responsible; and it is only right that I should congratulate him on his achievement and this foundation; and you on your fortune through your association with him.

That I should be asked to come from London to be the first to pay tribute to the spirit of this lectureship is indeed a privilege such as has rarely been offered me; and I appreciate the compliment more than I can easily say. I am told that the Prize is given for an original contribution to ophthalmology; and perhaps I can repay the compliment most happily by telling you of some of the things which at present interest me most in some research work we are carrying out, partly in the laboratories and partly in the research clinics, at the Institute of Ophthalmology, on the problems of glaucoma.

One of my reasons for choosing this subjcet, which may appear to be somewhat specialized for an audience which is not entirely ophthalmological, is that it exemplifies a tendency that is widespread in medicine, to mistake empiricism for fundamental truth. It is often very difficult to escape this easy tendency; for although we all pay lip service to the truism that an understanding of disease should be based on a sound knowledge of normal function, that medicine should be the hand-maid of physiology, the fact remains that our knowledge of the normal is often perfunctory and too often negligible. And when we are faced with patients with clamant symptoms demanding immediate relief, we would be failing in our duty if we did not apply every means available, even although we knew some of these means were based on premises we know are empirical or even suspect to be wrong. There is, however, sometimes a tendency among surgeons who are zealous in their craft, and sometimes for this reason the most able technically, to forget the empiricism of their methods, to think that by relieving a symptom they have cured a disease, and consequently to suffer disappointment because, despite their efforts, the more deeply-seated disease process goes on.

The problem of glaucoma is, of course, one of considerable antiquity, but since the chance and completely empirical demonstration by von Graefe in the 1850's of the effectivity of the operation of iridectomy in relieving the tension of the eye in certain cases, and, finally, after the pathological studies of Max Knies and Adolph Weber in Germany in 1876, who remarked histologically an obstruction to the circulation of the intra-ocular fluid at the angle of the anterior chamber in advanced cases of the disease, the consensus of ophthalmological opinion for almost a century has been practically unanimous in insisting that the essential feature of glaucoma was raised tension; its immediate local cause an embarrassment of drainage of the aqueous humour; and its adequate treatment measures by drugs or operation to improve the drainage. The problem was, therefore, one for the surgical plumber rather than for the medical physiologist. It must be admitted, however, that if the be-all and end-all of glaucoma resided in a raised tension and the raised tension itself were dependent upon the efficacy of drainage

of the intra-ocular fluids, then surely the anxieties of five generations of ophthalmologists and the tragedy of blindness that has overtaken countless numbers of their patients could be mechanically relieved by sufficiently enthusiastic surgery.

Let us start off by suggesting that a raised tension is merely a complication occurring in a more fundamental disease, and that the configuration of the angle of the anterior chamber merely a feature which aids the incidence and may increase the drama of this complication. If this were so, the concentration of the whole of our thoughts and energies almost exclusively on the aspect of drainage —important though it may be—may explain the undeniable fact that, in comparison with other diseases dependent upon a mechanical maladjustment amenable to surgical correction, the prognosis of glaucoma, taken as a whole, is bad.

In many forms of secondary glaucoma an obstruction of the angle of the anterior chamber undoubtedly exists. This is seen in its purest form in buphthalmos, when the angle is congenitally malformed, or in an epithelial ingrowth after a perforating wound. But in primary glaucoma the case is probably different. It is certainly true that once the disease is well established, an organic obstruction does occur in this region. In the congestive type of primary glaucoma it is usually due to a crowding of the narrow angle by the swollen tissues of the root of the iris and the ciliary body. In simple glaucoma it is probably the result of sclerosis of the tissues in the trabecular region—I say "probably" because we do not know for certain. But I am to suggest in this lecture that in both types of primary glaucoma these phenomena are really end-results — incidental in the ætiology although very important in their clinical effects—and that the primary cause of both types of the disease is an instability of the vascular control of the eye.

In the consideration of this problem a logical starting-off point is a study of the regular and rhythmic variations of tension which occur in the normal and glaucomatous eye.

The normal diurnal variation in intra-ocular tension, which never exceeds 5 mm. Hg, is a well-known phenomenon which has not received sufficient attention. It would seem that in this respect each individual has a characteristic rhythm which is obstinately maintained in spite of all environmental variations, and that both eyes vary together. It is important that the curve is unaltered by bodily posture or activity, and is unaffected even if the patient's habits are suddenly reversed and he remains up at night and spends the day in bed. Osmotic changes are not at fault for the rhythm is unaffected by rest or work, by changing the times or the richness of meals, or by feasting or fasting. Nor is the size of the pupil, which might hinder the flow of the aqueous humour at the angle of the anterior chamber, an effective factor, for it has been found that the rhythm occurs whether the pupil is fixed in dilatation or contraction by atropine or pilocarpine, if the continuity of the iris is broken by an iridectomy or a coloboma, or even if this tissue is congenitally absent in aniridia. Any action of light upon the ocular capillaries is negatived by the same monotonous persistence of the rhythm if a brilliant light is maintained all night and the day is spent in dark-

ness. It has been suggested that massage of the eye by muscular movements through the day aided the circulation of the intra-ocular fluid and lowered the pressure of the eye, while the relative immobility during sleep has the opposite hypertensive effect owing to stagnation of the aqueous humour; but again, the maintenance of the characteristic rhythm of the pressure despite the reversal of habits has disproved this.

The only circumstance in fact which has been shown to alter the incidence of these oscillation is a long-term and fundamental change of habits, for if a complete reversal of the habits of work and sleep are established over some time, a similar reversal of the variation in ocular tension occurs. It would, indeed, seem most probable that the basis of these diurnal changes is associated with the rhythmic variations which so commonly occur both in vegetable and in animal life — affecting, for example, sleep, the temperature, diuresis, the electrolytic content of the blood, and other basic functions. It would seem that each individual has a characteristic rhythm which is obstinately maintained, and that both eyes

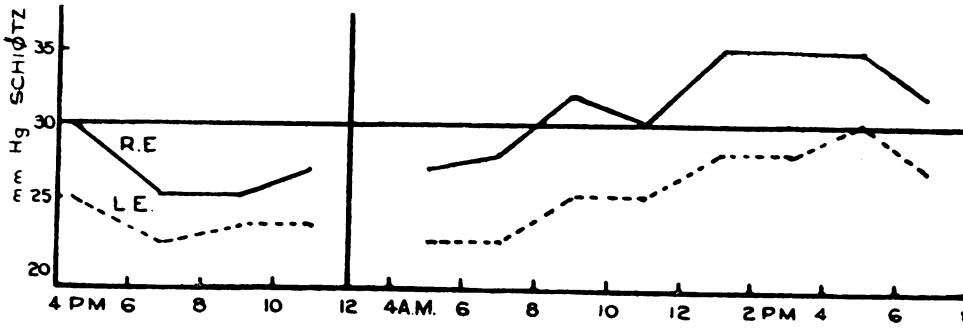

Fig. 1.
A typical diurnal phasic variation in glaucoma. The case is one of simple glaucoma showing a rising type of curve towards the afternoon. Abscissæ, ocular tension; ordinates, time of day.

habitually vary together, circumstances which make it likely that the periodic alteration is determined by a habitual hypothalamic rhythm imposed upon the organism by long-standing environmental conditions. The fact that such rhythms as the diurnal variation in temperature are apparent in the newborn infant indicates that these fluctuations are very fundamental and probably innate.

However that may be, it would seem that a regulating mechanism must exist which tends to maintain the intra-ocular pressure at a physiological level, within a slight habitual rhythmic variation, in spite of the drastic interference which operative procedures may entail. In early cases of glaucoma the first alteration in tension is not so much a rise as a distortion and exaggeration of this normal diurnal variation. It is as if the glaucomatous eye has lost some power of vascular control so that, instead of the normal slight variation of tension, a gross and uncompensated swing occurs.

Let us illustrate this from primary simple glaucoma. By simple glaucoma I mean the slowly progressive and insidious type of case characterized, in addition to the changes in ocular tension, by field defects and cupping of the disc from a relatively early stage of the malady, without congestion or episodic events, asymptomatic until its late stages, or associated only with vague but constant visual difficulties.

In this type of the disease three typical variations occur in the curve of the tension. First, a falling type of curve characterized by a high tension in the morning decreasing later in the day occurs in some 20 per cent of cases of simple glaucoma. In a second group the opposite phenomenon of a rising type of curve occurs in some 25 per cent of cases (Fig. 1). Finally, in a third group, comprising some 55 per cent of cases, a double variation appears in the daily curve which

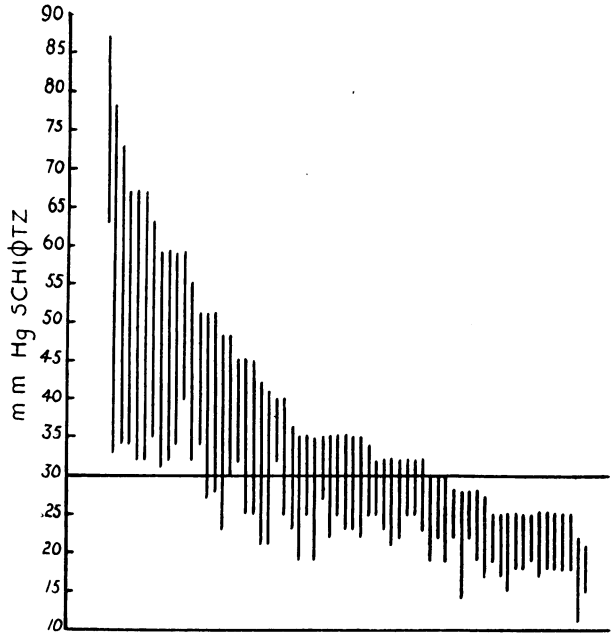

Fig. 2.

The excursion of the phasic variations in 63 cases of simple glaucoma represented by the height of the vertical lines. It will be noted that in a significant number of cases the tension is always below the limits generally accepted as normal, but the excursion is greater than 5 mm. Hg.

may, in a sense, be regarded as a combination of the other two types. These variations in simple glaucoma may be very dramatic. In Fig. 2, each vertical line shows the variations between the peak and base tension in a series of sixty-three unselected eyes affected with this type of the disease which had not been subjected to operation, either because they had recently come under observation, or because

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they appeared clinically not to be deteriorating with miotic treatment. In this series the greatest phasic variation was 45 and the smallest 5 mm. Hg during a period when miotic treatment had been stopped. In general, the higher the base pressure the greater the phasic excursion. It is important that in 18 cases the tension was never above 30 mm.—a significant proportion of almost 30 per cent.—and in two cases it remained consistently below 25, the level generally considered normal.

So far then as simple glaucoma is concerned, if I were to define it in terms of the ocular tension, I would say, not that it was a condition characterized by a high tension—above 30 mm. Hg, above 25, or what you will—but that it was characterized initially by an instability of tension which shows a diurnal phasic variation of more than 5 mm. Hg, a state which—usually but not invariably—results in a permanent increase of tension. I would stress that in its early diagnosis, the height of the tension is always below the level generally accepted as normal.

Before we leave this rhythmic variation in simple glaucoma there are several points which deserve attention. In the first place, the rhythm in its general sense is not fortuitous but is characteristic of the individual. It is independent of blood pressure, of age, sex and refractive condition, nor does it have any relation to the width or narrowness of the angle of the anterior chamber, phases as great occurring with proportionate frequency in cases with wide as with narrow angles. Moreover, it is seen in the earliest stages of the disease, often before any clinical evidences of glaucoma are apparent, as may be seen by its occurrence in an eye which seems clinically to be normal but whose fellow has obvious symptoms of the disease. It is also of unusual interest that, in general, the same individuality of the phasic variation is preserved after a successful drainage operation although the excursions are damped down.

Let us now turn to congestive glaucoma. By congestive glaucoma I mean that type of disease which, in contrast to simple glaucoma with its insidiously progressive course, is episodic in its nature, which occurs preferentially in females of an anxious disposition at an earlier age than the simple type of the malady, that shows no changes in the visual fields or optic discs until the disease is far advanced sometimes into the chronic congestive or the absolute stage, that usually has a narrow angle of the anterior chamber, and that is characterized initally by irregularly occurring rises in tension associated with transient attacks of halos and mistiness of vision which may culminate in an acute and incompensated attack of raised tension. While simple glaucoma is slowly and insidiously progressive, congestive glaucoma is violent and turbulent in its course; the former causes blindness quietly almost before its victim is aware, the latter with all the tragic drama of a catastrophe.

The investigation of the tension in such cases shows a characteristic evolution which can be divided into three stages.

In the first stage, which sometimes lasts for many years, the tension is generally normal, and it is important to remember that, in distinct contrast to simple glaucoma, it shows merely the normal but no abnormal diurnal rhythm.

Occasionally, however, a sudden rise of tension occurs, appearing as an isolated incident. It occurs particularly towards the end of the day, usually when the patient is tired or worried or excited. A family crisis, a business worry, an exciting game of cards, or a visit to the cinema are typical adequate stimuli. This phase may last for years; occasionally, however, an acute congestive attack may suddenly develop which the patient cannot fail to remark.

A second stage is reached when unusual events are not required to excite such a variation of tension, and a regular phasic rhythm sets in wherein, if no treatment is given, the tension may rise, regularly and periodically, every day to

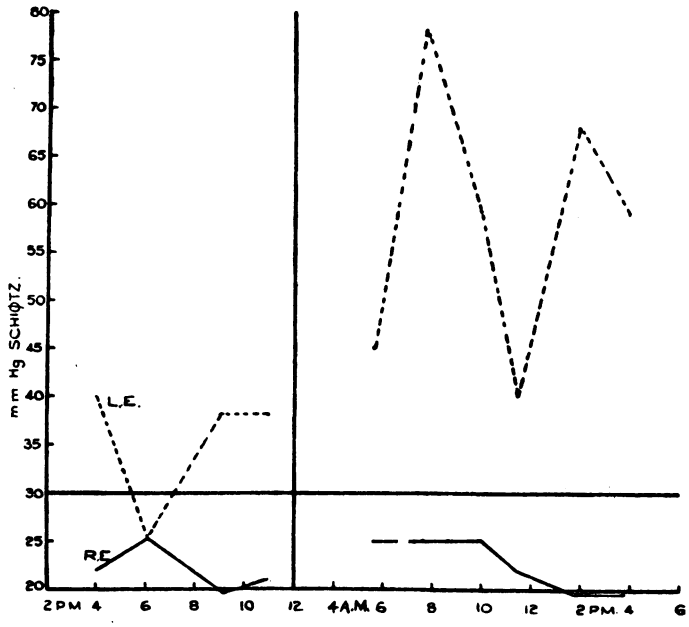

Fig. 3.

The excursion in a case of advanced congestive glaucoma affecting the left eye (dotted line). The right eye (continuous line) shows no pathological rise of pressure but a pathological variation indicating the presence of vasomotor instability.

heights sometimes of 60 or 80 mm. Hg. Again the eye remains white without congestion, and the patient meantime often suffers no inconvenience except regularly occurring and transient halos and mistiness of vision (Fig. 3). At this stage the height of the phasic rhythm of tension is usually controlled within adequate limits by miotics, but the character of the rhythm remains. This state of affairs may last for years. The optic discs remain pink and show no sign of cupping and the fields, both peripheral and central, are unimpaired, so that no disability—beyond the use of miotics—is experienced by the patient, nor does

objective harm affect the eyes. It is interesting, however, that after treatment with miotics has been begun, a failure in the natural control seems to be reached much more rapidly so that on the withdrawal of the drug, the tension rises rapidly to dangerous heights, and at this stage in the disease a congestive attack is likely to ensue.

The final stage is reached when miotics, even the most powerful, are without hypotensive effect; the tension suddenly rises and remains so; visual symptoms become sufficiently clamant to demand attention, and an acute strangulating circulatory crisis supervenes, unless it is forestalled by surgery. Something happens in the course of the usual transient, self-limited attack so that it becomes irreversible : some margin is crossed over which there is no easy return. There is one point of crucial importance which is not often stressed. In the ordinary prodromal attacks, whether they be intermittent and occasional or periodic and regular, there is no pain, there is little or no congestion, and the eye is white, and yet the tension is often 60 mm. Hg, and may occasionally reach 80. In the true congestive attack, the eye may certainly on occasion, be immeasurably hard, but the tension is often less than 60; and yet the eye is painful and intensely congested. Something new has happened : the whole clinical picture has changed; and the difference is qualitative not quantitive.

The pathological picture presented by a case such as this, when the eye has been examined shortly after an acute attack, is typical. It is obvious that the primary fault lies in an intense vaso-dilatation of the whole of the uveal circulation, associated with enormously increased capillary permeability and swelling of the tissues. The pathological picture shows that congestion affects particularly the ciliary body, wherein the blood vessels show a great dilatation with deposition of fibrin around them, and the entire ciliary region is so swollen that the root of the iris is pushed forward against the cornea, sometimes obliterating the angle of the anterior chamber. A discussion of this catastrophic phenomenon is not really germane to our immediate subject; but it may be that the prodromal phasic variations are due to a periodic sympathetico-tonia; it may be that when this becomes sufficiently frequent or severe, and the tension rises sufficiently high to cause tissue-damage, histamine-like substances are liberated and their effects upon the circulation change the entire picture.

In the meantime, let us enquire into the cause of these peculiar variations of tension which appear to be fundamental in primary glaucoma. It is certain that their cause does not lie in the width or narrowness of the angle of the anterior chamber, for similar variations occur whether the angle is wide or narrow, and in the same eye the angle remains of the same width during a rising and a falling phase of tension. Nor can it be due to a structural sclerotic impediment to drainage, for such an organic change cannot be effective at 10 o'clock and ineffective at 12 o'clock in the same day. Organic changes certainly develop at a later stage; but initially and fundamentally the cause must be equally variable as the effect, that is, it must be functional in nature.

These pressure changes could be due to one of three things—(1) a variation in the capillary blood pressure; (2) a variation in the volume of the intra-ocular fluid; or (3) a variation in its drainage.

With regard to the first question, it is impossible to see the uveal capillaries clinically or to measure the pressure within them, and the only evidence on this point which can be brought forward is indirect. The only part of the circulation we can observe is the exit veins as they emerge on the sclera, and invariably, contrary to what is frequently stated, and completely contrary to what happens in the congestive crises of acute glaucoma, in the early phasic stages a rise of tension is always associated with a constriction and a fall of tension with a dilatation of these vessels. It is also to be remembered that the entire uveal tract is virtually erectile tissue wherein arterioles of considerable size empty themselves into venous channels by direct anastomosis with little or no dichotomous branching. For this reason changes in vascular pressure will have dramatic effects and changes in capillary pressure will be readily reflected in the exit veins.

With regard to the second point, the formation of aqueous, recent work, on which there is now a considerable degree of unanimity, would seem to point to the conclusion that the intra-ocular fluids are formed by a basic process of controlled diffusion across the blood-aqueous barrier (essentially the ocular capillary walls), a process on which is superimposed a secretion elaborated in the ciliary region. Diffusion across the blood-aqueous barrier can be explored by studying the rate of the leakage of fluorescein into the anterior chamber after the dye has been injected intravenously. Normally the transfer of this substance across the blood-aqueous barrier follows a standard curve. With the exception of the acute crisis of congestive glaucoma, the phasic variations in tension in both simple and congestive glaucoma are associated with no significant alteration in the permeability curves, nor is it related in any way to the height of the ocular tension in a particular case, even although it may vary at different times of the day from 30 to 70 mm. Hg. We can, therefore, conclude that increased capillary permeability and increased diffusion do not enter into the causation of the periodic rises of tension in primary glaucoma.

It is of considerable importance that this mechanism is effective in certain types of secondary glaucoma—as in the inflammatory variety (hypertensive iridocyclitis) —and it is also interesting that the fluorescein pours into the anterior chamber in the acute congestive crisis of congestive glaucoma — but this, as we have suggested, is an entirely different mechanism from that seen in the early phasic stages.

Let us now consider any possible variation in secretion. If fluorescein is instilled into the conjunctival sac it diffuses through the cornea and appears in the aqueous humour in a concentration sufficient to be measured optically with considerable accuracy, and then slowly disappears. Its concentration and disappearance in the normal eye follow a fairly regular time-curve lasting some 18 hours. In glaucoma, if the tension is rising or high, the concentration of fluorescein in the aqueous remains high for a very much longer period. If the tension falls,

either spontaneously or on the exhibition of miotics, the concentration of fluorescein rapidly falls. If we were to assume that the rise in tension is due to over-secretion of new aqueous humour — which, of course, would contain no fluorescein — while the drainage facilities remained constant, a dilution of fluorescein in the anterior chamber would result; the concentration of fluorescein derived from the cornea during a period of high tension, and its disappearance with the fall of tension, prove that the increase of tension is not due to excessive secretion of aqueous but, suggest that it is due to a blockage of drainage, the relief of which accompanies the fall in tension.

This brings us to the drainage channels. A blockage of these channels may occur, first, at the angle of the anterior chamber if the root of the iris is pushed against the cornea. This can be shown not to occur in the early phasic stages of the disease of congestive glaucoma, although it does occur in the acute congestive crises. In the second place, a blockage may occur in the trabecula which may become impervious or sclerosed; this frequently happens in advanced cases of simple glaucoma, but cannot account for the early variable rise and fall. Finally, a functional block would occur if the pressure in the episcleral veins rose so that it became higher than the pressure in the anterior chamber. In the first two sets of circumstances it is possible that drainage may continue at a higher pressure level, but in the third case when the pressure in all the venous exits is raised, drainage would be impossible since aqueous cannot run from a lower pressure level in the anterior chamber into a high pressure vein.

Clinical observations show this to be the case, for in this respect the aqueous veins which drain directly from the canal of Schlemm into the episcleral veins emerging directly from the eye form a delightful and most accurate natural manometer. It can be observed clinically that in the increasing phase of tension there is little or no flow through the aqueous veins, the flow is of average dimensions when the tension is level no matter what the height may be, and that it is greatly increased in a decreasing phase. Similarly, if the glass-rod test is employed to a laminated aqueous vein, while a blood-influx phenomenon is the usual finding in the ascending phase when the recipient vessel of an aqueous vein is compressed, the conditions are reversed in the same vein in the descending phase, so that an aqueous influx is common (Fig. 4). That means that the venous pressure is higher than the aqueous in an ascending phase, and lower in a descending phase.

Finally, an occasional reversal of flow may occur spontaneously. An aqueous vein may appear laminated, containing for some distance parallel columns of aqueous and blood which have not yet intermingled, in a steady phase of tension: in these circumstances, the pressure of aqueous in the anterior chamber must equal the pressure in the vein. In the ascending phase of tension the same vein may become filled with blood, indicating a rise in the venous pressure; in the descending phase the flow may again become laminated and the vessels may eventually become filled with clear aqueous, indicating that in this phase the venous pressure has fallen below the aqueous pressure.

It would, therefore, seem obvious that, without the occurrence of any organic changes, the drainage of the aqueous humour is embarrassed or even abolished in the ascending phase of tension owing to the high venous pressure, an embarrassment which is relieved intermittently when the venous pressure descends, but would be unrelieved if the circulatory changes became permanent.

All this points definitely to a vascular change being responsible for the phenomenon. Let us enquire how it can be controlled.

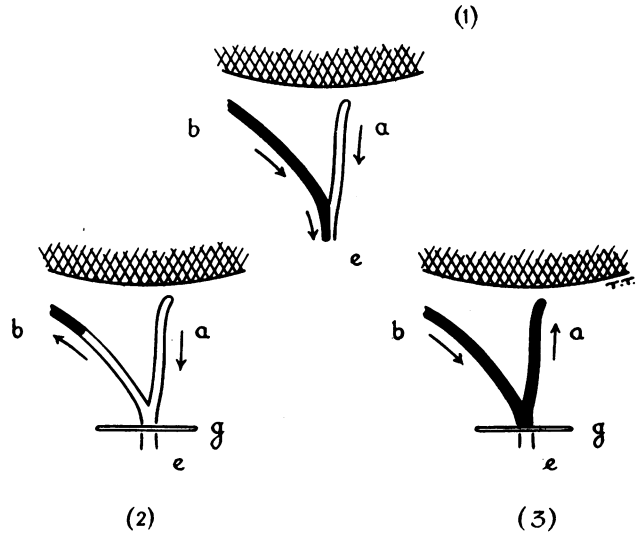

Fig. 4.

THE GLASS-ROD TEST. (1) Shows the normal condition. (*a*) Represents an aqueous vein full of clear fluid; (*b*) a blood vein full of blood; they join together to form a laminated vein filled partly with blood and partly with aqueous when the pressure in both feeding vessels is approximately equal.

Any gross difference in pressure is revealaed when the recipient vessel (*e*) is obstructed by pressure from a small glass rod (*g*). If the pressure in the aqueous vein (that is, in the anterior chamber) is greater than the pressure in the blood vein (that is, in the exit veins of the eye) there will be a reflex of aqueous from *a* to *b*, as seen in (2). If these pressure relationships are reversed there will be a reflex of blood into the aqueous vein, as seen in (3).

In the first place, the entire phasic variation is abolished if the ciliary ganglion is infiltrated with procaine. This, of course, abolishes both the sympathetic and parasympathetic nerve supply to the eye. It is also of interest that if the ciliary ganglion on one side is blocked in this way the phasic variation in the other eye is also damped down or ceases altogether, a fact which shows that this phasic variation is mediated between the two eyes by axon reflexes, an effect one sees in other connections. In the second place, a similar abolition of the phasic variation occurs on blocking the stellate ganglion in the neck, which indicates

that the sympathetic is primarily at fault. Similarly, an abolition of the phasic rises occurs after the administration of drugs which block sympathetic activity, such as hexamethonium or dibenamine, but in this case the evidence is somewhat obscured by the general fall of blood pressure.

Finally, we have the evidence of the hypotensive effect of cholinergic drugs such as pilocarpine and eserine. This has been known for a long time, and the classical view has always been that they act essentially by opening up the angle of the anterior chamber and thus encouraging draining by contracting the pupil. To some extent and in some cases, this is doubtless true, particularly in cases wherein the angle is narrow and temporarily embarrassed in an acute congestive attack. But this does not explain their effectivity in the more numerous cases wherein the angle is all the time demonstrably open; or when, on the contrary, it is organically closed by complete peripheral synechiæ; or when the sphincter of the iris is thrown out of action by an operation; or in cases of aniridia when the iris is absent or virtually so.

In addition to their miotic effects, however, these drugs produce a capillary dilatation and the opening out of new capillary districts, which, for the time being, may be functionally closed. This can well be seen by the naked eye in the iris of the albino rabbit. Normally in the iris of this animal, large radial vessels running from the circle of the iris are easily visible, with, however, only a few small vessels near the pupillary margin. On the instillation of pilocarpine or eserine, the picture is quite changed, for large numbers of dilated capillaries are seen among the terminal arcades. This effect is due not only to the dilatation of the few vessels previously seen, but to an apparently vast increase in their number.

The same effect can be observed by studying the permeability of the ocular capillaries before and after the instillation of pilocarpine in animals or man. In animals, for example, a particulate dye, such as Trypan blue, does not ordinarily get into the anterior chamber, but after the administration of eserine, the blue dye can be seen heavily staining the aqueous humour. In man this is most easily demonstrated by the technique we have already mentioned earlier in this lecture, of injecting fluorescein intravenously and observing the rate at which it appears in the anterior chamber in the beam of the slit-lamp when it is seen that the permeability is very considerably increased. This vasodilatory action of pilocarpine and eserine can be readily verified clinically after the instillation of these drugs by the observation of capillary dilatation in the conjunctiva, by the increase in the vascular pulse of the eye as registered with the tonometer, and very beautifully and dramatically by the apparent altered rate of the peri-foveal circulation as seen entoptically.

This effect is also seen in the behaviour of the aqueous veins after the instillation of miotics, for then a dilatation of these veins can be observed as well as an increase in their current. Indeed, these miotic drugs sometimes act so dramatically as to cause a change in the direction of flow so that a vessel which, before their instillation, seemed to be a blood vein, after their instillation becomes an obvious

aqueous vein; and in many vessels, on the application of the glass-rod test, an aqueous influx phenomenon can be observed after their use when before it could not.

If the phase of rising tension in glaucoma is due to a phase of irritability and constriction of the capillary circulation which induces a high capillary-venous pressure—a phase of sympathetico-tonia—while the phase of falling tension is associated with a recovery from this phase of irritability wherein the circulation resumes its normal equilibrium, it may seem reasonable to suggest that the essential action of miotics in these circumstances is to combat this irritable state, to counteract the adrenergic state by a cholinergic action, to cause a capillary dilatation and to open out capillary channels which have been temporarily occluded, so that the blood is dissipated over a wide capillary bed in such a way that its hydrostatic pressure is lowered and the pressure in the venous exits falls.

To summarize—it seems probable that the early stages of glaucoma of both types are characterized by a condition of vascular instability, periodic phases of sympathetico-tonia wherein a raised venous capillary-pressure occurs, being followed by phases wherein circulatory control reasserts itself.

In congestive glaucoma the changes are irregular, turbulent and dramatic, depending for a long time on specific stimuli which excite a condition of sympathetico-tonia; but since for a long time they are intermittent and since, in the quiet intervals, the circulation is adequately maintained, the eye as a rule maintains its integrity and its function for a longer period. But if the phases become a constant habit and the intermissions become incomplete, eventual damage is done; and if at any time they overstep themselves so that in an acute crisis circulatory strangulation becomes insupportable, the damage may be sudden and catastrophic.

In simple glaucoma the variations are regular, spontaneous, but slowly and remorselessly progressive, and they are accompanied by, or may even cause, organic changes of sclerosis in the ocular circulation. The first phase is associated with instability of tension, the second with its permanent elevation. So long as these vascular changes are intermittent and the circulation returns periodically to normal, so long as the eye gets periodic rest periods, its function may survive. But if these changes pass from the functional to the organic, from the reversible to the irreversible stage when compensation becomes difficult, infrequent and eventually impossible, permanent damage results. In the end the capillary circulation almost disappears, and all the tissues of the eye, including the trabeculæ at the angle of the anterior chamber and the tissues of the optic nerve, become degenerated and sclerosed; and even although, at this stage, if the tension—which may never have been very high—is surgically relieved, the degeneration and sclerosis may progress so that blindness—virtual or complete—may result.

That is not to say, of course, that the control of tension by operative treatment at as early a stage as possible is useless. Within the limits of our present knowledge, it is the only thing we can do; and if the raised tension is allowed to remain

and progress, most of those eyes would go blind. The poverty of our results is merely a natural result of our confining ourselves to relieving a symptom—albeit an important symptom—and leaving the primary disease untouched. To conceive glaucoma in terms of the drainage of the aqueous only, as is the habit among so many of us to-day, is to base our therapeusis on the evidence of the gross pathology which disease has left behind it, rather than on the more subtle initial changes depending on the underlying disordered physiology. The derangement of mechanics which appears as an end-result is so much more obvious than the initial failure in function: a rearrangement of mechanics is easy and since it gives relief, by all means let us practise it; but whatever we may say to our patients, do not let us say to ourselves that in this rearrangement we have solved the underlying problem or cured the disease. It may be that in the future we may be able to do better, but until that time comes, I am sure that Dr. Craig, with his great weight of wisdom and experience, will agree with me when I say, It is not what we say to others, particularly if they require psychological support, but what we say to ourselves, that really matters.

REVIEWS

THE JOURNAL OF CLINICAL NUTRITION, Vol. 1, No. 1. Published bi-monthly by The Nutritional Press, Allentown, Pennsylvania. Subscription 55s. to the agents for the British Commonwealth. London: Ballière, Tindall & Cox.

THIS is a new "international journal reporting the practical application of our newer knowledge of nutrition." The present number contains eight original papers, of which half are basically of the review type, and half present new observations. In addition, there is a section of abstracts of current literature.

The standard of printing and presentation is high, and the composition of the Editorial Boards suggests that this will be maintained. G. M. B.

JOURNAL OF THE AMERICAN GERIATRICS SOCIETY, Vol. 1, No. 1. Published by The American Geriatrics Society. (Pp. 76; illustrated. 82s. for one volume of six numbers.) Agents for British Commonwealth: Messrs. Ballière, Tindall and Cox, London. 1953.

THE American Geriatrics Society was established just over 10 years ago for "the clinical study of geriatric problems in the broadest sense, including the study of the causes, prevention and treatment of diseases of advancing years, the rehabilitation of patients, and the dissemination of this knowledge." The growing international membership of the Society has enabled the last objective to be fulfilled by the publication of the Journal of the American Geriatrics Society. The associate editors include Professor A. P. Thomson and Professor L. Brull. G. F. A.