MECHANISM OF PRODUCTION OF PAPILLOEDEMA*

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THE optic disc is an intriguingly small and intricate structure. Some of the pathological processes known or assumed in other conditions can be of help to us in elucidating the changes occurring in papilloedema. By papilloedema in this study I mean the non-inflammatory type found typically in cases of raised intracranial pressure, but also occurring, as we shall see, in some other conditions.

The tissue of the disc derives its blood supply from the arterial circle of Haller (or Zinn) (Fig. 1). Each trabecula of the lamina cribrosa (nourishing the nerve fibre bundle within it) is essentially the result of the ingrowth of a vessel derived from the circle of Haller accompanied by glial and connective tissue (Wolff, 1954). The circle of Haller is formed by about three of the short ciliary arteries which also supply the anterior end of the optic nerve. There are connexions usually on a capillary level across the cribriform plate with the inconstant artery of the optic nerve (François and Neetens, 1963), and with twigs from the central retinal artery arising just behind the cribriform plate. Although these are usually quite inadequate to maintain the vitality of the retina if there is a blockage of the central retinal artery, this may reflect

FIG. 1.—Arterial supply of anterior end of optic nerve (Hayreh, 1963b, Fig. 1).

ON Optic nerve
CAR Central retinal artery
PCA Posterior ciliary artery
CZ Circle of Zinn.

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the rapidity of retinal degeneration rather than the poverty of these anastomoses (Wybar, 1956). There are also connexions with the choroidal vessels immediately around the disc. Cilio-retinal anastomoses of any useful degree *via* the tissue of the disc have been disputed right back to the classical studies of Leber (1903), but there seems to be no doubt of the existence of numerous fine connexions *via* the pial branches of the central retinal artery and the recurrent pial branches of the circle of Haller (Fig. 2) (Singh and Dass, 1960; Hayreh, 1963a, b). The capillaries of the disc spread with the nerve fibres into the retina immediately around the disc and drain into the central retinal vein, there being no venous counterpart to the circle of Haller.

FIG. 2.—Fine arterial anastomoses between circle of Zinn and collateral branches of (mainly) the central retinal artery *via* the pial plexus of the anterior end of the optic nerve (Hayreh, 1963b, Fig. 2).

OA	Ophthalmic artery
CAR	Central retinal artery (depicted to avoid confusion only up to its point of entry into the nerve)
Col. Br.	Collateral branches
LPCA	Lateral posterior ciliary arteries
MPCA	Medial posterior ciliary arteries.

The tissue which becomes swollen in papilloedema is that supplied by the circle of Haller (Leinfelder, 1959), and it is the same tissue which atrophies away in chronic glaucoma. The survival of the nerve fibre bundles is of prime importance in chronic glaucoma, whatever the intra-ocular pressure or aqueous outflow may be, and these fibres depend for their nourishment on the blood supply of the disc and cribriform plate as they traverse it. The tissue of the disc is normally pink from the richness of its vascular bed, and, in separating a physiological cup from the edge of the disc, the rim is commonly known on ophthalmoscopic appearance as the border tissue. Loss of this tissue and the associated arcuate scotoma from interruption of the nerve fibres where the tissue is deficient are what distinguishes glaucomatous from physiological cupping. The picture of the disc in the non-glaucomatous atrophy which

may occur from a nerve lesion or from blockage of the central retinal artery is again different in that this tissue can still be discerned, but it becomes pale, the vascular bed closing down as the nerve atrophies. Moreover, in branch retinal artery occlusion, the field defects differ in important details from the glaucomatous scotoma. In these cases of blockage of the retinal artery or its branches, the blood supply to the rest of the eye and the intra-ocular pressure are unaltered, which differentiates the lesion from blockage involving the ophthalmic or carotid artery.

von Graefe (1854) wrote that, in chronic glaucoma (presumably chronic simple glaucoma), the arteries on the disc can be made to pulsate more readily than normal by gentle digital pressure on the globe, and in 1857, in a paper carefully describing the entity of low-tension glaucoma (amaurosis with excavation), he stated that this easily-induced arterial pulsation occurred also in cases in which the ocular tension was not raised. Various other workers confirmed these observations (Dimmer, 1887; Bailliart, 1940; Redslob, 1941; Sjögren, 1946), and related it to a low diastolic arterial pressure which can be measured by the ophthalmodynamometer. The extra pressure applied by the dynamometer until the retinal artery collapses added to the intra-ocular pressure gives the pressure in the ophthalmic artery (Duke-Elder, 1926), and there are tables to correct the figure on the machine for various intra-ocular pressures (Weigelin and Müller, 1951; de Laet, 1961) but, ignoring these corrections, the dynamometer reading indicates the pressure of the arterial supply relative to the basic resistance of the intra-ocular pressure (Lobstein, Bronner and Nordmann, 1960). As the blood supply to the whole eye normally comes in man from the ophthalmic artery and as all the arteries within the wall of the eye and subject to the intra-ocular pressure are assumed to function at similar pressures, this easily-induced pulsation seen in the retinal artery is an indication of impaired arterial pressure to all the intra-ocular structures (whether the impaired supply is from a failure to overcome the hindrance imposed by a raised intra-ocular pressure or from a primarily impaired arterial supply against a normal intra-ocular pressure). Ischaemia of the intra-ocular structures is one of the pathological features of chronic simple glaucoma. This is apparent on the disc, and it has been demonstrated in the choroid during life by Cristini, Forlani, and Scardovi (1962) without there being any definite relationship with the level of the intra-ocular pressure.

Gafner and Goldmann (1955), in considering how a raised intra-ocular pressure might affect the blood flow to the intra-ocular tissues, divided the arteries subjected to the intra-ocular pressure into three groups:

- (i) Those with virtually no anastomosis outside the eye (the central retinal artery).
- (ii) Those which, before entering the eye, give off branches smaller than the main stream and which therefore have a large resistance compared with the main stream (the short ciliary arteries).
- (iii) Those which give off branches of an alternative pathway as great outside the eyeball as within it (the circle of Haller).

Although the head of pressure (ophthalmic artery pressure) is the same for each group, a raised intra-ocular pressure will scarcely affect the flow in the central retinal artery, as there is virtually no alternative route for the blood, but it will particularly impair the blood supply to the disc as the blood from Haller's circle can be diverted

via its anastomotic connexions to tissues not subjected to the intra-ocular pressure (Fig. 3).

FIG. 3.—Diagrammatic representation of the shunt mechanism (From Gafner and Goldmann, 1955).

Vessels within the heavy circle are subjected to the intra-ocular pressure and thereby have the capillary resistance increased when the pressure rises. This would lead to a diversion of blood where an alternative extra-ocular bed is available, which is the case for the tissue of the disc, the shunt being mainly to the pial plexus. If the pressure is lowered (or the pial resistance raised) then blood is diverted selectively to the tissue of the disc which would now be the easier pathway.

- OA Ophthalmic artery
- CRA Central retinal artery
- SCA Short ciliary artery
- CRV Central retinal vein.
- RPA Recurrent pial arteries.

Furthermore, if the pressure in the ophthalmic artery is impaired and a normal intra-ocular pressure is maintained, a similar diversion of blood away from the tissue of the disc is to be expected, thus accounting in theory for cases of low-tension glaucoma. Christiansson (1962), on this assumption, looked for the development of glaucomatous cupping in thirteen patients who had undergone carotid ligation, but none had developed any, this perhaps being explained by the fact that most of them showed a slightly lowered intra-ocular pressure on the side of the ligation. Two further explanations for the lack of cupping, not mentioned by that author but apparent from the details of the paper, are that more than half the patients were hypertensive and that the average age (47 yrs) was younger than the average for glaucoma. It is known clinically that the disc in some cases may stand up to a raised tension for a long time without becoming cupped, *e.g.* in the younger age groups or where the blood vessels are congested (secondary glaucoma, diabetes, carotido-cavernous aneurysm), whereas in other cases it succumbs in spite of a normal tension. The development of cupping is related in certain well-authenticated instances to a fall in blood pressure (*e.g.* from coronary thrombosis, the onset of heart failure, or the use of centrally-acting cardiac depressant drugs: Reese and McGavie, 1942; McLean, 1957; Harrington, 1959; Lobstein and others, 1960). It is significant here to note that the main extra-ocular territory to which blood can be diverted from the disc is the pial plexus at the anterior end of the optic nerve and this of course is subject to the intracranial pressure. The diversion of blood to the pia had been

mentioned by Sautter and Seitz (1952), in another connexion—a theory of control by a glomus apparatus of the anastomotic channels between the central retinal artery and the circle of Haller to prevent overloading the retina with blood—this theory being a rather complicated explanation of the actual diversion which they found. A low intracranial pressure might be expected to aid the diversion of blood away from the disc and indeed Klar (1940), working on the basis of carotid sclerosis as a cause of low-tension glaucoma, found it to be around the lower limit of normality in three cases. I have had the intracranial pressure measured in two cases of low-tension glaucoma and have found it to be 85 and 95 cm. H₂O (by lumbar puncture in the horizontal position, without there being any spinal block when checked by Queckenstedt's test). In the second case the blood pressure was also low (115/70 mm. Hg), which would aggravate the ischaemia of the disc and might account for the rather low intracranial pressure as well as the failure of the intra-ocular pressure to rise above 23 mm. Hg (Schiötz) in the right eye and 27 mm. Hg in the left under provocation.

Now in papilloedema the tissues involved are those supplied by the circle of Haller and its connexions, most conspicuously the tissue of the disc. The vessel-bearing portion of the optic nerve is somewhat oedematous, principally adjacent to and involving the pial sheath (Fig. 4), but also around the central vessels and along

FIG. 4.—Case 1, died March 7, 1963. Longitudinal sections showing ampulliform swelling of the pia arachnoid (hydrops vaginae) around the vessel-bearing segment of the optic nerve which is also somewhat oedematous.

the septa, and the choroid immediately around the disc may share to a minor extent in this oedema (Paton and Holmes, 1911). The anterior layers of the lamina cribrosa are greatly separated and moved forward, but the posterior lamellae remain, as a rule, compact and normal in position, a result which could scarcely be attributed to propulsion from behind. The ophthalmoscopic appearance of developing cases was observed by Paton and Holmes (1911), and the process appears to comprise first hyperaemia (as evidenced by reddening of the disc), then dilatation of numerous small vessels visible on the surface of the disc as tiny curling vessels, and finally the established picture of oedema with protrusion forwards of the loose tissue of the disc in front of the lamina cribrosa and spreading for a very limited distance into the

retina in the nerve fibre layer. The other layers of the retina are, as a rule, not involved except by mechanical displacement and folding. Filling-in of the physiological cup is stated in various text-books to be one of the early signs of papilloedema, but in my experience this is not so, considerable mushrooming-forward of the border tissue occurring with persistence of a central cup. Greaves (1959) found congestion of the veins, obliteration of the physiological cup, and absence of the spontaneous venous pulse highly suspicious but not wholly reliable signs. He also stressed the importance of examination by the slit-lamp microscope for any signs of uveitis. This can of course be a cause of swelling of the disc and I have been confused by a case of this kind, which presented with bilateral swollen discs, with flare and cells in eyes which showed no ciliary injection or vitreous haze but which were rather soft—this hypotony would be a causative factor additional to the inflammatory process in such a case. Cook (1959) found that oedema starts between the fibres, firstly in the peripherally-placed bundles (of the rim of border tissue), and that the physiological cup becomes obliterated only when the oedema reaches the axial nerve bundles, the cup remaining open in some cases even in the presence of marked swelling. There is, from an early stage, congestion of the retinal veins in the immediate proximity of the disc, and when congestion becomes intense haemorrhages usually appear. The presence of haemorrhages, whilst indicating that the case is pathological, does not indicate what the pathology may be, and in fact if haemorrhages are a marked feature they make me think of some extra pathology or aggravating feature, such as severe anaemia, diabetes, or vascular occlusion, wherein the vessels or capillary bed are probably directly damaged.

I have been fortunate in observing the development of papilloedema in the following case:

Case 1, a man aged 49, presented on November 7, 1962, with blurring of the left eye of 3 weeks' duration, the visual acuity being "counting fingers" only. The left eye showed papilloedema of 3 to 4 D and a picture very similar to central vein thrombosis except that venous congestion and haemorrhages did not spread at that time more than about 2 disc diameters away from the disc. The right eye, in which the visual acuity was 6/5, showed these congested fine vessels on the border tissue of the disc and curling over the edge, a few tiny haemorrhages overlying the nasal edge of the disc, and fullness of the retinal veins. When the patient was admitted to hospital 5 days later in the care of the neurosurgeon, the right eye had developed a frank papilloedema of 3 D (Figs 5 and 6, opposite).

This early intense congestion was seen to be most marked in the parts of the disc which are normally most fleshy, that is in the nasal half including the upper and lower edges. Furthermore, the congestion was in the peripheral part of the disc and spread over the edge into the immediately surrounding retina. These congested fine vessels can be well seen by the ordinary ophthalmoscope, and though they become somewhat obscured when oedema develops the diagnosis is by then obvious.

I have had no difficulty in differentiating this congested appearance from the fleshy normal hypermetropic disc where the disc is reddened but its fine vessels are not engorged and the individual fine vessels can scarcely be discerned by the ordinary ophthalmoscope. I do not think that the degree of swelling and the occasional haemorrhage are of as much importance in the diagnosis of papilloedema as the underlying vascular changes—they are probably secondary effects from damage by the intense congestion, such as increased capillary permeability which the beautiful work of Dollery, Hodge, and Engel (1962) suggests.

FIG. 5.—Case 1, December 3, 1962, right fundus showing papilloedema in a case of inoperable astrocytoma of the mid-brain.

FIG. 6.—Case 1, same day, same eye, showing more detail of upper, half of disc which shows a mass of fine congested vessels extending over the edge into the retina, and also a few haemorrhages (dark blotches) overlying the upper edge.

Vascular congestion emerges as an invariable feature of papilloedema (Duke-Elder, 1940). Its distribution—most marked round the periphery of the disc and in the tissue in front of the cribriform plate, lessening as one reaches the posterior layer of the cribriform plate, where presumably the influence of the intra-ocular pressure would cease and that of the intracranial pressure take over, but still present in the vessels to which the circle of Haller has connexions—strongly suggests that it results from blood being diverted to those intra-ocular tissues supplied by the arterial circle because of increased resistance to flow in the pial plexus; a shunt similar to that

postulated by Gafner and Goldmann with respect to glaucoma but in the reverse direction. A raised intra-ocular pressure would hinder this diversion, and may explain why some cases of raised intracranial pressure fail to show papilloedema or develop it in one eye only. A low intra-ocular pressure would aid this diversion of blood to the disc and is known to facilitate the development of papilloedema in intracranial hypertension (Walsh, 1947). The intra-ocular pressure in my case was only 12.4 mm. Hg (Schiötz) in the right eye and 7.5 mm. Hg in the left, other readings of importance being an intracranial pressure of 200 to 240 mm. H₂O, dynamometer readings of 70 g. diastolic and 100 g. systolic (both eyes), and a brachial blood pressure of 158/92 mm. Hg. It is known that papilloedema does not develop on an atrophic disc whether the atrophy is due to pressure on the nerve or not. The usual explanation of the Foster Kennedy syndrome is that pressure on the vaginal sheath prevents the raised intracranial pressure reaching forward to affect the atrophic disc or the central retinal vein as it emerges from the nerve, but there are unilateral cases where this explanation could not apply (Smith, 1939). Cases are described where only a segment of a disc is atrophic and papilloedema fails to develop on that segment (*e.g.* Freusberg, 1938). These anomalies could, I think, be due to the closure of the vascular bed of the atrophic disc (or part thereof), thus preventing the occurrence of congestion or any subsequent developments.

We can now see why papilloedema without any increase in intracranial pressure may develop in a very soft eye, (papilloedema ex vacuo) as sometimes happens after a freely-draining trephine operation or other filtering scar, without there being any inflammatory signs and without any increase of pressure on the central retinal vein as it traverses the subarachnoid space. A low intra-ocular pressure would induce a diversion of blood from the extra-ocular territory especially to the tissue of the disc. The effectivity of a drainage operation in preventing further field loss in glaucoma probably depends on the improved blood supply to the disc which results from the hypotony, rather than on the improved drainage and circulation of the aqueous. It may be that, in the rare case of blockage of the central artery in which paracentesis has been used empirically and does sometimes restore sight, the beneficial effect derives from the congestion of the vessels of the disc produced by the hypotony opening up whatever anastomosis there is, rather than from the hypothetical dislodgement of a usually hypothetical embolus.

The pressure in the central retinal vein before it leaves the eye is thought in the normal state to be about 2 mm. Hg above the intra-ocular pressure (Duke-Elder, 1926) which, if we take an intra-ocular pressure of 16 mm. Hg, gives a venous pressure of 18 mm. Hg (or 244.8 mm. H₂O). We have no accurate figures for the pressure in the vein in cases of raised intracranial pressure, but the intracranial pressure would have to be in the region of 240 mm. H₂O or greater to cause venous back-pressure, and the forward pressure in the vein could easily pile up from the arterial pressure pushing on through the retinal capillaries until it was adequate to overcome any level of raised intra-cranial pressure. The venous pressure should rise somewhat with a rise in intracranial pressure, as Henderson (1912), Lauber (1935), and Sobański (1937) have shown. If this meant obstruction to the venous outflow then one would expect the whole retinal circulation to be impaired, with haemorrhages and venous

congestion spreading out to the periphery as occurs in central vein thrombosis; but in papilloedema the haemorrhages and venous congestion are restricted to the immediate environs of the disc. Furthermore, in papilloedema, as distinct from venous thrombosis, the vein can usually be emptied by light digital pressure, and I have seen one case in which a spontaneous venous pulse was present, indicating, I think, that the venous outflow in this case was unimpeded. In carotico-cavernous aneurysm there is usually marked venous congestion and a positive back-pressure, yet papilloedema is slight or absent—perhaps because there is also a raised intra-ocular pressure, especially with each pulsation, which counteracts any diversion of blood specifically to the disc. Let us therefore discount venous back-pressure as a prime cause of papilloedema and attribute the restricted distribution of the venous congestion to the fact that the veins are over-filled by the extra blood draining into them *via* the congested tissues of the disc.

A fairly constant finding with raised intracranial pressure is a high diastolic pressure in the cerebral arteries (Lobstein and Nordmann, 1959) arising from the increased capillary resistance of all tissues subjected to the intracranial pressure and, in cases of very high intracranial pressure, as a reaction produced by an ischaemic vasomotor centre to maintain the blood supply to the brain. This raised pressure in the cerebral arteries is said to occur even in cases where papilloedema is absent. Although ophthalmodynamometry measures the pressure in the ophthalmic artery, this gives a good indication of the pressure in the cerebral arteries because the ophthalmic artery is normally a direct branch of the internal carotid artery just before its final division into anterior and middle cerebral arteries. In malignant hypertension there may or may not be a raised intracranial pressure, but the diastolic pressure, as measured by the ophthalmodynamometer, and indeed throughout the whole body is markedly raised. Papilloedema as florid as that due to raised intracranial pressure can and does occur, though in these cases the oedema usually spreads further out into the retina and there is great attenuation of the arteries. Its occurrence is usually associated with a sudden and severe exacerbation of the hypertension and a deterioration of the general condition. The mechanism of production here is probably that the raised arterial pressure, unless balanced by an adequate rise in intra-ocular pressure, will selectively flood the blood vessels of the disc, just the reverse of the case in which glaucomatous atrophy ensues from a fall in blood pressure. A sudden rise in the arterial pressure might be expected to produce a raised intracranial pressure which would facilitate this diversion of blood, but it also produces a temporary rise in the intra-ocular pressure tending to neutralize this extra effect, and the development of papilloedema may depend on which rise is the greater in height and duration quite apart from the direct effect of raised pressure within the capillary bed of the disc.

The following case of malignant hypertension may help to clarify the situation:

Case 2, a man aged 70, attended on December 27, 1962, complaining of headache and blurring of vision coming on for 2 weeks associated with various stresses and a deterioration of his general condition. He had been seen on November 29, 1962, when the fundi showed signs of moderately severe hypertension with no papilloedema, and on two previous occasions since July, 1962, when he was under the care of the psychiatrist and the physician. The blood pressure had risen from 200/120 to 260–280/130–140 mm. Hg.

Moderate papilloedema had developed with many haemorrhages around the discs and engorgement of the fine vessels of the tissue of the discs (Fig. 7).

FIG. 7.—Case 2, January 11, 1963, right fundus showing papilloedema with congestion of the fine vessels of the tissue of the disc in malignant hypertension, also a fine macular star, crossings changes, and attenuation of the retinal arteries.

There was early macular star formation which accounted for the blurring of vision. The visual acuity was 6/18 in the right eye and 6/24 in the left. The retinal arteries, especially the lesser branches, were very attenuated and the veins somewhat full. The intra-ocular pressure was 35 mm. Hg (Schiötz) in the right eye, and 31 mm. Hg (left). The dynamometer readings were 105 g. (right) and 120 g. (left), only the diastolic level being measured at this great height.

The patient was admitted to hospital by the physician and treated at first by rest in bed and sedatives, and later by increasing doses of guanethidine (Ismelin). The blood pressure was still 260/130 mm. Hg on January 8, 1963, by which time the intra-ocular pressure had fallen to 22 mm. Hg (right) and 20 mm. Hg (left) and the dynamometer readings to 95 g. (diastolic) in both eyes. The intracranial pressure was not measured until February 4, 1963, when it was 180 mm. H₂O, so that it may well have been somewhat higher initially. By this time the blood pressure was 195/100 mm. Hg and the dynamometer readings were 57/100 g. (right) and 63/100 g. (left) (diastolic/systolic) with Schiötz measurements of 29 mm. Hg (right) and 25 mm. Hg (left).

The general condition had greatly improved and, apart from an episode of gravitational hypotension on February 19, 1963, when the blood pressure fell to 120–130/80–90 mm. Hg necessitating a reduction of the guanethidine, the patient has remained well with a blood pressure fluctuating around 170/90 mm. Hg.

4 months after the onset of the malignant episode the fundi and the vision were greatly improved, though there was still a residue of papilloedema and macular star.

We may now summarize what we have found respecting this shunt mechanism: that glaucomatous atrophy may arise from selective ischaemia of the disc as a result of a raised intra-ocular pressure, a lowered arterial pressure, or a lowered intracranial pressure, whereas papilloedema may arise from a lowered intra-ocular pressure, a raised arterial pressure, or a raised intracranial pressure.

Although there may be an element of venous back-pressure, this is not essential, the congestion underlying the oedema resulting from alterations affecting the arterial supply so as to overload the disc with blood. Whether papilloedema develops or

not in any particular case will depend on anatomical variations of the arterial supply and its anastomoses, on the balance between these three pressures, and on the rapidity of onset and the severity of the alterations.

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REFERENCES

- BAILLIART, P. (1940). In "Modern Trends in Ophthalmology", ed. F. Ridley and A. Sorsby, p. 195. Butterworth, London.
- COOK, C. (1959). *Trans. ophthal. Soc. U.K.*, **79**, 145.
- CRISTIANSSON, J. (1962). *Acta ophthal. (Kbh.)*, **40**, 271.
- CRISTINI, G., FORLANI, D., and SCARDOVI, C. (1962). *Brit. J. Ophthal.*, **46**, 99.
- DIMMER, F. (1887). "Der Augenspiegel und die ophthalmoskopische Diagnostik", 133. Toeplitz and Deuticke, Leipzig.
- DOLLERY, C. T., HODGE, J. V., and ENGEL, M. (1962). *Brit. med. J.*, **2**, 1210.
- DUKE-ELDER, S. (1926). *Brit. J. Ophthal.*, **10**, 513.
- (1940). "Text-book of Ophthalmology", vol. 3. Kimpton, London.
- FRANÇOIS, J., and NEETENS, A. (1963). *Brit. J. Ophthal.*, **47**, 21.
- FREUSBERG, O. (1938). *Klin. Mbl. Augenheilk.*, **101**, 494.
- GAFNER, F., and GOLDMANN, H. (1955). *Ophthalmologica (Basel)*, **130**, 357.
- GRAEFE, A. VON (1854). *v. Graefes Arch. Ophthal.*, **1**, pt 1, pp. 371, 382.
- (1857). *Ibid.*, **3**, pt 2, pp. 484, 546.
- GREAVES, D. P. (1959). *Trans. ophthal. Soc. U.K.*, **79**, 109.
- HARRINGTON, D. O. (1959). *Amer. J. Ophthal.*, **47**, no. 5, pt 2, p. 177.
- HAYREH, S. S. (1963a). *Anales del Instituto Barraquer*, vol. 4, no. 1.
- (1963b). *Brit. J. Ophthal.*, **47**, 651.
- HENDERSON, T. (1912). *Trans. ophthal. Soc. U.K.*, **32**, 82.
- KLAR, J. (1940). *Ber. dtsch. ophthal. Ges. Heidelberg.*, **53**, 162.
- LAET, H. de (1961). *Bull. Soc. belge Ophtal.*, No. 127.
- LAUBER, J. (1935). *Bull. Soc. franç. Ophtal.*, **48**, 429.
- LEBER, T. (1930). In "Graefe-Saemisch Handbuch der gesamten Augenheilkunde", 2nd ed., Bd. 2, Abt. 2. Engelmann, Leipzig.
- LEINFELDER, P. J. (1959). *Dig. Ophthal. Otolaryng.*, **21**, 130.
- LOBSTEIN, A., BRONNER, A., and NORDMANN, J. (1960). *Ophthalmologica (Basel)*, **139**, 271.
- and NORDMANN, J. (1959). *Docum. Ophthal.*, **13**, 397.
- MCLEAN, J. M. (1957). *Amer. J. Ophthal.*, **44**, 323.
- PATON, L., and HOLMES, G. (1911). *Trans. ophthal. Soc. U.K.*, **31**, 117.
- REDSLOB, E. (1941). *Ann. Oculist. (Paris)*, **177**, 323.
- REESE, A. B., and MCGAVIC, J. S. (1942). *Arch. Ophthal. (Chicago)*, **27**, 845.
- SAUTTER, H., and SEITZ, R. (1952). *v. Graefes Arch. Ophthal.*, **152**, 413.
- SINGH, S., and DASS, R. (1960). *Brit. J. Ophthal.*, **44**, 280.
- SJÖGREN, H. (1946). *Acta ophthal. (Kbh.)*, **24**, 239.
- SMITH, E. G. (1939). *Arch. Ophthal. (Chicago)*, **21**, 856.
- SOBĄŃSKI, J. (1937). *v. Graefes Arch. Ophthal.*, **137**, 84.
- WALSH, F. B. (1947). "Clinical Neuro-Ophthalmology", p. 331. Williams and Wilkins, Baltimore.
- WEIGELIN, E., and MÜLLER, H. K. (1951). *Docum. Ophthal.*, **5-6**, 366.
- WOLFF, E. (1954). "The Anatomy of the Eye and Orbit", 4th ed., p. 294. Lewis, London.
- WYBAR, K. C. (1956). *Brit. J. Ophthal.*, **40**, 65.