

- 1 Helveston EM, von Noorden GK. Microtropia: a newly defined entity. *Arch Ophthalmol* 1967;78:272-81.
- 2 Ingram RM. Amblyopia. *BMJ* 1989;298:204.
- 3 Almeder LM, Peck LB, Howland HC. Prevalence of anisometropia in volunteer laboratory and school screening populations. *Invest Ophthalmol Vis Sci* 1990;31:2448-55.
- 4 Howland HC. Early refractive development. In: Simons K, ed. *Early visual development, normal and abnormal*. New York: Oxford University Press, 1993:5-13.
- 5 Lepard CW. Comparative changes in the error of refraction between fixing and amblyopic eyes during growth and development. *Am J Ophthalmol* 1975;80:485-90.
- 6 Nastri G, Caccia Perugini C, Savastano S, Polzella A, Sbordone G. The evolution of refraction in the fixing and the amblyopic eye. *Doc Ophthalmol* 1984;56:265-74.
- 7 Saunders KJ. Early refractive development in humans. *Surv Ophthalmol* 1995;40:207-16.
- 8 Ingram RM, Barr A. Changes in refraction between the ages of 1 and 3½ years. *Br J Ophthalmol* 1979;63:339-42.
- 9 Abrahamsson M, Fabian G, Sjöstrand J. Changes in astigmatism between the ages of 1 and 4 years: a longitudinal study. *Br J Ophthalmol* 1988;72:145-9.
- 10 Abrahamsson M, Fabian G, Sjöstrand J. Refraction changes in children developing convergent or divergent strabismus. *Br J Ophthalmol* 1992;76:723-7.
- 11 Kiorpes L, Wallman J. Does experimentally-induced amblyopia cause hyperopia in monkeys? *Vision Res* 1995;35:1289-97.
- 12 Hung L-F, Crawford MLJ, Smith EL. Spectacle lenses alter eye growth and the refractive status of young monkeys. *Nature Med* 1995;1:761-5.
- 13 Stone RA, Laties AM, Fernandes A, Tigges M. Spectacles and young eyes. *Nature Med* 1996;2:610-11.
- 14 Atkinson J, Braddick O, Bobier B, Anker S, Ehrlich D, King J, et al. Two infant vision screening programmes: prediction and prevention of strabismus and amblyopia from photo- and videorefractive screening. *Eye* 1996;10:189-98.
- 15 Moseley MJ, Irwin M, Jones HS, Fielder AR, Auld R. Effect of spectacle wear and minimal occlusion therapy on the vision of amblyopic children. *Invest Ophthalmol Vis Sci* 1996;37:S941.

Blood pressure and glaucoma

The paper by Meyer *et al* in this issue of the *BJO* (p 864) adds another intriguing piece to the puzzle that represents the relation between blood pressure and glaucoma. Unfortunately, it often seems that we have an increasing number of pieces but less overall picture.

As long ago as 1857, von Graefe reported a patient with glaucomatous optic neuropathy but with a normal intraocular pressure (IOP), implying—even then—that glaucoma was about more than simply raised intraocular pressure.¹ Wolff,² in 1947, speculated that glaucoma was the result of optic nerve ischaemia while Duke-Elder³ considered arteriosclerosis to be an important factor in open angle glaucoma.

Systemic hypertension has been implicated for many years as a risk factor for developing glaucoma^{4,5} but results have been plagued by the use of single blood pressure measurements (the 'white coat effect') and the bias of hospital based studies. Major advances in our understanding of the relation have only come about with the advent of large scale population based surveys and 24 hour ambulatory blood pressure monitoring.

We have known for some years that systemic blood pressure and IOP were significantly correlated and this has been confirmed by the Baltimore Eye Study.⁶ However, the association between blood pressure and glaucoma is not so clear cut. The Baltimore Eye Study did show a small positive association of primary open angle glaucoma with higher systolic and diastolic blood pressure, the relation was non-linear and the systolic threshold was at 130 mm Hg—above which the risk increased. They also suggested, by using age as a surrogate for duration of systemic hypertension, a protective effect of hypertension in those under 60 and an adverse effect among those over 70 with respect to primary open angle glaucoma. The Rotterdam study⁷ found an association between primary open angle glaucoma and systolic blood pressure but not normal tension glaucoma (perhaps explained by the blood pressure-IOP association), while the Barbados Eye Study⁸ concluded that high blood pressure alone was not a risk factor for primary open angle glaucoma but did indicate, like the Framingham Eye Study,⁹ that people with field defects had significantly decreased blood pressure/IOP ratios.

Simply comparing blood pressure in individuals with and without glaucoma is never going to give us a definitive answer. This led the Baltimore Eye Study investigators to calculate vascular perfusion pressure in their subjects—this being the blood pressure (systolic, diastolic, or mean) minus the IOP—and showed that the lower the diastolic

perfusion pressure the higher the prevalence of primary open angle glaucoma.⁶ In fact, subjects with diastolic perfusion pressures below 30 mm Hg had an age adjusted risk of POAG six times higher than those with pressures of 50 mm Hg or greater.

However, the blood pressure measurements in the Baltimore Eye Study consisted of only two readings 5 minutes apart. It has been shown consistently that 24 hour ambulatory blood pressure monitoring gives lower readings than routine clinic measurements and correlates very well with direct intra-arterial recordings.¹⁰ There have now been a number of studies of 24 hour blood pressure monitoring in glaucomatous patients and the results are important.

Hayreh *et al*¹⁰ compared 24 hour blood pressures in patients with normal tension glaucoma, primary open angle glaucoma, and anterior ischaemic optic neuropathy and found a larger drop in mean systolic and diastolic blood pressure at night in the group with normal tension. This concept of 'nocturnal dips' in blood pressure has only come to light using 24 hour blood pressure readings and is now well recognised by cardiovascular physicians. Studies have shown that if hypertensive patients have their diastolic blood pressure reduced below a critical level then their rate of adverse cardiac events increases.¹¹ Hayreh *et al*¹⁰ extrapolated this to suggest that a similar process could occur in the optic nerve head and ocular ischaemic disorders.

Graham *et al*¹² showed that all nocturnal blood pressure variables were lower in (normal tension glaucoma or primary open angle glaucoma) patients with progressive field loss than in those with stable fields. Bechetoille and Bresson-Dumont¹³ found a lower diastolic and systolic blood pressure in patients with normal tension glaucoma compared with those with primary open angle glaucoma and a greater percentage of diurnal low readings in the former group. Kaiser *et al*¹⁴ also indicated that arterial hypotension was a risk factor for glaucomatous damage. The paper by Meyer *et al* also shows that patients with normal tension glaucoma have larger nocturnal blood pressure drops than normal controls.

Two potential confounders of any of these studies are the use of systemic and/or ocular antihypertensives by the subjects being studied. Hayreh *et al*¹⁰ showed a significant association between visual field loss and nocturnal hypotension in patients taking systemic antihypertensive medications. Graham *et al*'s paper¹² suggested that the nocturnal dip was exacerbated by systemic antihypertensives, but did not show an effect caused by topical β blockers.

The association of nocturnal blood pressure dips and

visual field loss seems very plausible. Twenty four hour blood pressure monitoring has shown that the vast majority of the population have their lowest blood pressure during sleep usually between 2 and 4 am (that is, nocturnal dips in blood pressure are physiological) but, of course, not everyone has progressive field loss. What may be different about those who lose field is that they have exaggerated nocturnal dips, which in some people seem to occur naturally while in others it may be the result of antihypertensive medications.¹² It is not inconceivable that this exaggerated drop could act on an already compromised optic nerve head and reduce ocular blood flow below a critical level. If large areas of infarction occurred, the picture would be of an anterior ischaemic optic neuropathy while a number of subclinical insults may eventually produce the picture of glaucomatous field loss. Certainly the evidence that the 'dippers' are at increased risk of field loss is growing.

We are all aware that IOP is the major risk factor for glaucomatous field loss but this does not explain field loss progression in those with IOP less than 21 mm Hg or lack of progression in those with IOP in the high 20s or 30s. Perfusion pressure is a link between blood pressure and IOP (blood pressure-IOP) and subsequently with blood flow (blood flow = perfusion pressure/resistance). Thus, a drop in perfusion pressure can be caused by a drop in blood pressure or rise in IOP and it is tempting to conclude that this balance determines whether field loss occurs. But what of the effect of vascular resistance? Tielsch *et al*⁶ speculated that their results, which showed hypertension protecting people from primary open angle glaucoma under the age of 60 but being detrimental over 70, indicated that initially raised blood pressure increased ocular blood flow (if their assumption was true that the older the subject the longer he had been hypertensive). Later, after a prolonged blood pressure rise, small vessel damage occurs and so there is increased resistance to flow with a reduction in ocular blood flow and subsequent ganglion cell loss. Thus, it is possible that those patients who have been hypertensive for some years have optic nerves that are experiencing both nocturnal drops in perfusion pressure and progressive hypertension induced vascular resistance, both of which decrease ocular blood flow.

Interestingly, reduced ocular blood velocities and increased vascular resistance have been demonstrated in the central retinal arteries of patients with glaucomatous field loss compared with controls.¹⁵ A similar inequality

existed for the less or undamaged eye in those with field loss in the fellow eye. Further, seemingly undamaged fellow eyes of those with glaucoma have been shown to have a reduced blood flow velocity and increased resistance indicating that circulatory abnormalities may precede glaucomatous damage.¹⁶

So, should we be checking the blood pressure of all the patients in the glaucoma clinic and suggesting alterations to their medications if the diastolic pressure is too low? The answer is, of course, that we need more evidence.

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- 1 Graefe A von. Amaurose mit Sehnervenexkavation. *Graefes Arch Ophthalmol* 1857;3:484.
- 2 Wolff E. Schnabel's cavernous atrophy. *Trans Ophthalmol UK* 1947;67:133-9.
- 3 Duke-Elder S. The problems of simple glaucoma. *Trans Ophthalmol Soc UK* 1962;82:307-13.
- 4 Kummell R. Untersuchungen uber Glaukom und Blutdruck. *Arch Ophthalmol Leipzig* 1911;79:183-209.
- 5 Leighton DA, Phillips CI. Systemic blood pressure in open-angle glaucoma, low tension glaucoma, and the normal eye. *Br J Ophthalmol* 1972;56:447-53.
- 6 Tielsch JM, Katz J, Sommer A, Quigley HA, Javitt JC. Hypertension, perfusion pressure and primary open-angle glaucoma. *Arch Ophthalmol* 1995;113:216-21.
- 7 Dielmans I, Vingerling JR, Algra D, Hofman A, Grobbee DE, de Jong PTVM. Primary open angle glaucoma, intraocular pressure and systemic blood pressure in the general elderly population. *Ophthalmology* 1995;102:54-60.
- 8 Leske MC, Conell AMS, Wu S-Y, Hyman LG, Schachat AP. Risk factors for openangle glaucoma. The Barbados Eye Study. *Arch Ophthalmol* 1995;113:918-24.
- 9 Leske MC, Pogdor MJ. Intraocular pressure, cardiovascular risk variables and visual field defects. *Am J Epidemiol* 1983;118:280-7.
- 10 Hayreh SS, Zimmerman B, Podhajsky P, Alward WLM. Nocturnal arterial hypotension and its role in optic nerve head and ocular ischemic disorders. *Am J Ophthalmol* 1994;117:603-24.
- 11 Floras JS. Antihypertensive treatment, myocardial infarction and nocturnal myocardial ischaemia. *Lancet* 1988;ii:994-6.
- 12 Graham SL, Drance SM, Wijsman K, Douglas GR, Mikelberg FS. Ambulatory blood pressure monitoring in laucoma. *Ophthalmology* 1995;102:61-9.
- 13 Bechetolle A, Bresson-Dumont H. Diurnal and nocturnal blood pressure drops in patients with focal ischemic glaucoma. *Graefes Arch Clin Exp Ophthalmol* 1994;32:675-9.
- 14 Kaiser HJ, Flammer J, Graf T, Stumpf D. Systemic blood pressure in glaucoma patients. *Graefes Arch Clin Exp Ophthalmol* 1993;31:677-80.
- 15 Nicoleta MT, Drance SM, Rankin SJA, Buckley AR, Walman BE. Color Doppler imaging in patients with asymmetric glaucoma and unilateral visual field loss. *Am J Ophthalmol* 1996;121:502-10.
- 16 Landau K, Winterkorn JMS, Mailloux LU, Vetter W, Napolitano B. 24-Hour blood pressure monitoring in patients with anterior ischemic optic neuropathy. *Arch Ophthalmol* 1996;114:570-5.