

# BjO

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## Editorials

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### Aging and vision

It might be no coincidence but as the 'baby boomers' approach advanced middle age there has been a commensurate interest in the effects of aging on normal physiology as well as obvious concerns in pathological terms. Aging processes are associated with many widespread general conditions such as hypertension, non-insulin dependent diabetes mellitus, and cardiovascular disease.<sup>1</sup> These conditions are, of course, widespread in developed countries but aging, indeed premature aging, affects many individuals in developing countries. Much of the ophthalmologist's workload is taken up with age related ocular disease such as cataract (the commonest cause of blindness worldwide<sup>2</sup>) and age related macular degeneration (ARMD), the major cause of blindness in developed countries.<sup>3,4</sup> In economic terms cataract presents a considerable burden of disease in countries such as the USA where some 100 000 operations are performed each year<sup>5</sup>; in contrast, in the Indian subcontinent, it is estimated that 50% of middle aged and elderly patients die blind from cataract.<sup>6</sup>

However, several other disorders affecting vision are more common in the middle aged and elderly. Open angle glaucoma has been predicted to overtake other causes of blindness in terms of frequency by the year 2000<sup>7</sup> while the pandemic in non-insulin dependent diabetes mellitus means that diabetes related blindness is also likely to increase, particularly since diabetic maculopathy, the predominant form of sight threatening retinopathy in this group of patients, is less amenable to therapy than neovascularisation. In addition, one of the commoner indications for keratoplasty, Fuchs' corneal dystrophy, manifests itself during the middle to late years of life.

The impact of aging on morbidity, mortality, and quality of life generally has induced the American Medical Association to nominate aging as the global theme issue for 1997. Accordingly, the October issues of many participating journals have been assigned to papers related to aging issues. In line with the prevalence of age related disease in ophthalmology, the *BjO* had no shortage of submissions when it solicited articles for this issue and its contents reflect many of the disorders that are discussed above. In particular, there are papers which deal with cataract and its surgical complications, with the investigation and treatment of glaucoma, and with age related macular degeneration. However, there are also other papers that highlight ophthalmological conditions which in the elderly behave somewhat differently than in younger patients. For

instance, Williams *et al* (p 835) show that age is a risk factor for graft rejection while Zamiri *et al* (p 827) emphasise the importance of fully investigating elderly patients with atypical chronic posterior uveitis to avoid missing intraocular lymphosarcoma, a rare but age restricted tumour. Other articles deal with ocular surface disease which is also much commoner among elderly patients.

While recognition of the numerous age related diseases increases, the mechanism of aging remains obscure. Genetic influences are suspected since patterns of aging seem to be familial; in addition, there is growing evidence that diseases such as ARMD<sup>8</sup> and open angle glaucoma<sup>9</sup> may be linked to specific gene defects, at least in some forms. Indeed, genetic studies have assisted our clinical understanding of several diseases in that genetic heterogeneity has directed clinicians to search for subtle phenotypic intradisease variation. Perinatal influences on aging have also been suggested, particularly periods of hypoxia which may have prolonged effects carried into old age.<sup>10</sup>

However, the current general hypothesis relating to aging centres on free radical damage for which there is considerable evidence.<sup>11</sup> Indeed, some interesting extensions to the concept suggest that increased cell death may relate to random mutations occurring in the respiratory chain enzymes in mitochondria thereby rendering them less susceptible to lysosomal degradation. This leads to slower turnover of mitochondria and reduces the cell's respiratory capability leading to early death.<sup>12</sup> Such a notion may have particular implications for lens, retinal, and optic nerve physiology. Free radicals are almost certainly also involved in other recognised mechanisms of aging such as advanced glycation end product accumulation<sup>13</sup> and loss of intracellular chaperones.<sup>14</sup> However, it is likely that the risk of increasing the rate of aging probably relates to relative loss of natural free radical scavengers more than any other specific mechanism.<sup>15</sup>

This of course implies that there is a progressive decline in function with age in the absence of overt disease. In addition to the ubiquitous problem of presbyopia, recent evidence suggests that other vision related functions apart from reduced accommodation may become impaired. For instance, a survey of individuals aged 45 and over in Melbourne has shown that reductions in the visual field occur more commonly in the elderly<sup>16</sup>; in addition, a variety of eye movement defects are also associated with advancing age.<sup>17</sup> In this way, the older patient's quality of life, including day to day activities such as driving, may be subtly affected

by minor functional visual disabilities which are absent in younger individuals. Therefore, in considering the effects of aging on vision, it is important to differentiate between reduced visual function in the normal healthy elderly individual and the elderly patient with specific age related disease. While the latter group deserve special research effort to be directed towards them, the former group's possible reduced quality of life also needs to be addressed.

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- Muller DC, Elahi D, Tobin JD, Andres R. The effect of age on insulin resistance and secretion: a review. *Nephrology* 1997;16:289-98.
- Thylefors B. Global data on blindness. *Bull World Hlth Org* 1997;73:115-21.
- Rosenberg T, Klie F. The incidence of registered blindness caused by age-related macular degeneration. *Acta Ophthalmol Scand* 1996;74:399-402.
- Rahmani B, Tielsch JM, Katz J, Gottsch J, Quigley H, Javitt J, et al. The cause-specific prevalence of visual impairment in an urban population. *Ophthalmology* 1996;103:1721-6.
- World Health Organisation. *Strategies for the prevention of blindness in national programmes*. Geneva: WHO, 1997:68.
- Limburg H, Kumar R, Bachani D. Monitoring and evaluating cataract intervention in India. *Br J Ophthalmol* 1996;80:951-5.

- Quigley HA, Vitale S. Models of open-angle glaucoma prevalence and incidence in the United States. *Invest Ophthalmol Vis Sci* 1997;38:83-91.
- Zhang K, Nguyen TH, Crandall A, Donoso LA. Genetic and molecular studies of macular dystrophies: recent developments. *Surv Ophthalmol* 1995;40:51-61.
- Belmouden A, Adam MF, Dupont de Dinechin S, Brezin AP, Rigault P, Chumakov I, et al. Recombinational and physical mapping of the locus for primary open-angle glaucoma (GLC1A) on chromosome 1q23-q25. *Genomics* 1997;39:348-58.
- Nyakas C, Buwalda B, Luiten PG. Hypoxia and brain development. *Prog Neurobiol* 1996;49:1-51.
- Taylor A, Jacques PF, Epstein EM. Relations among aging, antioxidant status, and cataract. *Am J Clin Nutr* 1995;62(6S):1439S-47S.
- de Grey AD. A proposed refinement of the mitochondrial free radical theory. *Bioessays* 1997;19:161-6.
- Booth AA, Khalifah RG, Todd P, Hudson BG. In vitro kinetic studies of formation of antigenic advanced glycation end products (AGEs). Novel inhibition of post-Amadori glycation pathways. *J Biol Chem* 1997;272:5430-7.
- Liu AY, Lee YK, Manalo D, Huang LE. Attenuated heat shock transcriptional response in aging: molecular mechanism and implications in the biology of aging. *EXS* 1996;77:393-408.
- Davies KJ. Oxidative stress: the paradox of the aerobic life. *Biochem Soc Symp* 1995;61:1-31.
- Taylor HR, Livingston PM, Stanislavsky YL, McCarty CA. Visual impairment in Australia: distance visual acuity, near vision, and visual field findings of the Melbourne Visual Impairment Project. *Am J Ophthalmol* 1997;123:328-37.
- Paige GD. Senescence of the human visual-vestibular interactions: smooth pursuit, optokinetic and vestibular control of eye movements with aging. *Exp Brain Res* 1994;98:355-72.

## Aging and the pathogenesis of retinal vein thrombosis

Venous thrombosis has a 'multiple hit' pathogenesis in which several adverse influences affecting the composition of the blood, the structure and function of the vessel wall, and blood flow together result in an acute thrombotic event.<sup>1</sup> This is exemplified by the long recognised clinical factors which predispose to thrombosis in the deep veins of the limbs. For example, the coagulation activation associated with surgical trauma combines with stasis of venous flow due to postoperative immobility to result in a high risk of venous thromboembolism (VTE) after major surgical procedures.

Other clinical risk factors for VTE include obesity, pregnancy, and use of the combined oral contraceptive or hormone replacement preparations. A range of diseases also predispose to VTE, especially malignancy, including myeloproliferative disorders, and less common conditions such as paroxysmal nocturnal haemoglobinuria and Behçet's disease. Among the biochemical and haemostatic variables which have been associated with VTE there has been considerable recent interest in hyperhomocysteinaemia, especially as this is partly determined by diet and it also predisposes to arterial occlusive events. Other notable associations with VTE are a raised plasma concentration of coagulation factor VIII and the antiphospholipid syndromes, where laboratory evidence of lupus anticoagulant and/or anticardiolipin is accompanied by arterial or venous thrombosis.

Over recent years our knowledge of inherited predisposition to VTE has expanded. Hereditary deficiencies of the anticoagulant proteins antithrombin, protein C, and protein S are rare disorders which are associated with a substantial incidence of VTE, often presenting in young adults and provoked by additional stimuli such as oestrogen use. In activated protein C resistance (APCR) there is a reduction of the efficiency of the inhibition of activated coagulation factor V by activated protein C resulting in a prothrombotic state. Other than during pregnancy, when APCR is a physiological response, this phenomenon is principally due to a mutation present at

polymorphic frequency in the gene for factor V (FV:Q<sup>506</sup>) which has been given the title factor V Leiden. The prevalence is high, the heterozygous state being present in around 3-5% in most European populations and up to 12% in some.

Age is also a major influence on the prevalence of VTE. There is a fourfold higher rate of limb venous thrombosis per capita among middle aged subjects (age 40-54 years) than young adults (15-24 years).<sup>2</sup> The elderly are at even higher risk. The mechanisms responsible for this are unclear but aging may introduce alterations to the composition of the blood or to the vessel wall which are prothrombotic.

Retinal venous occlusion (RVO) is a venous thrombotic disorder which also afflicts older subjects, 51% of cases occurring at more than 65 years of age.<sup>3</sup> The incidence in 70-79 year olds is threefold higher than that in those aged 50-59 years.<sup>4</sup> Undoubted associations exist with other conditions, especially hypertension, diabetes mellitus, sedentary lifestyle, and open angle glaucoma, each of which is also age related.<sup>5</sup>

Many of the acquired and inherited risk factors and conditions associated with limb deep venous thrombosis have been sought in subjects with RVO. Occasional cases in which there is deficiency of protein C, protein S, or antithrombin have been reported,<sup>6,7</sup> and others with antiphospholipid antibody,<sup>8-10</sup> myeloproliferative disease,<sup>11</sup> or hyperhomocysteinaemia.<sup>12</sup> The most persuasive evidence has been for a relation between RVO and altered blood rheology,<sup>13-16</sup> especially raised haematocrit and high plasma viscosity.

Recently Larsson *et al* reported a high prevalence of APCR in patients under 50 years of age who had suffered central retinal vein occlusion (CRVO).<sup>17</sup> No confirmatory test for factor V Leiden was performed. While this finding is consistent with the observation that a hypercoagulable state, with increased thrombin generation *in vivo*, is a feature of RVO,<sup>18</sup> other investigators have found no, or a much weaker, association between the occurrence of RVO and



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