British Journal of Ophthalmology 1993; 77: 214–217

Is the season of birth a risk factor in glaucoma?

Robert Weale

Abstract

Several lines of research suggest that some systemic diseases, often associated with age-related conditions, may present with enhanced prevalences owing to very early influences on human development. This paper describes an analysis of 1264 adult Caucasian patients presenting either with primary open angle or narrow angle/angle closure glaucoma on the one hand, or with age-related cataract on the other. In addition, data on cataracts and primary open angle glaucoma on 254 patients of Caribbean origin and 190 of south east Asian origin were also examined. Patients were classified with respect to sex and season of birth. These variables can play a statistically significant role in the prevalence of glaucoma, which raises the possibility that environmental influences may be involved.

(*Br J Ophthalmol* 1993; 77: 214–217)

Risk factors are pre-existing conditions, increasing the probability that a particular pathological entity is going to present in any one individual. A number have been described both for the glaucomas and for cataract. For example, hypermetropia is said to be a predisposing factor for narrow angle/angle closure glaucoma (NCAG), and myopia for primary open angle glaucoma (POAG)[1] and also for nuclear cataract.[2] People with relatively thin crystalline lenses, like the Bantu in southern Africa, are at a considerably reduced risk with respect to NCAG when compared with Danes for example.[3 4]

A barely noticed veterinary observation[5] suggests that environmental effects may also play a role. In a study of the mass and rate of growth of the crystalline lenses of newly-born Nigerian piglets, it was found that the season of birth of the animals plays a significant role. The lenses of animals born just after the cessation of the wet season were heavier than those born after the end of the dry season. The differences were 5% and 8% in wet and dry weights respectively. Conversely, the postnatal growth rate, monitored for 9 months, dropped by some 15% between the onset and end of the wet season. In Nigeria the temperature is fairly constant throughout the year,[6] and the authors speculate that their results may be influenced by light. The possibility that availability of food to the pregnant sows might be a determining factor[7] was not entertained.

The Nigerian piglets do not appear to be unique as regards a link between growth and season. Eveleth and Tanner[8] write: 'In temperate zones children tend to grow faster in height in the spring and slower in the autumn. In the tropics seasonal variation is governed more by dry and wet periods and the varying availability of food.' That seasonality plays an important role during antenatal development transpires also from detailed studies in the Gambia,[9] Tanzania,[10] and Japan.[11] Furthermore, Harding *et al*[12] found that men have heavier lenses than women, which suggests a variation with body weight.[13 14]

The possible relevance of these observations to ocular pathology appears to have been overlooked in the past: the brain seems to belong to the few organs to have received attention in the context of environmental antenatal effects.[15] If the size of the lens is subject to environmental factors then this might be revealed in corresponding variations in the prevalence at least of narrow/closed angle glaucoma. Admittedly, if the porcine data apply also to the human situation, then the effect to be expected would not be large. An increase in lenticular mass of 5% corresponds to barely 2% in thickness. This would correspondingly lead to a reduction in the depth of the anterior chamber only if the size of the eye were shown to be independent of the season of birth. No datum appears to have been published on this point.

Bantu lenses[3] have been shown to be about 0·4 mm thinner than those of (coeval) Caucasians. In Nigerians the difference is 0·25–0·3 mm.[4] These values correspond to about 5%. The burden of this argument is that if such a difference accounts for the observation that the prevalence of NCAG among negroes is only about one half of that found among northern Caucasians, then a smaller seasonal variation in lens thickness might yet be readily detectable and play a role in the aetiology of NCAG.

It may be noted that the prevalence of nuclear cataract in cattle has been shown to depend on the animal's season of birth.[16]

This paper analyses data on both types of glaucoma and on senile cataract obtained on Caribbean, Caucasian, and south east Asian patients; all the Caucasians had been born in the British Isles. A concurrent study relating to refraction will be presented separately.

Method

DATA COLLECTION

All the subjects of this study were attending Moorfields Eye Hospital, London. The criteria for selection were as follows. They were patients with diagnosed POAG or NCAG or senile (idiopathic) cataract. Pigmentary glaucomas and patients with ocular hypertension were excluded as were all those cases where there was any overt possibility that the diagnosed glaucoma or cataract was a sequela to other ocular pathologies. Only age-related cataracts were included: thus diabetic, traumatic, and steroid-induced cases were excluded. Once these criteria were satisfied the patients were included in the study. Their names, hospital number, date of attend-

Moorfields Eye Hospital, City Road, London EC1V 2PD and Age Concern Institute of Gerontology, King's College London, Waterloo Road, London SE1 8TX
R Weale

Accepted for publication 13 November 1992

ance, date of birth, sex, birthplace, and diagnosis were recorded.

The two types of disease serve to act as mutual controls. However, the average numbers of births in any one month are subject to a systematic seasonal variation. In the United Kingdom the data are easy to obtain from the annual reports of the office for Censuses and Population Statistics. A comparison of the averages for the central years of each of the three decades up to and including 1919 and of the subsequent four decades revealed that a systematic change ($p<0{\cdot}012$) had taken place in the seasonal pattern of births (SPB) just after the first world war (cf also ref 17). Care was taken lest this conclusion be vitiated by the influence exerted by the first and second world wars. SPB corrections for Caribbean and for south east Asian patients were also used.[18 19]

DATA ANALYSIS

The function describing seasonally cyclical data cannot be prejudged. What can be tested is whether the observed results differ significantly from what would be expected on the basis of the SPB. For example, if the prevalence of a condition followed a sinusoidal distribution throughout the year, peaking, for the sake of argument, in June-July, and the SPB varied in a similar manner, no seasonal effect on the disease could be inferred: more cases are observed for people born in the summer because more people are born in the summer. However, if the difference between the two distributions differs, a prima facie case may be made out for the existence of a seasonal effect of birth on the prevalence of the condition.

Tests for cyclical variations exist but depend on the availability of large numbers of data.[20] In the present case, tests were based on the goodness of fit, wherein one determines χ^2 between the observed data and the distribution one would expect on the basis of the SPB.

The classification of glaucoma patients was simpler than that of cataracts. Various classifications have been proposed from time to time, mixed cataracts forming the main obstacle to numerical analysis. In this study, no attention was paid to the severity, only to the presence of any condition. The types considered were cortical, nuclear, and posterior subcapsular cataracts respectively. Accordingly if one type was diagnosed, it was given the weight of 1, if two were present, each received the weighting of 0·5, and if three were diagnosed, each was weighted with 0·33.

Table 1 Average years of birth as a function of sex and disease (n=number of patients; S=*n (men)/n (women)) 1=<1920; 2=>1919*

Condition	*POAG*		*NCAG*		*Cataract*	
British Isles						
	1	2	1	2	1	2
Men	1911·84	1926·159	1912·28	1926·77	1911·32	1925·93
n	122	123	25	26	117	120
Women	1911·15	1928·17	1910·85	1926·57	1910·63	1926·69
n	133	69	48	53	296	143
S	0·92	1·78	0·52	0·49	0·4	0·84
Caribbean						
Men	1928·66				1924·42	
n	114				19	
Women	1927·53				1923·81	
n	79				42	
S	1·44				0·45	
South-East Asia						
Men	1927·58				1926·46	
n	43				60	
Women	1927·78				1926·33	
n	32				64	
S	1·34				0·94	

Results

AGE, NUMBERS, AND SEX

In view of the above mentioned change in the SPB numbers, the patients born in the British Isles were subdivided into two groups (1 and 2) depending on whether they were born before 1920 or after 1919. Table 1 thus gives the average years of birth for sex, group, and condition, and shows that the two diseases can act as effective controls for each other. The secular analysis was not possible for the two ethnic groups because detailed data on SPB are not available for them. The data were collected between 1990 to 1992.

Table 1 shows the ratio of men/women, *S*, as a function of condition. Although this indicates marked differences between the sexes, χ^2 tests did not reveal any significant difference in the seasonal variation between one sex and the other. The two sets of data were therefore amalgamated for each month.

Note that, as regards POAG, there is no contradiction between the data for the sexes in the two age groups. The number of male survivors in group 1 in the general population is significantly smaller than that of women. Therefore the number of male POAG cases per capita of the male population in this group is likely to be greater than is indicated by the near equality of male and female patient numbers. In other words, the sex ratio of ~1·8 for group 2 is probably representative: in this study men have been shown to be at greater risk of POAG than women.

The reverse argument would seem to apply to the two other conditions: in the present sample populations the relative prevalence of both NCAG and age-related cataract is greater among women than men.

The *S* values for glaucoma in the other ethnic groups does not differ greatly from the figures for the British Isles. However, it is noteworthy that the *S* value for cataracts among south east Asians is almost unity. The conventional wisdom is that in India there is considerable male prevalence 'because the men work in the fields', the implication being that they are more exposed to the sun than are their house-bound wives.

GLAUCOMA

It is convenient to consider the annual patient distribution in terms of four 3-monthly periods beginning with January. Application of the goodness of fit test applied to *all* the glaucoma patients born in the British Isles yielded a $\chi^2=6{\cdot}46$ with a significance level of $<0{\cdot}09$ (Fig 1). This is not statistically significant but does not rule out the possibility of a subset being significant. Accordingly the two age groups were separated: the younger group was found to show a seasonal variation with $\chi^2=11{\cdot}37$, $p<0{\cdot}01$ (Fig

2). Separation of the older age group diagnosed as having POAG shows no significant effect (Fig 3). In contrast, similar patients in the younger age group are characterised by a seasonal variation with $\chi^2=8{\cdot}7708$ ($p<0{\cdot}04$) (Fig 4). The data for NCAG, either separated into the two age groups or combined, fail to reach significance even though they show a variation (Fig 5) similar to that seen for POAG in Figure 4.

A similar test applied to all the results for patients born in south east Asia (n=75) yielded $\chi^2=10{\cdot}428$ with $p<0{\cdot}015$ (Fig 6). A non-significant value of $\chi^2=2{\cdot}993$ was obtained for the much larger number (193) of patients born in the Caribbean region.

The numbers of NCAG cases so far collected for patients born outside the British Isles are too small for a meaningful analysis.

There exists now a prima facie case for the view that at least one type of glaucoma exhibits prevalences throughout the year which depend on the patient's season and, probably, region of birth.

CATARACT

A similar analysis applied to the data for cataract failed to yield any significant value for either of the age groups or the three types of cataract. In view of the results obtained for cattle,[16] it is worth stressing that no seasonal effect was observed for the 306 cases of nuclear cataract (in the British Isles) analysed.

Cataracts among populations born outside the British Isles form the subject of a separate continuing study. Interim data for these patients also fail to reveal any seasonal effect on the prevalence of nuclear cataract. Judgment on the other types has to be reserved as yet.

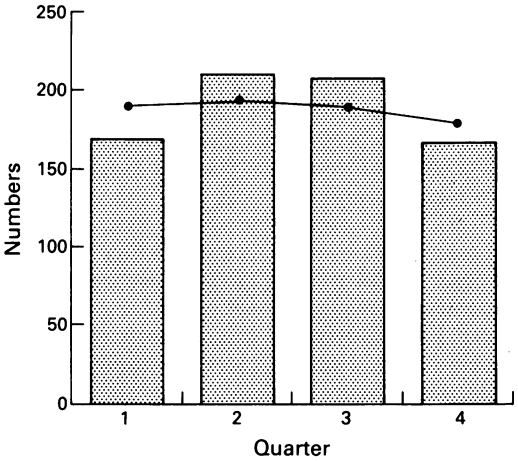

Figure 1 The quarterly prevalence for all cases of glaucoma in the British Isles. In this and in all subsequent figures, the continuous line joins the appropriate expected quarterly values based on the number of babies born in each quarter. Age groups 1 and 2, $\chi^2=6{\cdot}46$ ($p<0{\cdot}09$).

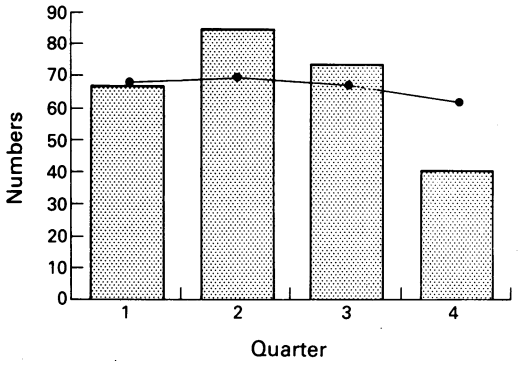

Figure 2 The quarterly prevalence for all cases of glaucoma in age group 2 in the British Isles. Age group 2, $\chi^2=11{\cdot}37$ ($p<0{\cdot}01$).

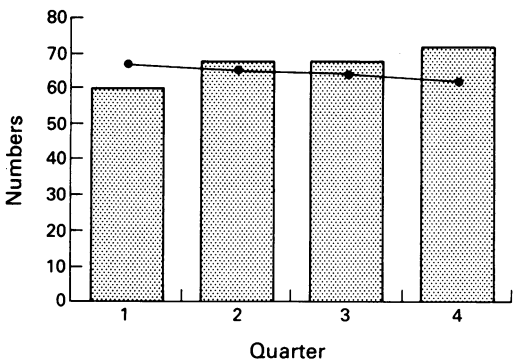

Figure 3 The quarterly prevalence for POAG in age group 1 in the British Isles. Age group 1 (not significant).

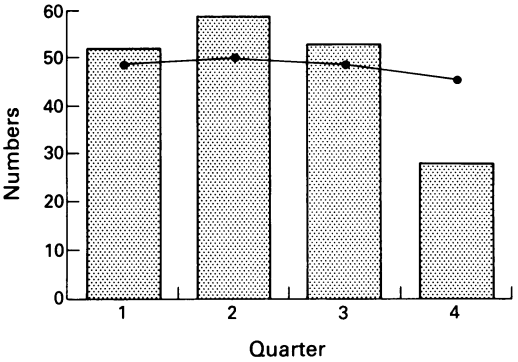

Figure 4 The quarterly prevalence for POAG in age group 2 in the British Isles. $\chi^2=8{\cdot}771$ ($p<0{\cdot}04$).

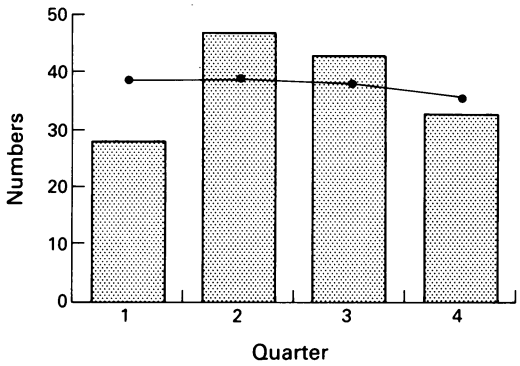

Figure 5 The quarterly prevalence for NCAG in both age groups in the British Isles. Age groups 1 and 2, $\chi^2=5{\cdot}52$ (not significant).

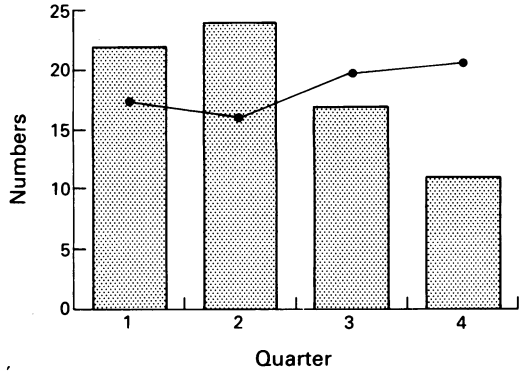

Figure 6 The quarterly prevalence for POAG in patients born in south east Asia. $\chi^2=10{\cdot}428$ ($p<0{\cdot}025$).

Discussion

The results for the glaucomas on the one hand and for cataract on the other support the view that the two conditions can be used as mutual controls.

The difference between the present and earlier results[7] is due in some measure to two new factors. In the first place, the earlier population sample included patients born outside the British Isles, and accommodated even those born in the Mediterranean basin and the Middle East, being all subsumed under the term of Caucasian. Secondly, although POAG was not then thought to reveal any significant seasonal effect, the division of the data for the British Isles into the above two age groups showed that the younger group exhibits a significant effect (Fig 4). The present marked difference between those born in the Caribbean region and in south east Asia respectively (Fig 6) is consistent with the earlier report.

As regards a tentative explanation of the results it may be noted that Caucasian women tend to be somewhat more myopic than men[14 21]; therefore one would expect POAG to be more prevalent among them[1] (but see Table 1). Both their eyeballs and lenses are smaller than those of men by approximately 1%,[12 14] but there is no obvious mechanical explanation for the difference in the prevalence of NCAG between the two sexes (Table 1).

The observation of a seasonal effect manifesting in connection with POAG is unexpected, and raises the question of whether lens size is the only hypothetical anatomical aetiological factor. There are established seasonal variations in preterm births,[11] in birth weight,[20] and in perinatal mortality,[22] and it would not be surprising if this were reflected in the development of organs reaching relative maturity late in term. Although the eye is largely developed by the end of the third month, noxious influences at this time may play a role much as is true at the end of pregnancy when the corneal shape, and therefore the forces acting on the globe, experience major changes.[23 24]

If certain crucial nutrients were unavailable during that season a few decades ago, then ocular development during the winter may have been so disadvantaged as to give rise to hazards among those born some 6 months later, which provides a hypothesis for the seasonal variation of the disease. On the other hand, the observed effects may be linked tentatively with problems relating to low birth weight,[25] a hypothesis consistent with the large prevalences both of this condition and POAG in some of the less industrialised countries.[7]

Conclusion

The prevalence of at least primary open angle glaucoma can depend on a patient's season of birth. In the three populations studied, the patterns differ probably owing to environmental influences in play at or before birth. However, the fact that angle closure glaucoma misses reaching the accepted level of significance in the British Isles does not rule out the possibility that there may be other populations where a clear seasonal effect on its prevalence may exist. Again, there may be other regions with different effects on POAG, and where secular influences may act differently from those reported here. This would not place seasonal effects in ophthalmology in a unique class.[17]

I thank Professor Alan Bird, Mr Roger Hitchings, Mr Arthur Steele, and Mr John Wright for allowing me to carry out this study largely in their clinics. Among others, the following have helped me in identifying patients: R Casey, P Courtney, P Doust, C Gilbert, R Gregson, A Harper, G Johnston, B Little, R Lobo, A Major, L Moodaney, S Nirmalananthan, D O'Neill, J J Preziosi, S Ritten, N Samanta, G Sheth, Z Shwe, J Sturmer, N Subramanian, E Wijayasinghe, R Wormald, and M Zeidan.

Generous support from the International Glaucoma Association is also gratefully acknowledged.

1 Shields MG. *Textbook of glaucoma.* 2nd ed. London: Williams & Wilkins, 1987: 149, 167.
2 Weale RA. A note on a possible relation between refraction and a disposition for senile nuclear cataract. *Br J Ophthalmol* 1980; **64**: 311–4.
3 Clemmesen V, Luntz MH. Lens thickness and angle-closure glaucoma. *Acta Ophthalmol (Kbh)* 1976; **54**: 193–7.
4 Clemmesen V, Olurin O. Lens thickness in Western Nigeria. *Acta Ophthalmol (Kbh)* 1985; **63**: 274–6.
5 Alaku O, Steinbach, J. Effects of season of birth and age on eye lenses weight in pigs in the humid equatorial tropics. *Growth* 1982; **46**: 22–5.
6 Fullard H, Darby HC, eds. *The library atlas.* London: George Philip & Son, 1987: XV, XXII.
7 Weale RA. Glaucoma and season of birth. *Lancet* 1991; **338**: 824.
8 Eveleth PB, Tanner JM. *Worldwide variations in human growth.* Cambridge: Cambridge University Press, 1990: 203.
9 Chambers R, Longhurst R, Paley A, eds. *Seasonal dimensions to rural poverty.* London: Frances Pinter, 1981.
10 Bantje H, Niemeyer R. Rainfall and birthweight distribution in rural Tanzania. *J Biosoc Sci* 1984; **16**: 375–84.
11 Matsuda S, Kahyo H. Seasonality of preterm births in Japan. *Intern J Epiderm* 1992; **21**: 91–100.
12 Harding JJ, Rixon KG, Marriott FHC. Men have heavier lenses than women of the same age. *Exp Eye Res* 1977; **25**: 651.
13 Brandt I. Dynamics of head circumference growth before and after term. In: Roberts DF, Thomson AM, eds. *The biology of human fetal growth.* London: Taylor & Francis, 1976: 109–36.
14 Weale RA. Ocular anatomy and refraction. *Doc Ophthalmol* 1983; **55**: 361–74.
15 Dobbing J. Vulnerable periods in brain growth and somatic growth. In: Roberts DF, Thomson AM, eds. *The biology of fetal growth.* London: Taylor & Francis, 1976: 137–47.
16 Ashton N, Barnett KC, Clay CE, Clegg FG. Congenital cataract in cattle. *Vet Rec* 1977; **100**: 505–8.
17 Golding J, Sunderland R. Month and day of delivery. In: Golding J, ed. *Social and biological effects on perinatal mortality.* WHO Bristol: University of Bristol, 1990: 105–50.
18 Becker S, Sardar M. Seasonal patterns of vital events in Matlab Thana, Bangladesh. In: Chambers R, Longhurst R, Paley A, eds. *Seasonal dimensions to rural poverty.* London: Frances Pinter, 1981: 151.
19 Rajagopalan S, Kymal PK, Pu-ai Pei. Births, work and nutrition in Tamil nadu, India. In: Chambers R, Longhurst R, Paley A, eds. *Seasonal dimensions to rural poverty.* London: Frances Pinter, 1981: 157.
20 Roberts DF. Environment and the fetus. In: Roberts DF, Thomson AM, eds. *The biology of fetal growth.* London: Taylor & Francis, 1976: 267–83.
21 Abrams D, Duke-Elder, Sir WS. *Ophthalmic optics and refraction.* London: Henry Kimpton, 1970: 234, 237–8.
22 Keller CA, Nugent RP. Seasonal patterns in perinatal mortality and preterm delivery. *Am J Epidemiol* 1983; **118**: 689–98.
23 Fledelius H. Prematurity and the eye. *Acta Ophthalmol* 1976; **54**: (suppl) 128.
24 Weale RA. *A biography of the eye – development, growth, age.* London: Lewis, 1982.
25 Boldman R, Reed DM. Worldwide variations in low birth weight. In: Reed DM, Stanley FJ, eds. *The epidemiology of prematurity.* Baltimore, Munich: Urban & Schwarzenberg, 1977: 39–51.