BJO at a glance

Creig Hoyt

Editorials

Pragmatism versus purity: effectiveness of the key informant methodology in a developing rural setting
C Williams and J M Sparrow

Surgical treatment of peripapillary choroidal neovascularisation
Susanne Binder

Night vision disturbances after refractive surgery: haloes are not just for angels
Stephen D Klyce

World view

The key informant method: a novel means of ascertaining blind children in Bangladesh
Mohammad A Muhit, Shaheen P Shah, Clare E Gilbert, Sally D Hartley, and Allen Foster
Causes of severe visual impairment and blindness in Bangladesh: a study of 1935 children
M A Muhit, S P Shah, C E Gilbert, and A Foster
doi:10.1136/bjo.2006.108019

Causes of blindness and visual impairment in Pakistan. The Pakistan national blindness and visual impairment survey
B Dineen, R R A Bourne, Z Jadoon, S P Shah, M A Khan, A Foster, C E Gilbert, M D Khan on behalf of the Pakistan National Eye Survey Study Group
doi:10.1136/bjo.2006.108035

Evolution of vision reducing cataract in skin smear positive lepromatous patients: does it have an inflammatory basis?
Ebenezer Daniel and P S S Sundar Rao
doi:10.1136/bjo.2006.112953

Cover

Eye in the sky
Ivan R Schwab

Letters

De novo mutation in the BIGH3/TGFB1 gene causing granular corneal dystrophy
E N Hilton, G C M Black, F D C Manson, D F Schorderet, and F L Munier

Multifocal electroretinography in dengue fever-associated maculopathy
Timothy Y Y Lai, Shaheeda Mohamed, Wai Man Chan, Ricky Y K Lai, and Dennis S C Lam

Interferon alpha eye drops: treatment of atypical lymphoid hyperplasia with secondary alopecia
P T Finger and D Reichstein
Bilateral symptomatic angle closure associated with a regular dose of citalopram, an SSRI antidepressant  
P Massaoutis, D Goh, and P J Foster  

Ocular surface toxicity associated with topical interferon α-2b  
Anthony J Aldave and Anne Nguyen  

Periorbital xanthogranuloma after blepharoplasty  
Christopher I Zoumalan, Melanie H Erb, Narsing A Rao, Robert See, Michael A Bernstine, Samir B Shah, and Timothy J McCulley  

The Finger iridectomy technique for glaucoma  
Paul T Finger  

Preimplantation genetic diagnosis for retinoblastoma predisposition  

Rise in intraocular pressure during haemodialysis in a patient with reduced outflow facility  
M Dominik Fischer, Johannes Fleischhauer, Gérald Keusch, and Mathias H Abegg  

Internal drainage in optic pit maculopathy  
Karen B Schaal, Julia Wrede, and Stefan Dithmar  

Botulinum toxin for the treatment of acute-onset concomitant esotropia in Chiari I malformation  
Alison Y Firth and John P Burke  

Microfoam surgical tape as practice object for scleral sutures  
Jan Niklas Ulrich and Thomas W Wilson  
The use of voriconazole in the treatment of *Aspergillus fumigatus* keratitis
Rosalind M K Stewart, Say Aun Quah, Timothy J Neal, and Stephen B Kaye

**Mailbox**

*Isotretinoin and night vision*
S Pushpoth and S Sandramouli

*Isotretinoin and night vision: authors’ response*
Susan P Mollan, Malcolm Woodcock, Peter Good, and Robert A H Scott

*Surgical embolus removal in retinal artery occlusion*
Sohan Singh Hayreh

**Corrections**

CORRECTION

**From the library**

From the Library

**Video reports**

*Pigmented free-floating iris cysts*
Gurdeep Singh, Kalpana Narendran, Veerappan R Saravanan, and V Narendran
Pragmatism versus purity: effectiveness of the key informant methodology in a developing rural setting

C Williams, J M Sparrow

The goal of the VISION2020 initiative is to eliminate avoidable blindness by the year 2020. The estimated prevalence of blindness and visual impairment in 2002 was lower than previously predicted (37 million instead of 52 million), suggesting that the three components of VISION2020 – disease control, human resource development and infrastructure development, have successfully helped millions of people escape visual impairment or blindness. However, the WHO point out that with an ageing population in many countries, the risk of visual impairment increases and therefore these early successes need to be developed and expanded to meet this challenge.

At the other end of the age range, an example of concrete progress in this worldwide effort is provided by Muhit et al. (see pages 995 and 1000) in this month’s BJO. The authors describe a method to add to the existing techniques to ascertain blind children in a developing country. Whereas many valuable studies have used data from children in schools for the blind to estimate the proportion due to different causes, this paper illustrates that important additional information may be obtained by also including children identified by local members of the community, who have been briefed by the study team on what to look for. These individuals, known as “key informants” (KIs) were unpaid volunteers who, after attending a half-day training session, spent 2–3 weeks in their communities actively seeking out blind or visually impaired children and encouraging their families to bring them to the eye examination carried out by the project team.

The first point to note is that the number of children ascertained by the KIs was nearly double that of the numbers recruited from special and integrated schools or community-based rehabilitation (CBR) programmes combined (1245, vs. 394 and 296, respectively). Second, the children recruited by the KIs were more likely to have severe visual impairment (SVI) rather than blindness; 9.8% SVI vs. 4.8% in blind schools and 7.8% in community programmes. Third, the cause of their vision loss was 40% more likely to be avoidable than for children identified in schools for the blind and, similarly, 30% more likely to be avoidable than for those identified in CBR programmes. Fourth, the children identified by the KIs were more likely to be female, aged 0–5 years, to live in rural areas and have infantile-onset eye problems, than children identified by the other two methods – groups which would otherwise have been under-represented.

The results described by Muhit et al. illustrate the value of this method in the search for accurate prevalence data, particularly for individuals who may benefit from treatment or who might have benefited from preventive strategies. Although this approach has limitations – for example, it is most suited to a society that is relatively open and in which people know others that are in their own geographic area, thereby being limited by transport rather than social convention – it is a valuable addition to existing techniques in population-based ophthalmological research. The “Gold Standard” of enumerating each person in households in geographically defined clusters and examining them all has been successfully used for common eye conditions, but the large sample sizes needed for rare conditions (such as blindness in children) make formal population-based surveys prohibitively expensive and logistically challenging. Even when identifying the population of interest from centralised databases and offering them transport to attend a central facility, it is difficult to achieve high enough compliance rates to provide accurate prevalence data and the databases may not include all individuals of interest. Thus, the use of KIs is a valuable addition to available methods for future studies on the prevalence of blindness and has the potential to make such studies more representative of the whole population. The additional cost of the KI component was only 25% of the whole study, therefore the additional ‘cost per case identified’ using the KI method was around a fifth of the ‘cost per case identified’ using traditional methodology. The marginal costs associated with the use of KIs were thus very small considering the large number of extra children identified, and the added value of these data to the statistical power and representativeness of the study as a whole.

Compared with the cost of carrying out conventional population-based research in established market economies such as the UK, the value for money represented by this method is impressive and may have applications in developed as well as developing countries.

Without quality population-based data on prevalence and causes of vision loss, control strategies cannot be devised, nor their effectiveness assessed. Improved data acquisition by this approach will strengthen confidence when making judgements of effectiveness and guide future policies towards better blindness prevention programmes.


Authors’ affiliations
C Williams, J M Sparrow, Bristol Eye Hospital, Lower Maudlin Street, Bristol BS1 2LX, UK

Correspondence to: Miss Cathy Williams, Bristol Eye Hospital, Lower Maudlin Street, Bristol BS1 2LX, UK; cathy.williams@bristol.ac.uk

Competing interests: None declared.

REFERENCES
2 http://www.iapb.org.
Peripapillary choroidal neovascularisation (PPCNV) comprises about 10% of all cases of choroidal neovascularisation. Starting at the nasal margin of the disc the condition does not become symptomatic until fluid, exude, blood, or the membrane itself have extended from the disc toward the macula, threatening central vision. Very large PPCNVs are defined as more than 3.5 disc areas or greater in size and involve 180° or more of the disc circumference. Although less common than smaller PPCNVs, the very large ones may lead to severe visual loss.

Over time, scar contraction at the edge of the PPCNV causes breaks in Bruch’s membrane, and the associated haemorrhage leads to a new circle of “reparative” fibrovascular ingrowth that manifests as progression or extension of the PPCNV complex.

PPCNVs can be idiopathic or secondary to various conditions. In a recent survey, Browning and Fraser reported that PPCNV was associated with age-related macular degeneration (AMD) in 45% of cases, while 39% were idiopathic, so at least 84% of the patients will be over the age of 55 years. Although the diagnosis of “idiopathic” PPCNV is unsatisfactory, the presence of these lesions in clinically normal eyes has been demonstrated in pathological studies. The remaining cases of PPCNV occur secondary to multifocal choroiditis, angioid streaks, histoplasmosis, choroidal osteoma, optic disc drusen, congenital disc anomaly, pattern dystrophy, and peripapillary pseudopod pigmentation epithelium and choroidal atrophy.

In patients over 70, involvement of the second eye in PPCNV can be expected in 20–62% of all cases. At this age, 75% of untreated cases have lost visual acuity (VA) to a level of 3/60 or less. The time between the involvement of the first and the second eye varies from simultaneous to seven years. On fluorescein angiography, PPCNV may contain a significant occult component, leading to slow and unpredictable growth; in fact more than half the AMD related and idiopathic cases are entirely or mainly occult. This makes PPCNVs difficult to treat by laser, which requires well defined lesion margins.

Results of laser photocoagulation for PPCNV vary. In 1988 Kies and Bird recommended that a large margin of normal tissue should be treated, and that there should be laser ablation of any angiographic abnormality around the lesion. In their series of 55 cases, only 13 (23.6%) received laser treatment, and recurrences were observed in three quarters of these. Once the centre was affected by fluid, bleeding, or choroidal neovascularisation, VA did not recover or improve spontaneously. Flaxel et al reported 1996 on their results with laser treatment for very large (massive) PPCNV, measuring 3.5 disc diameters or more, and with treatment limited to the temporal portion of the neovascular complexes. Six of 10 treated cases showed stabilisation while four progressed to severe visual loss. In PPCNV related to histoplasmosis, Turcotte et al reported stable vision in about 75% of cases after laser treatment. On the other hand, no statistical difference in final VA following laser treatment for AMD-PPCNV was reported by Ruben et al in 1994. In Browning and Fraser’s survey, 73 of 115 eyes with PPCNV of various origins underwent laser treatment; in 14 (19.2%) a recurrence was noted, and multiple recurrences occurred in four (5.5%).Comparable results with recurrence rates of 20% and 28% were reported by Annesley et al and Cialdini et al. Finally, in the Macular Photocoagulation Study PPCNV subgroup, there was no improvement in visual outcome with laser ablation over three years of untreated follow-up; furthermore, there was no significant difference in the rates of severe vision loss between treated and untreated eyes.

**WHAT ABOUT SURGICAL EXCISION FOR PPCNV?**

Since Thomas and Kaplan introduced subretinal surgery for foveal choroidal neovascular membranes in 1991, several groups have reported on membrane excision for PPCNV.

Successful surgery with improvement in vision was described in two single case reports of the surgical removal of AMD related extrafoveal PPCNV, where fluid accumulation had caused visual loss. In 2003, Sullu et al presented a case report of a nine-year-old girl with binocular PPCNV related to papillary drusen, who already had submacular involvement in her left eye. Wrongly diagnosed as having papilloedema, this child had undergone extensive neuro-ophthalmological examination. After surgery the VA improved in the left eye from 0.05 to 0.3, and no recurrence was observed. In 1998, Atebara et al reported on 17 young patients with extensive PPCNV related to histoplasmosis. In the majority (82%, 14/17), the PPCNV had already reached the fovea. While all cases with a preoperative extrafoveal location of the PPCNV reached a VA of 20/20 postoperatively, half the remaining 14 eyes achieved a final VA of 20/40 or better. After 32 months recurrences were observed in 24% (4/17). No surgical complications occurred. In 2004, Kertes described three patients aged 25–30 years with histoplasmosis and PPCNV, all of whom underwent surgery. The location of the PPCNV extended extrafoveally in two and was juxtapfoveal in the third. VA improved after surgery in all three eyes, two reaching 20/20 and the third, 20/50. Postoperatively, one peripheral tear needed laser treatment.

In 2003, Bains et al presented the surgical results in 17 patients over 55 years of age with extensive PPCNV, mainly AMD related or idiopathic. Preoperatively the PPCNV was located extrafoveally in seven cases (41%) but 11 eyes (59%) already showed foveal extension. Visual acuity was stable or improved in six eyes (35.2%) and worsened in 11 (63.8%). After an observation period of 30 months the investigators concluded that surgical excision yielded improvement or stabilisation of VA in about one third of their elderly patients. Complications such as retinal detachment, macular oedema, and preretinal membrane formation were observed in five eyes (29%).

Eleven AMD patients with massive PPCNV not eligible for laser treatment or refusing it were included in a study by Blinder et al in 2005. Cases were the PPCNV extended into the fovea were excluded, and the mean size of the membrane was 5 o’clock hours. After 23 months follow up seven cases (64%) had stable or improved VA, with a mean change of one line improvement. In three cases (27%), a recurrent membrane developed. In the same year, Kokame and
Yamaoka described the outcome of surgery in six elderly patients with extrafoveal PPCNV, where vision was threatened or affected by subretinal fluid, haemorrhage, exudate, or neovascular membrane growth. After three years of follow-up, VA was stable or had improved in five cases (83%) with a range of VA between 20/25 and 20/80. In three eyes there was early or late recurrence.

In this issue, Aisenbrey and coworkers report on the two-year functional and morphological outcome of subretinal membrane excision in eight patients with AMD related PPCNV (see page 1027).

Preoperatively, mean VA was logMAR 0.5; this improved to mean logMAR 0.3. Six of the eight cases gained vision. Although recent progression of the disease was the indication for surgery, in no case had the membrane extended into the fovea. Two years after surgery one recurrence was observed and was successfully removed surgically. The authors discuss newer treatment options, including photodynamic therapy, where a safety distance of 200 µm from the margin of the optic disc is recommended, and treatment with antiangiogenic agents. However, there is only one small case series on the successful treatment of PPCNV with photodynamic therapy, and none with antiangiogenic agents so far. Although small PPCNVs can be treated successfully with laser coagulation, the authors state correctly that large membranes may be ineligible for surgery because of the damage to the retinal pigment epithelium and the neurosensory retina that is caused by adhesions to the coagulated tissues. In agreement with the three recent reports cited above on the surgical excision of large PPCNVs, the authors recommend surgical intervention in older patients before the membrane has reached the centre of the fovea in order to maximise any improvement in vision.

Overall, younger patients with ocular histoplasmosis and other rare indications, with large, growing PPCNVs, have an excellent visual prognosis after subretinal surgery if the membrane is still extrafoveal. If the macula is already involved, there is a 50% chance of stabilisation or improvement, because the membrane in these cases tends to be located in the prepigment epithelium (type II), and because the patients are younger and so some regrowth of pigment epithelium can be expected. Clearly, the decision to undertake surgery is easier if the fovea is threatened or involved by fluid or exudates, and if the patient's vision is already compromised. In elderly patients, subretinal surgery to remove extrafoveal PPCNVs might also be a promising therapeutic option leading to visual improvement. However, little or no chance of regaining vision can be expected if the macula is already involved in the neovascularisation process.

Possible complications related to surgery include endophthalmitis, retinal detachment, and haemorrhage, but these are rare. Cataracts will develop in most of the elderly patients if the lens is not removed in combination with vitreous surgery. Over the past 15 years subretinal surgery has developed technically, and we have learned to keep the retinotomies small, to prevent haemorrhages, and to remove subretinal tissue with minimal trauma, making subretinal surgery for PPCNV a valuable therapeutic option which should not be performed too late!

There are, however, limitations to what we can conclude from the current studies because the numbers of cases are small and there have been no randomised comparisons with alternative treatments. Such studies are needed to define the place of surgery in the current therapeutic armamentarium. Other therapeutic options such as photodynamic therapy and antiangiogenic agents are being assessed, and there may be a place for combination therapies.


doi: 10.1136/bjo.2007.114009

Correspondence to: Professor Susanne Binder, Department of Ophthalmology, Rudolf Foundation Clinic, The Ludwig Boltzmann Institute for Retinology and Biomicroscopic Laser Surgery, Juchgasse 25, A 1030 Vienna, Austria; susanne.binder@wienkav.at

Competing interests: None.

REFERENCES

Night vision disturbances after refractive surgery

Stephen D Klyce

There has been considerable attention paid to the optical consequences of corneal refractive surgery, particularly those occurring during the night time when the pupil widens and larger areas of the sculpted cornea are included within the visual pathway. It seems a forgone conclusion that pupils larger than the functional optical zone (the area of the corneal surface after laser sculpting that provides quality vision) created by the surgery should cause problems for the patient and, in truth, this has occurred with night vision complaints that include starburst effects and haloes. Therefore, it has been the strategy over the course of technique development for laser algorithms to sculpt ever larger corneal areas encompassing the full correction zone (the zone of intended refractive correction) and to incorporate cleverly designed surrounding transition zones to blend in curvature changes in a smoother fashion. Taken together, these changes have reduced or eliminated many of the night vision complaints that were associated with pupil diameter, at least in some recent reports.

In this issue, Villa and associates (see page 1031), have re-examined this problem in successful LASIK patients by using a commercial device to measure a night vision disturbance metric, the “halo disturbance index.” They also measured the dark-adapted pupil size and the calculated optical aberrations arising from the corneal surface. In this careful study, the authors demonstrate that the halo disturbance index correlates strongly with specific aberrations: notably, spherical aberration, secondary astigmatism and coma. These aberrations, particularly spherical aberration and coma, are consistently reported in the literature as being the major culprits for the creation of visual disturbances following refractive surgery. However, in the current study, no correlation was found between the halo disturbance index and mesopic pupil diameter. This result is in contrast to the experience of many refractive surgeons, yet is consistent with findings published by some. This finding is encouraging, since it suggests that laser algorithms are improving to the extent where at least some of the lasers being used can treat patients with larger pupils without inducing night vision problems.

However, there is a caveat: the measurement of pupil diameter has been in standard use in refractive surgical screening procedures, and this should not be altered by the absence of statistically significant post-operative correlations being reported. Not only have these results been reported for an apparent minority of practices, but also, the absence of a correlation between two variables could mean that other variables confound or mask the effect. Simply, with the best of procedures and patient care, the occasional patient with large pupils will experience night vision complaints that are, rarely, debilitating. Still, the prudent course of action would be to evaluate the physical size of the functional optical zones that can be created with a particular laser system at various amounts of correction and compare these with patient mesopic pupil size along with the maximum expected decentration. If the expected functional optical zone can be expected to overlay the mesopic pupil nearly completely, the chance for inducing night vision difficulties after surgery should be minimal. Note that night vision complaints also occur in a substantial number of unoperated patients, and psychometric documentation of these would be a useful adjunct to the patient evaluation routine.

The principle aim of Villa and colleagues was to correlate corneal higher order aberrations with the halo phenomenon that occurs after what is currently accepted as successful refractive surgeries. Doing so should provide an objective measure of at least one of the forms of night vision disturbance. No psychometric evaluation was reported to determine any level of disability that the patients may have experienced. Rather, the authors used the Starlight device, which is said to measure the halo effect in patients. The Starlight instrument projects a central beam of light as a means to mimic gazing at a point light source under mesopic conditions. At intervals, near perception threshold peripheral point light sources are illuminated in serial fashion to obtain a visual field-like map of retinal sensitivity. When haloes are present, they will distort the peripheral test beams, so that these will not be detected. The output is a map of targets seen. For the normal unoperated eye, corrected for refractive error, the Starlight device demarcates nearly all the total projected field; normal eyes do not experience significant haloes. For the refractive surgical eye, the device demarcates the region of the visual field over which the near-threshold stimuli were visualised. The peripheral area not seen by these eyes is added up to calculate the halo disturbance index.

While it is clear that haloes will distort light rays and potentially dim the spot produced on the retina below the detection threshold, it also seems likely that other optical effects would have a similar consequence. Disturbances experienced by refractive surgical patients include glare, haloes, starburst, hazy vision, monocular polyopia, simultaneous vision, and defocus. The underlying causes of these phenomena are generally attributed to corneal surface aberrations left behind after refractive surgery. Every one of these symptoms has the potential to reduce the sensitivity of light projected by the Starlight instrument. Hence, while the measurements are objective and meaningful, it is unlikely that they can be used to uniquely identify haloes as the source of visual distortion. It would seem more appropriate to regard the data from the Starlight instrument as a “light distortion index” rather than a “halo disturbance index.”

Haloes are an optical phenomenon of nature and can be observed around the sun and stars as a consequence of light scatter caused by ice crystals or other substances in the atmosphere. In the eye, haloes have two main sources. One troublesome source from the past was the halo seen around bright lights particularly at night with hard, low-oxygen permeable contact lens wear. This produced Sattler’s Veil, a diffraction phenomenon caused by epithelial edema. There is the potential for haloes to be formed after surgery if periodic structures persist within the stroma, such as certain types of scar formation. A second type of halo effect in the eye is caused by refraction phenomena and is assumed to be due to the transition zone surrounding the treated area of the cornea. However, this type of halo is actually attributed to spherical aberration. While it is true that an abrupt transition zone can contribute to spherical aberration, it is the shape of the entire corneal region over the entrance pupil that contributes to spherical aberration. Hence, a very large treatment zone and a small pupil can still lead to haloes when there is significant residual ocular spherical aberration.

Despite these reservations regarding the interpretation of data from the
Starlight instrument, Villa and colleagues have provided means and data with which to examine success in refractive surgery in greater detail. Refraction, Snellen acuity, and contrast acuity are still the foundations for assessing refractive surgery, but to understand the causes of visual complaints remaining after treatment, we must look to the techniques Villa and colleagues have championed in their article.

REFERENCES

Eye in the sky

Most aquatic animals do not rely upon the cornea for refraction; in fact some do not even have a cornea. Evolutionarily, the cornea probably appeared early in vertebrate phylogeny although not for refraction. Rather, the cornea probably first appeared for protection, especially for the crystalline lens. Early fish developed a thin protective layer, and some species subsequently developed a second layer of cornea called the spectacle. In many fish neither layer of cornea is especially good optically, but they do not have to be. Parenthetically, echoes of those two separate layers still exist in our own cornea.

Neither of these two corneal layers has to be particularly smooth, because when the cornea is immersed in water, there is almost no refraction obtained from the cornea, permitting light to pass through unchanged. This creates a problem for any fish that must navigate the aerial world in any meaningful visual manner. What do such creatures do to overcome the generally poor visual characteristics of the lacklustre piscine cornea?

Conceptually, flying fish seem curious to us but these winged creatures simply occupy an unusual niche. Found in most oceans, flying fish seem to be concentrated in the Atlantic Ocean and the Caribbean Sea, although the largest species (cover illustration) is found in the Pacific. This fascinating creature feeds in the neustonic zone of the ocean (surface waters), and although this zone is very rich with plankton it is also very dangerous. Predators can use the sky as a backdrop and patrol beneath the surface of the water looking for prey. Hence, a neustonic fish must be primed to make a hasty escape. To escape, flying fish have chosen to fly.

The flying fish, then, must be prepared to navigate epipelagic waters as well as the aerial world above them. Just like many other animals, including some frogs, snakes, mammals and reptiles, the flying fish does actually become airborne for significant distances using pectoral fins as wings for gliding. Hence, it is a “flying fish”.

Cypselurus californicus will obtain the necessary speed by sculling with its pelvic fin, vaulting itself skyward but flying close to the water’s surface. The fish rapidly moves the lower lobe of its tail to propel itself forward once the rest of the body has already left the water. Eventually, even the tail leaves the water and the fish is airborne. While airborne, C. californicus does not “flap” its pectoral fins as wings, and, yet, it is very skillful at gliding. While gliding, the fish can almost double its swimming speed by using its tail, and has been documented to reach speeds of up to 70 km/h. Although each glide is usually short, up to 30–50 metres in length, some have been observed soaring for 200 metres or more using the updraft on the leading edges of waves. This remarkable feat can be done by making a series of glides. When the fish is airborne, it will descend towards the surface. Instead of dropping entirely into the water, the fish can simply dip its tail into the water to produce forward thrust. These fish generally fly approximately 1–2 metres above the sea, but have been recorded landing on ship’s decks 10 metres above the surface! The various genera of flying fish have a spectrum of flight capability that can be quantified based on wing area to body mass ratio and it probably correlates with visual capability out of water. The cover image exhibits the “S” trajectory that the fish follows, which is probably due to a large pelvic fin that continues to paddle with an enlarged lower tail lobe. In the Sargasso Sea, a closely related flying fish has consistent sites it prefers for launch and re-entry, and some element of visual recognition is required both in water and air, especially for takeoff and re-entry.

To do this, the flying fish has evolved a pyramidal cornea with an apex at its centre. This creates a three-windowed cornea, unique in the phylum Chordata. Its function remains a mystery. The cornea is relatively flat, approximately 180 μ thin, and quite clear, in contrast to the fish with thicker cornea mentioned above. Although the function of these three separate “windows” is unknown, it is logical to consider that the flying fish needs clear lines of sight posteriorly for possible predators, inferiorly for gauging distance to the water’s surface and possible predators, and anteriorly to look for a safe place to land. The lens of the flying fish eye is piscine—large and round with a high index of refraction. As a result, the cornea does not have to be highly refractive out of water and is relatively flat. The fish has been documented to be emmetropic in air and only mildly hyperopic in water. It is unknown if the measurements in water were in an accommodated state. The cornea is quite large with a diameter of 28 mm. The axial diameter in the specimen measured was 19 mm. Essentially, the cornea extends almost to the equator of the globe. The total length of the fish was only 36 cms. The corneal diameter is 8% of the body length!

Certainly, few animals would proceed in any medium without the sensory mechanism to interpret its surroundings, especially if moving with any speed. Vision through these separate windows is a logical sensory mechanism since other sensory mechanisms to manage aerial obstacles, re-entry sites, predators and such, are not developed in this species. This is a three-windowed eye in the sky.

Photograph by Robert Pittman NOAA.

Correspondence to: Ivan R Schwab, University of California, 4860 Y St, Suite 2400, Sacramento 95817, USA; irschwab@ucdavis.edu

REFERENCE

The key informant method: a novel means of ascertaining blind children in Bangladesh

Mohammad A Muhit, Shaheen P Shah, Clare E Gilbert, Sally D Hartley, Allen Foster

Background: Most information on the causes of blindness has come from examining children in special education. To obtain a more representative population-based sample of children, a novel method was developed for ascertaining severe visually impaired (SVI) or blind (BL) children by training local volunteers to act as key informants (KIs).

Objective: To compare the demography and cause of blindness in children recruited by KIs with other ascertainment methods.

Method: Children with SVI/BL were recruited in all 64 districts of Bangladesh. Three sources for case ascertainment were utilised: schools for the blind (SpEd), community-based rehabilitation (CBR) programmes and KIs. All data were recorded using the standard WHO/PBL Eye Examination Record.

Results: 1935 children were recruited. Approximately 800 KIs were trained. The majority of the children were recruited by the KIs (64.3%). Children recruited by KIs were more likely to be female (odds ratio (OR) 1.6, p < 0.001), from rural areas (OR 5.9, p < 0.001), be multiply impaired (OR 3.1, p = 0.005) and be suffering from treatable eye diseases (OR 1.3, p = 0.005) when compared with those in SpEd. Overall a child with an avoidable causes of SVI/BL had 40% (adjusted CI 1.1 to 1.7, p = 0.015) and 30% (CI 1.0 to 1.7, p = 0.033) higher odds of being ascertained using the KIs compared with SpEd and CBR methods, respectively.

Conclusion: Using this innovative approach has resulted in one of the largest studies of SVI/BL children to date. The findings indicate that KIs can recruit large numbers of children quickly, and that the children they recruit are more likely to be representative of all blind children in the community.

SUBJECTS AND METHODS

Children aged 0–15 years with severe visual impairment or blindness (SVI/BL) were eligible for inclusion. Ethical approval was obtained from the ethics review committee of BNSB Eye Hospital in Bangladesh.

Definitions and classifications

The World Health Organization (WHO) categories of visual impairment were used where SVI is defined as a presenting visual acuity of <6/60 in the better eye, and BL as a presenting visual acuity of <3/60 in the better eye.

Classification of causes

The WHO classification system was used to identify (1) the main anatomical site of abnormality and (2) the main underlying aetiology of SVI/BL for each eye, and then for each child. Causes were then categorised as preventable, treatable or unavoidable. Preventable causes were conditions which could have potentially been prevented through simple health promotion, prevention and education at community and household levels. Treatable causes were conditions where surgical, medical or optical interventions could have preserved or restored sight (eg cataract surgery). Avoidable causes were the sums of treatable and preventable causes, and unavoidable causes were all those that could not have been prevented or treated.

Abbreviations: BL, blindness; CBR, community-based rehabilitation; IQR, interquartile range; KI, key informant; NGOs, non-governmental organisations; OR, odds ratio; SpEd, special schools for the blind and integrated schools; SVI, severe visual impairment; WHO, World Health Organization
Case ascertainment methods
Recruitment through schools (SpEdu)
Systematic attempts were made to identify all schools providing education to blind children through (1) the Resource Directory of the International Council for the Education of the Visually Impaired,6 (2) by liaising with international and local non-governmental organisations (NGOs), and (3) records from the Ministry of Social Welfare. All eight special schools and the 69 “resource centres” for the integrated education of blind children in the country were visited. All children present on the day of the visit were examined by the ophthalmologist.

Recruitment from CBR programmes
All programmes catering for people with blindness were identified by networking with NGOs involved in disability or eye care, the Ministry of Social Welfare and other government departments. In addition, the study ophthalmologist also made specific inquiry during his visit to each district and through networking with local organisations to identify any other relevant local CBR programmes that had not been listed. Among the 507 subdistricts in the country, only 21 had active CBR programmes for SVI/BL children. All 21 CBR programmes in the country were visited.

Recruitment by KIs
The purpose of using KIs was to recruit blind children not enrolled in special schools. In each district, project officers identified approximately 15 local KIs during their preliminary visits. All the KIs were local volunteers and they did not receive any financial incentive. Two groups of KIs were most active and effective in this study (1) field workers and officers of the Directorate of Social Welfare of the Government of Bangladesh, and (2) field workers of various NGOs working in health, disability and social development projects at the community level. In addition, there were KIs who were school teachers, social workers, community leaders, religious leaders (Imams), local journalists and college students. In each district, the project officer, usually with support from the local administration and NGOs, organised a 1-day briefing meeting for the KIs to explain the overall purpose of the study, and why blind children were being ascertained. The KIs were shown how to measure vision in school-aged children using “finger counting” at 6 m. For young children, the KIs were told to observe the eyes carefully and look for any obvious abnormalities (eg, any abnormal looking eye including a white opacity in the central part of the front of the eye which could be due to a corneal scar or cataract). KIs were also encouraged to find and refer children whose mothers suspected them to have a “serious eye or vision problem” even if there did not appear to be anything obviously wrong with their eyes. The KIs were encouraged to network as widely as possible after the training so that children in remote rural areas would also be identified. The KIs did not give up their usual jobs and they were expected to disseminate what they had learnt during the training by talking to people they came across during their everyday activities. On the day of the training, they were also informed of the date and place where the eye examination would take place, so they could inform parents. The KIs were told that all the children they thought were blind would be examined by an ophthalmologist, and that all those who might benefit from treatment (medical, surgical or optical) would be referred to a collaborating eye hospital. After training, the KIs spent approximately 2–3 weeks in their communities, listing all children they “suspected” to be blind. These lists were given to the project officer who compiled a single list for each district. Approximately 800 KIs were trained throughout the country.

Eye examination and data recording procedure
A detailed description of the methods has been published previously.2 Socio-demographic data, and ophthalmic, medical and family histories were recorded before visual acuity measurements, refraction and ophthalmic examination. All data for each child were recorded on the WHO/PBL Eye Examination Record for Children with Blindness and Low Vision, in accordance with the coding instructions.4

Statistical analysis
An analysis of demographic variations between children ascertained by the case ascertainment methods was conducted. Logistic regression analyses with univariate and adjusted models were used to compare the KI method of case ascertainment with ascertainment from SpEdu and from CBR programmes with respect to age, gender, division, rural/urban dwelling, visual acuity, the presence of additional impairments and the causes of SVI/BL. All tests were two sided and the results are quoted as odds ratios (OR) with CI at the 95% level.

RESULTS
A detailed description of the anatomical and aetiological causes of childhood blindness in this national study has been reported previously.2 The majority of the 1935 BL/SVI children were recruited by KIs (n = 1245, 64.3%), followed by recruitment from SpEdu (n = 394, 20.4%) and CBR programmes (n = 296, 15.3%).

Age and gender, and visual acuity differences of the study population
The median age of the children was 132 (interquartile range (IQR) 96–168) months and, overall, there were more boys (n = 1220, 63.1%) recruited than girls. More than two-thirds of the children in the SpEdu group were aged between 11 and 15 years (n = 265, 67.26%) compared with 56.8% in the CBR group and 47.7% in the KI group. The vast majority of children aged 0–5 years were identified by KIs (247/297, 83.2%). Only 2.0% of children in the SpEdu group were aged 0–5 years, compared with 14.2% in the CBR group and 19.8% in the KI group (table 1). In the SpEdu group, 71.1% of the children were boys, compared with 60.8% in the CBR group and 61.0% in the KI group (table 1). A total of 140 children (35.23%) in SpEdu were congenitally blind compared with 112 (37.8%) in CBR programmes and 364 (29.2%) ascertained by the KIs. Children recruited by KIs had a higher proportion of SVI (9.8%) than children in the SpEdu group (4.8%). Of the children recruited from the CBR programmes, 7.8% had SVI. A higher proportion of children with an infantile (postnatal to <1 year) age of onset of impairment was found by KIs (25.2% vs 11.7% in SpEdu). Differences in anatomical cause and aetiology by ascertainment method are shown in table 2. A comparison of preventable causes showed that the children in the KI group were less likely to have a preventable condition than children in the other two groups (table 2). Approximately one in four children (95% CI 23.5 to 28.5) in the KI group had a preventable condition compared with 35.5%, (95% CI 29.8 to 39.4) in the SpEdu group. The main difference in this preventable group was seen in differences in vitamin A deficiency, which was responsible for 22.8% of the poor vision in SpEdu, 18.9% in CBR and 15.7% in KI groups.

In contrast, children with treatable conditions were more likely to be identified in the KI group than by the other methods of case ascertainment. Bilateral untreated cataract was identified most commonly in the children ascertained by the KIs. Nearly one-third of the children (n = 393, 31.6%) in the KI group had BL/SVI due to untreated cataract. This compared
with 22.3% in the CBR group and 17.5% in the SpEdu children. Children who had had unsuccessful cataract surgery were equally distributed amongst the three ascertainment methods. Children ascertained by KIs were most likely to have an avoidable cause of visual loss. Unavoidable causes such as retinal dystrophies were found more commonly in the SpEdu children (14.7% in SpEdu, 10.8% in CBR and 10.7% in KI children) and congenital anomalies were least commonly found amongst the KI children (10.3% in KI, SpEdu in 12.4% and 15.3% in CBR children).

Association analysis

When comparing children in the KI group with those in the SpEdu group, there were several statistically significant findings (table 3). Differences in age of the children as well as gender, level of visual acuity, associated disability and causes were identified.

In comparing children identified in CBR programmes with those identified by KIs, again age differences were apparent. The odds of ascertaining a child 0–5 years old compared with 11–15 years old was 70% more using the KI method (95% CI 1.1 to 2.4, p = 0.007). Lens-related abnormalities had a borderline higher odds of being ascertained using the KI method (p = 0.036), resulting in a borderline significantly higher odds of ascertaining an avoidable cause using the KI method (adjusted OR 1.3 95% CI 1.0 to 1.7, p = 0.033). No other significant differences were found.

Time frame and cost of case ascertainment

Field work took approximately 1 year. The main cost included salary for four local staff, extensive local travel and subsistence for the project team, and office costs. Approximately, US$50 000 (£25 300) was incurred for case ascertainment and data collection. However, the majority of the cost would have been incurred if only children in SpEdu had been recruited and examined. The authors estimate that 25% of the total cost and time was specifically needed for the ‘add-on’ KI component.

DISCUSSION

Large-scale population-based prevalence surveys would provide the most accurate data on the prevalence and causes of blindness in children. However, with a prevalence estimated to be about 8/10 000 children in Bangladesh, a very large sample (approximately 130 000 children, which would yield only 104 BL/SVI children) would be required to provide meaningful data on causes. Examination of children in SpEdu, with classification of causes using the WHO system, has been widely used to obtain data on causes, the advantage being that a relatively large number of blind children can be examined in a short period of time and at low cost. However, data from these blind school studies are likely to be biased for the following reasons: some causes of blindness are associated with high mortality rates (eg, measles, vitamin A deficiency, meningitis, congenital rubella) and only the survivors would be in school; cultural attitudes may make parents reluctant to acknowledge that they have a disabled child, and the child remains unidentified; in some cultures blind children provide an income for the family from begging; children with multiple impairments, and pre-school age children usually cannot be catered for in special education; and, lastly, most schools are in urban areas and parents in rural areas may be reluctant to send their child far away.

Table 1  Distribution by gender, age and division within the different methods of case ascertainment

<table>
<thead>
<tr>
<th></th>
<th>Special education n (%)</th>
<th>CBR n (%)</th>
<th>Key informants n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender p = 0.001*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>280 (71.1)</td>
<td>180 (60.8)</td>
<td>760 (61.0)</td>
<td>1220 (63.0)</td>
</tr>
<tr>
<td>Girls</td>
<td>114 (28.9)</td>
<td>116 (39.2)</td>
<td>485 (39.00)</td>
<td>715 (37.0)</td>
</tr>
<tr>
<td>Age (years) p = 0.001*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–5</td>
<td>8 (2.0)</td>
<td>42 (14.2)</td>
<td>247 (19.9)</td>
<td>297 (15.3)</td>
</tr>
<tr>
<td>6–10</td>
<td>121 (30.7)</td>
<td>86 (29.0)</td>
<td>168 (22.5)</td>
<td>411 (31.6)</td>
</tr>
<tr>
<td>11–15</td>
<td>265 (67.3)</td>
<td>168 (56.8)</td>
<td>594 (47.7)</td>
<td>1027 (53.1)</td>
</tr>
<tr>
<td>Visual acuity p = 0.008</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SVI</td>
<td>19 (4.8)</td>
<td>23 (7.8)</td>
<td>122 (9.8)</td>
<td>164 (8.5)</td>
</tr>
<tr>
<td>Blind</td>
<td>375 (95.2)</td>
<td>273 (92.2)</td>
<td>1123 (90.2)</td>
<td>1771 (91.5)</td>
</tr>
<tr>
<td>Dwelling p = 0.001*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>344 (87.3)</td>
<td>287 (97.0)</td>
<td>1216 (97.7)</td>
<td>1847 (95.5)</td>
</tr>
<tr>
<td>Urban</td>
<td>50 (12.7)</td>
<td>9 (3.0)</td>
<td>29 (2.3)</td>
<td>88 (4.5)</td>
</tr>
<tr>
<td>Family history p = 0.164</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>91 (23.1)</td>
<td>76 (25.8)</td>
<td>259 (20.9)</td>
<td>426 (22.1)</td>
</tr>
<tr>
<td>No</td>
<td>303 (76.9)</td>
<td>219 (74.2)</td>
<td>982 (79.1)</td>
<td>1504 (77.9)</td>
</tr>
<tr>
<td>History of consanguinity p = 0.77*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>62 (17.0)</td>
<td>56 (19.2)</td>
<td>222 (18.0)</td>
<td>340 (18.0)</td>
</tr>
<tr>
<td>No</td>
<td>302 (83.0)</td>
<td>235 (80.8)</td>
<td>1010 (82.0)</td>
<td>1547 (82.0)</td>
</tr>
<tr>
<td>Age of onset p = 0.001*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital</td>
<td>139 (35.3)</td>
<td>112 (37.8)</td>
<td>361 (29.0)</td>
<td>612 (31.6)</td>
</tr>
<tr>
<td>Infantile</td>
<td>46 (11.7)</td>
<td>56 (18.9)</td>
<td>321 (25.1)</td>
<td>414 (21.4)</td>
</tr>
<tr>
<td>1 to &lt;5 years</td>
<td>135 (34.3)</td>
<td>94 (31.8)</td>
<td>363 (29.2)</td>
<td>592 (30.6)</td>
</tr>
<tr>
<td>5 to &lt;10 years</td>
<td>74 (18.8)</td>
<td>34 (11.5)</td>
<td>209 (16.8)</td>
<td>317 (16.4)</td>
</tr>
<tr>
<td>Disability p = 0.005*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7 (1.8)</td>
<td>17 (5.7)</td>
<td>72 (5.8)</td>
<td>96 (5.0)</td>
</tr>
<tr>
<td>No</td>
<td>387 (98.2)</td>
<td>279 (94.3)</td>
<td>1173 (94.2)</td>
<td>1839 (95.0)</td>
</tr>
<tr>
<td>Total</td>
<td>394 (100)</td>
<td>296 (100)</td>
<td>1245 (100)</td>
<td>1935 (100)</td>
</tr>
</tbody>
</table>

*χ2 test showing significant differences between the ascertainment methods in gender, age, visual acuity, dwelling, age of onset and disability, postnatal to <1 year.

CBR, community-based rehabilitation; SVI, severe visual impairment.
defined structurally, are less useful where the condition of interest is defined functionally (e.g., visual loss). These registers, even in developed countries, are subject to under-reporting. There are also studies of blind children ascertained through CBR programmes in India and through active national surveillance schemes. However, in developing countries, where a large proportion of the rural population do not have access to specialised health services and referral linkages are not effective, national surveillance may prove to be more difficult to establish, exposing the system to underascertainment.

Using this innovative approach has resulted in one of the largest studies of blind children to date. This study also has the largest number of SVI/BL children recruited directly from the community, with almost two-thirds being ascertained by KIs, to have multiple impairments and to be from rural areas. Children were also more likely to be severely visually impaired rather than blind, which provides an opportunity for eye care programmes to employ KIs to find children early, before their sight deteriorates further and while the prognosis for sight-restoring surgery is good. A comparison of avoidable causes also reveals that significantly more children with avoidable causes were identified using the KI method than with either the SpEdu or the CBR methods (OR 1.6, p = 0.002 and OR 1.5, p = 0.003, respectively).

As no population-based studies have been undertaken anywhere which are large enough to determine the distribution of blindness in children by age, sex, place of residence and cause, one can only speculate how closely case ascertainment using KIs approaches the “truth” in the population. This is a complex area: many children are born blind from congenital anomalies, some of which are life threatening (e.g., congenital rubella). In developing countries, the most common age for children who were born sighted to become blind is from approximately 6 months to 5 years, when they are susceptible to vitamin A deficiency, measles, malaria, meningitis and other acquired conditions which potentially cause blindness. Many of these incident cases of blindness will die, due to complications of the condition causing blindness, or from inadequate medical care, or possibly from neglect. Acquired blindness beyond the age of 5 years is relatively unusual. Taken as a whole, one

---

Table 2: Anatomical site of abnormality, underlying aetiology and cause by method of ascertainment (special education, community-based rehabilitation and key informant)

<table>
<thead>
<tr>
<th>Main site</th>
<th>SpEdu group n (%)</th>
<th>CBR group n (%)</th>
<th>KI group n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole globe</td>
<td>71 (18.0)</td>
<td>45 (15.2)</td>
<td>137 (11.0)</td>
<td>253 (13.1)</td>
</tr>
<tr>
<td>Cornea</td>
<td>120 (30.5)</td>
<td>83 (28.0)</td>
<td>311 (25.0)</td>
<td>514 (26.6)</td>
</tr>
<tr>
<td>Lens</td>
<td>92 (23.4)</td>
<td>85 (28.7)</td>
<td>452 (36.3)</td>
<td>629 (32.5)</td>
</tr>
<tr>
<td>Uvea</td>
<td>5 (1.3)</td>
<td>7 (2.4)</td>
<td>26 (2.1)</td>
<td>38 (2.0)</td>
</tr>
<tr>
<td>Retina</td>
<td>65 (16.5)</td>
<td>33 (11.2)</td>
<td>147 (11.8)</td>
<td>245 (12.7)</td>
</tr>
<tr>
<td>Optic nerve</td>
<td>26 (6.4)</td>
<td>25 (8.5)</td>
<td>104 (8.4)</td>
<td>154 (8.0)</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>16 (4.1)</td>
<td>16 (5.4)</td>
<td>51 (4.1)</td>
<td>83 (4.3)</td>
</tr>
<tr>
<td>Other†</td>
<td>0 (0)</td>
<td>2 (0.7)</td>
<td>17 (1.4)</td>
<td>19 (1.0)</td>
</tr>
<tr>
<td>Total</td>
<td>394 (100)</td>
<td>296 (100)</td>
<td>1245 (100)</td>
<td>1935 (100)</td>
</tr>
</tbody>
</table>

Aetiology and cause p = 0.002†

| Hereditary      | 69 (17.5)         | 41 (13.9)       | 181 (14.5)     | 291 (15.0)  |
| Childhood factor| 151 (38.3)        | 86 (29.1)       | 356 (28.6)     | 593 (30.7)  |
| Unknown         | 171 (43.4)        | 165 (55.7)      | 698 (56.1)     | 1034 (53.4) |
| Other†          | 3 (0.8)           | 4 (1.4)         | 10 (0.8)       | 17 (0.9)    |
| Total           | 394 (100)         | 296 (100)       | 1245 (100)     | 1935 (100)  |

Aetiology p = 0.034†

| Preventable     | 136 (34.5)        | 78 (26.4)       | 323 (25.9)     | 537 (27.8)  |
| Treatable       | 124 (31.5)        | 114 (38.5)      | 563 (45.2)     | 801 (41.4)  |
| Unavoidable     | 134 (34.0)        | 104 (35.1)      | 359 (28.8)     | 597 (30.9)  |
| Total           | 394 (100)         | 296 (100)       | 1245 (100)     | 1935 (100)  |

*Pearson χ² test showing significant differences in site of abnormality, underlying aetiology and cause in the different case ascertainment methods.†Includes children that had either no anatomical abnormality (n = 14) or no anterior segment abnormality, but the posterior segment was not examined (n = 5) because the child was too young, uncooperative or had multiple disabilities.

Table 3: Analysis of likelihood of ascertaining children with blindness and severe visual impairment in Bangladesh in 2001: comparison of case ascertainment by the key informant method with recruitment through specialised schools for blind children (n = 1639)

<table>
<thead>
<tr>
<th>Age group</th>
<th>Univariate analysis</th>
<th>Adjusted for age andp</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6–10</td>
<td>1.5 (1.2 to 1.9)</td>
<td>1.5 (1.2 to 2.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>0–5</td>
<td>13.8 (6.7 to 28.3)</td>
<td>14.1 (6.9 to 28.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td>1.6 (1.2 to 2.0)</td>
<td>1.6 (1.3 to 2.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dwelling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>6.1 (3.8 to 9.8)</td>
<td>5.9 (3.6 to 9.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Visual acuity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SVI</td>
<td>2.1 (1.3 to 3.5)</td>
<td>2.5 (1.4 to 4.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Additional impairment</td>
<td>1 [1]</td>
<td>1 [1]</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3.4 (1.6 to 7.4)</td>
<td>3.1 (1.4 to 7.0)</td>
<td>0.005</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onset of visual loss</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infantile‡</td>
<td>2.6 (1.8 to 3.8)</td>
<td>2.5 (1.7 to 3.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;1 year to &lt;5</td>
<td>1.0 (0.8 to 1.4)</td>
<td>1.2 (0.9 to 1.6)</td>
<td>0.220</td>
</tr>
<tr>
<td>years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5 years</td>
<td>1.1 (0.8 to 1.5)</td>
<td>1.6 (1.2 to 2.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>Cause: lens</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lens</td>
<td>1.2 (1.1 to 1.3)</td>
<td>1.2 (1.1 to 1.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cause: cornea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cornea</td>
<td>0.9 (0.8 to 1.0)</td>
<td>1.0 (0.8 to 1.1)</td>
<td>0.448</td>
</tr>
<tr>
<td>Preventable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1 [1]</td>
<td>1 [1]</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.7 (0.5 to 0.9)</td>
<td>0.8 (0.6 to 1.0)</td>
<td>0.09</td>
</tr>
<tr>
<td>Treatable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1 [1]</td>
<td>1 [1]</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.3 (1.2 to 1.5)</td>
<td>1.3 (1.1 to 1.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Avoidable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1 [1]</td>
<td>1 [1]</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.3 (1.1 to 1.6)</td>
<td>1.4 (1.1 to 1.7)</td>
<td>0.015</td>
</tr>
</tbody>
</table>

*Sex adjusted; †age adjusted; ‡postnatal to <1 year of age. SVI, severe visual impairment.
would therefore expect the age distribution to increase from birth until the age of 5, and then stay relatively stable thereafter.

Although some conditions are more common in boys than in girls (eg, X-linked retinitis pigmentosa and ocular albinism), these conditions are rare. One would therefore expect approximately equal numbers of boys and girls to be blind, unless there are gender differences in accessing services and a different mortality rate by gender. The finding that, comparatively, more girls than boys were recruited by KIs illustrates that parents may be more willing to acknowledge the presence of a blind female child, or to take a blind girl for assessment if facilities are provided locally, without charge and with the support of a respected local person.

One would also expect a higher prevalence, and different causes, in children from rural communities compared with children living in urban areas. The latter are less likely to be vitamin A deficient (apart from slum populations), more likely to have had measles immunisation, and, as there is better access to eye care services, children in urban areas may be less likely to be blind from treatable conditions. One would therefore expect a higher prevalence of blindness in rural areas, and a greater proportion of rural children to be blind from preventable and treatable causes. In developing countries, one would also anticipate more children to come from rural than urban areas relative to the population distribution, with children from rural areas being more likely to suffer from avoidable causes. The data presented in this study suggest that the KI method of ascertaining blind children may come closer to this speculative "truth." However, further studies are needed to validate the KI approach—for example, by comparing the findings either with those of a house to house survey of all children or with those of a random sample survey.

In societies that have gender inequality, as in Bangladesh, the primary caregiver for the child is typically the mother or grandmother. As the majority of KIs recruited in our study were men, there was potential for incomplete ascertainment. There was also some variation in the effectiveness of the KI method in different districts, which was due to the varying level of commitment to volunteering. Lack of cheap transport and long travel times were other challenges faced by the KIs. Before implementation of any method that has potential to generate a large number of cases, it is essential to establish watertight referral systems to paediatric care centres and to set up financial structures that can cover the expenses of eye treatments.

The success of the KI method lies in its knowledge and use of active social networks (contacts among government and NGO staff and local leaders, etc), and with suitable training we found that KIs were very capable of limiting the number of false-positive referrals. The KI method can also be extended to case ascertainment of children with other impairments or conditions (eg, hearing and speech impairments, epilepsy) which can be recognised by community members. It is hoped that KIs can be empowered to reduce social stigma, increase awareness and improve health-seeking-behaviour among community members.

This novel method has the potential to identify the "difficult to reach" in developing countries, providing a mechanism for delivering services as well as providing population-based estimates of rare diseases and disability.

ACKNOWLEDGEMENTS

The authors wish to acknowledge the contribution of key informants in case ascertainment and the Childhood Blindness Project of Bangladesh (CRBP) team in data collection for the study.

Authors’ affiliations

Mohammad A Muhtit, Shaheen P Shah, Clare E Gilbert, Allen Foster, International Centre for Eye Health, Clinical Research Unit, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK

Sally D Hartley, Institute of Health, University of East Anglia, Norwich, UK

Funding organisations for the study: Christoffel Blindenmission, Muslim Aid, Sightsavers International, Royal College of Surgeons, England.

Competing interest. None declared.

REFERENCES


6 McDonald JR, Nataorajin T. Community care needs of people with AIDS—the key informant study: a research method for policy development, service planning, and achieving 1995;35:83–90.


Causes of severe visual impairment and blindness in Bangladesh: a study of 1935 children

M A Muhit, S P Shah, C E Gilbert, A Foster

WORLD VIEW

Objective: To identify the anatomical site and underlying aetiology of severe visual impairment and blindness (SVI/BL) in children in Bangladesh.

Design: A national case series.

Methods: Children were recruited from all 64 districts in Bangladesh through multiple sources. Causes were determined and categorised using standard World Health Organization methods.

Results: 1935 SVI/BL children were recruited. The median age was 132 months, and boys accounted for 63.1% of the sample. The main site of abnormality was lens (32.5%), mainly unoperated cataract, followed by corneal pathology (26.6%) and disorders of the whole eye (13.1%). Lens-related blindness was the leading cause in boys (37.0%) compared with corneal blindness in girls (29.8%). In 593 children, visual loss was due to childhood factors, over 75% being attributed to vitamin A deficiency. Overall 1338 children (69.2%) had avoidable causes. Only 2% of the country’s estimated SVI/BL children have access to education and rehabilitation services.

Conclusions: This is the first large-scale study of SVI/BL children in Bangladesh over two-thirds of whom had avoidable causes. Strategies for control are discussed.

With an estimated 1.4 million blind children worldwide, the World Health Organization’s (WHO) global initiative for the elimination of avoidable blindness (VISION 2020: The Right to Sight) has prioritised the control of blindness in children. The available data suggest that the prevalence and causes of blindness in children vary widely from country to country, reflecting differences in socio-economic development and health care provision. Accurate information on the prevalence and causes of blindness in children is difficult to obtain due to low prevalence—for example, only seven blind children were identified in a study of >10,000 children in India. Reliable data are needed, as strategies for the control of blindness in children are significantly different from those for adults: specific training, expertise and equipment, and a more comprehensive, multidisciplinary team approach are required. Early detection and prompt treatment are also essential to prevent irreversible amblyopia.

Bangladesh is one of the most densely populated countries in the world and is the seventh most populous nation, with 41% being children below the age of 16 years. The country is ranked 139th according to the United Nation’s Human Development Index. A recent survey provided data for adults, but to date no reliable data exist for children.

The purpose of this study of severely visually impaired or blind (SVI/BL) children was to identify the main anatomical site and underlying aetiology of blindness; to identify all preventable and treatable causes (i.e. avoidable causes); and to explore variation by socio-demographic variables.

SUBJECTS AND METHODS

Recruitment of SVI/BL children

The details of systematic attempts in each of the 64 districts of Bangladesh to identify SVI/BL children are described in another publication, but in brief the following sources were used:

- Schools (SpEdu): all eight special schools for the blind and 69 integrated schools.
- Community-based rehabilitation (CBR) programmes: all 21 active CBR programmes for SVI/BL children.
- Key informants (KIs): KIs were community volunteers who were trained by the study team to ascertain as many SVI/BL children as possible in their own locality.

Data collection

The team comprised an ophthalmologist (MM), three project officers and a project administrator. The project officers were responsible for contacting, visiting, networking, identifying and recruiting SVI/BL children in each district and for making arrangements for the visit by the mobile eye examination unit. The project administrator coordinated the team and maintained the data collection forms and equipment. Data on each child were recorded by the ophthalmologist on the WHO/PBL Eye Examination Record for Children with Blindness and Low Vision which has been widely used in other studies.

Method of eye examination

Examinations were conducted in the schools for the blind, or in suitable locations close to where the children lived. Each child was seen with his or her parent, class teacher, CBR coordinator or KI. Socio-demographic data, and relevant ophthalmic, medical, obstetric and family histories were elicited by the ophthalmologist. Presenting distance visual acuities (ie, with optical correction if usually worn) were measured in each eye separately and then in both eyes together using a reduced logarithm of minimum angle of resolution (logMAR) E chart, at 6 or 3 m. Cardiff acuity cards were used for pre-school children, employing the standard staircase method. Near vision was tested with an E chart with N5–30 font sizes with...
both eyes open. Visual fields were assessed by confrontation. Anterior segment examination was carried out using a magnifying loupe and torch. Cycloplegic refraction was performed unless it was considered clinically inappropriate (e.g., dense cataract), using retinoscopy and trial lenses. Posterior segments were examined by direct and indirect ophthalmoscopy. Intraocular pressure measurements were not made. Interobserver agreement studies conducted in the pilot study prior to the main study (between MM and CG) on the anatomical and aetiological causes of visual loss had good levels of agreement. All children needing surgical, medical or optical treatment were referred to one of four collaborating eye hospitals.

### Inclusion criteria
Children aged <16 years. The WHO categories of visual impairment were used: SVI was defined as a presenting visual acuity (ie, with glasses if normally worn) of <6/60 to 3/60 in the better eye. BL was defined as <3/60 in the better eye. As a result, children with unilateral blindness or impairment were not included in the study.

### Classification of causes
Three classification systems were used, the first two being those developed by the WHO.

#### Anatomical site of abnormality
All structural abnormalities were recorded for each eye, and one site selected for each eye, using the detailed definitions and criteria in the WHO Coding Instructions. Cataract, for example, is defined as central lens opacity sufficient to reduce visual acuity. One site, either that in the right eye or that in the left eye, was selected to represent the major site for the child, again following WHO guidelines. If the main sites differed between eyes, priority was given to treatable then to preventable causes.

#### Underlying aetiology
Based on family history, ocular history, clinical findings and diagnosis, attempts were made to determine the time of onset of the insult leading to visual loss. The following categories were used: hereditary, intrauterine, perinatal and childhood causes, and unavoidable causes were all other causes.

#### Preventable/treatable/unavoidable
Preventable causes (eg, vitamin A deficiency, measles) were diagnoses/conditions which could have potentially been prevented through simple health promotion, prevention and education at community and household levels by non-specialist, primary level health workers, volunteers or community members. Treatable causes were conditions where surgical, medical or optical interventions could have preserved or restored sight (eg, cataract and glaucoma surgery). Preventable, treatable and unavoidable categories were mutually exclusive for each diagnosis and subsequent analysis. Avoidable blindness was the sum of treatable and preventable causes, and unavoidable causes were all other causes.

### Ethical approval
Permission to visit schools was granted by the Ministry of Social Welfare. Ethical approval was obtained from the ethics review committee of the BNSB Eye Hospital in Bangladesh.

### Data management
Data were entered by a dedicated data entry officer into a database created in Microsoft Access (2000). All data entries were double checked by the project administrator. A random selection of the data set revealed an error rate of <0.1%. The data were exported to STATA 9.0 (Statacorp. Release 9.0., Stata Corporation, College Station, Texas) for statistical analysis. All tests are two sided, and CI are quoted at the 95% level.

### RESULTS
All identified participants (n = 2625) were asked to be present on the day of eye examination. All those who were present (n = 2322) on the day were examined by the ophthalmologist. After examination, 387 participants were excluded from the study as they were either too old or had visual acuity >6/60 in at least one eye. A total of 1935 children were included in this study.

### Demographic details of study children
More boys were recruited than girls (63.1% vs 36.9%) (table 1). Over half the study children were aged 11–15 years (1027, 53.1%) but there was no gender differences in age (p = 0.49). Children were largely ascertained from rural locations (1847, 95.4%), with no rural/urban gender differences (p = 0.74). The median age of rural children was 11 years (interquartile range IQR 7–14) compared with 13 years in urban children (IQR 9–15) (p<0.001).

### Table 1 Demographic characteristics of the study population, by gender

<table>
<thead>
<tr>
<th></th>
<th>Boys</th>
<th>Girls</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Division*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barisal</td>
<td>56 (4.6)</td>
<td>38 (5.3)</td>
<td>94 (4.9)</td>
</tr>
<tr>
<td>Khulna</td>
<td>240 (19.7)</td>
<td>124 (17.3)</td>
<td>364 (20.5)</td>
</tr>
<tr>
<td>Chittagong</td>
<td>432 (34.7)</td>
<td>259 (36.2)</td>
<td>691 (35.2)</td>
</tr>
<tr>
<td>Dhaka</td>
<td>237 (19.4)</td>
<td>160 (22.4)</td>
<td>682 (35.2)</td>
</tr>
<tr>
<td>Rajshahi</td>
<td>230 (18.9)</td>
<td>120 (16.8)</td>
<td>350 (18.1)</td>
</tr>
<tr>
<td>Sylhet</td>
<td>34 (2.8)</td>
<td>14 (2.0)</td>
<td>48 (2.5)</td>
</tr>
<tr>
<td>Level of VI†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blind</td>
<td>1100 (91.0)</td>
<td>661 (92.5)</td>
<td>1771 (91.5)</td>
</tr>
<tr>
<td>SVI</td>
<td>110 (9.0)</td>
<td>54 (7.5)</td>
<td>164 (8.5)</td>
</tr>
<tr>
<td>Near acuity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;N10</td>
<td>82 (6.7)</td>
<td>39 (5.5)</td>
<td>121 (6.3)</td>
</tr>
<tr>
<td>&gt;N30</td>
<td>138 (11.3)</td>
<td>66 (9.2)</td>
<td>204 (10.5)</td>
</tr>
<tr>
<td>&gt;N60</td>
<td>824 (67.5)</td>
<td>493 (68.9)</td>
<td>1317 (68.1)</td>
</tr>
<tr>
<td>Unable</td>
<td>176 (14.4)</td>
<td>117 (16.4)</td>
<td>293 (15.1)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–5</td>
<td>185 (15.2)</td>
<td>112 (15.7)</td>
<td>297 (15.4)</td>
</tr>
<tr>
<td>6–10</td>
<td>204 (33.1)</td>
<td>107 (29.0)</td>
<td>311 (31.4)</td>
</tr>
<tr>
<td>11–15</td>
<td>631 (51.7)</td>
<td>396 (57.5)</td>
<td>1027 (53.1)</td>
</tr>
<tr>
<td>Place of dwelling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>1166 (95.6)</td>
<td>681 (95.2)</td>
<td>1847 (95.5)</td>
</tr>
<tr>
<td>Urban</td>
<td>54 (4.4)</td>
<td>34 (4.8)</td>
<td>88 (4.5)</td>
</tr>
<tr>
<td>Other disability</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>64 (5.3)</td>
<td>32 (4.5)</td>
<td>96 (5.0)</td>
</tr>
<tr>
<td>No</td>
<td>1156 (94.7)</td>
<td>683 (95.5)</td>
<td>1839 (95.0)</td>
</tr>
<tr>
<td>Family history‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>255 (20.9)</td>
<td>171 (23.9)</td>
<td>426 (22.0)</td>
</tr>
<tr>
<td>No</td>
<td>963 (78.9)</td>
<td>541 (75.7)</td>
<td>1504 (77.7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (0.2)</td>
<td>3 (0.4)</td>
<td>5 (0.3)</td>
</tr>
<tr>
<td>History of consanguinity‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>208 (17.0)</td>
<td>132 (18.4)</td>
<td>340 (17.6)</td>
</tr>
<tr>
<td>No</td>
<td>983 (80.6)</td>
<td>564 (78.6)</td>
<td>1547 (80.0)</td>
</tr>
<tr>
<td>Unknown</td>
<td>29 (2.4)</td>
<td>19 (2.7)</td>
<td>48 (2.4)</td>
</tr>
<tr>
<td>Age of onset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital</td>
<td>373 (30.5)</td>
<td>239 (33.4)</td>
<td>612 (31.6)</td>
</tr>
<tr>
<td>Infantile*</td>
<td>290 (23.8)</td>
<td>124 (17.3)</td>
<td>414 (21.4)</td>
</tr>
<tr>
<td>&gt;1 to &lt;5 years</td>
<td>361 (29.6)</td>
<td>231 (32.3)</td>
<td>592 (30.6)</td>
</tr>
<tr>
<td>&gt;5 to &lt;16 years</td>
<td>195 (16.0)</td>
<td>122 (17.1)</td>
<td>317 (16.4)</td>
</tr>
<tr>
<td>Total</td>
<td>1220 (100%)</td>
<td>715 (100%)</td>
<td>1935 (100%)</td>
</tr>
</tbody>
</table>

*Arranged by adult population literacy, in descending order: Barisal (66.2%), Khulna (54.9%); Chittagong (52.0%); Dhaka (48.3%), Rajshahi (47.4%), and Sylhet (39.3%).

†VI, visual impairment. Blindness was defined as a presenting visual acuity (ie, with glasses if normally worn) of <3/60 in the better eye. Severe visual impairment (SVI) was defined as presenting <6/60 to 3/60 in the better eye.

‡The family history was unknown in five children.

§History of consanguinity was unknown in 48 children.

*Postnatal to <1 year.
The vast majority of children (n = 1839, 95%) had isolated visual loss. A positive family history of blindness was reported by 426 children (22%), and parental consanguinity by 340 children (17.6%). The odds of a positive family history was 3.2 (CI 2.4 to 4.1, p < 0.001) times higher in children whose parents had a consanguineous marriage. The vast majority of children recruited suffered from BL (91.5%) rather than SVI. A total of 130 children had optic atrophy, 30 following meningitis and 20 from raised intracranial pressure/intracranial tumours. Glaucoma was diagnosed in 83 children (4.3%) and uveal dystrophies (223 children). Lesions of the optic nerve affected 102 (5.3%), whereas other eye anomalies (eg anterior segment dysgenesis, microphthalmos, coloboma) accounted for 224 (11.6).

### Underlying aetiology of SVI/BL

In just over half of the cases, an underlying aetiology could not be determined (n = 1034, 53.4%) (table 2). The main sites of abnormality in these children were lens related (437, 42.3%).

### Table 2  Main anatomical site of abnormality, and underlying aetiology in 1935 severely visually impaired and blind children, by gender and age

<table>
<thead>
<tr>
<th>Anatomical Whole globe</th>
<th>Boys  (n = 715)</th>
<th>Girls (n = 297)</th>
<th>0–5 years</th>
<th>6–10 years</th>
<th>11–15 years</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Anatomical Whole globe</td>
<td>155 (12.7)</td>
<td>98 (13.7)</td>
<td>48 (16.2)</td>
<td>85 (13.9)</td>
<td>120 (11.7)</td>
<td>253 (13.1)</td>
</tr>
<tr>
<td>p&lt;0.001*  Cornea</td>
<td>301 (24.7)</td>
<td>213 (29.8)</td>
<td>39 (13.1)</td>
<td>140 (22.9)</td>
<td>335 (32.6)</td>
<td>514 (26.6)</td>
</tr>
<tr>
<td>p&lt;0.001† Lens</td>
<td>451 (37.0)</td>
<td>178 (24.9)</td>
<td>129 (43.4)</td>
<td>230 (37.6)</td>
<td>270 (26.3)</td>
<td>629 (32.5)</td>
</tr>
<tr>
<td>Retina</td>
<td>21 (1.7)</td>
<td>17 (2.4)</td>
<td>1 (0.3)</td>
<td>10 (1.6)</td>
<td>27 (2.6)</td>
<td>38 (2.0)</td>
</tr>
<tr>
<td>Optic nerve</td>
<td>148 (12.1)</td>
<td>97 (13.6)</td>
<td>12 (4.1)</td>
<td>71 (11.6)</td>
<td>138 (13.4)</td>
<td>245 (12.7)</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>47 (3.9)</td>
<td>36 (5.0)</td>
<td>19 (6.4)</td>
<td>26 (4.3)</td>
<td>38 (3.7)</td>
<td>83 (4.3)</td>
</tr>
<tr>
<td>Other†</td>
<td>9 (0.7)</td>
<td>10 (1.4)</td>
<td>4 (1.3)</td>
<td>4 (0.7)</td>
<td>11 (1.1)</td>
<td>19 (1.0)</td>
</tr>
<tr>
<td><strong>Aetiology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hereditary</td>
<td>176 (14.4)</td>
<td>115 (16.1)</td>
<td>55 (18.5)</td>
<td>98 (16.0)</td>
<td>138 (13.4)</td>
<td>291 (15.0)</td>
</tr>
<tr>
<td>Childhood factor</td>
<td>353 (28.9)</td>
<td>240 (33.6)</td>
<td>35 (11.8)</td>
<td>163 (26.7)</td>
<td>395 (38.5)</td>
<td>593 (30.7)</td>
</tr>
<tr>
<td>Preventable</td>
<td>10 (0.8)</td>
<td>7 (1.0)</td>
<td>4 (0.7)</td>
<td>4 (0.7)</td>
<td>11 (1.1)</td>
<td>17 (0.9)</td>
</tr>
<tr>
<td>Treatable</td>
<td>681 (55.8)</td>
<td>353 (49.4)</td>
<td>205 (69.0)</td>
<td>346 (56.6)</td>
<td>483 (47.0)</td>
<td>1034 (53.4)</td>
</tr>
<tr>
<td><em>Preventable</em></td>
<td>315 (25.8)</td>
<td>222 (31.1)</td>
<td>34 (11.5)</td>
<td>146 (23.9)</td>
<td>357 (43.8)</td>
<td>537 (27.8)</td>
</tr>
<tr>
<td><em>Treatable</em></td>
<td>549 (45.0)</td>
<td>252 (35.2)</td>
<td>157 (52.9)</td>
<td>272 (44.5)</td>
<td>372 (36.2)</td>
<td>801 (41.4)</td>
</tr>
<tr>
<td>Unavoidable</td>
<td>536 (29.2)</td>
<td>241 (33.7)</td>
<td>106 (35.7)</td>
<td>193 (31.6)</td>
<td>298 (29.0)</td>
<td>597 (30.8)</td>
</tr>
<tr>
<td><em>Unavoidable</em></td>
<td>1220 (100)</td>
<td>715 (100)</td>
<td>297 (100)</td>
<td>611 (100)</td>
<td>1027 (100)</td>
<td>1935 (100)</td>
</tr>
</tbody>
</table>

*‡*: showing significant differences between genders in anatomical site and type of blindness.

*§*: showing significant differences between age groups in anatomical site, aetiology and type of blindness.

**Table 3  Avoidable (preventable and treatable) and unavoidable causes of blindness and severe visual impairment in children**

<table>
<thead>
<tr>
<th>Cause</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preventable</td>
<td></td>
</tr>
<tr>
<td>Vitamin A deficiency plus other*</td>
<td>224 (11.6)</td>
</tr>
<tr>
<td>Vitamin A deficiency</td>
<td>118 (6.1)</td>
</tr>
<tr>
<td>Measles</td>
<td>118 (6.1)</td>
</tr>
<tr>
<td>Meningitis</td>
<td>30 (1.6)</td>
</tr>
<tr>
<td>Trauma</td>
<td>15 (0.8)</td>
</tr>
<tr>
<td>Ophthalmia neonatorum</td>
<td>14 (0.7)</td>
</tr>
<tr>
<td>Harmful traditional practice</td>
<td>7 (0.4)</td>
</tr>
<tr>
<td>Other (eg, toxoplasmosis, infectious keratitis)</td>
<td>11 (0.6)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>537 (27.8)</td>
</tr>
<tr>
<td>Treatable</td>
<td></td>
</tr>
<tr>
<td>Cataract</td>
<td>528 (27.3)</td>
</tr>
<tr>
<td>Pseudo/aphakia</td>
<td>101 (5.2)</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>83 (4.3)</td>
</tr>
<tr>
<td>Others (eg, ROP, raised ICP, tumours, epilepsy)</td>
<td>25 (1.3)</td>
</tr>
<tr>
<td>Uveitis</td>
<td>22 (1.1)</td>
</tr>
<tr>
<td>Keratoconus/dystrophy</td>
<td>21 (1.1)</td>
</tr>
<tr>
<td>Refractive error</td>
<td>11 (0.6)</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>10 (0.5)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>801 (41.4)</td>
</tr>
<tr>
<td>Unavoidable</td>
<td></td>
</tr>
<tr>
<td>CEA (microphthalmos, anophthalmos, coloboma)</td>
<td>223 (11.5)</td>
</tr>
<tr>
<td>Retinal dystrophies</td>
<td>223 (11.5)</td>
</tr>
<tr>
<td>Optic nerve disease (atrophy, hypoplasia)</td>
<td>102 (5.3)</td>
</tr>
<tr>
<td>Other*</td>
<td>33 (1.7)</td>
</tr>
<tr>
<td>Removed, phthisical, or disorganised</td>
<td>16 (0.8)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>597 (30.8)</td>
</tr>
<tr>
<td>Grand total</td>
<td>1935 (100)</td>
</tr>
</tbody>
</table>

*Strong history of severe febrile illness with or without diarrhoea
†Albinism, corneal blindness, congenital nystagmus, corneal opacity with other eye anomalies (eg anterior segment dysgenesis, microphthalmos, congenital cataract, slerolenciae)

ROP, retinopathy of prematurity; ICP, intracranial pressure; CEA, congenital eye anomaly.

www.bjophthalmol.com
Causes of severe visual impairment and blindness in Bangladesh

Table 4 Main anatomical site of abnormality, and underlying aetiology in 1935 severely visually impaired and blind children, by age of onset of disorder

<table>
<thead>
<tr>
<th>Anatomical</th>
<th>Congenital</th>
<th>Infantile*</th>
<th>&gt;1 to &lt;5 years</th>
<th>&gt;5 to &lt;16 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>p&lt;0.001†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole globe</td>
<td>199 (78.7)</td>
<td>14 (5.5)</td>
<td>26 (10.3)</td>
<td>14 (5.5)</td>
</tr>
<tr>
<td>Cornea</td>
<td>38 (7.4)</td>
<td>82 (16.0)</td>
<td>281 (54.7)</td>
<td>113 (22.0)</td>
</tr>
<tr>
<td>Lens</td>
<td>189 (30.1)</td>
<td>27 (15.6)</td>
<td>152 (24.2)</td>
<td>58 (9.2)</td>
</tr>
<tr>
<td>Uvea</td>
<td>15 (3.9)</td>
<td>5 (2.3)</td>
<td>5 (13.2)</td>
<td>16 (4.2)</td>
</tr>
<tr>
<td>Retina</td>
<td>105 (42.9)</td>
<td>39 (15.9)</td>
<td>59 (24.1)</td>
<td>42 (17.1)</td>
</tr>
<tr>
<td>Optic nerve</td>
<td>23 (14.9)</td>
<td>25 (16.2)</td>
<td>51 (33.1)</td>
<td>55 (35.7)</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>37 (44.6)</td>
<td>19 (22.9)</td>
<td>14 (16.9)</td>
<td>13 (15.7)</td>
</tr>
<tr>
<td>Others</td>
<td>6 (31.6)</td>
<td>3 (15.8)</td>
<td>4 (21.1)</td>
<td>6 (31.6)</td>
</tr>
<tr>
<td>p&lt;0.001†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hereditary</td>
<td>156 (53.6)</td>
<td>52 (17.9)</td>
<td>55 (18.9)</td>
<td>28 (9.6)</td>
</tr>
<tr>
<td>Childhood factor</td>
<td>20 (3.4)</td>
<td>103 (17.4)</td>
<td>319 (53.8)</td>
<td>151 (25.5)</td>
</tr>
<tr>
<td>Other†</td>
<td>12 (70.6)</td>
<td>2 (11.8)</td>
<td>2 (11.8)</td>
<td>1 (5.9)</td>
</tr>
<tr>
<td>Unknown</td>
<td>424 (41.0)</td>
<td>257 (24.9)</td>
<td>216 (20.9)</td>
<td>157 (13.3)</td>
</tr>
<tr>
<td>Total</td>
<td>612 (31.6)</td>
<td>414 (21.4)</td>
<td>592 (30.6)</td>
<td>317 (16.4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of blindness</th>
<th>Congenital</th>
<th>Infantile*</th>
<th>&gt;1 to &lt;5 years</th>
<th>&gt;5 to &lt;16 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>p&lt;0.001†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preventable</td>
<td>14 (2.6)</td>
<td>84 (15.6)</td>
<td>305 (56.8)</td>
<td>134 (25.0)</td>
</tr>
<tr>
<td>Treatable</td>
<td>246 (30.7)</td>
<td>259 (32.3)</td>
<td>183 (22.9)</td>
<td>113 (14.1)</td>
</tr>
<tr>
<td>Unavoidable</td>
<td>352 (59.0)</td>
<td>71 (11.9)</td>
<td>104 (17.4)</td>
<td>70 (11.7)</td>
</tr>
<tr>
<td>Total</td>
<td>612 (31.6)</td>
<td>414 (21.4)</td>
<td>592 (30.6)</td>
<td>317 (16.4)</td>
</tr>
</tbody>
</table>

*Postnatal to <1 year
†, showing significant differences in anatomical, ophthalmological and type of blindness by age of onset of disorder.
Includes children that had either no anatomical abnormality (n = 14) or no anterior segment abnormality, but the posterior segment was not examined (n = 5) because the child was too young and/or uncooperative and/or had multiple disabilities.
¶Parental, intrauterine.

followed by whole globe (215, 20.8%) and retinal conditions (128, 12.4%).

Among the known aetiologies, childhood factors predominated (593 children, 30.7%), the vast majority being diagnosed with corneal scarring (456, 76.9%) attributed principally to vitamin A deficiency, often precipitated by fever, diarrhoea or measles infection.

Two-hundred and ninety-one (15.0%) children had genetic disorders, mainly lens related (140, 48.1%) and retinal conditions (112, 38.5%). Modes of inheritance were as follows: autosomal dominant, 26 children (10.9%); autosomal recessive, 26 (10.9%), and could not be determined, 239 (82.1%). A history of parental consanguinity and a hereditary aetiology had retinal disorders, mainly lens related (140, 48.1%) and retinal dystrophies. Intrauterine and perinatal causes were both uncommon (17, 0.9%); two children had toxoplasmosis. Perinatal factors included corneal scarring attributed to ophthalmia neonatorum (14 children), and only one child was blind from retinopathy of prematurity.

Avoidable causes of BL/SVI

Overall, 1338 children (69.2%) had avoidable causes of SVI/BL: 537 children had preventable causes (27.8%) and a further 801 children (41.4%) had treatable conditions. Boys were significantly more likely to have an avoidable cause than girls (70.8% vs 66.3%, p = 0.037). Girls were more likely to have a preventable cause (31.1% vs 25.8%, p = 0.013), whereas boys were more likely to have treatable causes (45.0% vs 35.2%, p<0.001) (table 2). No significant age differences were apparent between children with and without avoidable causes (χ², p = 0.08). However, there was a trend, with older children being more likely to have avoidable causes than younger children (ie, age 0–5 years 64.3% avoidable; 6–10 years 68.4% avoidable; 11–15 years 70.2% avoidable). Preventable conditions were more likely in older children, whereas treatable conditions were more likely in younger children.

Approximately two-thirds of preventable causes were attributed to vitamin A deficiency either alone or following a febrile illness and/or diarrhoea (342, 63.7%) (table 3). Vitamin A deficiency was slightly more common in girls than in boys (19.3% vs 16.7%, p = 0.151). Measles was the next most common preventable cause, again being more common in girls (7.8% vs 5.1%, p = 0.015). Overall, 85% (460 children) of preventable causes of SVI/BL were attributed to vitamin A deficiency, measles, diarrhoeal diseases and febrile illness.

Over three-quarters of treatable causes were due to lens disorders (629, 78.5%) and 1 in 10 (4.3%) were SVI/BL from glaucoma. A total of 597 children (30.8%) had unavoidable causes of SVI/BL, 11.5% being due to congenital eye anomalies and 11.3% to retinal dystrophies (223 children in each group).

Causes in relation to the age at onset of visual loss

Nearly a third of the children reported being blind since birth, and 84% were SVI/BL before their fifth birthday (table 4). Two-thirds of lens-related SVI/BL occurred before the age of 1 year, whereas 92.7% of corneal conditions occurred after the child was 1 year old. Seventy-five per cent of preventable causes and 86% of treatable conditions led to SVI/BL before the age of 5 years.

DISCUSSION

This is the first large-scale study of SVI/BL children in Bangladesh and one of the largest case series of blind children reported from anywhere in the world. As in previous studies of blind children,26,27 boys outnumbered girls. There are several explanations: boys may be at greater risk of blinding conditions than girls, blind girls may have a higher mortality rate than blind boys, or parents of blind boys may be more willing to seek eye care (and education) than parents of blind girls. The last two reasons seem the more likely in this setting where parents are more willing to invest their limited resources in the welfare of sons.

In our study, disorders of the lens (mainly unoperated cataract) were the single most common cause of SVI/BL, particularly among younger children. This finding is similar to that of a large population-based survey of vitamin A deficiency undertaken in 1982–1985 in Bangladesh involving >22 000 children aged 3 months to 6 years, in which 5/11 blind children (45.5%) identified had cataracts.24

Our results are similar to those of a population-based study in India where 8/12 (66.7%) SVI/BL children had avoidable causes.25 However, our findings differ from those of most other studies in developing countries where disorders of the lens usually account for 10–20%.26 One explanation is that most previous studies have been of children in SpEdu, where children with cataract may have been identified and operated on, leaving these special schools after regaining their sight. Parents of children in SpEdu may also be more health care seeking than parents of children not attending school. Other reasons for the high proportion of lens-related SVI/BL are first, the incidence of cataract may be higher than in other countries, and, secondly, qualitative research undertaken at the time of the study suggests that parents delay taking their child for an ophthalmic opinion or are often given inappropriate advice, being told to delay surgery (unpublished data). The low rates of aphakia in young children in this study also suggest that young children are not receiving cataract surgery. Perhaps the most likely explanation lies in the lack of eye care services for children. A national situational analysis of paediatric eye care services in 2001–2002 identified only one fully trained paediatric
ophthalmologist and three other ophthalmologists who operate on older children with cataract.23 Paediatric ophthalmic services, were, therefore, totally inadequate, and likely to be inaccessible and too expensive for poor rural families.

Corneal pathology, mainly scarring, was the second most common cause of SVI/BL, and this is consistent with other studies from developing countries.11, 15 24 25 Other studies also suggest that scarring may be declining in importance as younger children are less affected than older children.26 30

The apparent decline noted in our study probably reflects the falling prevalence of vitamin A deficiency in Bangladesh in response to concerted control initiatives (from 3.6% in 1982–83, to 1.78% in 1989, and to 0.6% in 1996). Control includes intermittent vitamin A supplementation as part of the Expanded Programme of Immunization (EPI), home gardening and nutrition education. However, children who are borderline deficient can be precipitated into keratomalacia by episodes of febrile illness, diarrhoea or measles, all of which are highly prevalent in Bangladesh. In our study, a history of measles preceding blindness was reported by 6.1% of children. In Bangladesh, measles remains the fifth most common cause of childhood deaths (ie, 20 000 deaths annually). In response to this, the Measles Initiative, Bangladesh Campaign has been recently announced.22 This will be the largest ever measles immunisation campaign which will target approximately 33.5 million children aged 9 months to 10 years.

Retinopathy of prematurity (ROP) was not found to be a major cause of SVI/BL in Bangladesh. As the majority of communities are without access to paediatric intensive care units (ICUs) highly premature babies may not be surviving to develop ROP. However, particularly in the larger cities, as there is development of neonatal ICUs, more children are likely to develop ROP. In contrast to studies in developed countries,11 3 we found a much lower proportion of children with multiple disabilities. Possible reasons include lower survival rates of children with complex disabilities in developing countries, compounded by the fact that in more developed nations, as sight-restoring eye conditions are managed, only the more complex (typically those with multiple disabilities) remain. Furthermore, difficulty in case ascertainment due to the social stigma of disability in communities in developing countries makes this difference in proportions appear greater.

If one assumes the prevalence of blindness in children in Bangladesh to be approximately 0.7–0.8/1000, there are approximately 36 000–40 000 blind children in the country, two-thirds being of school age. Our study suggests that <2% of SVI/BL children have access to SpEdu and that coverage with CBR programmes is also inadequate.

The study findings led to the launch of the Bangladesh Childhood Cataract Campaign. Key elements include training paediatric ophthalmologists and clinical teams, developing a health education strategy, and community-based approaches for active case finding. There are now eight centres providing paediatric services, but eight more are needed to reach the VISION 2020 target of one Child Eye Care centre for every 10 million population by the year 2020.3

ACKNOWLEDGEMENTS

The authors wish to acknowledge the contribution of key informants in case ascertainment, and the Childhood Blindness Project of Bangladesh (CRBP) team in data collection for the study.

Authors’ affiliations
Mohammad A Muhit, Sheheen P Shah, Clare E Gilbert, Allen Foster, International Centre for Eye Health, Clinical Research Unit, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK

Funding organisations for the study: Christoffel Blinden Mission, Muslim Aid, Sightavers International, Royal College of Surgeons, UK

Competing interests: None declared.

REFERENCES

Causes of blindness and visual impairment in Pakistan. The Pakistan national blindness and visual impairment survey

B Dineen, R R A Bourne, Z Jadoon, S P Shah, M A Khan, A Foster, C E Gilbert, M D Khan, on behalf of the Pakistan National Eye Survey Study Group

Objective: To determine the causes of blindness and visual impairment in adults (>30 years old) in Pakistan, and to explore socio-demographic variations in cause.

Methods: A multi-stage, stratified, cluster random sampling survey was used to select a nationally representative sample of adults. Each subject was interviewed, had their visual acuity measured and underwent autorefraction and fundus/optic disc examination. Those with a visual acuity of <6/12 in either eye underwent a more detailed ophthalmic examination. Causes of visual impairment were classified according to the accepted World Health Organization (WHO) methodology. An exploration of demographic variables was conducted using regression modeling.

Results: A sample of 16,507 adults (95.5% of those enumerated) was examined. Cataract was the most common cause of blindness (51.5%; defined as <3/60 in the better eye on presentation) followed by corneal opacity (11.8%), uncorrected aphakia (8.6%) and glaucoma (7.1%). Posterior capsular opacification accounted for 3.6% of blindness. Among the moderately visually impaired (<6/18 to ≥6/60), refractive error was the most common cause (43%), followed by cataract (42%). Refractive error as a cause of severe visual impairment/blindness was significantly higher in rural dwellers than in urban dwellers (odds ratio (OR) 3.5, 95% CI 1.1 to 11.7). Significant provincial differences were also identified. Overall we estimate that 85.5% of causes were avoidable and that 904,000 adults in Pakistan have cataract (<6/60) requiring surgical intervention.

Conclusions: This comprehensive survey provides reliable estimates of the causes of blindness and visual impairment in Pakistan. Despite expanded surgical services, cataract still accounts for over half of the cases of blindness in Pakistan. One in eight blind adults has visual loss from sequelae of cataract surgery. Services for refractive errors need to be further expanded and integrated into eye care services, particularly those serving rural populations.

Pakistan, the sixth most populous country in the world, is a developing country situated in the World Health Organization’s (WHO) Eastern Mediterranean Region. The country ranks 135 in the United Nations Human Development Index, and a recent report has suggested that the country is facing significant hardship; a declining growth in gross domestic product (GDP) and a near doubling of the proportion of the population living below the poverty line between 1987 and 2003. The geography and climate of Pakistan are extremely diverse; the eastern and southern parts are dominated by the Indus River and its tributaries, the northern parts by the snow-covered Himalayan mountain range. The country’s four provinces are Punjab, Sindh, North West Frontier Province (NWFP) and Balochistan.

The evidence base on national blindness and visual impairment in Pakistan prior to this survey is extremely limited. One study, estimating the main cause of blindness to be cataract (66.7%), led the National Committee for the Prevention of Blindness (NCPB) to develop a Five Year National Plan for the Prevention of Blindness (1994–1999) with a particular focus on large-scale expansion of cataract surgical services.

The aim of this second national survey (conducted between 2002 and 2004) was to apply more rigorous survey methodologies to produce accurate data. Details of the prevalence of blindness among adults (aged >30 years) have been published and we now report on the causes of blindness and visual impairment, providing estimates of the magnitude of the major causes and exploring their demographic associations.

SUBJECTS AND METHODS

A detailed description of the methods used in the survey for sampling and training, and ocular examination protocols has already been published. A brief summary of the key methodological details is provided below.

Sample size

Based on an assumed prevalence of blindness of 1.8%, a random sampling error precision of 0.3%, a design effect of 2.0 and a 10% increase for non-response, the total sample size was calculated as 16,600.

Sampling strategy

Multi-stage stratified cluster random sampling, with probability proportional-to-size (PPS) procedures, was used. Enumeration, using the random walk method, was undertaken until the target number of adults was attained in each cluster. All enumerated individuals were asked to attend the survey station, set up in their community, for ophthalmic examination in the following days. Enumerated individuals who were unable to attend were examined in their home whenever necessary.

Abbreviations: BL, blindness; IOL, intraocular lens; logMAR, logarithm of minimum angle of acuity; MVI, moderate visual impairment; NCPB, National Committee for the Prevention of Blindness; NWFP, North West Frontier Province; OR, odds ratio; PCO, posterior capsule opacification; SVI, severe visual impairment; WHO, World Health Organization; YAG, yttrium–aluminium–garnet
possible. Three visits were made to homes before marking the subject as a non-responder.

**Ethical and official government approval**

Ethical approval was provided by the Pakistan Medical Research Council (PMRC) in March 2002. This study followed the tenets of the Declaration of Helsinki.

**Definitions used in the ophthalmic examination**

**Visual impairment**

The WHO categories of visual impairment were used in this study. Blindness (BL) was defined as a presenting visual acuity (ie, with glasses for distance if normally worn, or unaided) of <3/60 (<20/400 (logarithm of minimum angle of acuity (logMAR)) >1.30) in the better eye. Severe visual impairment (SVI) was defined as <6/60 to ≥3/60, and moderate visual impairment (MVI) as <6/18 to ≥6/60. A “near normal” category was also included as <6/12 but ≥6/18. Any person with an acuity of <6/12 in the better eye was regarded as visually impaired. As visual fields were only assessed on a subset of the sample, constricted visual fields were not included in the definition of blindness. The Snellen notation for visual acuity has been used herein for ease of comparison.

**Unilateral SVI/BL**

This was defined as a participant presenting with ≥6/12 in one eye and <6/60 in the other eye.

**Clinical examination**

Distance visual acuities were measured in all subjects using a reduced logMAR tumbling “E” chart. All study participants had a basic eye examination and all also underwent autorefrraction (Nikon Retinomax K-plus II Nikon, Tokyo, Japan). Individuals with <6/12 presenting visual acuity in one or both eyes (“red carders”) were subject to a more detailed examination. All “red carders” had their visual acuity retested with the autorefraction result in a trial frame and all had a slit-lamp examination with a dilated posterior segment examination. All “red carders” presenting with <6/18 with a treatable condition were referred to the nearest eye care facility.

**Identification of causes of visual loss**

The survey ophthalmologist, epidemiologist and the three clinical ophthalmologists determined the cause(s) of visual loss, following the principles outlined in the WHO Prevention of Blindness Proforma (Version III). For each eye, all pathological findings were recorded at the time of examination. Any degree of improvement in visual acuity when retested with a refractive correction was deemed evidence of refractive error present in that eye. One main cause was then selected for each eye, the WHO recommendations stipulating that (1) if any pathology is secondary to another, the primary pathology should be selected (eg, if the pathology was band keratopathy secondary to uveitis, uveitis should be selected), and/or (2) conditions amenable to treatment or (3) which could have been prevented are preferentially selected over and above unavoidable causes. Following this, the main cause in the right eye or the main cause in the left eye was chosen to represent the principal cause for the individual. If the main causes in the right eye and the left eye differed, the principal disorder for the individual was selected as the one most readily treatable or, if not treatable, the one which was more amenable to prevention (eg, if the main causes were right eye cataract and left eye optic atrophy, cataract was selected as the principal cause). Refractive error was considered more amenable to treatment than cataract. If refractive error and cataract co-existed in the same eye, cataract was given as the main cause if refractive error correction did not improve the visual acuity ≥6/18.

**Statistical analysis**

All data were double entered by two trained data processors. Conditions were subgrouped as preventable or treatable (ie, avoidable), or unavoidable. Cause-specific proportions of blindness and visual impairment were determined by age group, gender, province, location of household (rural/urban) and level of literacy. Univariate and age/gender-adjusted logistic regression modelling was used to explore associations of the major causes (eg, cataract vs all other causes) with demographic variables. Generalised estimating equations were used in the models to adjust for dependency in the data due to clustered sampling. Estimation of the cause-specific magnitude in Pakistan was calculated from age- and gender-standardised prevalence data (using the latest population data). Extrapolations for the year 2020 were calculated using projected population estimates derived from the US census bureau.

**RESULTS**

**Study population**

A total of 17 314 adults (≥30 years) were enumerated, 16 507 (95.3%) of whom were examined and included in this study. Of the study sample, 53.1% were women, their mean age being significantly lower than that of males (45.9 vs 48.9 years, respectively, p<0.001). The demographics of responders and non-responders, and details of the prevalence of visual impairment have been described in detail elsewhere. A total of 4416 subjects (27%, 95% CI 26.1% to 27.4%) were identified with a presenting visual acuity <6/12. Of these, 561 subjects (crude prevalence 3.4%, 95% CI: 3.1% to 3.7%) presented blind.

**Causes of bilateral blindness and visual impairment**

Initially, all possible pathologies of a reduced visual acuity in eyes that presented with <6/12 vision were recorded by the examining ophthalmologist (total of 14 881 eyes). Refractive error and cataract were recorded as causes in 5463 (36.7%) and 5345 (35.9%) eyes, respectively. The next most common cause was central corneal opacity (912 eyes, 6.1%), uncorrected aphakia (430 eyes, 2.9%) and macular degeneration (418 eyes, 2.8%).

Data were then analysed using the principal cause as shown in table 1. Overall, an extremely high proportion of all categories of visual loss were due to conditions which could have been treated or prevented. A striking 85.4% of blindness was due to avoidable causes. Unoperated cataract together with uncorrected aphakia and posterior capsule opacification (PCO) accounted for 46.8, 78.1 and 63.7% of MVI, SVI and blindness, respectively. Under/uncorrected refractive errors accounted for 70.2% of visual loss in individuals with <6/12, but only 2.7% of blindness.

Amongst the 47 blind from “other” causes, posterior segment disorders dominated, including retinitis pigmentosa (11 subjects), vitreous haemorrhage (six subjects) and retinal detachment (two subjects).

**Causes of unilateral SVI/BL**

The main causes of unilateral reduced vision are presented in fig 1. Overall, more men were uniocularly blind than women (238 men, 187 women, p<0.001).

**Demographic variation**

We have previously reported that the prevalence of blindness increased almost exponentially with increasing age. The
Causes of blindness and visual impairment in Pakistan

The refractive status of every individual was assessed by autorefraction, and, furthermore, subjects with a visual acuity of <6/12 in either eye had trial lens-corrected visual acuities measured. This allowed an accurate evaluation of refractive error in individuals with MVI. It is important to note that the prevalence was also associated with female gender, rural dwelling and illiteracy.

Among blind subjects, cataract was the main cause in all age groups. There were no persons blind as a result of glaucoma or uncorrected aphakia in the 30–39 year age group; however, among those aged 70 years and older, glaucoma and uncorrected aphakia accounted for 9 and 10%, respectively. PCO was not a cause of blindness in the younger age groups (ie, 30–59 years) but in older subjects it was a prominent treatable cause (6.3% in 60–69 year olds). In contrast amblyopia was a more common cause in younger subjects but was not reported as a cause in subjects ≥60 years. The highest proportion of phthisis/absent globe as a cause was found in the youngest age group (7.8%). The distribution in individuals with MVI is shown in fig 2.

The principal causes of MVI stratified by demographic variables are presented in table 2. In men, the principal cause was cataract (45.4%), whereas in women it was refractive error (45.4%). Provincial differences suggested that refractive error was more common in urban settings (47.5%) (whereas in rural settings cataract dominated (45.3%)) and in literate subjects (59.3%). The proportion attributed to corneal opacities was highest in Balochistan (9.9%).

**Association analysis**

The age- and gender-adjusted association analyses of the principal cause in participants with SVI/BL are presented in table 3. The odds of refractive error as a cause compared with any other cause steadily decreased with age (p = 0.025), whereas the odds of cataract and aphakia increased with each decade (p = 0.023 and p = 0.025, respectively).

**Estimate of the number of adults presenting with visual impairment in Pakistan by cause**

If the acuity level of <6/60 is used to denote “operable cataract”, there are 904 000 (95% CI 736 000 to 1 107 000) adults requiring surgery. A further 173 000 individuals have uncorrected aphakia or PCO. A total of 1 390 000 adults have a presenting visual acuity of <6/60 in the better eye due to avoidable causes (table 4). Assuming the prevalence and patterns of causes remain unchanged, the figures for the year 2020 show that a total of 2 560 000 adults will have avoidable causes of SVI and blindness. The estimate for “operable cataract” is predicted to increase to almost 2 million by the year 2020.

Projections for the year 2020 are shown in table 4. Regarding adults with MVI (<6/18 to ≥6/60, better eye), 2 140 000 would benefit from having their refractive error corrected, this number increasing to 4 320 000 adults in 2020.

**DISCUSSION**

The survey reported in this paper used a diagnostically rigorous methodology, similar to that used in the recent surveys in Bangladesh and India. The response rate was very high (95.3%), minimising potential non-response bias. The use of the WHO criteria for coding causes of visual loss allows comparisons with other similarly coded surveys.

The refractive status of every individual was assessed by autorefraction, and, furthermore, subjects with a visual acuity of <6/12 in either eye had trial lens-corrected visual acuities measured. This allowed an accurate evaluation of refractive error.
error as a cause of visual impairment, these data being important for planning refractive error services (a priority of the global initiative to eliminate avoidable blindness, VISION 2020: The Right to Sight\textsuperscript{11}). The examination process also involved a dilated examination of all eyes with a visual acuity <6/12, allowing the detection of posterior segment disease, which has often been overlooked in the presence of cataract.\textsuperscript{14} A survey conducted in rural NWFP identified uncorrected aphakia as the second most common cause of blindness.\textsuperscript{15} A hospital-based study in Lahore, Pakistan showed that only 50% of eyes among individuals returning for follow-up after cataract surgery had had intraocular lens (IOL) implantation.\textsuperscript{9} As low-cost, high-quality IOLs are now readily available, IOL surgery should be routine. Visual loss from PCO is certain to increase as cataract surgical rates increase, and YAG (yttrium–aluminium–garnet) lasers need to be made available for hospitals delivering high-volume cataract surgery, with training in their use, upkeep and repair made a priority.

After cataract and the sequelae of cataract surgery, glaucoma was the next most important cause of treatable blindness, accounting for 7.1%. This is lower than the 11% quoted for the WHO Eastern Mediterranean region, subregion D, which includes Pakistan,\textsuperscript{16} but much higher than in a similarly designed survey in Bangladesh (1.2%). A survey in India of adults aged $\geq$50 years, which used a blindness definition of <6/60, showed that 5.8% of blindness was due to glaucoma.\textsuperscript{17} The earlier study in Pakistan estimated the number of people blind “unavoidable” cases could have been treatable or preventable (misclassification bias).

We found 14,881 eyes with visual acuity <6/12. When all pathological findings in each eye were analysed together, refractive error caused as much visual loss as cataract (36.7 and 35.6%, respectively).

Almost 75% of individuals who were blind had treatable causes, and $\geq$90% of subjects had treatable causes of visual impairment. The two most important treatable causes of blindness were unoperated cataract (or uncorrected aphakia, 8.6%; and PCO, 3.6%) and glaucoma (7.1%), others being refractive error (2.7%) and diabetic retinopathy (0.2%). In the 1990 study,\textsuperscript{1} cataract accounted for 66.7% of blindness, whereas the current survey found unoperated cataract accounting for 51.5%. It is not possible to compare data for cataract between these studies directly, as different age groups were used, but the observed reduction almost certainly represents a real reduction, given the large-scale increase in cataract surgical service delivery in Pakistan. However, the finding that despite this increase nearly 1 in 10 adults in Pakistan were visually impaired (<6/12) due to unoperated cataract highlights the importance of continued support of the NCPB for extending cataract surgical services in Pakistan.

In this survey, >12% of blindness was due to the sequelae of cataract surgery (ie, uncorrected aphakia 8.6% and PCO 3.6%). A survey conducted in rural NWFP identified uncorrected aphakia as the second most common cause of blindness.\textsuperscript{15} Almost 75% of individuals who were blind had treatable causes of visual impairment. The two most important treatable causes of blindness were unoperated cataract (or uncorrected aphakia 8.6% and PCO 3.6%) and glaucoma (7.1%), others being refractive error (2.7%) and diabetic retinopathy (0.2%). In the 1990 study,\textsuperscript{1} cataract accounted for 66.7% of blindness, whereas the current survey found unoperated cataract accounting for 51.5%. It is not possible to compare data for cataract between these studies directly, as different age groups were used, but the observed reduction almost certainly represents a real reduction, given the large-scale increase in cataract surgical service delivery in Pakistan. However, the finding that despite this increase nearly 1 in 10 adults in Pakistan were visually impaired (<6/12) due to unoperated cataract highlights the importance of continued support of the NCPB for extending cataract surgical services in Pakistan.

In this survey, >12% of blindness was due to the sequelae of cataract surgery (ie, uncorrected aphakia 8.6% and PCO 3.6%). A survey conducted in rural NWFP identified uncorrected aphakia as the second most common cause of blindness.\textsuperscript{15} Almost 75% of individuals who were blind had treatable causes of visual impairment. The two most important treatable causes of blindness were unoperated cataract (or uncorrected aphakia 8.6% and PCO 3.6%) and glaucoma (7.1%), others being refractive error (2.7%) and diabetic retinopathy (0.2%). In the 1990 study,\textsuperscript{1} cataract accounted for 66.7% of blindness, whereas the current survey found unoperated cataract accounting for 51.5%. It is not possible to compare data for cataract between these studies directly, as different age groups were used, but the observed reduction almost certainly represents a real reduction, given the large-scale increase in cataract surgical service delivery in Pakistan. However, the finding that despite this increase nearly 1 in 10 adults in Pakistan were visually impaired (<6/12) due to unoperated cataract highlights the importance of continued support of the NCPB for extending cataract surgical services in Pakistan.

In this survey, >12% of blindness was due to the sequelae of cataract surgery (ie, uncorrected aphakia 8.6% and PCO 3.6%). A survey conducted in rural NWFP identified uncorrected aphakia as the second most common cause of blindness.\textsuperscript{15} A hospital-based study in Lahore, Pakistan showed that only 50% of eyes among individuals returning for follow-up after cataract surgery had had intraocular lens (IOL) implantation.\textsuperscript{9} As low-cost, high-quality IOLs are now readily available, IOL surgery should be routine. Visual loss from PCO is certain to increase as cataract surgical rates increase, and YAG (yttrium–aluminium–garnet) lasers need to be made available for hospitals delivering high-volume cataract surgery, with training in their use, upkeep and repair made a priority.

After cataract and the sequelae of cataract surgery, glaucoma was the next most important cause of treatable blindness, accounting for 7.1%. This is lower than the 11% quoted for the WHO Eastern Mediterranean region, subregion D, which includes Pakistan,\textsuperscript{16} but much higher than in a similarly designed survey in Bangladesh (1.2%). A survey in India of adults aged $\geq$50 years, which used a blindness definition of <6/60, showed that 5.8% of blindness was due to glaucoma.\textsuperscript{17} The earlier study in Pakistan estimated the number of people blind

### Table 2: Principal cause of visual loss for persons with moderate visual impairment (<6/18 but $\geq$6/60 in better eye)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Treatable (%)</th>
<th>Preventable (%)</th>
<th>Unavoidable (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RE</td>
<td>Cataract</td>
<td>PCO</td>
</tr>
<tr>
<td>Male</td>
<td>935</td>
<td>39.1</td>
<td>45.4</td>
</tr>
<tr>
<td>Female</td>
<td>1186</td>
<td>45.4</td>
<td>39.8</td>
</tr>
<tr>
<td>Province</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balochistan</td>
<td>101</td>
<td>38.6</td>
<td>29.7</td>
</tr>
<tr>
<td>NWFP</td>
<td>342</td>
<td>48.5</td>
<td>36.5</td>
</tr>
<tr>
<td>Punjab</td>
<td>1159</td>
<td>40.7</td>
<td>43.0</td>
</tr>
<tr>
<td>Sindh</td>
<td>519</td>
<td>43.9</td>
<td>44.3</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>729</td>
<td>47.5</td>
<td>34.6</td>
</tr>
<tr>
<td>Rural</td>
<td>1392</td>
<td>40.2</td>
<td>45.3</td>
</tr>
<tr>
<td>Literacy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiterate</td>
<td>290</td>
<td>59.3</td>
<td>28.6</td>
</tr>
<tr>
<td>Literate</td>
<td>1831</td>
<td>40.0</td>
<td>43.7</td>
</tr>
</tbody>
</table>

DR, diabetic retinopathy; MD, macular degeneration; NWFP, North West Frontier Province; PCO, posterior capsule opacification; RE, refractive error; UA, uncorrected aphakia.
from glaucoma to be 80,000,4 which is similar to the estimate from the current survey (89,000). As cataract is becoming increasingly controlled in developing countries, strategies for the detection and treatment of glaucoma will need to increase in profile. In this survey, glaucoma blindness was highest in the detection and treatment of glaucoma will need to increase increasingly controlled in developing countries, strategies for access to eye care services.

Diabetic retinopathy accounted for 0.2% of blindness. However, this is likely to underestimate the true burden of retinopathy in the population as diabetic patients are more likely to have cataract, which would be preferentially recorded as the cause of their visual loss, and vitreous haemorrhage (possibly from diabetic neovascularisation) was classified in the ‘other’ category. It is predicted that with rapid urbanisation, Pakistan will be among the five countries with the highest prevalence of diabetes by the year 2025.23 This is likely to alter the existing pattern of blindness and, in order to prevent a public health problem, preventive strategies need to be established.

In the 1990 Pakistan study, refractive error (including uncorrected aphakia) accounted for 11.4% of blindness,4 which is identical to the figure in the current survey, indicating that there has been minimal progress in addressing this highly treatable condition. Refractive error was the leading cause of MVI, particularly among the economically active working age group. Targeting this group, particularly with ready-made spectacles, should be made a priority as this would prove to be extremely cost effective. It must be recognised, however, that barriers exist—for example, the social implications of spectacle wear. In addition, many individuals have mild myopia and, as they have adequate near vision, they may not feel impaired.

Corneal pathalogy, the main preventable cause, was the second most common cause of blindness overall (11.8%), again similar to that found in the 1990 survey.4 There are many causes of corneal scarring, trachoma being one. Trachoma is still endemic in parts of the country, and a recent rapid assessment found that of 233 villages surveyed, 151 (64.8%) had individuals requiring trichiasis surgery.22 Pakistan has set up a dedicated national task force for trachoma control and is part of the GET 2020 alliance.23 Phthisis/absent globe was the most important cause of unavoidable blindness and the third most important cause of unilateral SVI/BL. This highlights the importance of ocular trauma in Pakistan. A previous study on ocular trauma in NWFP found that 57.7% of cases had a perforating injury and that men outnumbered women by 5:1.24 A similar gender difference in unilateral blindness was noted in our survey.

A comparison of the findings of this survey with others in the region shows that Pakistan has the lowest proportion of SVI/BL (57%) due to cataract (India 62.4%,20 Bangladesh 82%).11 Refractive error (including uncorrected aphakia) was lowest in Bangladesh (7.5%), followed by Pakistan (12%) and India (19.7%). Corneal opacity, responsible for nearly 1 in 10 cases of SVI/BL, was particularly prevalent in Pakistan but accounted for <1% of SVI/BL in India20 and Bangladesh.12 The reason for this high disparity is unclear but warrants further investigation. In subjects with <6/12, cataract and refractive error were of similar importance in Pakistan; however, this contrasts with Bangladesh where the main cause was cataract (73.4%), with refractive error only accounting for 18.9%.12

Our findings are markedly different from the findings in high income countries where the primary causes of blindness are age-related macular degeneration, diabetic retinopathy and myopic degeneration, one survey in the USA indicating that these causes accounted for 63% of blindness.25

Based on the findings from this survey and future population dynamics, eye care service delivery needs to continue to expand in Pakistan, focusing principally on high-quality cataract surgery and aftercare, and on increased capacity for the correction of refractive errors. This recommendation is consistent with the prioritised areas of action for the region as outlined by the WHO South-East Asia policy VISION 2020: The Right to Sight. The more challenging conditions to control,
namely glaucoma, macular degeneration and diabetic retinopathy, are also emerging as priorities.26–27

ACKNOWLEDGEMENTS

The authors are grateful for the contribution of the “Pakistan National Eye Health Survey Group” and for the support of the following individuals: Professor Shahed Mohammed, Professor Zia Uddin Sheik, Professor Asad Aslam, Professor Nasim Panazai, Dr Shabbir Mir Dr Niaz Ali. Mr Pak Sang Lee (Technical Coordinator, International Centre for Eye Health, London), Ikram Ullah Khan (Biomedical Engineer, Pakistan Institute of Community Ophthalmology), Dr Haroon (Sight Savers International), Dr Rubina Gillani (Fred Hollows Foundation), Dr Babar Qureshi (Christoffel Blindenmission), Dr Mohammed Shabbir and Dr Falak Naz (Clinical and Community Ophthalmologists, respectively, North West Frontier Province team), Dr Abdul Ghafoor and Dr Kiramatullah (Survey Ophthalmologists, Punjab and Baluchistan Teams), and Dr Waheed Shaikh and Dr Amjad Shaikh (Survey Ophthalmologists, Sindh Team). The survey was financially supported by the “International Blindness Prevention Collaborative Group” which consisted of: The Government of Pakistan, the World Health Organization East Mediterranean Regional Office and Pakistan Office, Sight Savers International, Christoffel Blinden Mission, and the Fred Hollows Foundation. The authors also wish to thank Mr Tauqueer Abbas and Mr Fakhr-e Alam for data entry, Dr Mahwash Akhtar-Khan, Yelena Alexander and Rahul Shah for assisting in data cleaning, and Mr Fazl-Subhan for assisting with financial management. Heidelberg Engineering (Heidelberg, Germany) kindly lent two HRT-II instruments. Later, Brodies, J Vincent and S. Haq Amerdin and Sons, both based in Lahore, Pakistan, were generous in their instrument support. Ophthalmic medications were generously donated by the NWFP divisions of the companies Remington and Kocbe. This study was supported financially by the “International Blindness Prevention Collaborative Group”:


Authors’ affiliations

B Dineen, R R A Bourne, S P Shah, A Foster, C E Gilbert, International Centre for Eye Health, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK

Z Jadoon, M A Khan, M D Khan, Pakistan Institute of Community Ophthalmology, Kyber Institute of Ophthalmic Medical Sciences, Peshawar, Pakistan

Competing interests: None declared.

REFERENCES


Evolution of vision reducing cataract in skin smear positive lepromatous patients: does it have an inflammatory basis?

Ebenezer Daniel, P S S Sundar Rao

Cataract is recognised to be the leading cause of blindness in the world. As the world’s population ages, cataract induced visual dysfunction and blindness is on the increase.

The cure for cataract has been almost entirely through surgical methods, but this is not equally available to all, and the surgery which is available does not produce equal outcomes. The challenge is to prevent or delay cataract formation, and ongoing efforts are increasingly focused on factors that initiate and sustain the development of cataract. For reasons that are still largely elusive, populations from the Indian subcontinent have a very high incidence of cataract.

The Indian subcontinent is also home to more than half the world’s leprosy population. Although recent estimates of new cases show a gradually declining trend, in early 2006 around 220 000 new cases of leprosy were diagnosed worldwide. Largely because of the extensive coverage of multidrug therapy (MDT) and improved socioeconomic conditions in endemic nations, there were an estimated 14 million cured leprosy patients worldwide by the end of 2006. A significant number of these will continue to bear the consequences of disability and disfigurement, and ocular complications would occur during their MDT as well as during periods after completion of therapy.

Cataract, a major cause of visual impairment among leprosy patients, may not merely be related to aging but linked in some way to the disease process. Factors that could influence its evolution in leprosy patients include steroid treatment and intraocular inflammation. Knowledge of possible associated risk factors would help in formulating measures to prevent or delay the onset of cataract in patients affected with leprosy.

METHODS

All newly diagnosed multibacillary (MB) leprosy patients resident within the leprosy control area of the Schieffelin Leprosy Research and Training Centre in the Vellore District of South India were invited to participate in a longitudinal ocular study. Patient recruitment started in 1991 and was completed in 1997. Consenting study patients received a baseline ocular examination followed by prospective biannual examinations during the two year period they were on MDT and for five years thereafter. Patients were actively followed up in the field by public health workers belonging to their own community and encouraged to come for regular biannual check up examinations. Research methods and protocols were approved by the institutional review board of the Schieffelin Leprosy Research and Training Centre, and were conducted in accordance with the principles of the Declaration of Helsinki. All patients were provided with examinations and treatment free of charge.

At enrollment, the following leprosy characteristics were recorded: the type of MB leprosy based on the WHO classification; deformity grading of hands and legs based on the World Health Organisation classification; the bacterial index calculated from the results of the acid-fast staining of smears from specific skin sites; the presence of type 1 (reversal reaction) or type 2 (erythema nodosum leprosum) reactions; and a history of hypopigmented or erythematous patches on the face.

At each visit, the following ophthalmic characteristics were recorded: visual acuity (with and without correction); presence of orbicularis oculi weakness, lagophthalmos, entropion, trichiasis, corneal opacity, corneal ulcer, episcleritis, scleritis, clofazamine crystals on the cornea, flare and cells, posterior synechia, iris atrophy, and cataract. Best corrected visual acuity was measured with Snellen’s chart by a trained examiner. After examination of the adnexae, slit lamp biomicroscopy was done on all patients. Applanation tension was recorded in the upright position. Direct ophthalmoscopy without dilatation was carried out in all patients during each visit, and those with decreased vision or intraocular inflammation were referred to同志 for further examination.

Abbreviations: MB, multibacillary; MDT, multidrug therapy
complications underwent pupil dilatation and were examined with an indirect ophthalmoscope.

Cataract was defined as the presence of any lens opacity observed during slit lamp examination and confirmed by distant direct ophthalmoscopy after dilatation, and consistent with a corrected visual acuity of 6/18 or worse. For analytical purposes, patients free of cataract at enrolment who underwent cataract surgery during follow up also were also considered to have developed cataract.

The incidence of cataract was calculated as the number of patients with cataract observed per person year of cataract-free follow up while taking MDT and for a period of five years after completion of therapy, among patients who did not have cataract at baseline. Patients were followed either until completion of the study in June 2004 or until death or migration, whichever occurred earlier. Statistical analysis was conducted, with the unit of observation being the individual rather than the eye. Cox proportional hazards regression was used to analyse the occurrence of cataract according to demographic and clinical characteristics associated (p<0.05) with pathology by univariate analysis. Probability (p) values, hazard ratios (HR), and 95% confidence intervals (CI) were generated. Patients who did not have positive skin smears for M leprae at enrolment and those who had no follow up visits were excluded from analysis.

## RESULTS

In all, 301 MB patients were enrolled. Fifty five of them were negative for M leprae at enrolment. Of the remaining 246 patients, 27 presented with cataracts and seven did not have any follow up visits after enrolment. Thus the analysis was on 212 smear positive lepromatous patients who had no cataracts at diagnosis. None of the patients had central corneal opacities or significant peripheral corneal opacities that compromised vision.

There were 154 male and 58 female patients. Age ranged from 7 years to 74 years with a mean (SD) of 39.3 (13.4) years; 33 had lepromatous leprosy and 179 had borderline lepromatous leprosy. Eighty one had either grade 1 or grade 2 deformity in one or more limbs, and 30 had grade 1 or grade 2 deformity in all limbs.

Forty nine individuals (2.87%/person year (95% CI, 2.17% to 3.80%)) developed cataract during a total follow up period of 1704 person years. Forty five of these were 41 years or older and were followed up for a total of 638 person years with an incident rate of 0.070/person year (95% CI, 0.0523 to 0.094).

Risk factors that were analysed for an association with vision reducing cataract are given in table 1. Although several significant associations were found on univariate analysis, stepwise multiple regression confirmed the association of only age (per decade) (HR = 2.50 (95% CI, 1.82 to 2.78), p<0.001), 3663 crystals on the cornea (HR = 49.92 (95% CI, 5.48 to 454.82), p = 0.001), grade 2 deformity in all limbs (HR =3.17 (95% CI, 1.12 to 8.97), p = 0.029), and uveal involvement (HR = 3.52 (95% CI, 1.42 to 8.67), p = 0.006).

## DISCUSSION

Multibacillary leprosy, as defined by the WHO, includes all cases with more than five hypopigmented skin patches on clinical examination. Although we followed up a cohort of newly diagnosed MB leprosy patients, our analysis was based only on patients with positive skin smears. This excluded patients belonging to the tuberculoid spectrum of the disease who are known to have fewer intraocular complications than lepromatous patients.

Our study shows that vision reducing cataract (vision ≤6/18) develops at the rate of 3% per person year among lepromatous patients. When patients 41 years or older are taken to be the population at risk, the figure goes up to 7% per person year. Comparison with other incident studies is difficult as our definition of cataract was based on visual impairment, distant direct ophthalmoscopy, and slit lamp biomicroscopy. Most studies have described only prevalence data on cataracts. Progression of cataract has been described in a population similar to the one from which our cohort was derived but the methodology used was more refined. A study defining cataract by using distant direct ophthalmoscopy in an Indian population had estimated that 3.8 million people go blind in India because of cataract every year. Despite the limitation of not categorising the cataracts anatomically or grading them by severity or photographing them, the study highlights the need for continued specialised ophthalmic care, including cataract surgery, for a large microbiologically cured aging leprosy population.

Intraocular inflammation and oral steroids are two other important factors associated with the development of cataract in leprosy affected persons. It is evident from our study that uveal inflammation plays a major role in the evolution of cataract in smear positive lepromatous patients. None of the patients had florid anterior uveitis during the follow up period. The subtle and low grade nature of the inflammation will not readily be apparent unless carefully screened using a slit lamp, which is not appropriate for diagnosis in a community setting. It does, however, raise the possibility of potential interventions. M leprae or its remnants can remain in the uveal tissue long

---

### Table 1 Risk factors for developing cataract in smear positive lepromatous patients

<table>
<thead>
<tr>
<th>Factor</th>
<th>Hazard ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (per decade)</td>
<td>2.315 (1.890 to 2.836)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex (female v male)</td>
<td>1.053 (0.556 to 1.998)</td>
<td>0.870</td>
</tr>
<tr>
<td><strong>Leprosy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Classification (LL v BL)</td>
<td>1.178 (0.552 to 2.515)</td>
<td>0.671</td>
</tr>
<tr>
<td>Duration of leprosy (&gt;1 v &lt;1 year)</td>
<td>1.840 (1.001 to 3.381)</td>
<td>0.049</td>
</tr>
<tr>
<td>History of face patch</td>
<td>0.888 (0.496 to 1.588)</td>
<td>0.688</td>
</tr>
<tr>
<td>Face patch</td>
<td>0.938 (0.696 to 1.263)</td>
<td>0.674</td>
</tr>
<tr>
<td>History of reactions</td>
<td>0.632 (0.250 to 1.598)</td>
<td>0.332</td>
</tr>
<tr>
<td>No reaction v type 1 reaction</td>
<td>0.971 (0.505 to 1.866)</td>
<td>0.929</td>
</tr>
<tr>
<td>No reaction v type 2 reaction</td>
<td>1.845 (0.252 to 13.481)</td>
<td>0.546</td>
</tr>
<tr>
<td>Skin smear (≥3.00 v &lt;3.00)</td>
<td>0.748 (0.363 to 1.543)</td>
<td>0.432</td>
</tr>
<tr>
<td>Grade 1 or 2 in any limb v no deformity</td>
<td>1.701 (3.341 to 0.123)</td>
<td>0.866</td>
</tr>
<tr>
<td>Grade 1 or 2 in all limbs v no deformity</td>
<td>3.528 (1.607 to 7.747)</td>
<td>0.002</td>
</tr>
<tr>
<td>Grade 2 deformity in all limbs v no deformity</td>
<td>1.874 (1.253 to 2.804)</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Ocular</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lagophthalmos</td>
<td>0.638 (0.088 to 4.623)</td>
<td>0.656</td>
</tr>
<tr>
<td>Impaired corneal sensation</td>
<td>1.896 (0.918 to 3.913)</td>
<td>0.084</td>
</tr>
<tr>
<td>Peripheral corneal opacity</td>
<td>0.901 (0.324 to 2.508)</td>
<td>0.842</td>
</tr>
<tr>
<td>Punctate keratitis</td>
<td>0.904 (0.125 to 6.550)</td>
<td>0.920</td>
</tr>
<tr>
<td>Flare and/or cells</td>
<td>29.297 (3.604 to 238.125)</td>
<td>0.002</td>
</tr>
<tr>
<td>Keratic precipitates</td>
<td>4.691 (1.680 to 13.097)</td>
<td>0.003</td>
</tr>
<tr>
<td>Iris atrophy</td>
<td>11.699 (3.483 to 39.289)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Uveal inflammation*</td>
<td>5.814 (2.453 to 13.777)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Naso-lacrimal duct potency</td>
<td>6.256 (2.237 to 17.493)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pterygium</td>
<td>2.715 (1.384 to 5.327)</td>
<td>0.004</td>
</tr>
<tr>
<td>Intraocular pressure†</td>
<td>1.741 (0.903 to 3.358)</td>
<td>0.098</td>
</tr>
<tr>
<td><strong>Drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral steroids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cumulative dose &lt;2000 mg v no steroids</td>
<td>0.789 (0.593 to 0.332)</td>
<td>1.880</td>
</tr>
<tr>
<td>Cumulative dose &gt;2000 mg v no steroids</td>
<td>0.805 (0.547 to 0.397)</td>
<td>1.632</td>
</tr>
<tr>
<td>Corneal B663 crystals</td>
<td>51.847 (5.795 to 463.876)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Uveal inflammation includes flare and cells and/or keratic precipitates and/or iris atrophy.
†Pressure <10 mm Hg v pressure between 10 and 20 mm Hg.
BL, borderline lepromatous leprosy; LL, lepromatous leprosy.
after completion of treatment with MDT and can stimulate inflammation.\(^1\) Even though increasing loads of mycobacteria in the skin were not associated with cataract formation it may be possible to destroy bacilli that are resident in the ocular tissues by using topical bactericidal drugs such as fluoroquinolones.\(^2\) Several studies have also proved that histopathology discloses many more meaningful association but their role in lenticular changes has not been acknowledged.\(^3\)

Lepromatous leprosy and borderline lepromatous leprosy can develop reactions or erythema nodosum leprosum that necessitate treatment with oral steroids, usually for periods of three months or more.\(^4\) In our cohort even cumulative doses of more than 2000 mg of prednisone were not significantly associated with the development of cataract. Crystalline corneal deposits of clofazamine can occur in an occasional patient on MDT.\(^5\) The numbers were too small in our cohort to infer any meaningful association but their role in lenticular changes has been acknowledged.\(^6\)

Persons with severe disabilities had an increased likelihood of cataract formation. Lepromatous patients with deformity are more undernourished than those without deformity,\(^7\) and deficiency of factors such as essential amino acids, minerals, and vitamins in the diet can lead to cataract formation. An animal experiment has shown that a combination of vitamin E deficiency and long term prednisolone treatment can cause cataracts. Singly, however, both conditions were found to be subliminal cataractogeneric risk factors.\(^8\)

Conclusions
In summary, the risk of developing vision reducing cataract during and after MDT in skin smear positive lepromatous patients over the age of 40 years is 7% per person year and is associated with subclinical intraocular inflammation and severe forms of limb deformity, after adjusting for age. These patients are likely to be at a higher risk of further injury, and continued ophthalmic care—even after completion of MDT—is a necessary component in programmes for which prevention of disability is a major goal.

ACKNOWLEDGEMENTS
Funding for the study was provided by LEPRA. We are grateful for this support over the years. We acknowledge the help extended to the project by Dr Paul Courtright, Dr Timothy Flytche, and Dr John Kempen. We thank Mr Paramanandam Yowan, non-medical supervisor, for coordinating the field work and supervising the clinic visits.

\[\text{References}\]
Pigmented free-floating iris cysts

Gurdeep Singh, Kalpana Narendran, Department of Pediatric Ophthalmology, Aravind Eye Hospital and Post Graduate Institute of Ophthalmology, Tamil Nadu, India
Veerappan R Saravanan, V Narendran, Retina and vitreous services, Aravind Eye Hospital and Post Graduate Institute of Ophthalmology, Tamil Nadu, India

ABSTRACT

Free-floating iris cysts are rare. These cysts may be located in the vitreous or the anterior chamber. Anterior chamber cysts can be idiopathic or induced by trauma or surgery. Vitreous cysts may be associated with the remnants of the hyaloid system and therefore be congenital, or can result from trauma or ocular disease.

Case 1: An 8-year-old girl presented for routine follow-up with a past history of undergoing traumatic cataract extraction with intraocular lens implantation OD one year prior. Slit lamp examination showed a free floating dark brown, pigmented round iris cyst in the anterior chamber OD.

Case 2: A 9-year-old boy presented for routine eye examination. Examination of the anterior vitreous showed a large pigmented cystic lesion. It was free floating and appeared to be composed of pigmented cells joined together by a semi-translucent membrane, probably composed of pigmented epithelium.

Discussion: Free-floating iris cysts in the anterior chamber are rare, and can be congenital or associated with trauma, surgery, medications or tumors. The wall usually comprises iris pigment epithelium containing pigment granules. The cysts can get detached from the iris surface and float freely in the anterior chamber, or can get reattached to the iris at some other location. They can remain stable or can grow and cause visual disturbance or secondary glaucoma. Visually symptomatic cysts or cysts causing glaucoma need to be removed surgically or collapsed using NdYAG laser.

The origin of vitreous cysts has been the source of controversy. It has been proposed that they may be associated with the remnants of the hyaloid system and therefore be congenital, or they can result from trauma, retinal surgery or other ocular disease. Bilateral cases have been reported in patients with retinitis pigmentosa. Rarely, vitreous cysts can lead to visual disturbances if they are imposed on the visual axis. Orellana and colleagues removed a vitreous cyst via a pars plana approach, aspirating it with a 20-gauge needle. Awan suggested disrupting the cyst with argon laser photocystotomy as a simpler and safer method.

In our series the patient with the anterior chamber cyst was followed up for a period of two years and the patient with vitreous cyst was followed up for a period of three years without any increase in the size of the cysts or the occurrence of complications.

Correspondence to: Dr Gurdeep Singh, Department of Pediatric Ophthalmology, Aravind Eye Care System, Aravind Eye Hospital and Post Graduate Institute of Ophthalmology, Avinashi Road, Coimbatore- 641 014, Tamilnadu, India; email: gurdeep9999@yahoo.co.in

To view the full report and accompanying video please go to: http://bjo.bmj.com/cgi/content/full/91/8/1037/DC1

All videos from the BJO video report collection are available from http://bjo.bmj.com/video/collection.dtl
De novo mutation in the BIGH3/TGFB1 gene causing granular corneal dystrophy

Introduction

Allelic mutations in the BIGH3/TGFB1 gene are responsible for a clinically heterogeneous group of corneal dystrophies inherited in an autosomal-dominant manner. At least seven corneal dystrophies are caused by such mutations and strong genotype-phenotype correlations have allowed classification at the genetic level. Two mutation hotspots exist at codons 124 and 555, and over 95% of granular corneal dystrophy (CDG3G; OMIM no. 121900) cases have been associated with a Arg555Trp mutation. Patients typically present in the first decade with discrete, grey–white, “crumb-like” granules in the anterior corneal stroma, with sparing of the peripheral cornea and of the stroma between the opacities. We report a nuclear family with a mutation in BIGH3/TGFB1, causing granular corneal dystrophy. The daughter presented with granular corneal dystrophy caused by a Arg555Trp mutation in exon 12 of BIGH3/TGFB1. Her father also presented with granular corneal dystrophy (but with few corneal opacities) but had no detectable mutation. This family represents the first de novo instance of a mutation in BIGH3/TGFB1 causing granular corneal dystrophy.

Case reports

The proband, an 18-year-old female, presented to the optician at age 18 with mild photophobia and minimally reduced vision. She had no history of recurrent erosions. On examination she had corrected visual acuities of 6/9 R and L and her corneas demonstrated classical granular corneal dystrophy, with numerous discrete midstromal and anterior stromal whitish opacities that did not extend to the limbus (not shown). Her general health was good. The provisional diagnosis was of classical granular corneal dystrophy. There was no family history of granular corneal dystrophy.

Both parents were examined. The proband’s mother had a normal corneal examination. The father was asymptomatic with corrected visual acuities of 6/5 R and L. However, on examination he had a small number (<5) of small, midstromal, semi-translucent opacities in both eyes (fig 1). These were not visually significant. He had no significant ocular history of trauma or infection, and had not previously sought specialist ophthalmic advice.

To confirm the diagnosis, DNA was extracted from peripheral leucocytes of the proband. Exon 12 of BIGH3/TGFB1 was amplified by polymerase chain reaction and directly sequenced and compared with the published NCBI sequence using the Blast2seq tool. A single heterozygous C to T base pair transition at position 1710 (c.1710C>T, fig 2a) was found that gives rise to a p.Arg555Trp change at the protein level. This missense mutation has previously, and repeatedly, been reported as the major cause of classical granular corneal dystrophy.

After counselling, both parents gave consent for DNA to be extracted from peripheral leucocytes for both mutation analysis and paternity testing. Analysis of BIGH3/TGFB1 exon 12 sequence from both parents revealed no mutation and maternality and paternity were confirmed (data not shown). The possibility of mosaicism in the father was evaluated by direct sequencing of subcloned polymerase chain reaction products. All products cloned (n = 23) were found to be wild-type exon 12 sequences. The patient declined any further analysis from other tissues.

Comment

Granular corneal dystrophy is an autosomal dominant disorder characterised by discrete white corneal opacities within the anterior stroma. Onset is within the first decade of life and the deterioration in vision is associated with a progressive opacification of the cornea. The condition is caused by a variety of mutations in the BIGH3/TGFB1 gene, with the p.Arg555Trp mis-sense alteration being by far the most common. In all previously reported cases the mutation has been familial and has been inherited in an autosomal dominant fashion.

Here we describe an instance of granular corneal dystrophy in a nuclear family comprising of the proband and her two parents. The proband was confirmed to have classical granular corneal dystrophy caused by a p.Arg555Trp mis-sense mutation in BIGH3/TGFB1. Sequencing of both parents, who were asymptomatic, did not reveal the existence of this mutation. Paternality and maternality were confirmed. Importantly, examination of the father demonstrated bilateral semi-opaque midstromal corneal opacities of low frequency. The corneal phenotype and the lack of the c.1710C>T mutation in white blood cell genomic DNA suggests that the father is mosaic for the BIGH3/TGFB1 mutation observed in the proband. For a mosaic individual, the novel genetic change may be present in some, but not all, of his or her cells. In this case we propose that the c.1710C>T mutation is carried within a proportion of the father’s germ cells as well as his corneal cells and possibly at low levels in other tissues. It is of interest that the small number of opacities observed in the father’s corneas was present

Figure 1 Slit lamp photographs of the left (A) and right (B) eyes of the proband’s father. Small white opacities were observed in the anterior cornea at low frequency (arrows). Electropherograms of exon 12 of the BIGH3 gene. (C) The proband has a heterozygous C to T transition at nucleotide position 1710 (arrow). Sequence obtained from the proband’s father (D) and mother (E) was wild type.
within the stroma and that there was no clinical evidence of epithelial disturbance or of disruption at the level of Bowman's layer. This is similar to primary granular dystrophy and lends support to the suggestion that the primary disease may be of stromal (keratocyte) origin.

In the event of mosaicism a genetic change may not be observed in DNA from all tissue types and in this case the c.1710C>T mutation was absent in the affected father's blood leucocytes. As sequencing would normally only identify a mutation if it was present at a level of 10–20% of the total DNA, further sequencing analysis of multiple ampiclon clones was performed and confirmed that mutation is unlikely to be present in the father's leucocytes down to a level of 5% of the normal allele. Germline mosaicism would result in vertical transmission of the mutated gene, with offspring displaying 100% penetrance in the case of an autosomal dominant disorder. Furthermore, the risk for the daughter of passing the mutant allele to her children would be 50%, as for any other individual affected by an autosomal dominant condition.

To date, all described cases of granular corneal dystrophy type I have been familial. The family in this study represents the first reported example of de novo granular corneal dystrophy type I – importantly, Tanhecho et al. have also recently reported the occurrence of two patients with a de novo prezygotic Arg124Leu mutation causing granular corneal dystrophy type III (CDB1; OMIM no. 608470). While the daughter may be considered as the first de novo case of true granular corneal dystrophy we propose that the mild phenotype of the father suggests that it is actually he who represents the first case of an individual carrying a de novo postzygotic mutation in the BIGH3/TGFBI gene.

Acknowledgements
This work is supported by the Swiss National Science Foundation grant no. 32-111948. GB is a Wellcome Trust Senior Clinical Research Fellow.

E N Hilton, G C M Black, F D C Manson
Centre for Molecular Medicine, University of Manchester, Manchester, UK

E N Hilton, F D C Manson
Department of Clinical Genetics, Central Manchester and Manchester Children’s University Hospitals NHS Trust, St Mary’s Hospital, Manchester, UK

D F Schorderet
Institut de Recherche en Ophtalmologie (IRO), 1950 Sion, Department of Ophthalmology, University of Lausanne and Swiss Institute of Technology (EPFL), Lausanne, Switzerland

G C M Black
Department of Ophthalmology, Manchester Royal Eye Hospital, Manchester, UK

F L Munier
Jules Gérin Eye Hospital, Lausanne, Switzerland

Correspondence to: Professor G C M Black, Department of Clinical Genetics, Central Manchester and Manchester Children’s University Hospitals NHS Trust, St Mary’s Hospital, Hathersage Road, Manchester, M13 9JH, UK; gcblick@manchester.ac.uk
doi: 10.1136/bjo.2006.103283

Accepted 20 October 2006

Competing interests: None declared.

References

Multifocal electroretinography in dengue fever-associated maculopathy

Dengue fever is a viral disease transmitted by Aedes mosquitoes and is endemic in the tropics. The severity of dengue fever varies from mild non-specific febrile illness to potentially fatal dengue haemorrhagic fever causing thrombocytopenia and shock. Patients with dengue fever may develop various ophthalmic manifestations causing visual loss, including macular oedema, macular haemorrhage, retinal vasculitis, “cotton-wool” spots and optic disc swelling. We report the use of multifocal electroretinography (mfERG) in the assessment of a patient with dengue fever-associated maculopathy in whom there were no clinical or angiographic abnormalities.

Case report
A 16-year-old girl with serologically confirmed dengue fever presented with left relative scotoma and reduced vision 7 days after the onset of fever. Her visual acuity was 20/20 and 20/40 in the right and left eye, respectively. Anterior segment examination was unremarkable. Fundus examination showed no abnormality and particularly no retinal haemorrhage. Optical coherence tomography demonstrated normal foveal depression and retinal thickness. Fluorescein and indocyanine green angiographies showed no abnormal leakage (fig 1). Owing to the lack of clinical evidence of maculopathy, mfERG was performed to evaluate the macular function. mfERG demonstrated reductions in both N1 and P1 response amplitudes at the central and nasal macula, corresponding to the scotoma on perimeter (fig 2). The patient was managed conservatively without treatment. After 1 year, her visual acuity remained at 20/40 with absence of fundus abnormality. Repeat mfERG recording showed persistent response abnormalities.

Comment
Ocular manifestations in dengue fever have been reported in several case series, and the commonest fundus findings are retinal haemorrhage and macular oedema. The onset of visual symptoms usually coincides with the resolution of fever and the lowest point of thrombocytopenia. In our patient and in previous reports, the interval between fever onset and ophthalmic symptoms was around 7 days. It has been postulated that this time interval corresponds to the time of antibody formation, deposition of immune complexes or production of autoantibodies. Visual disturbances in dengue fever-associated maculopathy were suggested to be because of retinal haemorrhages, or retinal and choroidal vasculopathy. In our patient, visual loss developed in the absence of fundus abnormality including retinal haemorrhages or oedema, and without any angiographic abnormality. With the use of mfERG, retinal dysfunction in the central and nasal macula corresponding to the scotoma was detected. As both the N1 and P1 responses were reduced, the findings suggested that dengue fever-associated maculopathy might be due to damage to the photoreceptors or bipolar cells. After 1 year, the mfERG abnormalities were found to be persisting in the absence of any fundus changes.

Our mfERG and clinical findings support the hypothesis that formation of autoantibodies against the retina could cause visual loss in dengue fever-associated maculopathy, and that the functional changes could be irreversible. A similar clinical picture and mfERG findings

Figure 1 (A) Mid-phase fluorescein angiography and (B) mid-phase indocyanine green angiography of the left eye showing normal retinal and choroidal vasculature and the absence of abnormal hyperfluorescence, hypofluorescence or blocked fluorescence at the macula.
may also occur in acute zonal occult outer retinopathy, and dengue fever-related maculopathy could therefore be an acute zonal occult outer retinopathy-like disorder. The use of mFERG enabled the diagnosis of dengue fever-associated maculopathy, which would otherwise be difficult to confirm in the absence of clinical or angiographic abnormalities.

**Case report**

A 33-year old female presented with bilateral conjunctival tumours and no history of hair loss. No systemic disease was found on preoperative examination. Slit-lamp examination demonstrated bilateral pink coloured masses in each fornix, bilateral diffuse conjunctival injection and eyelid oedema (Fig 1). No proptosis, corneal exposure or evidence of optic neuropathy was noted. A biopsy was required to determine that the tumours were benign (ALH), then “observation as treatment” was prescribed. Three months after her postoperative recovery, she continued to note ocular discomfort, eyelid oedema and ptosis (partially obscuring her vision).

After a discussion of the known risks and benefits of observation, steroid therapy, external beam irradiation, and topical chemotherapy, our

---

**References**


patient consented to topical interferon-alpha therapy. The risks and benefits of therapy were explained in a discussion that adhered to the tenets of the Declaration of Helsinki and complied with the United States Health Insurance Portability and Privacy Act of 1996 (HIPPA).

Treatment involved placement of a punctal plug into the left lower eyelid followed by application of interferon-alpha eye drops (1-million units per milliliter four times per day for three months). She was taking no other medications during treatment. Ophthalmic examinations included a visual acuity determination, intraocular pressure measurement, slit-lamp examination and indirect ophthalmoscopy.

During her monthly examinations, a progressive reduction in tumour size and eyelid oedema was noted. However, at the end of treatment she complained of hair loss from her head temporarily associated with topical interferon-alpha therapy (fig 2).

Comment
Interferon induced a partial reduction in ALH and decreased eyelid oedema (a palliative treatment with no apparent ocular side effects). However, our patient noted scaphoid alopecia during treatment.

Though hair loss is a known side effect associated with systemic interferon alpha administration, searching the National Library of Congress online database (PubMed) with the key words (interferon, eye cancer, conjunctiva, alopecia, Intron) revealed no other reported case of alopecia induced by interferon alpha eye drops. As seen after systemic interferon alpha administration, her hair has started to grow back. However, it’s reasonable to warn patients that alopecia can be associated with even the small dose used during topical interferon-alpha treatment of conjunctival tumours.

References

Bilateral symptomatic angle closure associated with a regular dose of citalopram, an SSRI antidepressant

Symptomatic angle closure (also called acute angle closure, AAC) is a rare complication in patients receiving antidepressant treatment. The main mechanisms of AAC proposed in the literature are through the antimuscarinic and the serotoninergic action of certain antidepressants or through the development of choroidal effusions. In this unusual case, two different classes of antidepressants are highlighted, both of which seem to have had a direct effect of precipitating angle closure in our patient, but with differing timescales.

Case report
In December 2005, a 55-year-old Caucasian woman presented with a sudden onset of bilateral blurred vision, described as “grey net curtain”. The symptoms lasted for a few hours and then the vision returned to normal, leaving her with a mild headache. Her medical history revealed depression and an episode of thyrotoxicosis in September 2005 for which she had radioactive iodine treatment. She was initially taking imipramine which was switched to citalopram 20 mg/day in July 2005 and thyroxine since September 2005. She wore hypermetropic glasses with a prescription of +3.75 D (diploïd) OD, +4.75 D OS, and had axial length measurements of 22.8 mm OD and 22.5 mm OS. On examination, visual acuities were 6/6 and both corneas were clear and intraocular pressures (IOPs), however, were measured at 56 mm Hg OD and 34 mm Hg OS.

The pupils were mid-dilated and showed a sluggish reaction to light. Gonioscopy revealed appositional angle closure >270° right and around 200° left. There was no significant cataract present in either eye. Optic discs had no features of glaucomatous damage.

The diagnosis of bilateral symptomatic (“sub-acute”) angle closure was made, and medical treatment was given according to our institutional protocol. The treatment consisted of intravenous acetazolamide 500 mg and G pilocarpine 2%, in addition to G apraclonidine and G levobunolol in both eyes. The above treatment brought the left IOP down to 18 mm Hg but the right eye required argon laser iridoplasty to achieve pressure control. These treatments were followed by bilateral NdYAG laser iridotomies. She was discharged with IOPs of 16 mm Hg right, 14 mm Hg left and patent iridotomies, and was prescribed G pilocarpine 2% and G prednisolone 1% both to be used in both eyes four times a day. With the consent of her doctor, she also stopped her citalopram tablets.

In subsequent follow-up visits, the topical citalopram was stopped and up to 3 months later she retained open drainage angles with no peripheral anterior synchiae, patent iridotomies and IOPs in the range of 15–16 mm Hg. During the same period, she developed increasing symptoms of a chronic anxiety disorder and her doctors restarted her on imipramine 25 mg/day on 9 May 2006. Fortuitously, she had a glaucoma clinic appointment 2 days later, at which point she was found to have over 270° appositional angle closure despite patent iridotomies, and IOPs measured at 28 mm Hg right and 23 mm Hg left. She was put on pilocarpine 1% twice daily.

Figure 2 Topical Interferon Alopecia: Left, hair loss (arrow) from cranium is viewed at low and at higher magnification (right). Informed consent was obtained for publication of this figure.

Correspondence to: Paul T Finger, MD, The New York Eye Cancer Centre, 115 East 61st Street, New York City, New York, USA 10021; pfinger@eyecancer.com

doi: 10.1136/bjo.2006.106930

Accepted 2 October 2006

Supported by The EyeCare Foundation, Inc., New York City, New York, USA. http://eyecarefoundation.org

Competing interests: The authors have no proprietary

s details in this report.

Informed consent was obtained for publication of the person’s details in this report.

in both eyes and continued on imipramine until 7 July 2006. On the 7 July 2006, she was switched to mirtazapin 30 mg, which is her current antidepressant. IOPs and angles have now normalised, and she continues with her topical treatment.

Discussion

There have been reports of tricyclic antidepressants (such as amitryptiline and imipramine) being associated with angle closure in patients using paroxetine, which is a selective serotonin re-uptake inhibitor (SSRI) with a weak antimuscarinic effect. A similar association was reported in six patients using paroxetine, which is a selective serotonin re-uptake inhibitor (SSRI) with a weak antimuscarinic effect. Croos et al. have reported a case of bilateral angle closure after a cataract operation and alcohol overdose. In a recent case report Zelefski et al. have highlighted the association of escitalopram with choroidal effusion and secondary angle closure. This has also been described extensively in association with the use of topiramate and is thought to be an idiosyncratic reaction to the drug. It usually manifests clinically within 2–4 weeks of administration.

Although anterior chamber depth measurements and ultrasonography were not performed on our patient, the possibility of a choroidal effusion-related angle closure is unlikely as: (a) the visual acuity was normal on presentation; (b) there was no myopic shift; (c) the onset was delayed; and (d) the angle closure responded to conventional treatment with acetazolamide, miotics and peripheral iridotomy.

There is evidence of the presence of serotonin receptors in the human iris, cornea and ciliary body, but the effects of long-term SSRI administration on IOP or the angle are unclear. In animal studies, serotonin stimulation may cause mydriasis and have an independent effect in raising the IOP.

The salient points in our case were that the episode of angle closure occurred 5 months after our patient started cataract and also that there was a rapid onsets relapse into angle closure 2 days after re-administration of imipramine, despite having patent iridotomy.

Although we have only an indirect indication of the tendency to angle closure (from axial length measurements and hypermetropic prescription), the sequence of events suggest a pharmacological factor influencing the course of disease. We propose a slow (possibly partially serotoninergic) effect on the iris and/or ciliary body attributable to cataract! given in the delay in the onset of symptoms, and a more direct antimuscarinic effect of imipramine, which had an almost immediate effect.

From the current literature, the risk of angle closure related with the use of SSRIs appears small but can lead to significant morbidity. More laboratory-based studies are needed to further elucidate the pharmacological effects of SSRIs on the iris, angle and the IOP.

In reality, it is impractical to screen all the new patients on SSRIs for narrow angles. However, ophthalmic examination should be recommended in high-risk individuals before starting antidepressants and all patients need to be made aware of the symptoms of angle closure and the need for regular optometric eye examinations even in the presence of patent iridotomy.

Ocular surface toxicity associated with topical interferon α-2b

 Conjunctival intraepithelial neoplasia (CIN) has traditionally been managed with surgical excision, combined with cryotherapy, with a wide range of reported recurrence rates. In cases of CIN that are too extensive to perform a complete surgical excision or in cases in which the surgical margins are involved, ophthalmologists are now using adjunctive topical anti-neoplastic agents such as mitomycin C and interferon α-2b (IFNα-2b) in place of, or in combination with, repeat surgical excision. Although the toxicity associated with the topical ophthalmic use of mitomycin C is well recognised, IFNα-2b has been reported not to cause ocular surface toxicity. We report a case of cornel toxicity, manifest as epithelial microcyst formation, associated with the use of topical IFNα-2b.

Case report

A 64-year-old man with a history of biopsy-proven CIN of the left eye presented to one of the authors (JA) for evaluation. Twenty-two years earlier, he had undergone a superficial keratectomy and excision of a papillomatous conjunctival lesion from the left eye. Six years before presentation he had undergone a superficial keratectomy, and a limbal conjunctival biopsy 3 years later demonstrated epithelial squamous cell carcinoma in situ. The patient was treated with a 4-week course of topical mitomycin C (0.02% initially, then 0.01%), which was discontinued secondary to poor tolerance.

On presentation, the patient’s visual acuity was limited to counting fingers in the left eye secondary to a dense cataract. Unilateral 360° micropannus and scattered punctate epithelial keratopathy (PEK) were noted in the cornea of the left eye. Several foci of fine papilliform vessels were noted in the nasal and limbal bulbar conjunctiva (figs 1A,B); biopsy specimens taken from these regions demonstrated marked atypia of the epithelial cells, consistent with CIN, extending to the edges of the submitted specimens.

As the extensive conjunctival vascular abnormalities were too diffuse to perform a complete surgical excision, adjunctive topical treatment with mitomycin C was considered. However, given the previous poor tolerance of mitomycin C and concern about exacerbation of corneal limbal stem cell compromise secondary to the previous limbal keratectomies and mitomycin C-associated toxicity, the patient was started on topical IFNα-2b (1 million IU/mL; prepared from injectable powder mixed with preservative-free normal saline) four times daily. Four weeks later, diffusely

Correspondence to: P Massaoutis, Moorfields Eye Hospital, 19 Worfield St London, London SW11 4RB, UK
doi: 10.1136/bjo.2006.107185

Accepted 24 November 2006

Competing interests: None declared.

References


Ocular surface toxicity associated with topical interferon α-2b

Conjunctival intraepithelial neoplasia (CIN) has traditionally been managed with surgical excision, combined with cryotherapy, with a wide range of reported recurrence rates. In cases of CIN that are too extensive to perform a complete surgical excision or in cases in which the surgical margins are involved, ophthalmologists are now using adjunctive topical anti-neoplastic agents such as mitomycin C and interferon α-2b (IFNα-2b) in place of, or in combination with, repeat surgical excision. Although the toxicity associated with the topical ophthalmic use of mitomycin C is well recognised, IFNα-2b has been reported not to cause ocular surface toxicity. We report a case of cornel toxicity, manifest as epithelial microcyst formation, associated with the use of topical IFNα-2b.

Figure 1 Slit lamp photomicrographs demonstrating fine corkscrew vessels in the inferonasal bulbar (A) and superior limbal (B) conjunctiva of the left eye.
The development of corneal epithelial microcysts in the case reported here is evidence of the ocular surface toxicity that may be seen in patients treated with topical IFN-z-2b. Corneal epithelial microcystic formation, identical to that noted in the patient reported here, has been reported with the use of systemic interferon treatment, and is a well-recognised complication of the systemic administration of the antineoplastic agent cytarabine (Ara-C).19–20 Corneal toxicity associated with high-dose systemic cytarabine is thought to be secondary to the inhibition of DNA synthesis in the rapidly dividing basal corneal epithelial cells.21 Similarly, the antineoplastic actions of interferon involve immune-enhancing properties as well as inhibition of cellular proliferation.22 An alternative mechanism that has been proposed to explain corneal epithelial microcyst formation in association with systemic interferon treatment is increased intercellular adhesion and altered corneal epithelial cell migration via an interferon-mediated increased expression of intercellular adhesion molecule-1.18 The development of the epithelial cysts several weeks after the initiation of topical interferon treatment, whether through inhibition of DNA synthesis, alteration of epithelial cell migration or another mechanism, indicates that IFN-z-2b-related corneal epithelial cell toxicity is the most likely explanation for the origin of the microcysts. Ophthalmologists should be aware of the fact that ocular surface toxicity may be associated with topical IFN-z-2b treatment, and that it should be used judiciously in patients with conjunctival intraepithelial neoplasia.

Anthony J Aldave, Anne Nguyen
The Cornea Service, The Jules Stein Eye Institute, University of California Los Angeles Medical Center, Los Angeles, California, USA

Correspondence to: Dr A J Aldave, The Jules Stein Eye Institute, 100 Stein Plaza, UCLA, Los Angeles, CA 90095, USA; aldave@jsei.ucla.edu
Accepted 12 October 2006

Competing interests: None declared.

References

Periorbital xanthogranuloma after blepharoplasty
Periorcular xanthogranulomas is a rare inflammatory condition characterised by histiocytoses and Touton giant cells. It is encountered in several settings: juvenile xanthogranuloma, Erdheim–Chester disease (ECD) and necrobio- tic xanthogranuloma. Recently, cases with an adult onset not associated with ECD have been described, with frequent involvement of the eyelids and orbit.1 In this report, we describe a unique case of adult-onset periorcular xanthogranuloma precipitated by blepharoplasty.

Case report
A 57-year-old woman was referred for persistent postoperative oedema/inflammation 18 months after bilateral upper and lower blepharoplasty. On the basis of a review of her medical record and a conversation with her cosmetic surgeon, there was no suggestion of disease before surgery: her periorcular involutional changes were typical and no abnormalities were noted intraoperatively. Her initial postoperative course was unremarkable, with mild swelling/ecchymosis. In contrast with the ecchymosis, which resolved within 2 weeks, the oedema unremarkingly progressed. No photographs were taken during the immediate postoperative period.

Examination revealed infiltration of all four eyelids, which were rubbery to palpation, bilateral blepharoptosis, palpably enlarged
nuclei and peripheral foamy/vacuolated tissue displaying the characteristic central fibrous tissue as well as multiple Touton giant cells laden histiocytes infiltrating the muscle fibres and

Figure 2 Periocular xanthogranuloma. (A) Clinical appearance with infiltration of all four eyelids and mild blepharoptosis with an S-shape configuration. (B) Visibly enlarged lacrimal gland. (C) Coronal T1 fat-suppressed gadolinium-enhanced orbital MRI demonstrating diffuse hyperintensity of the periocular tissues including the lacrimal gland. Informed consent was obtained for publication of this figure.

The lacrimal glands and follicular conjunctivitis (fig 1). Ophthalmological examination was otherwise unremarkable, with normal symmetric exophthalmometry measurements and full extraocular motility. Orbital MRI demonstrated bilateral diffuse periocular infiltration with lacrimal gland involvement (fig 1C). A left anterior inferior orbitotomy was performed. All tissue planes (epidermis to orbit fat) were involved and obscured with diffusely infiltrative, firm, bright yellow material.

H&E-stained sections displayed several large follicles surrounded by lipid-laden histiocytes and Touton giant cells infiltrating the fat, muscle and fibrous tissue (fig 2). Immunohistochemical staining confirmed the benign nature of the follicles, staining positive for CD20 and negative for κ, λ, and bcl-2. A few CD3 cells were seen in the mantle zone and scattered throughout the surrounding tissue, particularly around the xanthogranulomatous cells. They stained positive for κ and λ, with a ratio of 5:1. Flow cytometry suggested a κ monoclonal B cell population (ratio 10:1). PCR using three sets of primers (FR3A/VIJN, FR2A/VIJH and FR2B/VIJH) detected no heavy-chain gene rearrangements. No abnormality consistent with a lymphoproliferative disorder or ECD was detected on systemic evaluation (chest and abdominal CT, bone scan, extremity plain films and protein electrophoresis of serum and urine).

Oral prednisone (60 mg daily) achieved a partial response, with recurrence on tapering the drug. External beam radiation (2080 rad in 13 divided doses) resulted in complete clinical resolution, which persisted 1 year later.

Comment

This report is unique in that xanthogranulomatous inflammation seems to have been caused or at least precipitated by periocular surgery. In most reported cases, no mention is made of periocular surgery. However, this is not the first case presumably related to trauma. A recent report suggested a relationship between xanthogranuloma of the ear lobes and mechanical injury due to earrings. In our patient, an entirely causal relationship seems unlikely; however, surgical insult might have stimulated/activated subclinical disease. Admittedly, even this is unconfirmed and the exact nature of the relationship between surgical insult and xanthogranulomatous inflammation remains to be determined.

Christopher I Zoumalan
Department of Ophthalmology, University of California San Francisco, San Francisco, California, USA

Melanie H Erb, Narsing A Rao, Robert See, Michael A Bernstine
University of Southern California, Doheny Eye Institute, Los Angeles, California, USA

Samir B Shah, Timothy J McCulley
Department of Ophthalmology, University of California San Francisco, San Francisco, California, USA

Correspondence to: Dr T J McCulley, Department of Ophthalmology, University of California San Francisco, 10 Koret Way, San Francisco, CA 94143-0336, USA; mcculley@vision.ucsf.edu

This paper was presented in part at the Walsh Society meeting at Snowbird, Utah, February 2003.

doi: 10.1136/bjo.2006.107821
Accepted 9 December 2006

Competing interests: None declared.

References

The Finger iridectomy technique for glaucoma

Surgical iridectomy is a standard method of treatment for narrow-angle glaucoma. However, the development of laser iridectomy has largely replaced the need for incisional surgery. There are cases where patients are unable or unwilling to submit to laser iridectomy, when surgical manipulation of the iris is required and when the cornea is not sufficiently clear. This case demonstrates the first use of a 25-gauge aspiration cutter through a 1 mm self-sealing corneal incision to perform a surgical iridectomy for glaucoma.

Case report

An 80-year-old woman was noted to have a variably pigmented inferonasal iris tumour, lenticular pseudoxfoliation and narrow angles in her left eye. The tumour was documented to grow and cause a sector cataract (prompting her referral to The New York Eye Cancer
Centre, New York City, New York, USA). Ophthalmic examination included a 35 MHz high-frequency ultrasound (ultrasound biomicroscopy) in movie mode. Both her narrow angles and tumour were evaluated (fig 1).

Methods of procedure

This study conformed to the tenets of the Declaration of Helsinki and the Health Insurance Portability and Accountability Act of 1996. The Finger iridectomy technique (FIT) was performed for glaucoma immediately after an FIT the iris tumour biopsy was found positive for melanoma. A 0.3 forceps was used to stabilise the eye at the limbus. A 25-gauge trochar was used to create an incision through the superonasal iridotomy demonstrates its patency. A 35 MHz high-frequency B-scan ultrasonography (ultrasound biomicroscopy) prior to FIT iridectomy demonstrates a severely narrowed anterior chamber angle (before small-incision surgical iridotomy for glaucoma). (D) At 3 weeks after successful FIT iridotomy, the anterior chamber angle has widened.

Comment

A review of the literature shows that relatively large aspiration cutters have been used to perform iridectomy. For example, Ghanem et al used an aspiration cutter during phacoemulsification in patients with iridochisis. The FIT is different in that it is a minimally invasive approach using a smaller 25-gauge aspiration cutter probe to perform localised iridectomy through a self-sealing 25-gauge incision. No large incision, irrigation or sutures are required in FIT.

The FIT introduces the concept of using a 25-gauge aspiration cutter to perform a minimally invasive iridectomy for glaucoma. Unlike standard surgical iridectomy, the FIT 25-gauge corneal incision allows for a relatively safe self-sealing corneal wound.

Paul T Finger

The New York Eye and Ear Infirmary, New York City, New York, USA.

Correspondence to: Dr P T Finger, The New York Eye Cancer Center, 115 East 61st Street, New York City, NY 10021, USA; pfinger@paultfingermd.com
doi: 10.1136/bjo.2006.108126
Accepted 18 October 2006

Funding: This work was supported by The EyeCare Foundation, New York City, NY, USA.

Competing interests: None.

References


Preimplantation genetic diagnosis for retinoblastoma predisposition

Heritable mutations in the RBL gene cause an autosomal dominant condition resulting in retinoblastoma and an increased risk of malignancies including pineoblastoma, neuroblastoma, chondrosarcoma, rhabdomyosarcoma, glioma, leukaemia, sebaceous carcinoma, squamous cell carcinoma and cutaneous melanoma. Individuals with heritable retinoblastoma can undergo prenatal diagnosis followed by termination to avoid passing on the mutation to the next generation. Preimplantation genetic diagnosis (PGD) offers a means of achieving an unaffected pregnancy from the outset. IVF is required for PGD to allow cell biopsy from embryos for genetic testing. Embryos without the germline RBL1 mutation are transferred to the mother for implantation and pregnancy.

Case study

A 24-year-old woman with bilateral retinoblastoma (RBL1, OMIM 180200), had a de novo M708R mutation in RBL1 and was referred for PGD. She had a one-year-old child with the mutation and also had had a miscarriage and two terminations of affected pregnancies. Following ovarian stimulation, 15 eggs were collected, of which 12 oocytes matured and eight fertilised normally 18–20 hours post-intracytoplasmic sperm injection (ICSI). Seven embryos were suitable for biopsy on day 3. DNA from biopsied cells was amplified by PCR using fluorescently labelled intragenic (RB1) and linked polymorphic micro-satellite markers (D13S168 and D13S262). The PCR products were analysed using an ABI 3730 Prism. Three embryos (E4, E6 and E7) were diagnosed as carrying the maternal affected chromosome, while two embryos (E5 and E1) did not give clear results. Embryos E3 and E8 were diagnosed as unaffected. Figure 1 shows the haplotype for the family and figure 2 shows electropherograms of the parental DNA, a normal and an affected blastomere. All cell negatives and PCR negatives showed no DNA amplification.

On day 4 post-insemination unaffected embryos E3 (5 cell) and E8 (morula) were transferred to the uterus. Six-weeks gestation ultrasound showed two sacs, one with a viable fetal pole while the other was anembryonic. A healthy boy was delivered at 35/40 weeks. Here we report the first successful use of PGD for retinoblastoma in the UK.
Comment

This report highlights the feasibility of PGD for rare cancer predispositions. The indirect mutation detection strategy by haplotyping that we have reported may be applied to more than one family with different germline mutations provided DNA is available from other affected family members in order to identify the chromosome carrying the mutation. The difficulty in doing PGD for heritable retinoblastoma is that a large number of germline mutations have been identified and approximately half of these are new mutations. Separate PGD protocols need to be developed for each de novo germline mutation. PGD for cancer predisposition is therefore labour intensive and expensive, however, the value of PGD for retinoblastoma should be considered within the context of childhood manifestation of the disorder and a lifetime cancer risk in multiple organs. Inherited predisposition to retinoblastoma is very rare with a yearly UK incidence of approximately 20 cases. PGD could significantly reduce the incidence of this inherited disorder.

Seema Dhanjal, Georgia Kakourou, Thalia Mamas, Natasha Saleh
UCL Centre for Preimplantation Genetic Diagnosis, Department of Obstetrics and Gynaecology, University College London, London, UK

Alpesh Doshi, Sarah Gatts, Sarah Nuttall
Assisted Conception Unit, University College Hospital, Eastman Dental Hospital, London, UK

Karen Fordham
UCL Centre for Preimplantation Genetic Diagnosis, Department of Obstetrics and Gynaecology, University College London, UK

Paul Serhal
Assisted Conception Unit, University College Hospital, Eastman Dental Hospital, London, UK

Joy Delhanty, Joyce Harper, Sioban SenGupta
UCL Centre for Preimplantation Genetic Diagnosis, Department of Obstetrics and Gynaecology, University College London, UK

Correspondence to: Sioban SenGupta, UCL Centre for Preimplantation Genetic Diagnosis, Department of Obstetrics and Gynaecology, University College London, London, UK

doi: 10.1136/bjophthalmol.2006.108597

Case report

A 68-year-old HD patient with end-stage renal disease of unknown aetiology presented with central retinal vein occlusion in the right eye, which was followed by rheuroid iritis. Despite local antiglaucomatous medication, IOP reached levels up to 36 mm Hg, whereas the IOP of the left eye remained normal (10 mm Hg). The patient reported severe headache confined to the right frontal region during HD, which ceased without need of medication within hours after HD was completed. The patient was otherwise asymptomatic and had no personal or family history of headache and/or migraine. Due to persistent high IOP in the right eye, cyclocycocoulcation was successfully performed, with IOP declining to levels around 15 mm Hg (4 weeks postprocedure). The HD-associated pain also ceased. The fact that the pain was confined to the right orbita led to the hypothesis that it might be caused by a transient rise in IOP. To investigate this hypothesis, we measured IOP at 10 min intervals in both eyes prior to (baseline) and during HD on three independent occasions. A Medronic Tono-Pen XL application tonometer (Jacksonville, Florida, USA) was used. There was no significant difference between the two eyes at baseline and during the first 90 min of HD treatment (fig 1). However, IOP in the right eye rose after 90 min by 4.0 (1.3) mm Hg (mean (SEM)) to result in a significant IOP difference between the right eye and the healthy left eye of 7.9 (4.0) mmHg (p<0.01).

Rise in intraocular pressure during haemodialysis in a patient with reduced outflow facility

Intraocular pressure (IOP) during haemodialysis (HD) has previously been measured with ambiguous results. Some studies have shown that HD does not affect the IOP, whereas others have shown an increase or decrease in IOP during HD. The discrepancy in these results may be due in part to functional differences in the ocular system of the investigated patients. Indeed, there is some evidence that outflow facility status plays a significant role in IOP fluctuation during HD treatment. We present a case of unilateral reduction of outflow facility showing an increase in IOP during HD, which persisted even after active aqueous humour secretion is reduced by cyclocycocoulcation.

References

for the remaining duration of HD treatment. As expected, urea and serum osmolality decreased (urea from 18.4 (2.0) mmol litre$^{-1}$ to 4.7 (0.9) mmol litre$^{-1}$ (p = 0.01), whereas the concentration of total protein rose from 72.7 (1.6) g litre$^{-1}$ to 78.3 (1.6) g litre$^{-1}$ (p = 0.03).

Comment
In eyes with normal aqueous outflow facility, an increased influx of extracellular fluid, as may happen during HD, is thought to be met by adaptive outflow mechanisms, thus avoiding a rise in IOP. However, in eyes with compromised aqueous outflow facility (eg, narrow angle or outflow obstruction due to neovascularisation), IOP may rise to pathological levels and potentially trigger acute glaucoma. The patient we report here exhibits secondary neovascular glaucoma with reduced outflow facility in the right eye. The fact that the rise in IOP during HD is still evident after active secretion was reduced by cyclocryocagulation points to a critical role of the impaired outflow facility in the HD-associated rise in IOP. We thus suggest that HD leads to increased aqueous humour formation, which in turn is insufficiently counter-regulated by the hampered outflow facility and thus leads to an increase of IOP. We further suggest that influx is also increased in the healthy left eye during HD, where a functional adaptation of outflow mechanisms prevents a rise in IOP. We conclude that there should be critical awareness regarding IOP changes during HD treatment especially in high-risk patients with glaucoma, narrow angle and/or altered aqueous outflow facility.

Acknowledgements
The authors thank Drs Daniel Barthelmes, Florian Sutter and Horst Helbig for insightful comments and helpful discussions.

M Dominik Fischer, Johannes Fleischhauer
Department of Ophthalmology, University of Zurich, Switzerland

Gérald Keusch
Department of Nephrology, City Hospital Waid, Zürich, Switzerland

Mathias H Abegg
Department of Ophthalmology, University of Zurich, Switzerland

Correspondence to: Mathias Abegg, MD PhD, Department of Ophthalmology, University Hospital Zürich, Frauenklinikstrasse 24, CH-8091 Zürich, Switzerland; mhabegg@hispeed.ch
doi: 10.1136/bjo.2006.110072

References
The macular hole. (C) OCT scan 13 months after operation. (D) OCT scan 16 months after operation.

Figure 2

Optic disc pit with associated serous macular detachment has a poor visual prognosis if left to its natural course. It has been suspected that the subretinal fluid originates from the vitreous cavity via an inner retinoschisis-like separation within the papillomacular bundle between the optic disc pit and the central retinal detachment. We report a surgical approach on the basis of this assumed pathomechanism.

Case report

A 20-year-old man presented with decreased vision in OD (right eye) due to macular detachment in association with an optic nerve pit (fig 1). Visual acuity was 20/400 OD and 20/20 OS (left eye). Optical coherence tomography revealed parapapillary retinoschisis-like separation of the outer retinal layers and extended full-thickness neurosensory retinal detachment. There was a round full-thickness macular hole covered by the posterior hyaloid. The posterior hyaloid was partially detached nasally. After giving informed consent, the patient underwent surgery in May 2004. Limited preretinal vitrectomy and retinal incision in the area of the schisis-like separation was performed to create a link between the outer schisis-like separation and the vitreous cavity and thus to interrupt the continuous flow into the subretinal space (fig 1). The incision was made parallel to the papillomacular bundle, approximately 3/4 deep into the retina using a bent 27-gauge cannula. No active suction of subretinal fluid or gas tamponade was performed. Postoperatively, the schisis-like separation was flattened and resolved completely, the macular hole was closed and the retina was reattached (fig 2). Visual acuity was 20/100 after 1 month, 20/40 after 3 months and 20/20 after 9 months. During a follow-up of 29 months, vision remained stable and no recurrence of the maculopathy occurred.

Comment

Various treatment modalities for optic pits with associated macular involvement have been tried with variable success. The surgical procedure presented here seems to offer a promising alternative. Drainage of the intraretinal fluid resulted in collapsing of the schisis-like separation, and thus interrupted the continuous flow into the subretinal space. After the schisis-like separation was closed, the subretinal fluid was resorbed. Complete resorption took several months, indicating that the central retinal detachment had been present for a long time. During the follow-up of 29 months, no reopening of the schisis-like separation occurred, even though the retinal incision is likely to have closed in the meantime. It might be assumed that once the schisis has collapsed, it will not separate again. Recently, Spaide et al reported successful retinal incision in optic pit maculopathy in a patient with schisis-like cavity of the inner retina. The patient presented in our study shows that pathological fluid accumulation can be successfully drained even if it is located in deeper retinal layers such as the outer plexiform layer, resulting in disappearance of the schisis-like separation.

In conclusion, if there is evidence for intraretinal fluid accumulation in a patient with optic pit maculopathy, internal drainage procedure might be considered regardless of the depth of the affected retinal layer.

Karen B Schaal, Julia Wrede, Stefan Dithmar
Department of Ophthalmology, University of Heidelberg, Heidelberg, Germany

Correspondence to: Professor S Dithmar, Department of Ophthalmology, University of Heidelberg, Im Neuenheimer Feld 400, 69120 Heidelberg, Germany; stefan.dithmar@med.uni-heidelberg.de
doi: 10.1136/bjo.2006.110304
Accepted 22 November 2006
Competing interests: None declared.

References

**Botulinum toxin for the treatment of acute-onset concomitant esotropia in Chiari I malformation**

Acute-onset esotropia (ET) is a rare presentation of Chiari I malformation. The ET may resolve following neurosurgical decompression, although this is not usually immediate. Where neurosurgery is not undertaken, Kowal et al. suggest prismatic correction or strabismus surgery. The latter may result in temporary correction of the strabismus, as the strabismus can recur and resolves only following decompression. Botulinum toxin (BT) has been reported as successful in one case where the ET did not resolve following neurosurgery. Despite BT being a common treatment for acute acquired concomitant ET, no previous case has been reported in which BT was used prior to neurosurgical decompression for Chiari I malformation.

**Case report**

A 16-year-old girl experienced diplopia during swimming, and presented to the A&E Department on the day of onset. She gave a history of occasional, brief diplopia. On examination, there was 16Δ ET at near and 20Δ ET at distance. The angle of deviation reduced on versions. Saccade to the right was possibly hypometric; no nystagmus was present. Over 2 weeks, the angle increased to 40Δ ET, saccades to the right became definitely hypometric and abducting nystagmus developed. MRI scan revealed Chiari I malformation with tonsillar descent approximately 12 mm below the foramen magnum, with loss of cerebrospinal fluid (CSF) spaces around the foramen magnum indicative of impaction of neural tissue.

Foramen magnum with loss of cerebrospinal fluid and impaction of neural tissue. Neurosurgery was discussed, but BT was used in the expectation that repeat injections would be necessary as the aetiological cause had not been treated at this time. Following the BT, BSV was maintained for 8 months prior to decompression surgery. Recurrence of ET following strabismus surgery has occurred over a variety of time frames upwards from 3 months following strabismus surgery. Surgical decompression improves ocular manifestations such as nystagmus, but this may not be for several months. In our case, nystagmus and hypometria had not resolved 3 months following surgery.

BT should be considered as a treatment option to restore alignment in acute-onset ET due to Chiari I malformation. Further case series are required to determine the effectiveness of BT compared with strabismus surgery.

**Comment**

BT restored binocular single vision (BSV) in a patient awaiting neurosurgical decompression for Chiari I malformation. Neurosurgery was delayed to fit in with the patient’s education. BT was used in the expectation that repeat injections would be necessary as the aetiological cause had not been treated at this time. Following the BT, BSV was maintained for 8 months prior to decompression surgery. Recurrence of ET following strabismus surgery has occurred over a variety of time frames upwards from 3 months following strabismus surgery.

The human sclera consists of collagen and elastin, with a thickness ranging between 0.33 mm beneath the recti muscles, 0.66 mm at the muscle insertion and 1 mm posteriorly.

**Microfoam surgical tape as practice object for scleral sutures**

Performing scleral sutures in strabismus and retinal surgery poses a challenge for residents as it requires high precision and allows only little room for error, with possible complications including endophthalmitis and retinal detachment from scleral perforation or muscle desinsertion.

The human sclera consists of collagen and elastin, with a thickness ranging between 0.33 mm beneath the recti muscles, 0.66 mm at the muscle insertion and 1 mm posteriorly.

The three layers of the sclera are ill defined and comprise episclera, sclera proper and lamina fusca. Pig eyes, which are commonly used as practice objects for surgical procedures, are not always readily available, change their consistency after conservation and potentially present a risk for contamination or infection. Other commonly used practice objects include fruits such as oranges, bananas and grapes, or hard-boiled eggs.

Microfoam surgical tape manufactured by 3M consists of rolls of closed-cell foam and is designed for securing dressings and compression applications to joints, with a thickness of 0.8 mm and width of 1, 2 or 3 inches (fig 1). It is elastic and has an adhesive lower surface. When used as a practice object for scleral bites, achievement of appropriate suture depth can be easily checked by lifting the superficial layer from underlying layers (fig 2). In addition, the elastic tape can be easily stretched to 0.4 mm for simulation of a thinner sclera.

Our department’s retina and strabismus specialists evaluated Microfoam surgical tape as a practice object and uniformly agreed on its authentic feel, resistance, thickness and curvature when compared with the actual human sclera.

In conclusion, Microfoam surgical tape represents a readily available, cheap, storable and easily transportable alternative to pig eyes or fruits for practicing the placement of scleral sutures with authentic characteristics and immediate feedback.

**References**


9. Jan Niklas Ulrich, Thomas W Wilson Geisinger Medical Center, Danville, Pennsylvania, USA

Correspondence to: Dr J N Ulrich, Geisinger Medical Center, 500 Pine Street, Apt 5, Danville, PA 17821, USA; npilic@web.de

doi: 10.1136/bjo.2006.111133

Competing interests: None declared.

**References**


**The use of voriconazole in the treatment of Aspergillus fumigatus keratitis**

There are a few reports of the use of voriconazole for the treatment of fungal keratitis. We report another case of its apparent success in *Aspergillus fumigatus* keratitis and discuss the dilemma of...
prescribing an expensive drug in the absence of defined ophthalmic therapeutic levels.

A 51 year old diabetic man presented a week after being poked in his eye by a child’s finger, with a 3.0×3.5 mm central corneal ulcer overlying full thickness stromal infiltrate with associated hypopyon (fig 1). Pinhole visual acuity was 2/60 in this eye. Topical ciprofloxacin 0.3% was started. Aspergillus fumigatus was isolated after 48 hours’ incubation and topical amphotericin B 0.15%, voriconazole 1% hourly, and oral voriconazole 800 mg twice daily were introduced, the latter reducing to 400 mg twice daily after 48 hours. Topical voriconazole was prepared aseptically with 0.9% sodium chloride, with 48 hour expiry (24 hours from opening). The ulcer size, infiltrate, and hypopyon slowly reduced, although recurrent hypopyon at day 13 led to rescraping, aqueous paracentesis, and administration of intracameral amphotericin. A bacillus and coagulase-negative staphylococcus were isolated following enrichment culture. With no further treatment alteration the ulcer healed. At six weeks the eye appeared quiet with a corneal scar, 30% stromal thinning and visual acuity of 6/24; oral voriconazole was discontinued and topical treatments four weeks later.

Comment

Fungal keratitis is difficult to treat and carries a significant risk of intraocular involvement. Traditional antifungals usually have good topical transcorneal penetration, but even systemic therapy has limited intraocular penetration. Primary treatment failure is reported in 31%, with predictive factors being Aspergillus infection, large ulcer size, and hypopyon. We therefore used a novel agent in this high risk case.

Voriconazole is a highly potent triazole, with 100% in vitro susceptibility reported in 34 common ocular fungal pathogens, compared to only 60–82.4% for fluconazole, itraconazole, amphotericin B, and ketoconazole. Although unlicensed in this capacity, topical and oral voriconazole (4–6 mg/kg twice daily for 4–12 weeks) are reported in the successful treatment of Fusarium, Scedosporium, Alternaria, Candida albicans, and Aspergillus fumigatus keratitis. Despite initial good response, two of these cases also showed disease exacerbation at 10 to 14 days which settled with intracameral infusion or further/increased systemic treatment or both. Intracameral amphotericin may have been instrumental in our case, but this is difficult to disentangle from the voriconazole effect.

Orally administered, voriconazole reaches therapeutic levels in the aqueous and vitreous of the non-inflamed eye, and aqueous of the infected eye. Its penetration topically is less clear; although levels exceeding the minimum inhibitory concentration are reported in the cornea, vitreous, and choriorretina of rabbit control and infected eyes, human data are conflicting.

The good ocular penetration of oral voriconazole has encouraged its use. Although the properties of this agent are attractive its cost far exceeds that of traditional antifungals. A 28 day course costs £3645.44 orally (400 mg twice daily) and £2884.00 topically (hourly), compared with only £86.24 for oral fluconazole (200 mg four times a day) and £190.40 for topical (hourly) amphotericin B.

Restricting voriconazole use to cases involving resistant organisms is difficult as there are no ophthalmic data on resistance and susceptibility breakpoints. Guidelines for the treatment of fungal keratitis need to be established.

Figure 1  Central corneal ulcer with dense elevated infiltrate and hypopyon.

Figure 2  Scleral bites of different depth (top left, bottom left and bottom centre): too superficial (left suture), too deep (centre suture) and adequate depth (right suture). View from underneath (top right, bottom right): suture too superficial (left suture, not visible), suture perforates sclera (centre suture) and adequate depth (right suture).
Isotretinoin and night vision

We read with interest the article by Mollan et al. who have concluded that previous isotretinoin use does not cause a clinically significant reduction in night vision in most people, and that the retinal toxic effects of isotretinoin may be measurable by electroretinography (ERG) and dark adaptation (DA). Although the authors have successfully highlighted the importance of counselling patients for potential irreversible loss of DA following isotretinoin use, their report, in our opinion, has failed to substantiate the need for routine screening of potential military and civilian commercial aviators.

In their study, 2 of 47 patients had both abnormal ERG and DA, whereas 11 others had certain abnormal ERG parameters that may or may not be of practical significance. The interpretation of this finding is debatable in the context of this study being a retrospective analysis, where we cannot assess the electrodiagnostic status of the patients in the study group before treatment. Only two patients in the study had abnormalities in both ERG and DA. Those two patients, X and Y, received treatment for a comparatively shorter period of time (8 and 12 weeks, respectively) than others (treatment range 6 weeks to 6 months). Whether these patients had a higher dose of isotretinoin or had any predisposing retinal problems are not adequately explained in the report. It would have been informative if the authors had compared the dose-effect relationships among patients in whom the dose of treatment was known (8 patients with abnormal ERG and 23 patients with normal ERG in the isotretinoin group).

In this particular study, the authors have mentioned a patient who continued to show signs of retinal toxicity 8 years after cessation of treatment, presumably with changes in ERG, but there is no description of this patient either in table 1 or elsewhere in the article. Further, the authors have compared the persistence of retinal toxicity in this particular patient with the study conducted by Oner et al. In their study, Oner et al. have looked into the visual acuity, anterior segment changes, intraocular pressure, Schirmer`s test, tear film break-up time, colour vision and changes in microbial flora. They specifically mention in their article that they did not perform any electrodiagnostic studies in their patients. Perhaps it is inappropriate to compare the two studies, which have looked at entirely different aspects of side effects of isotretinoin.

Although Mollan et al. have mentioned in their methods that colour vision was tested in their patents, they have not elaborated on the relevant results in the article. It is interesting to note that the authors have not justified in the main report their recommendation for routine electrophysiological screening for professions that are critical for night vision, except in the abstract. It would be appropriate to conduct a prospective study to look into the effects of isotretinoin and other described ocular changes following the use of isotretinoin, to precisely address their question.

S Pushpoth, S Sandramouli
Wolverhampton and Midland Counties Eye Infirmary, Wolverhampton, UK

Correspondence to: Dr S Pushpoth, Wolverhampton and Midland Counties Eye Infirmary, Compton Road, Wolverhampton WV3 9QR, UK; drsree@tiscali.co.uk

Accepted 24 October 2006

Competing interests: None declared.

References

Surgical embolus removal in retinal artery occlusion

I was interested to read the article by Garcia-Arumi and colleagues on “Surgical embolus removal in retinal artery occlusion”1. The authors claim that “Surgical removal of retinal arterial emboli seems to be an effective and safe treatment for RAO (retinal artery occlusion)” Brieﬂy, the study was based on six eyes with temporal branch retinal artery occlusion (BRAO) and one with central retinal artery occlusion (CRAO). The surgery was performed in the eyes with BRAO 4, 12, 19, 22, 28, and 33 h after onset and in the eye with CRAO 29 h after visual loss. The first intervention for STA-MRA, 48 h after surgery, showed reperfusion of the occluded branch retinal artery in four and none in one; in...
involved retina, visual fields, particularly with a Goldmann perimeter, provide much better information about the extent of visual loss and change. In my study, every eye with BRAO had visual fields plotted with a Goldmann perimeter, which showed that in eyes with BRAO there is often a reduction in the size of the visual field defect as part of the natural history. Garcia-Arumi and colleagues state that they recorded the visual fields with the Humphrey perimeter but give no information on the visual fields of their cases. Moreover, unlike the Goldmann perimeter, the Humphrey perimeter provides information about only the central 24° to 30° and not the entire involved retina.

(4) In the series of Garcia-Arumi and colleagues, six of seven eyes had had acute retinal ischaemia for 12–33 h and one for 4 h. We evaluated the retinal tolerance time to acute ischaemia experimentally in rhesus monkeys’ and found that, in CRAO, ischaemic retina can recover normal function from acute ischaemia of 97 min, but, after that, the longer the ischaemia, the more extensive the irreversible damage, so that acute ischaemia lasting 240 min results in massive irreversible retinal damage. Therefore, it does not seem logical that restoration of circulation in BRAO 4–33 hours after the occlusion would restore function in an already irreversibly damaged retina. Moreover, they found restoration of circulation in four of the six eyes on fluorescein angiography first performed 48 h after surgery. They argue that, “in branch RAO... some degree of perfusion at the macular area may be supplied by the contralateral temporal artery.” This may be true, but it may also be another factor in the spontaneous marked visual recovery in such eyes as part of the natural history.

In conclusion, on the basis of my studies on the natural history of eyes with BRAO, I believe that the improvement in visual acuity attributed by Garcia-Arumi and colleagues to embolectomy simply represents natural history.

Soham Singh Hayreh
Department of Ophthalmology and Visual Sciences, University Hospitals & Clinics, Iowa City, IA 52242, USA

Competing interests: None declared

References

NOTICES

Glucoma

The latest issue of Community Eye Health (No 59) discussing new treatments for glaucoma in the developing world, with an editorial by leading specialist Richard Wormald. For further information please contact: Journal of Community Eye Health, International Resource Centre, International Centre for Eye, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK (tel: +44 (0)20 7612 7964; email: Ana.Habib@lshtm.ac.uk; online edition: www.jceh.co.uk). Annual subscription (4 issues) UK £28/US$45. Free to developing country applicants.

9th IOIS International Symposium

The 9th International ocular Inflammation Society international symposium will be held in Paris from 17–20 September 2007. For further information on registration please call +33 (0)1 70 08 69 82, or fax +33 (0)1 42 93 29 28, or email andrelamyl@wanadoo.fr. Or you can visit the website www.iois-paris-2007.com.

IAPB 8th General Assembly – 2008

The 2008 International Agency for the Prevention of Blindness Eighth General Assembly: “Excellence and Equity in Eye Care” will be taking place at the Centre de Conventions Reboxo, in Sao Paulo, Brazil on 28 July–2 August. For further information please email: agency@iapi.org.

Second Sight

Second Sight would like to hear from experienced Indian eye surgeons returning to India after training/working in the UK. Second Sight is a London based charity dedicated to the elimination of cataract blindness in India. For further information please contact Dr Lucy Mathen, email: lucymathen@yahoo.com.

Singapore National Eye Centre

The Singapore National Eye Centre will be holding its 18th Anniversary International Meeting from 14–17 March 2008 at Suntec City Convention Centre, Singapore. For further information please call +65 6227 7290 or email meet@snec.com.sg.

Inaugural Asia Cornea Society Scientific Meeting

The Asia Cornea Society will be holding its inaugural meeting on 13–14 March 2008 at the Shangri La’s Rasa Sentosa Resort, Singapore. For further information please fax +65 6227 7291 or email acs@snnec.co.sg.

International Ocular Blood Flow Symposium

The International Ocular Blood Flow Symposium will be taking place on 13 October 2007 at the Sutton Place Hotel, Toronto, Canada. For further information please telephone +416 978 2719 or +1 888 512 8173, fax +416 946 7028 or email cc.med@utoronto.ca.

Neuro-Ophthalmology and Strabismus – 2008 EUPO Residents’ Course

The 2008 European Residents in Ophthalmology (EUPO) Course will be held in Geneva, Switzerland, on September 5-6, 2008. The course organized by Prof. Avinoam Mathen, email: lucymathen@yahoo.com.

CORRECTION

doi: 10.1136/bjo.2007.92965corr1

In the paper by Tranos et al (Br J Ophthalmol 2006;90:1107–10) the spelling of the third author is incorrect. The correct spelling is Zambarakji. We apologise for this error.
Alzheimer’s disease a specific pattern of retinal nerve fibre loss occurs in association with narrowing of retinal veins and decreased retinal blood flow in these veins. The authors emphasise that at least part of the visual loss in Alzheimer’s disease appears to be of retinal origin. (Invest Ophthalmol Vis Sci 2007;48:2285–89)

The potential therapies for statins continue to be expanded. Among the many positive effects of statins appears to be its ability to lower blood pressure. This response appears to be unrelated to age, serum cholesterol changes or the duration of the trial. Effects were greatest in patients with the highest baseline blood pressure. (Hypertension 2007;49:792–8)

The harmful effects of hormone replacement therapy are significant. A recent report suggests that hormone replacement therapy is associated with an increased risk of ovarian cancer in post-menopausal women. Although the risk is small, the authors contended it was potentially important and would add one extra ovarian cancer for every 2500 women taking hormonal replacement therapy over a 5-year period. (Lancet 2007 doi: 10.1016/S0140-6736(07)60534-2)

Many studies have documented that reducing sodium intake lowers one’s blood pressure and in some cases prevents the onset of hypertension. Now, a study of patients who reduced dietary sodium intake has documented that by doing so these patients reduced their long-term risk of adverse cardiovascular events. The authors conclude that at public health programs aimed at lowering dietary sodium intake in the general population could have a significant effect on preventing cardiovascular disease. (BMJ 2007;334:885–8)

Ophthalmologists are now aware of the intraoperative floppy iris syndrome being associated with systemic alpha-blockers. When unrecognised this can cause an increased risk of cataract surgery complications. In a prospective multi-center non-randomised observational series surgeons documented that the intraoperative floppy iris syndrome occurred in 90% of eyes enrolled in the study. Nevertheless, experienced surgeons could anticipate the syndrome and employ compensatory surgical techniques resulting in low complication rates and excellent visual outcomes. (Ophthalmology 2007;114:957–64)

Dysmetropsia is a disorder of visual perception, in which there appears to be modification of the size of perceived objects. It is commonly associated with retinal pathology although it has also been reported in association with extra-cerebral visual pathways. Investigators from Korea have now described the syndrome of hemimacropsia in association with medial temporop-occipital infarction. This is in contrast to patients who have been reported with hemimicropsia in whom the lesions are usually located in the lateral aspect of the temporo-occipital lobe. (J Neurol Neurosurg Psychiatry 2007;78:547)

At the present time there is no proven therapy to prevent the development of advanced age related macular degeneration. The use of high dose antioxidant vitamin therapy has been recommended by some. The question of lifestyle risk factors in age related macular degeneration has been addressed by several studies. The Age Related Eye Disease Study has now reported on the association of dietary lipid intake and the risk of age related macular degeneration. In this study a higher intake of long chain polyunsaturated fatty acids and fish was associated with a decreased likelihood of having neovascular age related macular degeneration. (Arch Ophthalmol 2007;125:671–9)

Carpal tunnel syndrome is a common finding in many populations. Although it has been suggested in the past, it may be associated with systemic disease, investigators have recently studied 516 consecutive patients with carpal tunnel syndrome. They found only four patients in whom systemic disease was associated with the problem. Two patients were found to have diabetes mellitus and two were hypothyroid. (J Neurol Neurosurg Psychiatry 2006 doi:10.1136/jnnp.2006.102143)

“But Groopman reserved some of his most bitter criticism for his colleagues within academic medicine. They had fostered a belief that anyone can take care of patients. This arrogance has created a culture at academic centres where research is applauded and teaching is taken for granted, where writing scientific papers (for journals like the Lancet) take precedence over developing clinical skills.” (Horton R. What’s Wrong with Doctors. NYRB 2007; LIV: 16-20)