

- 1 Latchman D, ed. *Genetic manipulation of the nervous system*. London: Academic Press, 1996:1–276.
- 2 Blomer U, Naldini L, Verma IM, Trono D, Gage FH. Applications of gene therapy to the CNS. *Hum Mol Genet* 1996;5:1397–404.
- 3 Johnson E. Gene therapy companies: launching against the tide. *Gene Therapy* 1996;3:841–2.
- 4 Friedmann T. Human gene therapy—an immature genie, but certainly out of the bottle. *Nature Med* 1996;2:144–7.
- 5 Marshall E. Less hype, more biology needed for gene therapy. *Science* 1995; 270:175.
- 6 Sullivan LS, Daiger SP. Inherited retinal degeneration: exceptional genetic and clinical heterogeneity. *Mol Med Today* 1996;2:380–6.
- 7 Faktorovich EG, Steinberg RH, Yasumura D, Matthes MT, LaVail MM. Photoreceptor degeneration in inherited retinal dystrophy delayed by basic fibroblast growth factor. *Nature* 1990;347:83–6.
- 8 Bennett J, Wilson J, Sun D, Forbes B, Maguire A. Adenovirus vector-mediated in vivo gene transfer into adult murine retina. *Invest Ophthalmol Vis Sci* 1994;35:2535–42.
- 9 Li T, Adamian M, Roof DJ, Berson EL, Dryja TP, Roessler BJ, et al. In vivo transfer of a reporter gene to the retina mediated by an adenoviral vector. *Invest Ophthalmol Vis Sci* 1994;35:2543–9.
- 10 Jomary C, Piper TA, Dickson G, Couture LA, Smith AE, Neal MJ, et al. Adenovirus-mediated gene transfer to murine retinal cells in vitro and in vivo. *FEBS Lett* 1994;347:117–22.
- 11 Jomary C, Vincent KA, Muzyczka N, Wadsworth SC, Smith AE, Neal MJ, et al. Adenoassociated virus vector-mediated gene transfer to retinal cells in vitro and in vivo. *Invest Ophthalmol Vis Sci* 1995;36:S772 (Abstract 3569).
- 12 Hauswirth WW, Zolotukhin S, Muzyczka N, Flannery JG. Adeno-associated virus delivery of an opsin promoter driven reporter gene to the mouse and rabbit retina. *Invest Ophthalmol Vis Sci* 1995;36:S845 (Abstract 3884).
- 13 Ali RR, Reichel MB, Thrasher AJ, Levinsky RJ, Kinnon C, Kanuga N, et al. Gene transfer into the mouse retina mediated by an adeno-associated viral vector. *Hum Molec Genet* 1996;5:591–4.
- 14 Bennett J, Tanabe T, Sun D, Zeng Y, Kjeldbye, Gouras P, Maguire AM. Photoreceptor cell rescue in retinal degeneration (*rd*) mice by in vivo gene therapy. *Nature Med* 1996;2:649–54.
- 15 Yang NS. Gene transfer into mammalian somatic cells in vivo. *Crit Rev Biotechnol* 1992;12:335–56.
- 16 McCarthy M. DNA vaccination: a direct line to the immune system. *Lancet* 1996;348:1232.
- 17 Grunzburg WH, Salmans B. Virus vector design in gene therapy. *Mol Med Today* 1995;1:411–7.
- 18 Fisher K, Guang-Ping G, Weitzman MD, DeMatteo R, Burda JF, Wilson JM. Transduction with recombinant adeno-associated virus for gene therapy is limited by leading-strand synthesis. *J Virol* 1996;70:520–32.
- 19 Ferrari F, Samulski T, Shenk T, Samulski RJ. Second-strand synthesis is a rate-limiting step for efficient transduction by recombinant adeno-associated virus vectors. *J Virol* 1996;70:3227–34.
- 20 Hart SL, harbottle RP, Cooper R, Miller A, Williamson R, Coutelle C. Gene delivery and expression mediated by an integrin-binding peptide. *Gene Therapy* 1995;2:552–4. (Corrigendum in 1996;3:1032–3.)
- 21 Hodgson CP, Solaiman R. Viroosomes: cationic liposomes enhance retroviral transduction. *Nature Biotech* 1996;14:339–42.
- 22 Hangai M, Kaneda Y, Tanihara H, Honda Y. In vivo gene transfer into the retina mediated by a novel liposome system. *Invest Ophthalmol Vis Sci* 1996;37:2678–85.
- 23 Senut M-C, Suhr ST, Gage FH. Transplantation of genetically modified non-neuronal cells in the central nervous system. In: Latchman D, ed. *Genetic manipulation of the nervous system*. London: Academic Press, 1996: 181–202.
- 24 Naldini L, Blomer U, Gallay P, Ory D, Mulligan R, Gage FH, et al. In vivo gene delivery and stable transduction of nondividing cells by a lentiviral vector. *Science* 1996;272:263–7.
- 25 Campbell KHS, McWhir J, Ritchie WA, Wilmut I. Sheep cloned by nuclear transfer from a cultured cell line. *Nature* 1996;380:64–6.

Corneal ulceration in the developing world—a silent epidemic

Anyone who has spent time in Asia or Africa can invariably recall a vivid image of a blind beggar, sometimes an elderly person but frequently a child with opaque corneas, haunting the bazaars and marketplaces of cities and villages. The spectre is so common that it almost passes unnoticed, but these individuals who are bilaterally blind represent only a small fraction of the millions who suffer monocular blindness as a result of corneal trauma and subsequent microbial keratitis.

With the global figure of blindness rapidly approaching 40 million, attention naturally is focused on cataract, which is responsible for 50% or more of all visual disability, and trachoma which is still an enormous public health problem affecting 500 million people worldwide and responsible for 25% of all bilaterally blind individuals.¹ Xerophthalmia, onchocerciasis, and glaucoma account for several millions more of the 85% of the world's blind individuals who live in developing countries in Asia and Africa.²

While corneal blindness in the developing world has traditionally been attributed to trachoma, xerophthalmia, measles, neonatal ophthalmia, and leprosy, Thylefors³ contends that the importance of superficial corneal trauma in agricultural work, which frequently leads to rapidly progressing corneal ulceration and visual loss, has been overlooked as a worldwide cause of monocular blindness. He estimates that up to 5% of all blinding conditions are directly related to ocular trauma and subsequent infection. Population based studies in several countries tend to support this assumption. In the Nepal blindness survey corneal trauma and ulceration were found to be the second leading cause of unilateral visual loss after cataract, accounting for 7.9% of all blind eyes.⁴ In Malawi,⁵ Tanzania,⁶ and Bangladesh,⁷ corneal scarring was found to be responsible for 39–55% of all cases of unilateral blindness. Surveys of blind children in Africa have shown that approximately 70% of all visual disability in this group is caused by corneal opacification.⁸

Even though the prevalence of corneal scarring in a population may be used as an indication of the occurrence of corneal ulceration, the true incidence of keratitis can only be determined by a large population based survey. In the USA Erie *et al*⁹ reported the incidence of ulcerative keratitis in a carefully defined population in Olmsted County, Minnesota over a 39 year period from 1950 to 1988. In this retrospective population based survey the mean age and sex adjusted incidence of ulcerative keratitis was 5.3 per 100 000 population increasing to 11.0 per 100 000 during the 1980s, the increase corresponding to the widespread use of cosmetic contact lenses. Until recently, a similar population based study in a developing country had not been documented. In 1996 Gonzales *et al*¹⁰ reported the incidence of corneal ulceration in Madurai District, Tamilnadu, south India. This retrospective population based study surveyed all of the corneal ulcers occurring in 1993 in Madurai District, an administrative area in the state of Tamilnadu with a population of over three and a half million. There were 1148 cases of corneal ulceration recorded in medical records in the district, yielding an annual incidence of 3.4 cases of corneal ulceration per 10 000 population. But, by carefully questioning all of the medical practitioners in the district and examining hospital records and patient charts in ophthalmologists' offices, Gonzales *et al* were able to extrapolate a much truer estimated annual incidence of corneal ulceration of 11.3 per 10 000 population.

To put these figures in perspective, the incidence of corneal ulceration in Olmsted County, Minnesota from 1980 to 1988 was 11.0 per 100 000 population. The estimated true incidence of corneal ulceration in Madurai District, Tamilnadu, south India in 1993 was 113.0 per 100 000 population, or 10 times the incidence reported in the USA. Applying the 1980–8 incidence rate in Olmsted County to the 1990 US population yields an estimate of 27 000 corneal ulcers annually. Applying the 1993 incidence rate in

Madurai District to the state of Tamilnadu alone yields an estimate of 50 000 new ulcers every year. If these statistics are generalised to all of India, an estimated 840 000 people a year in that country develop a corneal ulcer. In absolute numbers this is 30 times the number of ulcers seen annually in the USA.

Undoubtedly, true estimates of the magnitude of blindness from corneal ulceration in the developing world remain elusive because of the unilateral nature of keratitis. However, data from the Madurai study indicate that corneal ulceration is much more frequent in developing countries than previously recognised, and it also appears to be occurring in epidemic proportions. A comparison of population based studies in the USA and India indicates that there is at least a tenfold higher incidence of corneal ulceration in India. In absolute numbers microbial keratitis in the developing world is a previously undocumented significant cause of monocular blindness. As such, even by conservative estimates it is responsible for well over one and a half million new cases of unilateral blindness worldwide each year. These findings should encourage further epidemiological research in the pathogenesis of corneal ulceration and the development of comprehensive programmes for risk reduction and antibiotic prophylaxis for superficial corneal trauma.

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- 1 Thylefors B. Present challenges in the global prevention of blindness. *Aust N Z J Ophthalmol* 1992;20:89-94.
- 2 Foster A, Johnson G. Magnitude and causes of blindness in the developing world. *Int Ophthalmol* 1990;14:135-40.
- 3 Thylefors B. Epidemiological patterns of ocular trauma. *Aust NZ J Ophthalmol* 1992;20:95-8.
- 4 Brilliant LB, Pokhrel RP, Grosset NC, Lepkowski J. Epidemiology of blindness in Nepal. *Bull WHO* 1985;63:375-86.
- 5 Chirambo MC, Tielsch JM, West KP, Katz J. Blindness and visual impairment in Southern Malawi. *Bull WHO* 1986;64:567-72.
- 6 Rapoza PA, West SK, Katala SJ, Taylor HR. Prevalence and causes of vision loss in central Tanzania. *Int Ophthalmol* 1991;15:123-9.
- 7 Khan MU, Haque MR, Khan MR. Prevalence and causes of blindness in rural Bangladesh. *Ind J Med Res* 1985;82:257-62.
- 8 Foster A, Sommer A. Childhood blindness from corneal ulceration in Africa: causes, prevention, and treatment. *Bull WHO* 1986;64:619-23.
- 9 Erie JC, Nevitt MP, Hodge DO, Ballard DJ. Incidence of ulcerative keratitis in a defined population from 1950-1988. *Arch Ophthalmol* 1993;111:1665-71.
- 10 Gonzales CA, Srinivasan M, Whitcher JP, Smolin GS. Incidence of corneal ulceration in Madurai District, South India. *Ophthalmic Epidemiol* 1996;3:159-66.