LETTERS TO THE EDITOR

Amitosis in human donor corneal endothelium – a serendipity?

SIR,—It is generally accepted that the human corneal endothelium does not usually replicate, Kaufman *et al*¹ described a single dividing (amitotic) cell in the donor cornea of a 50-year-old man, and more recently Laing *et al*² reported a putative mitotic figure by clinical specular micrographs in a case of graft rejection. They suggested that mitosis represents an additional healing mechanism to repair by cell reorganisation, migration, and enlargement. Since the human endothelium cannot at present be studied continuously but at short intervals in vivo, a given cell cannot be monitored at different phases of division. Hence evidence for mitosis or amitosis must be circumstantial and based on isolated clinical or histological observations. Any report of suspected cell division adds to this circumstantial evidence.

We wish to report the finding of binucleate cells by scanning electron microscopy (SEM) in the endothelium of purportedly normal adult and infant donor corneas. One cornea was from a 65-year-old woman with a normal ocular history. The cause of death was cardiac failure, and the globe was enucleated 12 hours post mortem. The other was from a case of cot death at the age of 3 months. The eye was enucleated four hours post mortem. A corneoscleral button was excised from each and prepared for SEM. During random scanning a single binucleate cell was found in the adult corneal endothelium. It was larger than the adjacent cells and its posterior plasmalemma appeared intact. At higher magnification, an apparent cleavage line was visible between the nuclei (Fig 1). Owing to the suspicion that mitosis occurs in infant corneas used for keratoplasty,³ dividing cells were specifically sought in the infant endothelium. A single binucleate cell was found (Fig 2).

Recently coalescence of endothelial cells, which creates bi- or multinucleate cells, has been implicated as a repair mechanism.⁴ However, as indicated by other observers,⁵ the binucleate state is equally explained by nuclear division. A consideration of the binucleate state should include normal mitosis, amitosis, cell fusion, cell rest, or indeed artefact. The lack of cytoplasmic cleavage in the cases reported here suggests incomplete mitosis or amitosis – a process in which the nucleus divides without cytoplasmic cleavage.

It is not known when human corneal endothelial cells lose their ability to divide, and conclusions regarding endothelial cell regeneration cannot be drawn from the chance findings of binucleate cells. However, the circumstantial evidence to date indicates that complete cell division, if it occurs in the mature corneal endothelium in vivo, is very infrequent and cannot adequately replace damaged or dead cells. Therefore all care should be taken to avoid the loss of cells during the preparation of donor corneas for transplantation, and, if methods of handling infant corneas (which possess twice the number of cells of adult corneas and which may be in the process of cell multiplication) can be improved, then the very young donor cornea is to be recommended.

The authors wish to thank Mr R J Buckley, FRCS, for reading the manuscript, the Department of Medical Illustration for photographic processing, and Miss Sheila Work for secretarial assistance.

ISRAEL N NARTEY
Moorfields Eye Bank

EMIL S SHERRARD
WILLIAM N G
Department of Clinical Ophthalmology,
Institute of Ophthalmology,
City Road, London EC1 2PD

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Correspondence to Dr I N Nartey, Moorfields Eye Hospital, City Road, London EC1 2PD.

Measurement of corneal diameter

SIR,—The measurement of corneal diameter was the subject of a recent paper by Robinson *et al*.¹ The ocular dimensions, and changes due to normal or abnormal processes, are of particular interest to ophthalmology.² While Robinson *et al*¹ address important issues, several aspects of their paper deserve further comment.

The definition of corneal diameter is critically important to the resultant measurements and, arguably, to the biological import of such measurements. Previous values of corneal diameter reflect a lack of uniformity in definition and method.³ Robinson *et al*¹ apparently adopted the horizontal visible iris diameter (HVID) as their definition of the horizontal corneal diameter (HCD).

Figure 1: SEM of adult corneal endothelium (x 860). Arrowhead indicates binucleate cell.

Figure 2: SEM of infant corneal endothelium (x 2800). Arrowhead indicates binucleate cell with cleavage line.

Anatomically HCD can be measured with reference to the external scleral sulcus, a small furrow at the corneoscleral transition zone.³ The visible iris will vary with peripheral thickness and transparency, and thus HVID would be expected to be a variable underestimate of HCD. Parenthetically, plane-projected distances such as HVID and HCD underestimate the true curvilinear surface distance.⁴ The difference between HVID (measured by Robinson *et al.*¹) and HCD may have non-trivial effects on recording corneal size. For example, peripheral corneal thickness changes with age,⁵ and measurements of HVID may not accurately reflect corneal growth.

The authors claim (p 572) that 'the photographic method is more accurate: diameters may be measured to the nearest 0.05 mm from the photographs compared with ± 0.25 mm with calipers or ± 0.5 mm with a ruler'. The photographic method has undoubtedly the best resolution, and hence probably the best repeatability, but nowhere do Robinson *et al.*¹ establish the superior accuracy of the photographic method. In other words, photographic determination may provide HVID estimates of good precision, but HVID itself may be an inaccurate indicator of HCD, or the true corneal diameter. One study³ found that $HVID < HCD$, and, while HVID and HCD are reasonably correlated, HVID can be an inaccurate predictor of HCD. For an $HVID = 11.6$ mm, the 95% confidence range for HCD was 12.1 to 13.7 mm.

The problem of reconciling the need for measurement accuracy with that of simplicity and suitability for clinical application was nicely resolved by Martin and Holden, of Sydney, Australia.³ Martin found that fluorescent tubes can be positioned in front of the eye such that the catoptric images are discontinuous at the external scleral sulcus, thus disclosing the true corneal diameter (HCD) as the horizontal distance between the discontinuities.³ Combined with the advantages of photography, Martin's method offers a simple yet accurate means of monitoring corneal diameter.

L STEPHEN KWOK
Lions Eye Research Laboratories,
LSU Eye Center,
Louisiana State University School of
Medicine Medical Center,
New Orleans,
LA, USA

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Correspondence to L Stephen Kwok, PhD, LSU Eye Center, 2020 Gravier Street, Suite B, New Orleans, LA 70112-2234, USA.

SIR,—We thank Dr Kwok for his interest in our article.¹ We agree that the definition of corneal diameter is critically important, but unfortunately no satisfactory definition is forthcoming. The problem is exemplified by the statement, 'there is a gradual transition of clear cornea to opaque sclera, the superficial third becoming opaque earlier than the deeper two thirds'.² Later on these same authors comment on the difficulty of defining this junction histologically, as there is a gradual

transition from cornea to sclera. It is implicit therefore that no single measurement can adequately define the corneal boundaries, and it is not surprising that a wide range of values is quoted in the literature.³ We therefore elected to measure the parameter most readily identified—that is, white-to-white.

The long-term aim of our study, albeit not stated in the article, was to develop a technique using a portable apparatus, which would enable 'corneal diameter' to be measured simply and repeatedly in preterm neonates and children, some of whom may have ocular malformations or infantile glaucoma. We did not use the corneoscleral furrow as a measuring point for the following reasons: it is difficult to see; there is no information as to its presence in the neonate, infantile glaucoma, or other globe malformations; and finally its relationship to limbal histology has not been defined. We do not doubt the value of the method using catoptric imagery and the corneoscleral furrow but question its application to the study of corneal growth in preterm neonates. Martin and Holden⁴ used catoptric imagery to measure both the white-to-white and corneal diameter in 50 eyes, but eye casts were made in only five of these patients. For these eyes no comparison was made between either the white-to-white or corneal diameters measured using catoptric imagery and the white-to-white or corneal diameter in vivo.

We concur with Dr Kwok that we have not established the superior accuracy of our method as a measure of the 'true' corneal diameter, but for the reasons stated above this probably cannot be contained in a single measurement.

JUDITH ROBINSON
ALISTAIR R FIELDER
Department of Ophthalmology,
University of Birmingham,
Birmingham and Midland Eye Hospital,
Church Street,
Birmingham B3 2NS

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BOOK REVIEWS

Vitamin A Supplements. Prepared by a WHO/UNICEF/IVACG Task Force. Pp. 24. Sw fr 8.00. World Health Organisation: Geneva, 1988.

This short publication gives precise information on the rationale and recommendations for the treatment and prevention of vitamin A deficiency. Details of alternative strategies for the prevention of xerophthalmia are discussed as well as matters pertaining to the logistics of implementing various programmes. It is essential reading for all physicians involved in child care in developing countries.

A FOSTER

A Colour Atlas of AIDS and HIV Disease. 2nd Edn. By Charles F Farthing, Simon E Brown, Richard C D Staughton. Pp. 115. £16.00. Wolfe: London, 1988.

This is a well-illustrated short atlas of all the manifestations of AIDS. It has a good basic introduction on aetiology, immunology, and the origin and spectrum of the disease. A description of diseases in the different systems of the body follows. The section on eyes is rather brief. It finishes with some good advice on counselling of patients and prevention of transmission of the disease, with a particular note on cautions for doctors. I think this is a good book for those needing an overview of the disease in easily palatable form.

RONALD J MARSH

NOTES

Public health ophthalmology

A special master degree programme in preventive ophthalmology will again be offered during 1990-1 by the Johns Hopkins Medical Institutions under the auspices of its Dana Center for Preventive Ophthalmology, a World Health Organisation collaborating centre. The programme is designed for individuals interested in initiating, developing and providing leadership to national or regional blindness prevention activities and in conducting serious clinical epidemiological research. Five to 10 places are available for participants from developing and developed countries. A small stipend may be available to some participants to help defray living expenses. Further information from: Program Coordinator, Preventive Ophthalmology Program, DCPO, Wilmer Institute, Room 120, Johns Hopkins Hospital, 600 N Wolfe Street, Baltimore, Maryland 21205, USA.

Preventive ophthalmology

The Dana Center for Preventive Ophthalmology of the Wilmer Eye Institute and Johns Hopkins School of Public Health will hold the third Master's Degree Program in Preventive Ophthalmology during the 1990-1 academic year. The course is designed to educate ophthalmologists from developed and developing countries in the application of epidemiological and other public health techniques to prepare them to assume leadership positions in clinical and public health research activities and prevention of blindness programmes. Some funds are available to help supplement the costs of participants from developing countries. Further information from PHO Program Coordinator, Dana Center for Preventive Ophthalmology, Wilmer Institute, Room 120, Johns Hopkins Hospital, 600 N Wolfe Street, Baltimore, MD 21205, USA.

AIDS and loss of vision

The first International Conference on 'AIDS and vision loss' will be held on 25-26 January at the Marriott Hotel, San Francisco, USA. Further details from American Foundation for the Blind (Fay Ellis), 15 West 16 Street, New York NY 10011, USA (tel 212 620-2029).