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Lens Epithelial Cells Adhere Less to HEMA Than to PMMA Intraocular Lenses

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Summary
Following cataract surgery proliferation of residual lens epithelial cells may occur causing secondary opacification and loss of visual acuity. Using an *in vitro* system the abilities of bovine and porcine lens epithelial cells to adhere to two types of intraocular lens have been assessed. Lens epithelial cells adhere significantly less to lenses composed of poly 2 hydroxyethylmethacrylate (HEMA) than to polymethylmethacrylate (PMMA).

The proliferation of human lens epithelium (HLE) cells may reduce visual acuity following extra-capsular cataract surgery in two ways. Firstly, the HLE cells may proliferate and opacify the posterior capsule behind the intraocular lens (IOL)[1] and secondly, they may undergo metaplasia to contractile myoblasts which cause wrinkling of the posterior capsule.[2] In both normal and cataractous lenses HLE cells from all parts of the anterior lens capsule have equal growth capacity while HLE cells from younger donors have a greater growth capacity.[3]

Table I. *Cumulative Capsulotomy Rates*

	1 year	*3 years*
Hydrogel*	1.9% (n = 157)	22.6% (n = 53)
PMMA[4] (convex posterior)	2%	5%
PMMA[4] (laser ridge)	21%	42%
PMMA[5] (Modified J Loop)	4.5%	7.0%

*WJCCR personal results

A new material, Poly 2-hydroxyethylmethacrylate (HEMA), is now available for the manufacture of IOLs. One of us (WJCCR) has been implanting these lenses for over three years.

Our assessments at the first year were initially very encouraging suggesting a low incidence of posterior capsule opacification. At three years, however, the capsulotomy rate exceeds that of polymethylmethacrylate (PMMA) posterior-convex or biconvex lenses although it is less than that reported of laser ridge lenses[4] (Table I).

These *in-vitro* investigations were intended to evaluate the hypothesis that the physicochemical composition of the IOL exerts an effect on the ability of lens epithelial cells to adhere to these polymers.

Materials and Methods

The anterior capsules from three pairs each of porcine and bovine eyes were dissected and prepared by a standard technique[6] and the lens and epithelial cells removed from the capsule by treatment with 0.01% trypsin and

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0.02% EDTA. After numerous standardising experiments to determine the optimum seeding density and substrate exposure time, the cells were suspended in Dulbecco's Minimal Essential Medium with 10% fetal calf serum at a cell density of $1.0 - 9.9 \times 1;^4$ cells/ml. Aliquots of 1 mL of cell suspension were placed in chambers of 6×4 multiwell plate and incubated at 35.5°C for one hour. During this time the cells were able to adhere to the substrate.

There were two components to the experiment. Firstly, in order to assess the possible effect of substrate shape on the adhesion of cells to the IOLs, HEMA IOLs were embedded planar and convex faces uppermost in 1% agarose coated multiwell chambers. Secondly, in order to compare any difference in adhesion between PMMA and HEMA the two IOL types were embedded planar surface uppermost in the agarose coated wells. In each experiment an agarose coated well without an embedded IOL was used as a control. Five replicates of each experiment were performed. Following the incubation period the IOLs and suspensions were removed and the cells detached from the IOL substrates by trypsinisation. Duplicate aliquots of ten microlitres were taken from each sample and counted using a haemocytometer and phase contrast optics. The surface areas over which the cells had adhered were measured and the number of cells adhered per mm^2 calculated in each case. The results were analysed using orthogonal comparisons within an analysis of variance.

Results

Cell Adhesion to Planar Compared with Convex Surfaces of HEMA IOLs

Figures 1 and 2 represent the ratio of five replicate experiments for Porcine Lens Epithelial (PLE) cells and five replicate experiments for Bovine Lens Epithelial (BLE) cells adhering to the convex and planar surfaces of the HEMA IOL when placed uppermost. Formal statistical analyses using orthogonal comparisons within an analysis of variance show that there is no significant difference between the planar and convex surfaces of HEMA lens with respect to the number of PLE and BLE cells adhering. $F_{1,20} = 1.90$ for PLE cells and $F_{1,20} = 0.36$ for BLE cells.

Cell Adhesion to PMMA IOLs Compared With HEMA IOLs

Figures 3 and 4 represent the ratio of five replicate experiments each for PLE and BLE cells adhering to the planar surface of HEMA and PMMA IOLs. Formal statistical analyses using orthogonal comparisons within an analysis of variance show that the number of PLE and BLE cells/mm^2 adhering to the HEMA IOLs is significantly less than the number of PLE and BLE cells/mm^2 adhering to the PMMA IOs. $F_{1,20} = 6.35$ for PLE cells and $F_{1,20} = 7.96$ for BLE cells, $p < 0.05$.

Discussion

These results demonstrate that there is less adhesion of PLE and BLE cells to HEMA than to PMMA. This is not related to the shape of the IOL. This difference in ability of PLE and BLE cells to adhere to PMMA and HEMA IOLs may be due to a number of factors. Scanning electron microscopy of these IOLs reveal that they present similarly smooth surfaces—therefore surface texture is unlikely to be the cause of this observed difference.

While electrostatic and Van der Waal forces

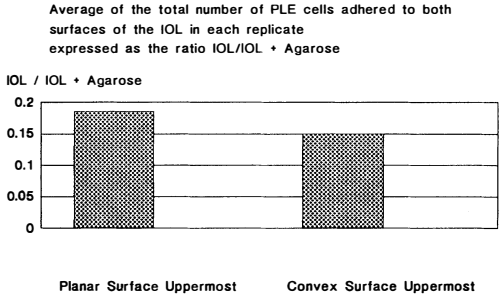

Fig. 1.

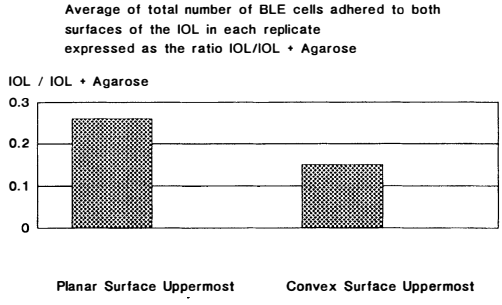

Fig. 2.

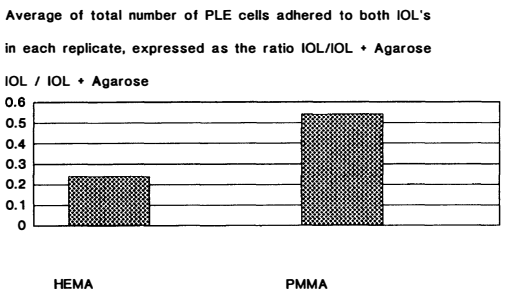

Fig. 3.

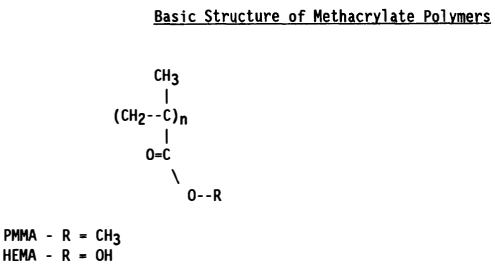

Fig. 5.

may play a part, a more likely explanation for the varying cell adhesive properties of these two types of IOL may be due to differences in their surface tensions. The hydroxyl groups of HEMA IOLs render them hydrophilic whereas PMMA is hydrophobic (Fig. 5). Reich *et al.*[7] have described a technique to measure tissue-polymer adhesion forces. Their experiments revealed a comparatively high adhesion force for PMMA compared with that for HEMA (Table II). King and co-workers[8] studied the hydrogel-water interfacial tensions of various methacrylate polymers including PMMA and HEMA in order to determine their biological behaviour in terms of protein adsorption and cell adhesion properties. By measuring the contact angle between an underwater captive air or octane bubble and the polymer they also found a higher solid-water interfacial tension with PMMA than HEMA. Therefore it seems likely that the difference in the capacity of lens epithelial cells to adhere to the two polymers investigated in this study may well be due to differences in their surface properties.

There are two known advantages and two theoretical advantages to using hydrophilic IOLs:

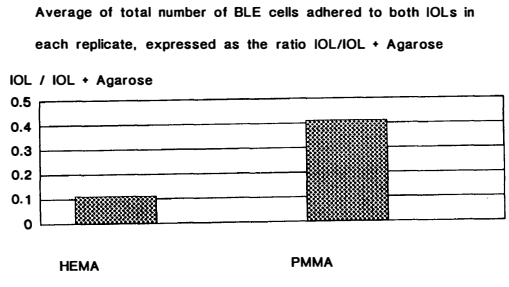

Fig. 4.

(1) The high adhesion forces exerted by PMMA explain the damage that can occur to the corneal endothelium during intra-operative contact. There is less damage if contact occurs with a HEMA lens.[9]

(2) The adherence of inflammatory cells and keratic or pigmentary precipitates to the IOL can be a post operative feature of pseudophakia.[10] PMMA IOLs removed from human eyes, either surgically or at post mortem, may have a variety of cells on their surfaces. In particular macrophages appear to settle and change into fibroblast-like cells.[11] HEMA IOLs implanted in cats displayed no fibroblast-like coating when they were removed at six weeks post-implantation.[12] In order to minimise such precipitates, by modifying the lens surface hydrophobicity, PMMA IOLs are now available chemically bonded with heparin. HEMA IOLs are inherently hydrophilic and the quiet post operative course and reduced IO debris have been noted as a feature.[13]

(3) The lower adhesion of cells to HEMA may also be important in minimising the introduction of particles, bacteria or other contaminants into the eye. It has been reported that, during routine cataract extraction, 19.4% of IOLs become contaminated by bacteria if the IOLs are allowed to rest on the eye. Of these 66% are contaminated by Staphylococcus Epidermidis identical to that cultured from the operating room air.[14] Further studies

Table II. *IOL endothelial interface adhesive forces*

	Average stress gm/cm²
PMMA	0.66
PMMA+ Healon	0.19
HEMA	0.09

Reich S, *et al.* 1984.[7]

would be useful to determine the adhesion of coagulase negative staphylococci to the two IOL types.

(4) Lens epithelial cells require a substrate on which to proliferate. A large area or reverse optic IOL reduces the extent of cell proliferation on the posterior capsule—possibly by a barrier effect.[15] Although on theoretical grounds an IOL rendered less receptive to cellular adhesion may be anticipated to impede cell proliferation, this has not yet been borne out by our long term clinical follow-up.

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