spatial frequency decline which flicker sensitivity did not. Also, flicker sensitivity declined at low temporal frequencies whereas pattern sensitivity did not. This suggests different information channels for pattern and flicker information, which may be, respectively, the sustained and transient systems with their different spatial frequency preferences. Our data show that alternation rates where subjects typically find the grating to be just continuous are far slower than the fastest temporal modulation (critical flicker fusion) (*15*) that can be detected at this luminance. At our point of continuity-discontinuity of grating appearance, there is obvious flicker in the field even though the pattern seems constant.

One might suspect that the increase in STVS reflects increased response persistence in the sustained system with increasing spatial frequencies. Breitmeyer and Ganz (*13*) cite evidence indicating that higher spatial frequencies increase persistence in the sustained channel.

It is interesting that gratings repeated for 500 msec on and 500 msec off appeared stationary at spatial frequencies greater than 1.2 cycles per degree, whereas lower spatial frequencies appeared temporally modulated (*12*). The appearance of stationariness of the higher spatial frequencies through a 500-msec offset is analogous to our estimates for long icons in the same spatial frequency range. These reports indicate a longer persistence in approximately the same spatial frequency region where the STVS durations increase, and support our suggestion that the higher spatial frequencies are responsible for longer icon durations [see (*16*)]. Physiological data also demonstrate longer response persistences to brief stimuli in cells classified as sustained (*10*).

These data imply that STVS has a post-photoreceptor component and thus conflict with Sakitt's proposal (*3*) that the major locus of the icon is in the rod photoreceptors. Our experiments suggest that major cone and post-photoreceptor processes are active in STVS. First, if only rods mediated STVS one would expect a "foveal" hole in the perceived icon because of the predominance of cones in central vision (*17*). In our study with fixation controlled, no such phenomenon was evident. Second, the increase in STVS duration with spatial frequency speaks against a pure photoreceptor icon. We can find no obvious reason to predict on a rod or cone level that finer gratings would produce longer icons. In fact, since the 15 cycle-per-degree grating yielded the longest perceived durations, one would have to postulate that if photoreceptors produced this icon, some neural process shortened the icons for the other gratings. More parsimonious is the suggestion of increasing sustained channel mediation of the icon with increasing spatial frequency.

The long duration of the 15 cycle-per-degree icon is doubly interesting. Such a grating, with its bars of 2 minutes of arc, is beyond or at best at the limits of rod acuity (*18*). It is unlikely that rods mediate the icon of a grating, centrally fixated, photopically illuminated and to which they have little resolution.

In summary, the duration of STVS increased with spatial frequency in a manner consistent with increasing sustained channel mediation. In cognitive psychology, the icon is assumed to maintain pattern vision despite interruptions of input and for further processing. Sustained channels may have the requisite properties for this task. Breitmeyer and Ganz (*13*) distinguish between a central, contour-specific iconic store called ISc and a peripheral icon, or ISp. Our data seem to represent manipulations of the ISc stage while Sakitt's (*5*) may refer to the ISp. However, a rod STVS would seem largely irrelevant to our normal photopic vision which includes fine acuity, foveal mediation, color, and bright lights, and not of major importance to most human information-processing paradigms. Cone or neural loci, or both, for STVS are certainly not excluded.

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Corneal Endothelium Damage with Intraocular Lenses: Contact Adhesion Between Surgical Materials and Tissue

Abstract. *Intraocular lenses destroy corneal endothelial cells by contact adhesion between the acrylic lens and endothelial surfaces during cataract surgery. Glass and rubber surgical glove surfaces produce similar cell damage. This phenomenon may be important in many surgical procedures and appears to be preventable if a hydrophilic polymer interface is interposed between contacting tissue and the surfaces of materials used.*

We became interested in the problem of cellular damage caused by surface adhesion from the standpoint of ophthalmic surgery and from the finding that corneal endothelial damage occurs during intraocular acrylic lens insertion. The cornea, the anterior transparent membrane of the eye, depends upon an intact living endothelial monolayer for its clarity. The endothelium serves as an aqueous barrier

and a pump to remove fluid from the cornea. If this barrier is damaged, leakage of fluid into the cornea will cause clouding and damage vision. Our studies and those of others indicate that the endothelial cells are essentially nonregenerative in man and heal primarily by spreading (*1*). Damage to this tissue is therefore quite serious in view of its very limited healing capability. In addition, endothelial cells are progressively depleted with age, and clarity may be lost years after initial cell damage. This tissue property, combined with the increasing use of intraocular lens implants for optical correction of aphakia following cataract surgery, and the possible damage done by them, was a cause of concern. Although the surgical complications associated with plastic lens insertion have been generally recognized, there has been little appreciation of the function of the plastic-tissue interface in promoting tissue damage.

We have found by specular microscopic examination that ordinary cataract extraction promotes the loss of 7 to 8 percent of the central corneal endothelial cells, and insertion of a plastic intraocular lens following cataract surgery can produce central endothelial cell loss of 50 percent or more. This dramatic cell loss is observed for several different types of commercially available acrylic (polymethyl methacrylate) intraocular lenses (*2*).

In view of the extensive endothelial damage that occurs during intraocular manipulation, we studied the surface interaction between the acrylic lens and the corneal endothelium. Corneas from rabbit eyes and human eyes (donated to the eye bank) were gently contacted with (i) acrylic rod surfaces moistened with a balanced salt solution and machined to the corneal curvature and (ii) several different types of commercial acrylic lenses. Cell damage was assessed by dye penetration of *p*-nitrotetrazolium blue into ruptured cells (*3*) and by scanning electron microscopy (SEM) (*2*) of tissue and plastic surfaces. In all of these tests, extensive damage was evident after even 1-second contacts and was uniquely different from mechanical damage produced by rubbing materials across the endothelial surface. The cell membrane was torn from the surface by this adhesion, revealing either empty spaces or cell interiors with nuclei present (Fig. 1, A and B). The cell membrane adhered to the acrylic lens surface (Fig. 1C). This type of damage did not occur when human or animal lenses or hydrophilic soft contact-lens material (polyhydroxyethyl methacrylate) was placed against corneas.

Contact occurs because the eye tends to collapse when opened, so that the iris and vitreous body push the intraocular lens against the cornea. With recognition of this contact damage, ophthalmic surgeons can often prevent contact by trying to maintain an air bubble cushion between the lens and the cornea. However, it is not always possible to completely prevent touch during insertion of the lens.

These results prompted further experiments with other materials that might be used during surgery and that might therefore contact sensitive tissue surfaces. The same type of tissue damage to rabbit and human corneal endothelium resulting from momentary contact adhesion was observed for surfaces of glass and surgical rubber gloves (Fig. 1D) as

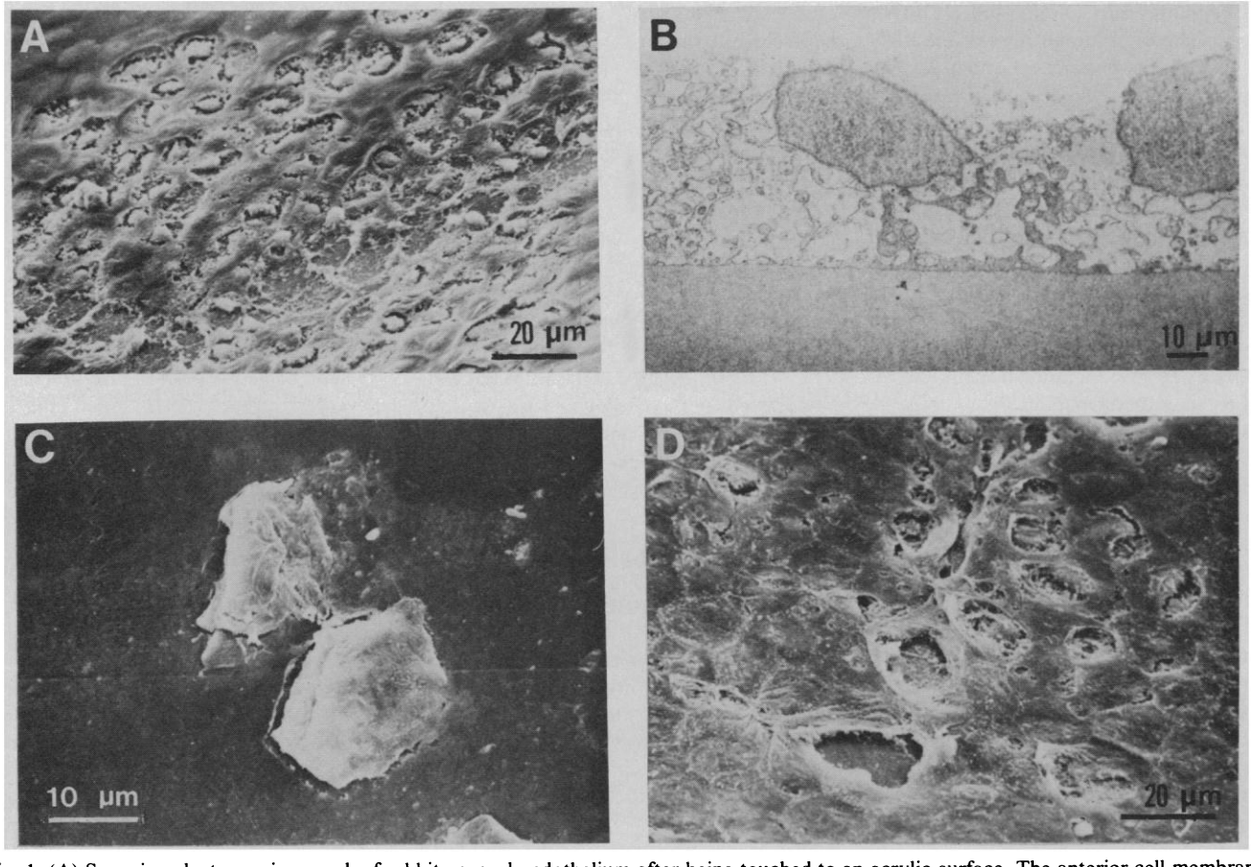

Fig. 1. (A) Scanning electron micrograph of rabbit corneal endothelium after being touched to an acrylic surface. The anterior cell membranes have been torn free exposing cell nuclei (×700). (B) Transmission electron micrograph of specimen shown in (A) demonstrating loss of anterior cell membrane, although the nuclei are present (×1950). (C) Scanning electron micrograph of acrylic lens surface showing adhering cell membrane after endothelium contact (×1750). (D) Scanning electron micrograph of rabbit corneal endothelium after being touched to a surgical rubber glove (×900).

shown by SEM photomicrographs. In addition, touch to a smooth stainless steel sphere caused complete loss of endothelial cells in several areas. This type of damage induced by metal instruments will be examined further.

The acrylic polymer used for intraocular lenses has good optical and mechanical properties and has demonstrated a reasonable degree of bioacceptance during many years of ophthalmic application. It is a rigid, hydrophobic material and is not readily wet by physiological fluids or saline solution. Since the immediate tissue interactions are primarily biophysical and probably involve a hydrophobic interaction between the plastic and cell surfaces, our initial approach to interfering with adhesion was to apply a hydrophilic polymer (polyvinylpyrrolidone, PVP) solution in an attempt to produce an adhesion barrier–lubricant boundary layer (*2*). Both PVP and other hydrophilic polymer solutions completely eliminated adhesion damage to the endothelial cells.

The tissue–materials interface has been extensively studied from the standpoint of polymer biocompatibility for nonthrombogenic and tissue-compatible implants or prostheses (*4*). Short-term toxicology and thrombogenicity as well as long-term tissue acceptance have been major points of concern. However, except for attention to cell adhesion to plastic surfaces pertinent to tissue culture studies, cell binding to polymer surfaces from the standpoint of blood and tissue compatibility, and some studies related to surgical adhesives, dental restoratives, and the changes of the adhesive properties of cell surfaces accompanying tumor cell metastasis, there has been relatively little attention devoted to the fundamentals of short-term bioadhesion phenomena. The literature on protein and cell adhesion to hydrophobic polymer surfaces (*5*) does suggest that increasing surface hydrophilicity tends to reduce adhesion. Only a very qualitative understanding of the basis for improvement in what is loosely termed "biocompatibility" as a result of increased wettability or hydrophilicity of surfaces seems yet to exist.

Our research indicates that contact adhesion by hydrophobic or electrostatic surface interactions (or both) may be an important general phenomenon that occurs in many surgical procedures when foreign surfaces, such as plastic, rubber, metal, and glass, contact exposed tissue. Our finding that the elimination of such adherence is achieved by interposing a hydrophilic polymer at the interface suggests (i) a mechanism by which hydrophobic and electrostatic surface interactions can be masked and (ii) a role for the hydrophilic polymer as a lubricating boundary layer to minimize frictional shearing forces and so limit cell membrane damage.

We may be dealing with a phenomenon in surgery whose importance is not generally recognized because tissue damage of this type is not obvious and because postoperative complications are often complex in their origins. However, we believe that careful investigation of contacts with surgical gloves, surgical instruments, and catheter surfaces is likely to reveal tissue damage that is now unsuspected but that may significantly affect tissue healing and repair mechanisms. For example, abdominal adhesions may occur after contact with rubber gloves. Efforts have in fact been reported to minimize adhesions by intraperitoneal injection of hydrophilic polymer solutions. Although PVP and dextran appeared to produce significant improvements in animal experiments, the technique used for administering the antiadhesive polymer solution was not practical and unfortunately appears to have received little further attention (*6*).

In the case of vascular and urinary tract catheters, ample clinical evidence exists that tissue damage produces thrombosis, inflammatory reactions, phlebitis, and urinary tract infection, all of which may be lessened by hydrophilic coating (*7, 8*). We believe that such coatings are effective primarily because they produce a hydrophilic, nonadherent surface with a low coefficient of friction so as to minimize the damage to the vascular endothelium or the urethral mucosa surfaces. Further studies in these areas are important because it may be relatively easy to favorably alter the surfaces that contact living cells to minimize tissue damage and so to avoid unnecessary surgical complications.

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Retinoyl Complexes in Batten Disease

A retinoyl complex was identified as the autofluorescent component of the neuronal storage material in Batten disease in a recent report by Wolfe *et al.* (*1*). Part of the evidence presented was based on their interpretation of the mass spectrum of lipid-free curvilinear bodies (CLB's). Prominent fragment ions included were those with a mass-to-charge ratio (*m/e*) of 255, 213, 185, 173, 159, 145, 133, 121, 119, 107, 105, 95, 93, 91, 81, 69, 55, 43, and 41. They compared these peaks with mass spectra of retinol, retinoic acid, and methyl retinoate obtained in our laboratory (*2*), as summarized by Elliott and Waller (*3*). The ions with *m/e* greater than 255 were not included in the report (*1*), but were shown in the mass spectrum of lipid-free CLB's at a recent meeting in Chicago (*4*). The mass spectrum showed a parent molecular ion at *m/e* 386 with fragment ions at *m/e* 368, 353, 301, and 275. These ions are not characteristic of vitamin A compounds but, when included with the fragment ions in the previous report (*1*), are identical to those of cholesterol (*5*). The nuclear magnetic resonance (NMR) data for the lipid-free CLB's are not inconsistent with the published NMR spectrum of cholesterol (*6*). The observed protons at 3.62 and 5.15–5.32 parts per million downfield from tetramethylsilane do not correspond to signals in published NMR spectra of the vitamins A (*7*). It should be noted that we have identified cholesterol as a contaminant in supposedly purified metabolites of retinoic acid many times. For example, cholesterol has cochromatographed with ^{14}C-labeled metabolites of retinoic acid on a silicic acid column, followed by sequential separation by thin-layer chromatography in four different solvent systems, and final-