A major story of the last 2 decades of the 20th century has been the emergence of refractive surgery. Initially extremely controversial, with modest predictability and debatable safety and long-term stability,1 surgical modification of corneal curvature has come to be well accepted by the profession and the public. The number of these procedures that will be performed in 2000 may exceed 1.5 million. These procedures will continue to be refined over time, and new procedures designed to treat extreme refractive errors (eg, phakic intraocular lenses) or other problems not currently treatable (eg, presbyopia) will fuel growth in this area. Ultimately, the genetic and environmental influences that result in excessive axial elongation and myopia will be identified, and the progression of myopia in school-aged children will be arrested. The benefit to society of eliminating myopia and other refractive errors in the next century will be enormous, allowing the reallocation of enormous resources away from corrective lenses and toward research into treatments for blinding diseases.

Corneal infections will become much less of an important concern to the corneal and external disease specialist. Herpetic corneal disease and bacterial keratitis are commonly encountered. The likelihood is that the mechanism of viral latency will be understood in detail, permitting the problem of viral reactivation to be conquered during the next century, eliminating or dramatically reducing the problem of corneal scarring and inflammation due to recurrent episodes of herpes simplex keratitis.2,3 Bacterial keratitis will become much less common owing to a combination of factors: (1) With the dramatic and ongoing improvements in the outcomes of refractive surgical procedures and increased acceptance of this option by the public, the use of contact lenses will decline dramatically. (2) Improvements in contact lens design and material composition will provide a much more physiologic environment for the corneal epithelium.4 The reduction of lens-induced hypoxia of the corneal epithelium will reduce the frequency of microbial keratitis. Emergence of resistant organisms will continue to be a major issue for corneal infection, as was the case for all types of ocular and systemic infections during the latter half of the 20th century. In the last decade or so, ophthalmologists have benefited tremendously from the remarkably broad spectrum of activity enjoyed with some of the topical fluoroquinolones.5 As resistance emerges, pharmaceutical companies will be challenged to devise new agents, including peptides, that will deal with the common infectious organisms but be nontoxic to the cornea. It is possible that the spectrum of activity of our antimicrobials will narrow, reducing the success rate of empirical therapy and increasing the need for microbiologic studies to identify the causative organism and its sensitivities to a panel of possible therapeutic agents.6

Penetrating keratoplasty will be performed much less frequently. Improvements in instrumentation and surgical technique will reduce endothelial cell loss from surgical trauma. Pseudophakic corneal edema, the most common indication for first-time penetrating kerato-
plasty in most series, therefore, will be less commonly encountered and will be treatable by mechanisms other than full-thickness grafting. Either endothelial cell transplantation, or use of gene therapy to induce endothelial cell replication and repopulation, will address the problem of corneal edema in a manner that is much less traumatic and associated with less morbidity (rejection, postoperative astigmatism, need for contact lens wear) than keratoplasty. Gene therapy may have value for limiting corneal scarring and favorably influencing outcomes in other wound healing situations.9,10

Keratoconjunctivitis sicca will be conquered. This condition is a major source of ocular morbidity in developed nations, occurring in 10% or more of the population in some studies, with a disproportionate number of women afflicted. Available therapy, basically consisting of simple lubricants and/or punctal occlusion, is clearly inadequate in many individuals and does not address the underlying pathophysiology of this condition.11 The recognition of an immune-mediated inflammatory mechanism contributing to the development of the dry eye state (possibly related to changes in systemic hormonal status) offers the expectation that the condition of severe end-stage dry eye can be prevented or at least partially reversed. The relative roles of traditional immunomodulatory agents such as cyclosporine vs possible hormonal therapy will be elucidated, and this major source of ocular morbidity will be addressed.

An intraocular lens or injectable material will be used to replace the cataractous crystalline lens and restore accommodation. Development and refinement of intraocular lenses has been one of the great success stories in ophthalmology during the last few decades. Foldable lenses that can be placed through incisions 3 mm in length or shorter have allowed for astigmatically neutral cataract surgery. The remaining challenges in this field include increasing the predictability of postoperative refractive error, especially for very long and very short eyes, and restoring accommodation. Intraocular lenses that can be adjusted in situ to eliminate residual refractive error due to intraocular lenses power prediction errors, and intraocular lenses capable of moving within the eye and thereby increasing refractive power in response to ciliary muscle action are under development, and might serve to address these issues. Endocapsular cataract surgery, in which the lens nucleus and cortex are removed and the capsular bag subsequently filled with a clear polymer capable of restoring flexibility to the lens and accommodation, has been under study for 2 decades and might prove useful.

Proliferation of residual lens epithelial cell and resulting posterior capsular opacification continues to limit the success of current cataract extraction techniques. Preservation of an intact capsule may protect against retinal problems, including retinal detachment and macular edema, especially in children. Prevention of capsule opacification is also a precondition for successful endocapsular cataract surgery. It is likely that new developments in gene therapy and cell targeting will allow this problem to be solved in the coming decades, so that selective inhibition of this cell population can be achieved in a manner that will not induce significant toxic effects to other intraocular cell populations.

The next several decades will see advances in the surgical and nonsurgical management of corneal diseases, cataract, and refractive error, resulting in improved outcomes and quality of life. The tools that will allow us to realize these advances are high technology and molecular medicine.

Accepted for publication April 18, 1999.

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