# MANAGEMENT OF BULLOUS KERATOPATHY

Thesis

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**The Master Degree in** *(Ophthalmology)*

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بسم الله الرحمن الرحيم

وما اوتيتم من العلم إلا قليلاً

صدق الله العظيم

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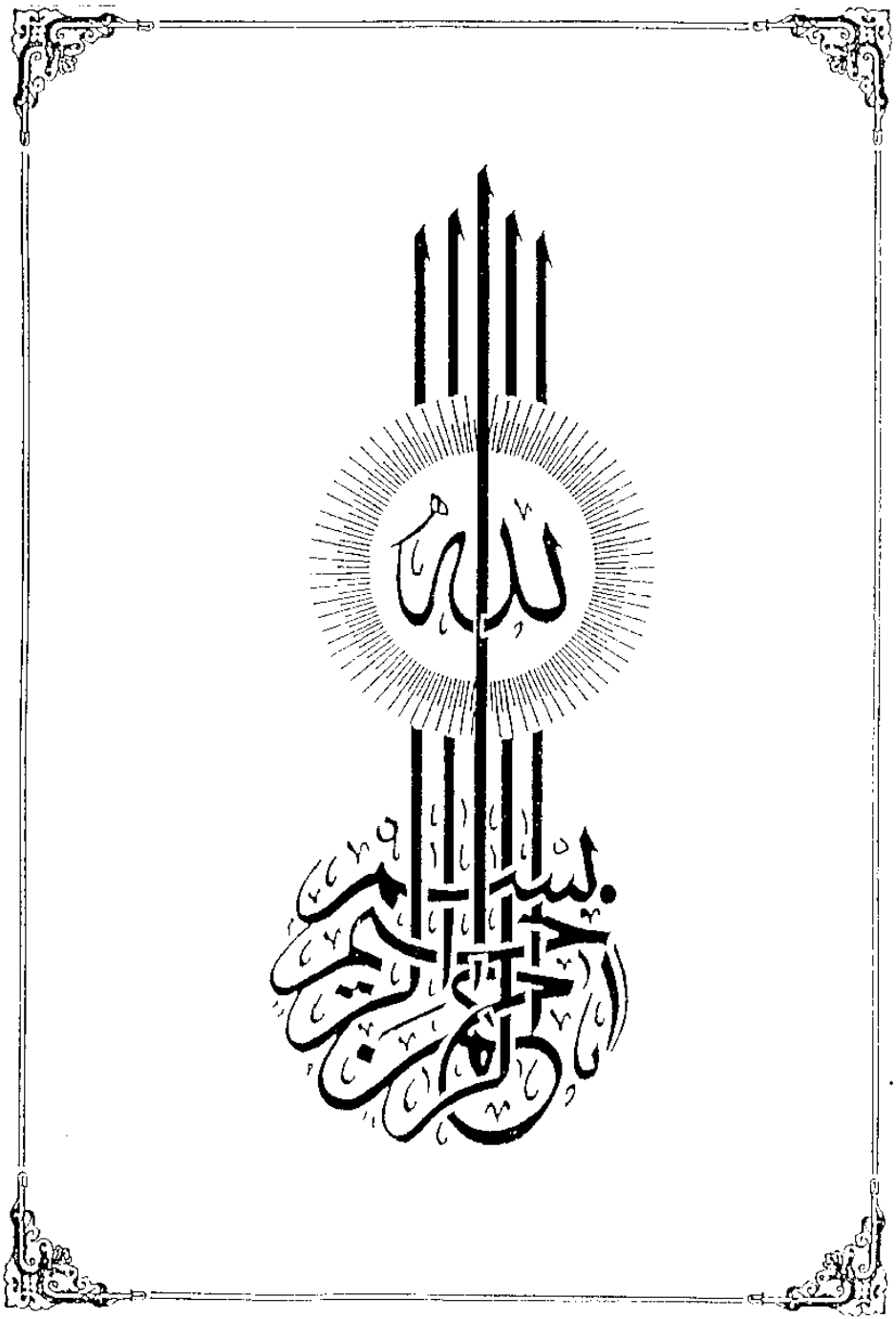

*To My Father*

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# INTRODUCTION

# INTRODUCTION

## Anatomy of the Corneal Endothelium

It is the most posterior layer of the cornea. It consists of a single layer of flat, hexagonal cells which together form a mosaic *(Kestenbaum, 1963).*

Specular microscopy of the endothelium adds to the above that the cells being regularly spaced, with equal sizes, having uniform shape and homogenous colour *(Hefni et al., 1982).* Each endothelial cell measures 18 to 20 um in width and 4 to 5 um in height *(Mayer, 1984)* (Fig. 1).

The normal endothelial cell count is 3000 to 3500 cells per square millimeter in the young adult, decreasing to about two-thirds of that value in old age. This decrease in number is coupled with increased cell size and pleomorphism *(Bourne and Kaufman, 1976).*

The normal endothelial cell contains a large oblong nucleus and cytoplasmic organelles *(Iwamoto and Smelser, 1965).*

The endothelial surface shows low flat bulges caused by the nuclei *(Svedbergh and Bill, 1972).*

The lateral plasma membranes of adjacent cells are extensively interdigitated and have shown to be the location of a $Na^+$-$K^+$ ATPase-dependent pump *(Hodson, 1977).*

Intercellular junctions along these membranes near their apical borders are mainly composed of gap junctions with tight junctions evident in only some areas *(Ottersen and Vegge, 1977).*

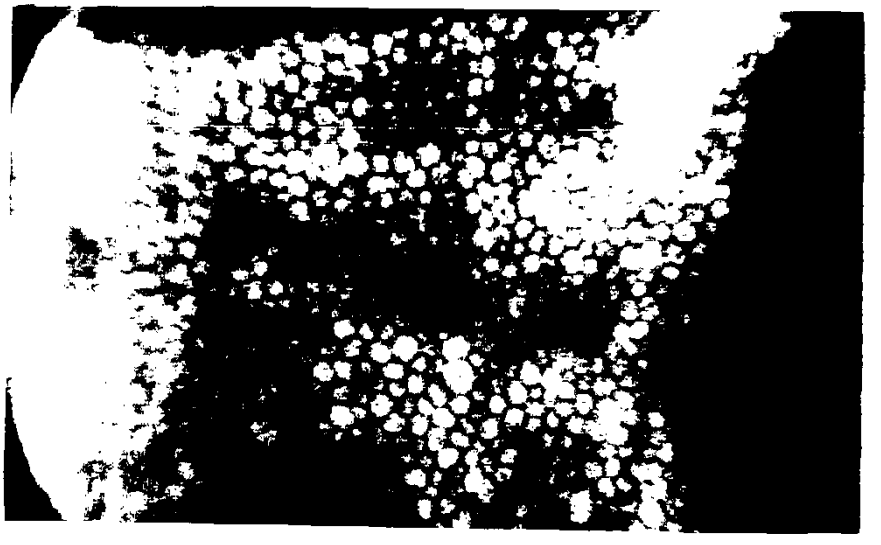

Fig. 1: Wide-angle specular microscopy showing normal endothelial mosaic [From: Dohlman (1983)].

**Physiology of the Corneal Endothelium**

In respect to the regulation of the corneal hydration, the endothelium has 2 types of functions.

*1. Barrier Function of the Endothelium*

The endothelium acts as a semipermeable membrane, creating a barrier to diffusion of electrolytes and to flow of water *(Doughman, 1985).*

The barrier function of the endothelium is calcium dependent. The junctions between the endothelial cells are dependent upon calcium ions for tight linkage. In their absence, the cells are separated by wide intercellular spaces that allow corneal swelling owing to the loss of the endothelial barrier *(Kaye et al., 1968).*

The breakdown of this barrier can also result from improper irrigating solutions, drugs, and trauma, which may lead to corneal oedema *(Edelhauser et al., 1985).*

*2. Pump Function of the Endothelium*

Experimental demonstration of a fluid transport ability clearly implicates the endothelium as the layer responsible for the active dehydration of the cornea *(Mishima and Kudo, 1967).*

The endothelial pump consists of enzymes in lateral plasma membrane that catalyze the movement of ions from the stroma to aqueous humour, creating an osmotic gradient that draws water out of the stroma. Bicarbonate may be the cation that is actively transported across the endothelium *(Hodson, 1971, 1977).*

The pump function can be inhibited with ouabain, a specific inhibitor of $Na^+/K^+$ ATPase. In this case the cornea will swell; however, the barrier function remains *(Mishima, 1982).*

Thus, as a continuous monolayer of closely apposed metabolically capable cells, the corneal endothelium is suited for its functions as a barrier to fluid flow and as an actively transporting ion pump *(Kenyon, 1983).*

**Clinical Evaluation of the Corneal Endothelium**

Until recently, evaluation of the corneal endothelium was limited to slit lamp biomicroscopic examination for guttata, folds or keratic precipitates. Such limited observation made it difficult to evaluate endothelial function and functional reserve, to predict the future course of a disease, or to determine the eye's ability to withstand surgery. It is also difficult by mere slit lamp examination to compare the relative merits of different surgical procedures or to diagnose drug toxicity in terms of endothelial damage. More recently, however, better techniques for in vivo evaluation of the endothelium have been introduced. These include specular microscopy, pachometry, and fluorophotometry. Endothelial morphology, pump function and permeability characteristics can be quantitated with these aids *(Dohlman, 1983).*

*Specular Microscopy*

Specular microscopy allows direct visual inspection of the endothelial cells in vivo *(Laing et al., 1975).*

Endothelial diseases can be followed quite accurately with specular microscopy. Thus, in early Fuchs' dystrophy, endothelial abnormalities and Descemet's membrane excrescenses can be diagnosed by specular microscopy before become visible by slit lamp observation. The guttate excrescenses are seen as irregular dark areas where the endothelial cell contours can not be distinguished *(Bigar et al., 1978).*

Similarly, larger or smaller keratic precipitates deposited on the endothelium can be readily observed by specular microscopy, and any gradual cell loss can be followed *(Roberts and Koester, 1981).*

Specular microscopy has its greatest value in determining the relative trauma to the endothelium resulting from various surgical procedures, particularly cataract extraction techniques, intraocular lens implantations, and penetrating keratoplasty *(Dohlman, 1983).*

Specular microscopy may also find routine use for in vitro evaluation of endothelial quality in donor tissue for keratoplasty *(Roberts et al., 1981).*

*Pachometry*

Corneal (or stromal) thickness can be measured with an optical device called a pachometer *(Mishima, 1968).*

Measuring corneal thickness is often a useful maneuver when subclinical oedema is suspected in the presence of guttata or after disease or surgery. The value of pachometry lies in estimating the functional reserve of the endothelium in a clear cornea. A reading close to 0.50 mm is reassuring for the future, whereas one around 0.70 mm means borderline decompensation and risk of imminent epithelial oedema *(Dohlman, 1983).*

*Slit Lamp Fluorophotometry*

It is a method of studying the barrier function of the corneal endothelium *(Waltman and Kaufman, 1970).*

This technique allows measurements of fluorescein exchange between cornea and aqueous humor and can be utilized to determine endothelial permeability *(Ota et al., 1974).*

The fluorescein can be injected intravenously and the diffusion across the endothelium can be followed. In this way it has been shown that patients

with guttata and some corneal thickness increase also have increased permeability to fluorescein, suggesting that in early Fuchs' dystrophy swelling is due to a breakdown of the barrier function rather than to a low endothelial pump rate *(Burns et al., 1981).*

This technique may prove to be a useful adjuvant in evaluating endothelial damage following intraocular surgery *(Raber and Yanoff, 1984).*

# PATHOGENESIS OF BULLOUS KERATOPATHY