SOME OF THE CORNEAL EFFECTS PRODUCED BY WEARING HYDROGEL CONTACT LENSES SOAKED IN A NON-ISOTONIC SALINE

by

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Study of some of the corneal effects produced by wearing hydrogel contact lenses soaked in a non-isotonic saline

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Summary

The corneal response to daily and extended wear hydrogel contact lenses was evaluated when the lenses were soaked in non-isotonic solutions varying from 0.7 to 1.2 percent.

The naturally occuring diurnal variations of the cornea were examined to discover what effect they may have on contact lens wear. It was noted that there were significant corneal hydration changes. Initially there was swelling of the cornea which subsided after four hours. There were no changes in the central anterior radius of the cornea.

No realtionship could be found between intraocular pressure and corneal hydration in different eyes. It appears that intraocular pressure is an independent parameter.

Animal work using rabbits was undertaken, using hypotonic solution and five hours of wear, this was done to ensure that the solution used would not cause irreversible damage to human eyes. It was already known from previous work that hypertonic solutions were safe. The animal study produced greater changes than had been expected so the human experiments were curtailed to three hours wearing time.

Corneal hydration changes were investigated in six male volunteers, using corneal thickness as a measure, so that the effects of the various tonicities of soaking solution could be established. It was found that slightly hypertonic solutions produced the least disturbance in corneal hydration, not normal saline as would have been expected.

To verify the results of the volunteer experiments five contact lens patients were supplied with both daily and extended wear hydrogel lenses which had been soaked and stored in an hypertonic solution. The lenses were worn for nineteen weeks after which time no changes could be detected in corneal hydration as measured by pachymetry; tonicity of the tears as measured by chloride ion titration; or in the corneal endothelium as observed by non-contact specular microscopy.

Key words
Central corneal thickness/ tear tonicity/ corneal endothelium/ non-isotonic saline/ contact lenses.

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$\mathring{A}$	=	$\mathring{A}$ngstrom
C.C.T.	=	Central corneal thickness
C.G.	=	Control group
Cl^-	=	Chloride ion
cm	=	Centimeter
C.S.G.	=	Chronic simple glaucoma
HCO_3^-	=	Bicarbonate ion
I.O.P.	=	Intraocular pressure
I.P.	=	Imbibation pressure
K.Rdg.H	=	Ophthalmometer reading horizontal
K.Rdg.V	=	Ophthalmometer reading vertical
λ	=	Wavelength of light
L.T.G.	=	Low tension glaucoma
ml	=	Millilitre
mm	=	Millimeter
mm Hg	=	Millimeters of Mercury
Na^+	=	Sodium ion
N.S.	=	Not significant
O_2	=	Oxygen
O.H.	=	Ocular hypertensive
R.E.M.	=	Rapid eye movement
S.D.	=	Standard deviation
Sec	=	Second
S.P.	=	Swelling pressure

CHAPTER 1

Introduction

Any contact lens is a foreign body to which the eye may produce rejection symtoms. The particular structures which are most likely to be affected are the eyelids, tears, conjunctiva, and cornea. The cornea is the only structure which may be efrected so as to cause physiological or pathological changes which would be severe enough to produce lasting visual damage. The cornea is responsible for seventy five percent of the refraction of the eye, and it is absolutely essential that it is maintained in a transparent condition.

Experienced contact lens fitters have known for many years that hard scleral and corneal contact lenses will produce both reversible and irreversible corneal changes. To a certain extent hard contact lenses have an inbuilt self limiting effect, because if they are worn too long they either become uncomfortable, or after removal of the lenses the patients vision is distorted due to corneal oedema, this means that it is relatively unusual for these lenses to be abused. Experience with all types of soft contact lenses would indicate that because of the initial comfort, these lenses do not have this advantage and they are frequently

overworn with subsequent complications.

Contact lens practitioners have been searching for an ideal solution to maintain the osmotic balance within the cornea for many years. In 1935 Obrig used many different tonicities of solution in order to try to reduce Ficks Phenomena, or corneal oedema, in patients wearing sealed scleral contact lenses (which were the lenses predominately being worn at that time). He achieved partial success only, this can probably be ascribed to the fact that as well as tonicity changes causing corneal oedema the anoxic condition of the stagnant tear pool would also have some effect, and as the length of time of wearing the lenses increased so would the oedema due to anoxia. Many of the problems such as Ficks Phenomena were reduced when scleral lenses were fitted as fenestrated rather than sealed; corneal lenses had an even greater effect on reducing corneal oedema, and its associated problems. Hydrogel contact lenses produce similar problems to those seen when fitting the old fashioned sealed scleral contact lenses. Why should this occur? Could it be that the hydrogel lenses have an insufficient oxygen permeability, or is the tonicity of the saline used for soaking and inserting the lenses sufficienty different to that of the tears and cornea to cause osmotic oedema. These two suggestions

are not new, the contact lens literature over the past few years has been full of articles on oxygen permeability and all contact lens fitters are well aware of Fatt's Dk value of oxygen permeability for hydrogel contact lenses. The importance of tonicity of contact lens solutions goes back many years, in 1827 Hershel advised the use of transparent gelatin for use with haptic lenses; in 1887 Fick suggested the use of two percent grape sugar. In 1892 Dor was the first person to suggest physiological saline. In 1922 Obrig suggested the use of 1.4 percent saline using a buffered solution this was found to give far better results when scleral lenses were worn than physiological saline (0.9 percent). By 1935 normal and half normal saline solutions were used exclusively in contact lens fitting, all sorts of other solutions have been tried including artificial blood filtrates, egg white, saliva, sea water, gum arabic in 0.6 percent saline, cerebrospinal fluid, castor oil, patient's own tears, sodium bicarbonate (Obrig 1935) none, however, seemed to give any great improvement over normal saline. It is easy to see with hind sight that the problems encountered in the 1930s with haptic contact lenses were possibly due to poor understanding of corneal physiology and the fitting techniques used, rather than the solutions that were being used to fill the contact lenses, being of the incorrect tonicity.

Why then in the 1980's is the author concerned with the tonicity of solutions when physiological saline has been relatively trouble free for fifty years? One of the main reasons why a practitioner will withdraw contact lenses from an established wearer is because of corneal oedema, and its attendant problems; could it be that by slightly changing the tonicity of the soaking solution that it may be possible to maintain a better osmotic balance within the cornea. It seems that where soft contact lenses are concerned because they are soaked in solution that the effect of the saline either directly or indirectly on the cornea is likely to be greater than the effect of the soaking solution on corneal lenses. Corneal lenses, now, are usually stored wet, and in this hydrated condition they contain two percent of the soaking solution; this is not readily exchanged with the tears. Any solutions that are used to clean, soak and wet corneal lenses are very quickly washed away by the involuntary tearing which is produced with the introduction of any foreign body into the eye. Soft contact lenses can be used as drug carriers to sustain release of drugs over a long period of time, and in fact the ocusert method of administration of ocular drugs is essentially a modified hydrophilic contact lens. The very fact that the lenses contain up to eighty percent solution means that there must be, at the very least, an exchange between the tears and the lens, if there are

tonicity differences there will be a tendency for the osmotic balance to be restored. It therefore, would not seem unreasonable to expect that soaking solutions of different tonicities will produce changes in the tears, or the cornea, or both and that lenses made from the same polymer combination, but with different water contents will produce proportional variations. It is necessary to have some idea of corneal anatomy and physiology before these effects can be adequately discussed.

CHAPTER 2

Anatomy and Physiology of the Cornea

Section 2.1 Structure of the Cornea

According to the Oxford English Dictionary the definition of cornea is from the medieval Latin meaning horny tissue or coating. It is the most anterior surface of the eye and has two main functions:-

(1) To act as a barrier membrane, which means that it has to be tough so that it can withstand the intraocular pressure and also mechanical trauma from the environment hence the definition of the name.

(2) It is the main refracting surface of the eye, therefore, it is essential that the membrane is transparent, smooth, curved and stable. The fact that the cornea is transparent makes it a unique membrane in the body, because it has to be avascular and yet capable of maintaining and regenerating itself.

According to Davson, Duke Elder, Mandell, Spooner, Wolff, and many other authors the cornea can be divided anatomically into two main sections:-

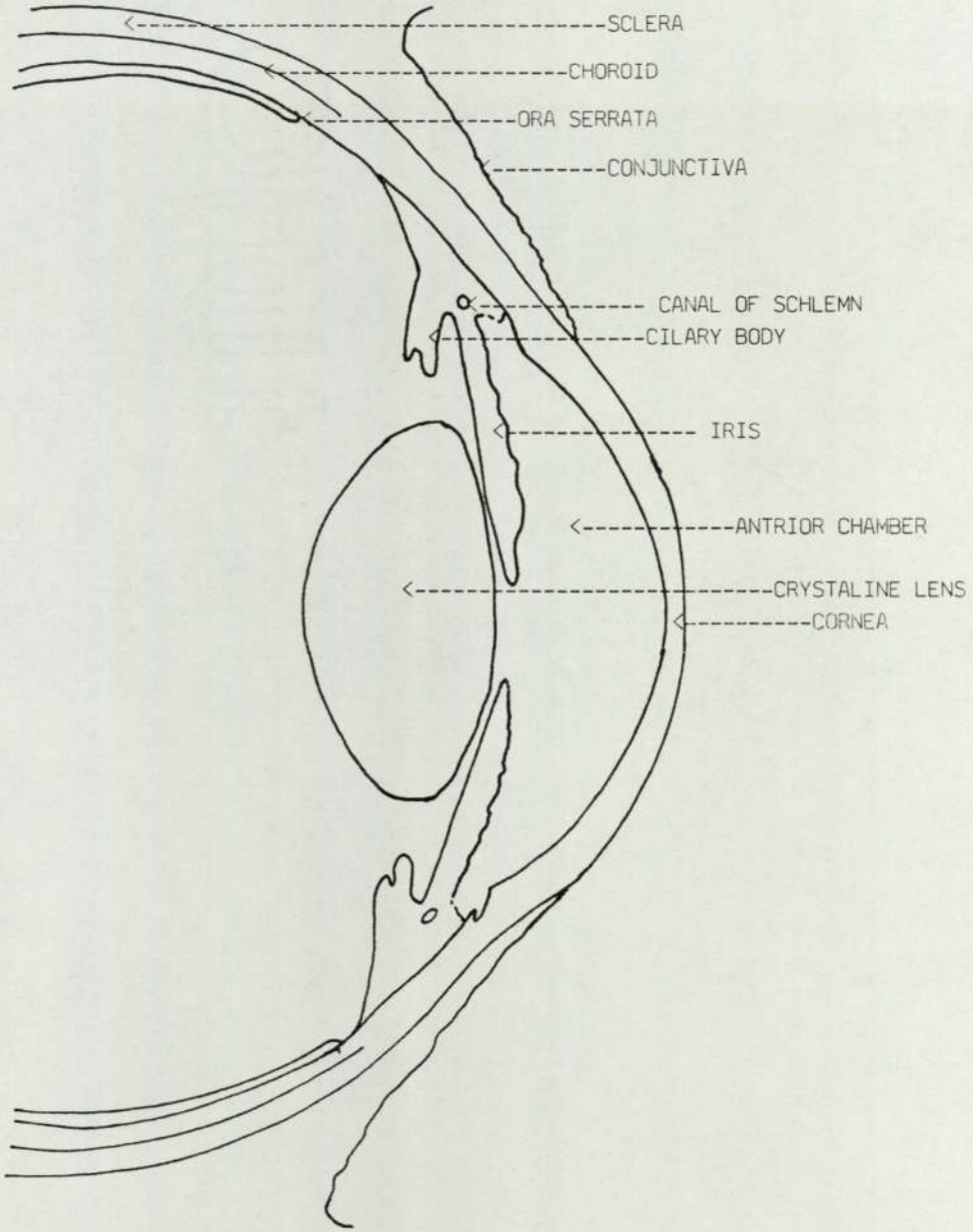
(1) The Cornea Proper

(2) The Limbus

The limbus is a zone approximately one millimeter wide.

Its histological structure is different from that of the cornea proper, also it contains blood vessels, and lymphatics which are not found in the normal cornea.

The cornea proper has classically been said to consist of five layers, but more recently most authors have described three layers, the epithelium, the stroma, and the endothelium. The layers of Bowman and Descemet have been ascribed to the stroma and endothelium respectively.



TRANSVERSE SECTION OF ANTERIOR HALF OF THE EYE(AFTER BOND)

Figure 2.1.

MICROSCOPIC STRUCTURE OF THE CORNEA (AFTER BOND)

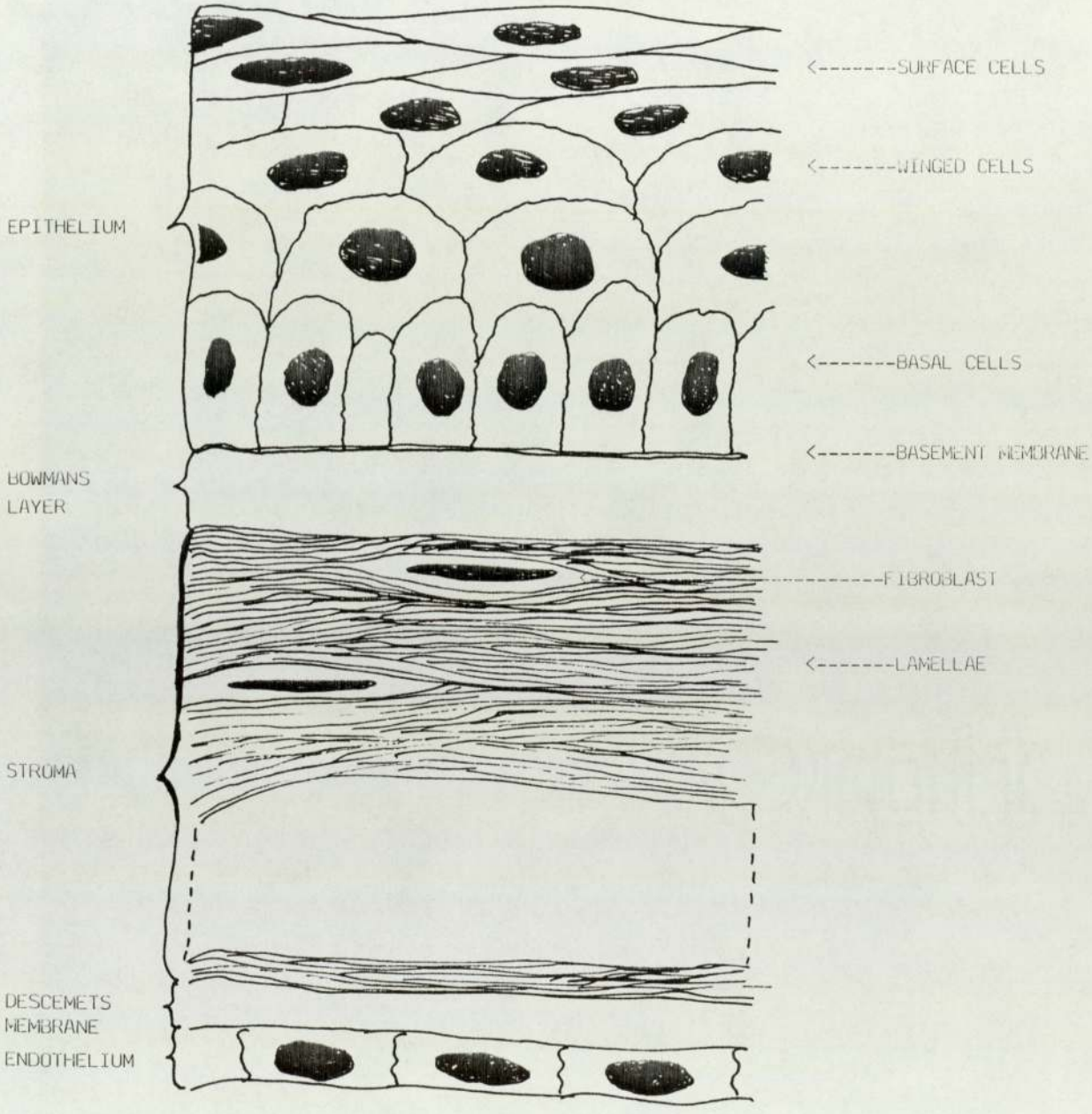


Figure 2.2

Section 2.2.

The Epithelium (Epithelium Anterius Corneae)

The outermost of the layers, the epithelium has a regular thickness (50 - 100 microns) in the adult eye, it becomes thicker, and folded at the point of attachment to the conjunctiva.

It is a specialised, modified, form of epithelium consisting of five or six layers of cells resting on a basement membrane.

The cells can be divided into three main groups, and are described according to their shape and position within the epithelium.

(1) Basal cells

(2) Winged cells

(3) Surface cells

The basal cells are collumnar in shape, with spherical nuclei which are displaced towards the head of the cell. Nearer to the surface of the cornea the cells gradually become much flatter until eventually they are winged shaped, and the nuclei become oval with the long axis

parallel to the corneal surface. On top of these cells there are two or three layers of surface squamous epithelial cells. The nuclei project inwards so that the surface layer is smooth. Unlike surface cells of the skin those of the cornea are not keratonised and retain their organells which indicate according to Ruskell (1980) that the metabolic processes are still functioning.

The outermost cellular surface is covered with fine projections which are similar to gut microvilli according to Jakus (1962) scanning electron microscopy has revealed in rabbit that the surface of the epithelium has mircoplica (ridges) as well as microvilli. It has been suggested that the microplica and microvilli enable better adherence of tears to the cornea, however, Ruskell (1980) has shown that contary to other opinion in primates these microvilli and microplica are absent at the apex of the cornea, therefore it seems unlikely that they form a tear cornea attachment. According to Kawabara (1970) the rabbit has microplica but no microvilli. Pfister (1973) has also shown by use of paired stereophotography that all animals have microvilli and that microplica were in fact microvilli that had been flattened into the underlying membrane. He could not demonstrate microplica in rat, cat, dog or rabbit. Pfister concluded that the presence of microvilli was probably to increase the surface area

of the membrane and therby enhancing the absorbtion of mucin. He suggested that additional mucin could be stored as a reserve between the microvilli in an unabsorbed form so that a continuous supply was available for the plasma membrane. The microscopically irregular corneal surface that the microvilli produce means that the cornea has a far greater potential for wettability than if it was completely smooth.

Hoffman (1972) has suggested that the different number and patterns of microplica in the rabbit cornea may be a means of classifying the difference between dark, medium, and light surface corneal epithelial cells. Pfister (1972) has shown by the use of ultra violet irradiation that the dark, medium, and light cells are not separate types, but one type of cell at different stages of growth the most immature being the lightest. He concluded that the dark cells were at a hypermature stage and were covered by a thin layer of mucin adsorbed during its surface life. as the surface ages it becomes very hydrophilic, thinner, and increases its surface area. As part of the pattern of exfoliation a normal dark cell develops a depression or elevation as the plasma membrane retracts lining the edge of the cell at the perimeter with insoluble cellular components. At the bottom is a new hydrophobic light cell with microvilli. Pfister (1973) suggests that

as the light cell is exposed to the tear film mucin is adsorbed by the microvilli. Gradually with age the hydrophobic cell becomes hydrophilic. He believes that the finding of thehole formation in surface epithelial cells is the first demonstration of localised lysis leading to cellular exfoliation, and further suggests that the hole may develop as part of a self generating process built into the genetic programme of cell life.

New cells are mainly generated by mitosis in the basal cell layer and also to some extent in the second layer according to Machemer (1966). The basal cells make room for new ones by migrating towards the surface where they are eventually sloughed off by the blink action of the eyelids.

Bertalanffy and Lau (1962) have shown that fourteen and a half percent of cells are renewed each day in rats which would indicate that complete epithelial regeneration would take place within seven days. This correlates well with Kikkawa's (1972) observation of an increase in corneal desquamation every four days in rabbit; and also with the work of Hanna et al (1961) who have shown by isotope study that the life expectancy of a human epithelial cell is seven days. According to Cardossa et al (1968) in rats there is a circadian rhythm, mitosis occuring most often at 07.00 hours and least frequently at 19.30 hours.

The disappearance of the ageing hydrophilic dark cells by formation of a hole occurs synchronously with gradual increasing wettability and maturity of the underlying surfacing immature hydrophobic light cells as the distribution of these dark cells with holes is random the influence of these hydrophobic areas is decreased so that the cornea will have an overall wettable surface. This randomness may explain the clinical finding of a variable tear break up time found in the general population. The corneal surface must possess unique properties to enable the maintenance of a stable tear film for optical purposes which is normally achieved despite surface cellular activity.

Engleman (1867) first described atypical corneal epithelial cells these have been observed and variously specified as Langerhans cells (Ribbert, 1878; Pau and Conrads , 1957) Polymorph elements (Schareberg; 1955), Basal layer branched cells (Whitear; 1960), Secretory cells (Teng 1961 and 1963), Polyganal cells (Seriura; 1965) and Dendritic cells (Segara; 1964). In man these have been identified at basal cell level and their processes are long and thin. Perera (1969) has questioned the existance of these cells attributing the dendritic appearance to a fixation artefact.

The epithelium is a strange membrane as it has a barrier function and yet allows a relatively free passage of

molecules. The permeability is not very selective any molecule small enough can be transported once it is through the corneal barrier this resistance is quite considerable. Maurice (1969) has estimated that it is equivalent to a layer of water one meter thick when the diffusion equilibrium is established across the epithelial layer.

Dohlman (1971) has suggested that the barrier activity of the epithelium is due to the close packing and interdigitation of the epithelial cells. This may be the reason why the stroma does not continually imbibe water. Eventually fluid will leak across the limbus, and corneal oedema becomes inevitable; unless there is a dehydrating mechanism within the cornea. He indicates that since the epithelium actively secretes salt into the stroma it is unlikely to have anything to do with the control of corneal thickness. In further support of this he showed that in humans if an artificial epithelium is glued peripherally to Bowmans layer the corneal thickness is maintained. There does not seem to be a concensus of opinion on whether the corneal epithelium is actively involved in corneal hydration control. Green (1966) suggested that there is a direct correlation between corneal thickness and the rate of inward sodium transport from the tear film into the stroma. In 1968 he stated that there was strong evidence to show that the corneal epithelium can reduce the

thickness of a swollen cornea by means of a transport system providing that there is some type of barrier in the endothelial surface. He found that a decrease in the epithelial transport system caused a decrease in the endothelial transport system which caused a decrease in the rate of sodium secreation into the stroma which causes changes in the mucopolysaccahrides which then take up the excess water in the presence of decreasing amounts of sodium thus producing the change in hydration. Green (1981) has shown conclusively that in man there is an active sodium chloride pump in the corneal epithelium although this is six or seven times less efficient, i.e. slower, than the endothelial pump. He has shown beyond doubt that there is an active transport of ions into the stroma and an active transport of chloride ions out of the stroma.

If this is the case it becomes very important for the contact lens practitioner, when a patient is fitted with a contact lens imbibed in a saline solution that has a different tonicity to that of the tears and the epithelium; then the epithelium will not be in equilibrium with the surrounding fliud and there is likely to be a change in corneal hydration. Prior to the work of Green, Potts and Mandrell (1957) found a small transcorneal potential which they attributed to the epithelium; this also implied

an active transport of sodium across the epithelium rather than or as well as the endothelium.

Several reasons have been put forward for the cause of epithelial oedema. According to Cogan (1940) fluid accumulates in the epithelium, because of absorption of tear fluid. Dohlman (1965) has suggested that fluids from the aqueous humour, and the stroma are pushed forward into the epithelium by the force of the intra ocular pressure, this would only occur if the endothelium was not functioning and the intra ocular pressure was normal or conversley if the endothelium was normal and the intra ocular pressure raised. Dohlman found in a survey of ninety patients that the majority who had epithelial oedema also had a positive imbibation pressure. That is the stromal pressure was positive to the epithelium not negative as in the normal cornea this causes a flow of fluid across the cornea and into the epithelium. He concluded that the epithelial oedema was caused by raised intra ocular pressure and its own impermeability to the electrolytes. Pfister (1977) in an anatomical study of epithelial oedema found that in all specimens the epithelial surface was very irregular. This parallels the clinical situation seen with the slit lamp microscope, and the mire distortion seen with the ophthalmometer. He suggested that this irregularity is produced by detached epithelial

cells lying on the surface, the oedematous cells bulging forwards, again, this explains the clinical findings of steeper ophthalmometer readings in patients with corneal oedema. He also found greater spaces between the cells, and finally he found rounded shallow depressions having variable diameters up to that of a surface cell. Usually the surface cells were covered with the normal number of microprojections. Again, this explains the clinical appearance of the ' ground glass ' cornea when it is oedematous.

Section 2.3.

Stroma (Substantia Propria Cornea) and Bowmans Layer (Laminar Limitans Anterior)

Section 2.3. i. Bowmans Layer

Bowmans membrane was described by the English anatomist Sir William Bowman (1847) as the anterior elastic membrane. This was not a particularly good name since it has subsequently been shown that this layer does not consist of elastic tissue but should be considered as a modified superficial layer of the stroma. Teng (1962) has shown using an electron microscope that this thin (approximately 12 microns) apparently structureless, transparent, layer contains a very fine randomely orientated fibre network the elements of which are similar to collagen fibres found in the stroma. This layer is very tough, and resistant to injury, but once damaged it is never renewed, but is replaced by fibrous tissue.
Over the whole of its area the layer is penetrated by fine unmyelinated nerve fibres which pass from the stroma to the epithelial cells.

Section 2.3.ii Stroma

The stroma is ninety percent of the total thickness of the cornea approximately 480 microns. It provides the structural support consisting of fibroblasts, macrophages collagen fibres, and matrix. The collagen fibres are arranged in bundles which appear with the light microscope as alternating lamellae lying parallel to the corneal surface. Water forms the main bulk of the cornea approximately eighty percent, and the chief solid constituent is collagen, fifteen percent, this is found in the fibrous stromal lamellae which are continuous with those of the sclera. According to Ruskell (1980) the lamellae probably extend uninterupted across the cornea without changing direction laterally. Most of the lamellae are of similar thickness and lie parallel to one another like the pages of a book. The fibres which are buried in the mucoid matrix have an angled orientation in adjacent lamellae. Kokott (1938), Jakus (1961), and Polock (1961) have all shown that towards the periphery of the cornea the lamellae are concentric with the limbus and are responsible for increasing the thickness in this area. In this region there is some interweaving of the lamellae, but the fibrils remain parallel to one another.

The other cells which are found throughout the stroma are mainly modified fibroblasts (keratocytes, or fixed cells)

CHEMICAL COMPOSITION OF THE STROMA

Water	78%
Collagen	15%
Other Proteins	5%
Mucopolysaccharides	1%
Salts	1%
Total	100%

After Fatt 1978

these are not found in Bowmans layer. There is some disagreement between authors as to whether these cells lie inside or outside the lamellae. Jakus (1954), Smelser and Ozanics (1965), say that the cells lie within the lamellae, whilst McTighe (1965) states that they are outside. Goldman (1968). indicates that in the irregular anterior layer the cells lie within the lamellae, whilst in the more regular posterior layer the cells lie between the lamellae. These cells have fine long processes which connect with processes from similar cells at the same level thus giving the impression of continuity of all junctions according to Jakus (1964). Ruskell (1980) has stated that the cell is disposed at the interface between lamellae. In a single interface the cell bodies are well spaced across the cornea, however the thin long processes are so extensive that many come into contact with processes from neighbouring cells giving the appearance of a delicate wide lace pattern, also there may be more than one nucleus present. According to Klintworth (1969) the fibrocytes of the cornea are execptional in displaying a phagocytic function.

If there were no difference in the refractive index of the collagen fibres and the ground matrix of the stroma then it would automatically be tranparent. All the available evidence indicates that this is not the case, and

therefore, each fibril is capable of scattering light in all directions. The theories of corneal transparency will be discussed more fully in section 2.5.

Maurice (1951) states that the stroma is about four times more resistant to sodium penetration than the epithelium. It is therefore conceivable that the stroma could be the site of metabolic change. By 1969 Maurice thought that this was unlikely because it would be unreasonable to assume that the stroma could move fluid out by its own action unless there were internal forces within the tissue which could excrete the fluid.

Green (1960) suggested that there could be a connection with the binding of cations onto the acid mucoplysaccharides in the stroma, and an active pump mechanism, which could control the number of ions available, and therefore act as a dehydrating mechanism. In 1969 Green described a seemingly detrimental net transport of sodium and water across the epithelium into the stroma. He postulated that this was due to the sodium ion concentration within the stroma, but has subsequently proved that this is not the case and now thinks that the epithelium and endothelium are the major sites for corneal hydration control (Green; 1982)

Section 2.4.

Endothelium (Endothelium Camerae Anteriors) and Descemets Membrane (Lamina Limitans Posterior)

Section 2.4.i. Descemets Membrane

When examined by light microscopy this layer appears to be an homogeneous, structureless layer approximately five to seven microns thick, about half the thickness of Bowmans layer. The thickness increases towards the limbus and in old age to between ten and thirty microns. It would appear to be the basement membrane of the endothelium, Jakus (1964) observed with the electron microscope that anteriorly the layer consisted of a fine, regular, two dimensional hexagonal lace pattern. Posteriorly the pattern becomes disorganised and has a fine granular appearance. It is the last structure in the cornea to succomb to inflammation and does have some elastic properties.

Section 2.4.ii Endothelium

The deepest layer of the cornea the endothelium acts as a barrier between the aqueous humour and the stroma, and controls interchange between the two. It consists of a single layer of flattened epithelial like cells, which form an hexagonal mosaic presenting a smooth surface to the anterior chamber. In tangentional section the cell borders are ill defined, according to Ruskell (1980) this is because of the oblique cell interfaces, and the interdigitation of broad processes of adjacent cells. The nucleus is oval or kidney shaped and the cytoplasm has a granular appearance; by electron microscopy the endothelial cells all show features of having a very active metabolism, that is, large numbers of mitrochondria, granules, vessels, well defined golgi body,and endoplasmic reticulum. Iwato and Smelser (1965) have described terminal bars (now known as zonula ocludentes) near the posterior border, which they postulated restrict movement in and out of the cornea. Shanthaverrappa and Bourne (1963) have described pores in the intracellular spaces of the endothelium between half and two microns in diameter which appear black with the light microscope. They suggested that these are responsible for the nutrition of the cornea from the aqueous humour possibly by pinocytosis. Otterson and Verge (1977) studied the intercellular junctions of the endothelium and observed gap junctions or

nexuses in monkey and man corneal endothelium have also been shown in rats, (Luxenberger; 1973), and rabbits (Kaye; 1973). They also observed tight junctions as described by Iwamata and Smelser (1965) and by Hogan and Alvarado (1969). They concluded that the human endothelium is encircled by an incomplete zonula ocludentes and speculated that these particular patterns have a similar function to that described by McNutt and Weinstein (1973) for epithelium. It is suggested that the junction acts as a site of communication for large molecules and ions. Stocker (1953) stated that although the regenerative power of corneal endothelium in rabbit is greater than in man the rabbit can be used as a human model. Peter (1889), Nagano (1914), Fuchs (1917), Stocker (1953), Fuchs (1953), Binder and Binder (1957), Heydenreich (1958), Chi, Teng and Katzin (1960), have all described the effect of injury or disease as the vacuolation of the cytoplasm or the nucleus, contraction of the nucleus, and shrinkage of the endothelial cells, granulation of the cytoplasm, and disappearance of the intercellular cement substance. Defects of the endothelial layer heal by migration of the adjacent cells into the area, and by multiplication and regeneration of the cells. Van Horn et al (1977) found in a study of rabbit and cat endothelium that in the wounded endothelium of rabbit extensive cellular division occured in the healing process

and the corneal thickness returned to normal within four to thirty days. Whereas in cat the endothelial cells became enlarged and spread over the injured area the cells remain enlarged and irregular for up to one month following the original injury, corneal thickness remaining elevated for the same length of time. They concluded that the cat is more similar to man than rabbit in this respect.

Laing et al (1976) have also reported that in man the individual cell area doubles with age; Bourne and Kaufman (1976) found a thirty five to seventy percent decrease in endothelial cells per millimeter one week after cataract extraction. Ridgway personal communication (1980) suggests that this is due to the folding of the endothelium during operation. Blatt et al (1979) have divided the corneal endothelium into two types:-

(i) Homomegethos - that is those endothelium which have one cell size, and in these cases the cell count decreases with age.

(ii) Polymegethos - that is those endothelium which have cells of different sizes, in these types the cell count does not decrease with age.

Laing et al (1976) have indicated that there is an increase in polmegethism with age and a decrease in cell count this is in disagreement with Blatt et al (1979)

who have suggested that there is a great variation in central cell density with the polymegethous type compared with the homomegethous group, but no absolute decrease in numbers. Rao et al (1979) have shown that there is a difference in healing rates with the different types of endothelium. They described a series of patients who had undergone cataract surgery; in the group of polymegethous endothelium the mean increase in corneal thickness four weeks post operatively was eighteen percent, whereas in sixty five percent of the homomegethous group the cornea had returned to normal thickness four weeks post operatively. They did not find any one segment of the cornea where the cells were significantly different in size, however, Ridgway (1980) has observed that in man the superior cells in the endothelium are larger than those inferiorly. The work of Rao et al (1979) would tend to suggest that there is no sharp cut off between the homomegethous and the polymegethous type of endothelium but that there is in fact a continuum. Kaufman, capella and Robbins (1966) and Capella and Kaufman (1969) have shown that as the cornea grows during childhood cell density decreases by half, and gradually the cells become larger until the eye reaches maturity, when the endothelium has uniform hexagonal cells in old age the corneal endothelium shows polmegethism and the endothelium is a mixture of enormous as well as small cells.

Thus it has been established that injury and old age do have an effect on the corneal endothelium, but the exact nature still has to be established.

It would seem therefore that a contact lens may also have some effect on the endothelium, however, Guillon (1980) has shown that there is no significant difference between wearing a variety of contact lenses compared to a control group of non- wearers. Zantos and Holden (1977) have described changes in appearance of the corneal endothelial mosaic in patients wearing both hard corneal contact lenses and hydrogel contact lenses. They suggested that the changes were due to an increased separation between the cells and also circumscribed black zones obscuring or displacing the mosaic. Sherrard (1978) concluded that although different types of affection have been seen within the endothelial cells by use of the specular microscope, there are in fact only two ways that the cells can be affected either due to intracellular vacuoles or due to cell rupture.

The endothelial layer is thought to have similar barrier properties to that of the epithelium. According to Stanley, Mishima and Klyce (1966) , and Stanley (1972) the endothelium is not just a barrier to maintenance of normal corneal thickness, but may contain a pumping mechanism for

corneal hydration. He suggests that damage to the corneal pump may be the cause of oedema, although he found no active ionic transport in the endothelium to account for this pump.

After considering all the possible sites for a metabolic pump in the cornea Maurice (1969) concluded that it must be in the endothelial layer simply by exclusion of all the other positions which could be used. He also suggested that the stroma exchanged fluids exclusively with the aqueous humour, because the endothelial layer is much less resistant than the epithelium. He postulated that this exchange was probably through a system of pores, which is most likely to be through the endothelial vacuoles. The endothelium is a strange membrane because it appears to have a dual function, from the available evidence Hodson (1971) concluded that it pumped water out by a metabolic action and yet simultaneously leaked water back into the stroma. He further explains (1971[2] and 1975) that the control of stromal hydration which resides in the endothelium is in essence a sodium bicarbonate pump coupled to water movement. This fliud movement which dehydrates the stroma to physiological thickness represents an equilibrium between the sodium bicarbonate pump and sodium bicarbonate leak this

ionic equilibrium is reflected in water equilibrium.

Green (1982) has shown conclusively that there is an active transport of bicarbonate ions, sodium ions and chloride ions at the endothelium, and that this active transport in conjunction with that of the epithelium is the method of hydration control. There must be another positive ion which acts to control corneal hydration otherwise the system would be totally out of control. So far this ion has not been isolated Green postulated that this may be a protan, but as yet this has not been proven.

CORNEAL HYDRATION CONTROL AFTER GREEN 1982

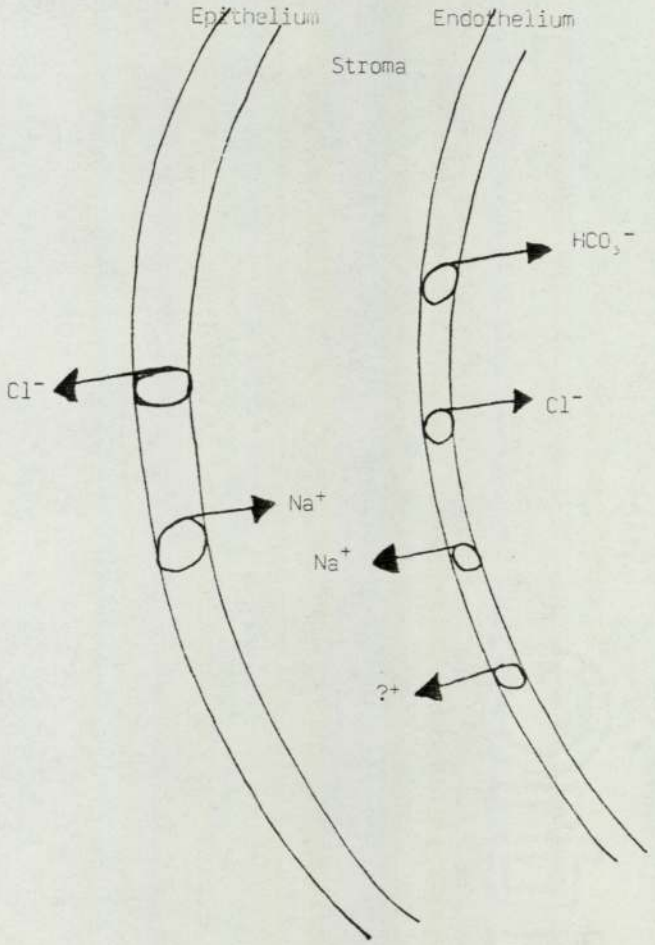


Figure 2.3

Section 2.5.

Corneal Transparency

If the contact lens eye combination is to maintain its optical function then it is important that the cornea remains clear. The main contributors to corneal transparency are:-

(1) The regular arrangement of all of the corneal components particularly those of the stroma as this makes up the bulk of the cornea.

(2) The integrity of all of the components within the cornea.

(3) The stromal structure which retains the embryonic state of the collagen fibres and mucoid matrix.

(4) Bowmans and Descemets membranes with their homogeneous properties, and high degree of resisitance to injury plus their transparency.

Any situation which alters any one or any combination of these features could result in some loss of transparency. It has been known since 1684 when Van Lurwenhock immersed

the isolated cornea in water that it will swell and this causes significant loss of transparency. In water it increases five and a half times in weight after eight hours and its water concentration increases from seventy eight percent to ninety eight percent by weight, with this degree of hydration the cornea looks like a coagulated piece of egg white. Thus it is the matrix which swells and not the collagen fibres.

Although the cornea is not perfectly transparent it will transmit approximately ninety percent of incident light, corneal hydration changes appear to alter the spectral transmission of the stroma; according to Kinsey (1948) under normal circumstances the ultra violet and wavelengths shorter than 3100 Å are all absorbed by the stroma. At the infra red end of the spectrum, the absorbtion curve of the cornea is similar to that of water approximately two thirds is absorbed according to Kenshalo (1960) ; Boether and Worter (1962). Payrau et al (1967) have shown that in beef corneae which have been immersed in water for twenty minutes there is a differential reduction of transmission for different wavelengths of light from 3100Å there is a reduction of transmission of fifteen percent for 4100 Å the reduction is thirty five percent whereas for 7100 Å the reduction is only twenty percent. This would indicate why a 'rainbow' effect is seen by a patient

suffering from corneal oedema. Maurice (1969) has shown that there is a small scattering of light in the stroma which he thought was due to discrete elements of the stromal cells and their nuclei. Much of the light is scattered in a forward direction which again could be a potential explanation of the 'halo' appearance round lights which is enhanced with stromal swelling. The fact that the stroma scatters light is used to advantage in the clinical situation, because this is why it is possible to distinguish the stromal layer of the cornea when using a slit lamp biomicroscope to view the in vivo human cornea. Zucker (1966) has shown that moderate stromal swelling has little effect on corneal transparency a seventy per-cent increase in stromal thickness reduces visual acuity by twenty three percent that is equivalent to a change from 6/6 to 6/9 further increases in thickness had a very much more marked effect on vision, therefore it would seem that the stromal thickness can be increased by three quaters before any marked change in acuity is noticed, this is equivalent to a total increase in corneal thickness of sixty three percent, which is rarely seen clinically, if it is assumed that the average corneal thickness is 0.5 mm then a sixty three percent increase would mean a thickness of 0.83mm which is only observed in frankly pathological eyes. It is more usual in the experience of the writer to see oedema of the epithelium, and certainly a relatively

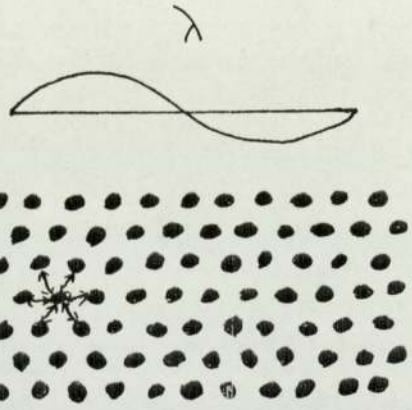
small epithelial disturbance would seem to cause a disturbance of vision a typical example is after wearing hard corneal contact lenses when the epithelial disturbance is only just visible by slit lamp biomicroscopy examination and yet the subjective acuity can be markedly reduced. This is particularly noticeable if the disturbance is in a clearly defined central zone of the cornea, it is assumed that this is due to scattering of light similar to the effect seen when looking through a chavasse glass. If the oedema is over the complete diameter of the epithelium then the subjective visual disturbance seems to be less marked; this is one of the reasons why hydrogel contact lenses can be worn to the detriment of the cornea without the patient realising the problem.

By far the simplest explanation of corneal transparency is that of equal refractive indices of the corneal components, for many years this was thought to be the case. In 1881 Ranvier suggested that the refractive indices of the ground substance and the matrix were different, but because the differences were so small the refraction between the two was reduced. Cogan and Kinsey (1942 [2]) suggested that the reason was because the interstitial fliud was kept to a minimum. Schwarz (1953) and Davson (1955) suggested that the function of the mucopolysaccharides was to raise the refractive index of the

ground substance to that of the collagen. Maurice (1969) measured the refractive index of the dried collagen material to be 1.55 and calculated that the refractive index of the ground substance (mucoid) to be 1.345 roughly the same as water. He postulated that in fresh tissue the collagen is unlikely to maintain the same refractive index as a certain amount of water will be absorbed and the diameter of the fibrils will be increased thus the refractive index could be expected to approach that of the mucoid substance. However, at the same time the ground substance will inevitably loose some of its water and thus the refractive index will approach that of the collagen fibres. He calculated that for the two refractive indices to be equal the fibrils would have to increase their diameter by four and a half times. This just does not happen as has been proved by examination of the stroma by electron microscopy, if it did occur then there would be no space between the fibrils, and it is known that molecules as large as fluorescein and heamaglobin can diffuse across the stroma as this has been observed by slit lamp biomicroscopy examination in the clinical situation. Maurice (1953) then described the lattice theory of corneal transparency, which has ever since seemed to be the most plausible explanation of this phenomenon. He postulated that the reason for corneal transparency was because of the spacing of the stromal lamellae. It

has been known since His (1856) that the stromal lamellae are doubly refracting and the direction of the optic axis is in the direction of the fibres that is the stroma has an optic axis perpendicular to the cornea. The electron microscope has subsequently shown that the stromal lamellae are made up of straight parallel collagen fibres. Maurice (1969) has shown experimentally by observing the diffusion rate of heamaglobin through the cornea that the stromal diffusion system is limited by the structural system which becomes more open as the tissue swells. He concluded that as the swelling takes place in the interstitial spaces which in turn leads to a separation of the fibrils then these fibrils are responsible for limiting diffusion. He also showed that the diffusion of sodium ions through the stroma was five to six times less than in a free solution therefore the ground substance plays a part in resisting diffusion it is not solely a question of fibril spacing. Maurice (1969) calculated that the light scatter produced by a structure with the anatomical properties of the stroma would theoretically scatter most of the light falling on it and thus be opaque. Maurice showed that the two cases of corneal clouding, that produced by corneal swelling, and that produced by raised intraocular pressure could be explained by his lattice theory. He stated that the stromal fibres are spaced

FIBRIL PATTERN FOR CORNEAL TRANSPARENCY AFTER MAURICE 1957



Fibril lattice diagram representing a section of fibrils arranged in a lattice providing a basis for transparency.

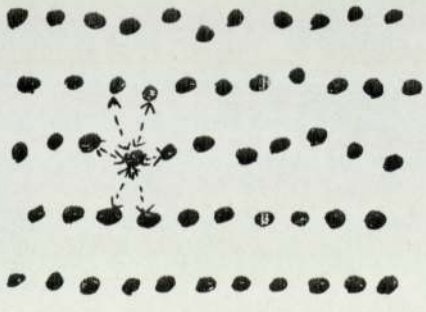


Diagram representing the separation of the rows of fibrils in the swollen cornea, their dearrangement being the result of the weakening of the forces of alignment and consequently the loss of transparency of the stroma.

Figure 2.5

in a regular order within the lamellae, and act as a diffraction grating, thus the individual scattered waves of light show distructive interference, except that of the incident beam. The scattered light being projected entirely in the direction of the incident beam and therefore the tissue appears transparent. He then suggested that the regular arrangement must be three dimensional because if the regular distribution of the fibres was only in one direction the tissue would reflect a fraction of the light falling on it in any direction of the regular tissue arrangement. Maurice stated that if the cornea is to remain transparent then in this fibre arrangement of the lattice the fibrils must be parallel and equal in diameter. Hart and Farrell (1969 and 1971) have shown by further electron micrographs that the collagen fibres do not conform to a perfect lattice, but, nonetheless the spacing is regular enough, and all that is necessary is for the spacing to be equal (not an exact lattice pattern) and less than a wavelength of light. They found that the spacing between the centre of one fibre and the centre of the next is 600 Å, and as the average fibre diameter is 300 Å this gives a spacing of 300 Å, which is considerably less than the wavelength of the visible spectrum.

Maurice (1972) also noted that all the swelling takes place in the ground substance not in the collagen fibres.

He indicated that the cornea will swell for two reasons:-

(1) Changes in osmosis

(2) Changes of a mechanical nature

or a combination of both.

Theile and Jaraschky (1966) have shown that the loss of transparency is due to droplets of water being trapped between the intrafibrillar spaces, however this has not been observed by any other author nor has it been seen clinically.

The tendancy for the corneal stroma to swell results from pressure exerted against Descemets membrane and the endothelium. In humans Dohlman (1960) has measured this pressure to be 50 - 80 mm Hg. The swelling pressure is reduced when the cornea swells as this swelling pressure is dependent upon hydration, and this can be correlated to corneal thickness as it has been well established that corneal hydration and thickness have a constant relationship. In humans Zucker (1966) has shown that :-

$$H = 7.0q - 0.64$$

where H = hydration water weight per dry weight and q = thickness in millimeters

Since the stroma is approxomately eighty percent by volume of the cornea it is the main structure concerned with transparency. The greatest changes in transparency occur with variation in water content, and this has to be regulated very carefully, because when there is excessive swelling inevitably clouding of the cornea will occur. The water is contained within very fine fibrils that make up the ribbons of connective tissue. This arrangement is very easily disturbed by such features as trauma, vascularisation and inflammation.

In the normal situation the cornea is kept in a relatively deturgesed state, the amount of dehydration is controlled by the metabolic activity of the cornea.

When an excised piece of stroma is immersed in water it undergoes swelling, Ehlers (1966) has shown that the excised human stroma will absorb fluid up to two and a half times its dry weight; to the point where the stroma takes on the appearance of the white of a boiled egg.

The cornea is bathed by fluids on both sides, therefore, there must be forces exerted which keep the cornea in equilibrium. The external force drawing fluid into the cornea in this way is called the swelling pressure. According to Fatt (1978) this force can be measured by

placing a piece of tissue between two porous plates the upper plate being weighted and the complete sample being immersed in a water bath. When the outward force from the stroma is balanced by the external pressure applied through the weighted porous block the stroma reverts to its original dimensions, that is being neither thinner nor thicker than the original sample. Fatt concluded that the inter fibrillar mucopolysaccharides are the main source of the outwardly directed force. He also supported this by observing that when cetyl pyridium chloride (which is known to precipitate mucopolysaccharides) is applied to the stroma the tissue collapses. Bert and Fatt (1970) have further shown that the collagen in swelling is essentially perpendicular to the surface of the collagen fibres. Under free swelling conditions they state that the stroma will swell up to thirty times its normal thickness.

Hedbys and Dohlman (1963) have shown that the swelling pressure hydration relationship for the stroma appears to be similar for man. rabbit and stear, and also the relationship remains almost constant with solutions of very different tonicities; they used ten and one percent saline and water. This indicates that swelling pressure is not just a simple osmotic process.

When the stromal disc is in a situation of equilibrium

the mechanical load and the swelling pressure are equal. If the load is increased the stromal specimen will attenuate, due to a loss of water, and conversely if the load is decreased the stroma will swell, due to the uptake of water; this produces a negative pressure inside the sample which is known as the imbibation pressure and is equal and opposite to the swelling pressure.

The swelling of the stroma is almost entirely due to the increased separation of the fibrils and lamellae, which lie parallel to the surface. If the lamellae and fibres were less well organised then obviously the swelling would not be solely in one direction; it is this well organised lattice that contributes to the swelling thickness relationship.

Section 2.6

Oxygen Utilization of the Cornea.

Whatever type of mechanism is involved with maintaining a normal corneal thickness metabolic energy is essential.

The metabolism of the cornea is maintained by both aerobic and anaerobic glycolysis. Aerobic glycolysis consists of a breakdown of glucose to lactic acid and then a further oxidation of the lactic acid to carbon dioxide and water. This action occurs mainly in the limiting membranes, because the two main supply routes of oxygen to the cornea are the atmosphere and the aqueous humour. Anerobic glycolysis which is the breakdown of glucose to lactic acid occurs mainly in the stroma probably because this layer has no direct access to oxygen.

Since the late nineteenth century, when contact lenses were first worn, it has been known that they cause ' veiling ' of the cornea, however it was not until 1946 that Josef Dallos postulated that this effect was caused by corneal oedema possibly due to oxygen starvation of the epithelial surface. It was another twenty years before Hill and Fatt (1963) reported the use of a polarographic oxygen sensor to monitor the depletion of oxygen from the air trapped under a scleral contact lens.

This method of measuring oxygen tension was not suitable for clinical use. Hill and Fatt subsequently (1964) simplified their technique and used an oxygen sensor covered by a thin polythene membrane, when this sensor is held against the cornea the oxygen is depleted in about one minute. Unfortunately although a simpler technique it is not as accurate as the original method and can only be used for comparison of oxygen uptake rates.

The work of Hill and Fatt and coworkers has greatly increased the understanding of oxygen consumption by the cornea; they have stated that the cornea breathes solely across its surface; Fatt and Bieber (1968) have further shown that approximately one tenth of the oxygen flux across the epithelial surface reaches the anterior chamber via the endothelium.

In the closed eye situation the air is replaced by the capillaries in the palpebral conjunctiva, the oxygen tension is therefore decreased at the epithelial surface to being the same as at the endothelial surface that is 55 mm Hg.

There is a great deal of difference between the hydrogel contact lens, and the corneal contact lens wearer as far

as oxygen requirements are concerned. In the later case because the lens moves with each blink, when fitted correctly, there is a continuing replenishing of the oxygen supply to the cornea, dissolved in the tears, thus allowing reoxygenation and aerobic glycolysis. In the former case the lens does not move in the same way, and the cornea remains covered for the majority of the time that the lens is being worn. For practical purposes it has been shown by Hill (1967) that there is a specific thickness and water content which will allow sufficient oxygen depression for adequate corneal respiration. In the daily wear open eye situation the average thickness for a seventy percent water content lens is 0.47millimeters, however, in the closed eye, extended wear condition the maximum average thickness is 0.14 millimeters; if the water content is reduced to forty percent then for the daily wear lens the average thickness must not exceed 0.13 millimeters, and in the closed eye, extended wear situation the maximum average thickness is 0.04 millimeters. It can therefore be seen that the new, thinner, high water content hydrogel contact lenses, if fitted correctly, will theoretically allow sufficient oxygen for aerobic glycolysis to take place.

Miashima, Kaye, Takahashi, Kudo, and Trenberth (1969) have shown that if the oxygen supply to the epithelium

is withdrawn then there is only oedema of the epithelium, thus they concluded that the endothelium is the critical membrane which causes corneal swelling.

CHAPTER 3

ANATOMY OF THE PRECORNEAL TEAR FILM

Section 3.1 Uses of Tears

The tears which are essentially the secretion of the lacrimal gland have six main functions:-

(1) To maintain the optical surface of the eye.

(2) To act as a wetting agent.

(3) To protect the eye.

(4) To collect and remove waste products.

(5) To provide some nutrition for the cornea.

(6) To supply the epithelium with atmospheric oxygen dissolved in the tears.

The precorneal tear film has been classically described as consisting of three layers by Wolff (1946). Holly et al (1973) have subsequently shown that there are essentially

four layers; the middle aqueous layer being divided into two sections.

(1) Superficial lipid layer.

(2) Aqueous phase dilute mucin layer

(3) Aqueous phase mucin layer

(4) Mucoid layer.

STRUCTURE OF THE TEAR FILM AFTER HOLLY 1973

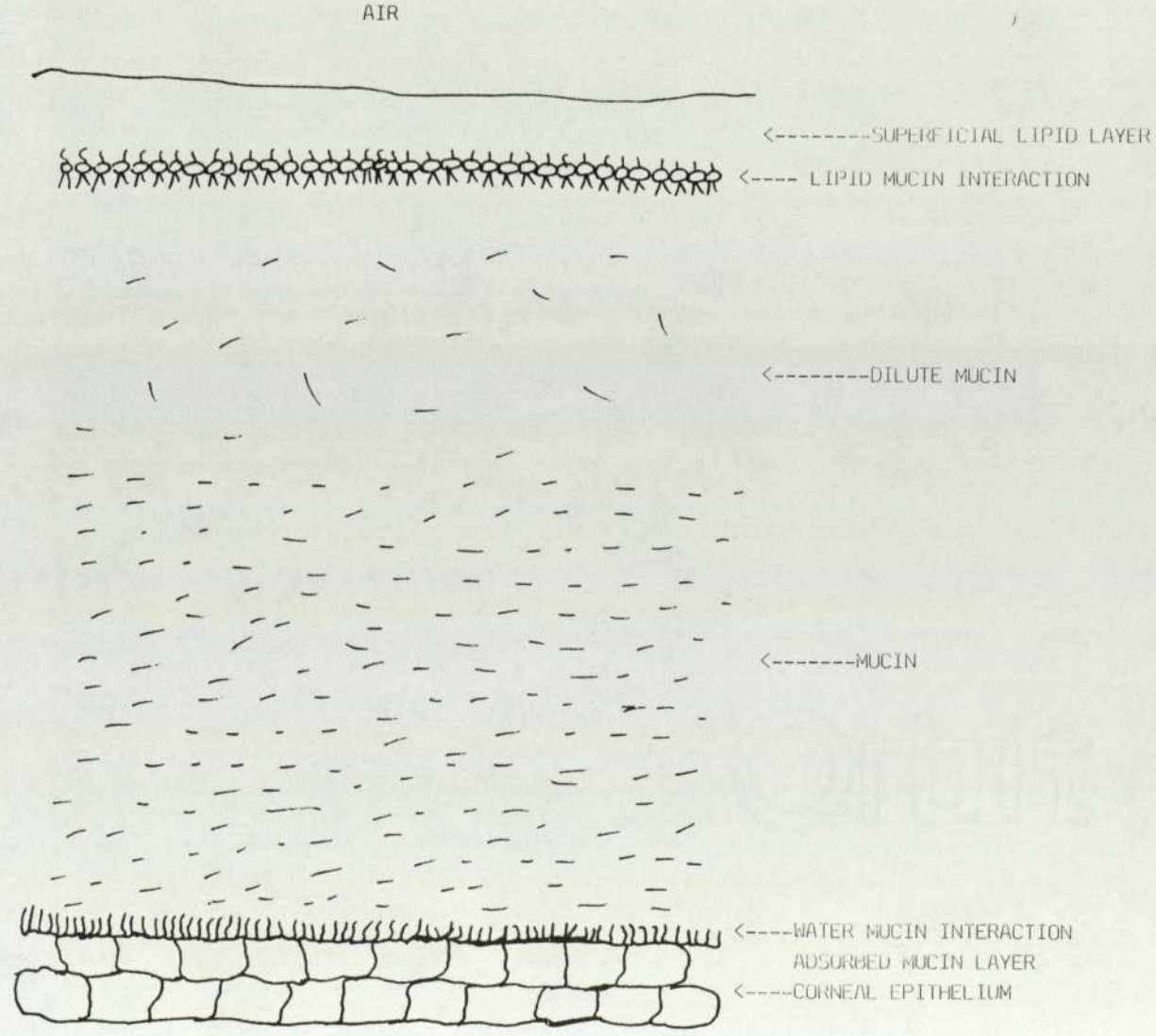


Figure 3.1

Section 3.2.

The superficial lipid layer.

Lipids are compounds which are insoluble in water, but soluble in fat solvents. They include simple lipids (waxes, true fats) made up of alcohol and free fatty acids and compound lipids (phospolipids, glycolipids) made up of simple lipids with additional elements.

Wolff (1946) observed the precorneal tear film by using the slit lamp biomicroscope and suggested that this outermost layer was essentially oily, and he postulated that it originated from the meibomian glands of the eyelids. Ehlers in 1965 using chemical methods also concluded that the outermost layer was oily in nature being a cholesterol lipid layer. In 1972 Brauniger, Shah and Kaufman demonstrated using physical methods that the precorneal film was composed of oily elements. They exposed the surface of a normal human subject to minute particles of oil and water in turn their results showed that water droplets below a certain size bounced and rolled off the cornea whereas oil droplets were immediately absorbed into the precorneal tear film, thus an hydrophobic oily anterior layer was demontrated.

The thickness of this layer varies between 500 Å and 5000Å

its hydrophobic nature is thought to reduce tear evaporation as suggested by Maurice and Mishima (1961) and Iwata et al (1969), however, this is not certain since the work of Brown and Dervichian (1969) who have shown that when the oily secretion from the tarsal glands of humans was spread over saline there was no reduction in evaporation of the solution.

Section 3.3

Aqueous Phase

This watery portion of the pre corneal tear film is six or seven microns thick and is the main constituent of the tears, according to Wolff (1946) it is secreted by the lacrimal gland, and the accessory glands of Krause and Wolfring. It consists of approximately ninety eight percent water, the remaining two percent being made up of dissolved solids which are essentially proteins, mainly albumin, globulin, and lysozyme. McEwan et al (1958) have shown that these are secreted to different extents by the lacrimal gland proper, accessory lacrimal gland and the conjunctival goblet cells. Gachen et al (1979) have shown that the tear proteins are very complex and there may be a mixture of as many as sixty different proteins.

This middle layer has been subdivided into two sections by Holly (1973), a more concentrated semi gel phase and a highly dilute one. He has shown that mucin is distrubuted throughout the tears, and agrees with Wolff (1946) that the mucoid material at the epithelial aqueous interface is composed of mucopolysaccharides and glycoproteins.

The two most obvious cations in the precorneal tear film are sodium and potassium according to Thaysen and Thorn (1954)

Their concentration according to McEwan (1958) are 144 to 146 micro equivalents per millilitre and 16 to 24 micro equivalents per millilitre of tears respectively. Calcium is also found in the tears according to McEwan in the concentration of 26 micro equivalents per millilitre which may have some long term effects in extended contact lens wear according to Winder and Ruben (1977). The chloride ion content of tears is slightly greater than in serum 128 to 145 micro equivalents per millilitre according to McEwan (1958). He stated that the concentration of bicarbonate ions is 26 micro equivalents per microlitre, these together with carbonate ions according to Carney and Hill(1976) may contribute to the regulation of the ph of tears, however, Tapaszto (1973) has suggested that they plus proteins are the essential elements that give the tears their ability to buffer. Green (1982) has shown that sodium, chloride and bicarbonate ions are all involved in the regulation of corneal hydration therefore these ions are not only important to the tears but also to the cornea.

Section 3.4

Mucoid Layer

Wolff (1946) describes a mucoid layer deepest in the tears next to the corneal epithelium; it has been suggested that this layer ensures that the contact angle between the tears and the epithelium is such that the tears spread evenly over the corneal surface. Ehlers (1965) disagrees with this suggestion of Wolff's and has shown that the outermost parts of the epithelium of the cornea are infiltrated by lipids which are produced by the tarsal glands, and the mucoproteins which are secreted by the conjunctival glands which are dispersed throughout the watery layer of the tears. Holly (1973) also describes the mucin as being distributed throughout the tear layer. The glycoproteins from the goblet cells are the savengers of the tears and they remove the debris. In other animals the glycoproteins are much more specific than in man, Smelser and Chen (1974) Have shown that in the eel if the glycoprotein is rubbed from the eye, the eye swells when the fish is returned to the water, so obviously in this case the glycoproteins act as a seal for the epithelium. When the eel resecretes the specific glycoprotein the eye returns to normal. It is unknown if the glycoproteins are specific in man in the same way. It has been shown by Kempster et al (1979) that there is an

increase in mucous when hard contact lenses are worn, this could be a specific response to the presence of a foreign body. Ehlers, Kessing and Norn (1972) have suggested that the production of mucous may alter under various pathological conditions.

Section 3.5.

Collection of tears.

The pattern of tear flow is such that the tears flow around the eye not across the eye, so gravity has nothing to do with tear flow. This is also why it is difficult to collect tears from the lower conjunctival cul de sac. When contact lenses are fitted the delicate balance of the tears is inevitably greatly disturbed, however, no contact lens material has been found that does not have an effect on the cornea and tears, so all that can be hoped to be achieved is a situation where this disturbance is kept to a minimum.

The collection of unstimulated tears is very difficult indeed, the method used in this work was to collect the tears by means of a standard small capillary tube, ensuring that the end of the tube was smooth, by examination under the slit lamp biomicroscope. The capillary tube was held at the outer canthus of the volunteers, whilst the observer was looking through the slit lamp biomicroscope to make sure that the capillary tube only came into contact with the tear prism, once the capillary attraction was broken the tube filled reasonably quickly. Great care was taken not to stimulate the tears in any way whatsoever, to this end the illumination on the slit

lamp biomicroscope was kept to an absolute minimum, frequently the blue or green illumination was used. The tears were then immediatley analysed in a CMT 10 Chloride titrator so that there was the least possible chance of evaporation of the tears. Once the capillary tube was partially full of tears the contents were expelled onto a clean microscope slide and then a one micro litre pipette was used to measure the correct quantity and the results analysed. Three one micro litre samples were used and the results averaged, this was done to reduce experimental errors. It was not possible to obtain more than three samples from each volunteer, this is simply because of the small quantaties involved.

TEAR FLOW PATTERN AFTER HOLLY 1973

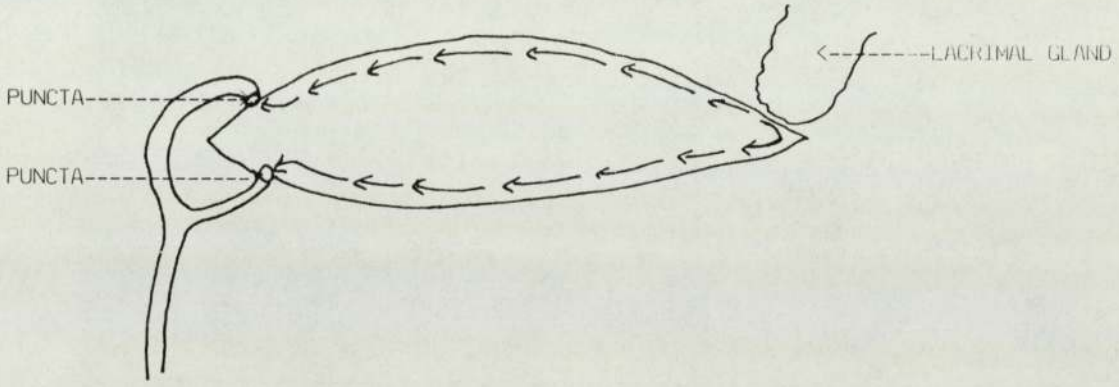


Figure 3.2

CROSS SECTION OF TEAR PATTERN AFTER HOLLY 1973

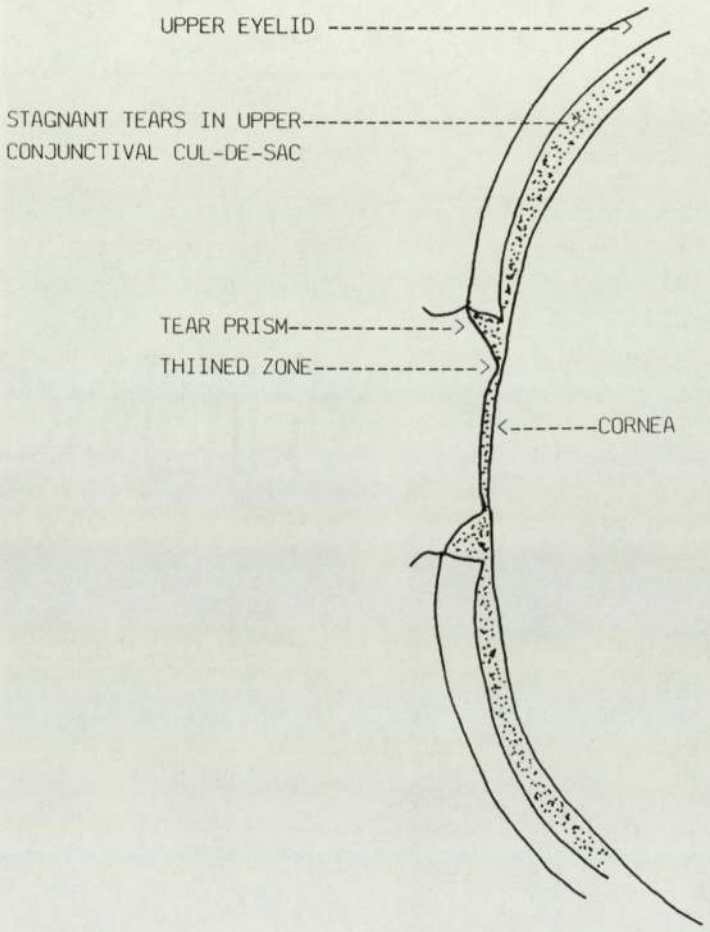


Figure 3.3

PLATE 3.1

Micropipette for measuring 1 microlitre of tears

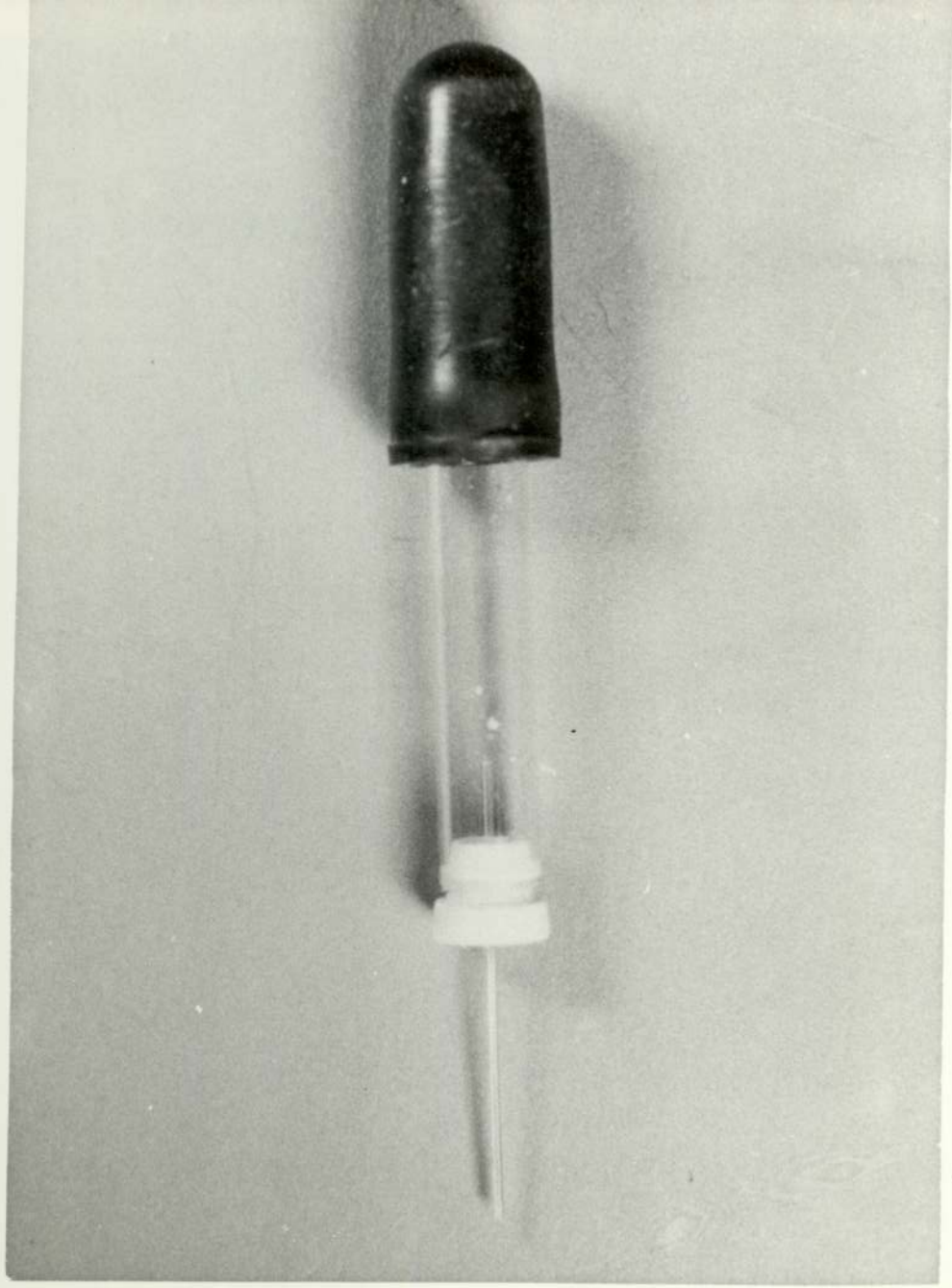
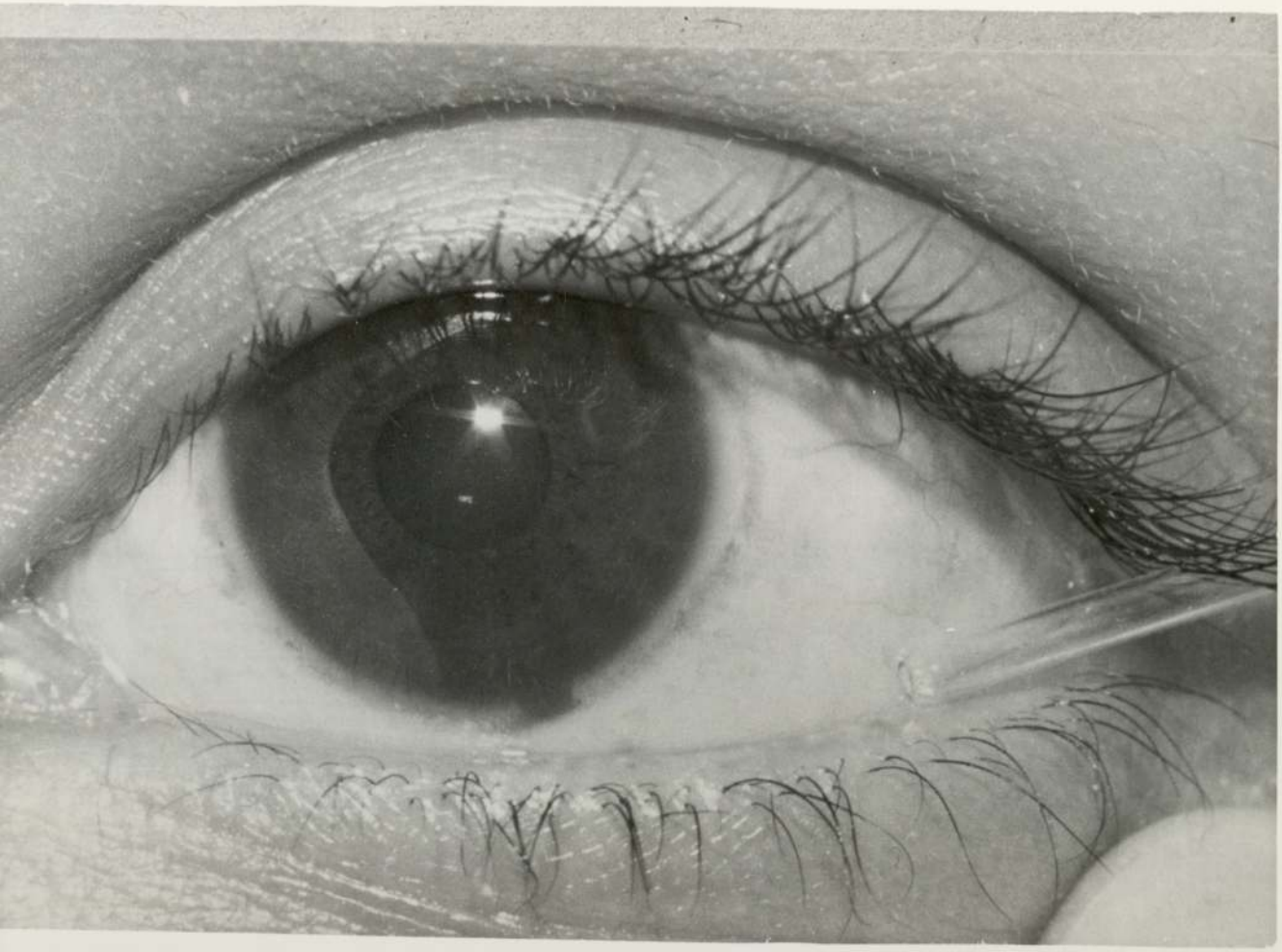


PLATE 3.2

Method of tear collection

PLATE 3.3

Close up showing position of pipette for collection of tears.



CHAPTER 4

INSTRUMENTATION

Section 4.1.

Pachymetry

The measurement of apparent corneal thickness in the human living eye was first performed by Blix in 1880. He used a modified ophthalmometer and found values between o.482 and 0.576 millimeters in ten eyes. The apparatus consisted of two horizontally arranged microscope tubes with optical systems of equal power, which were converged to an angle of approximately 40° at a point in front of the tubes. One of the tubes contained an illuminated diaphragm adjusted so that it was imaged at the point of intersection of the axes of the microscopes. The tubes moved symmetrically along their axes, by simultaneous movement of the image of the diaphragm it was first observed as being reflected from the epithelial surface and then the apparatus was adjusted so that the endothelial reflex was coincident with the point at which the epithelial reflex was originally seen. The distance between the two image points was transferred to a scale and thus the apparent corneal thickness was measured.

In order to calculate the actual corneal thickness it is

necessary to know both the anterior corneal radius of curvature and the refractive index.

After Blix, in 1909 Gullstrand introduced a new method for measuring the apparent depth of the cornea. His method never gained popularity because it was a time consuming and complicated process, nevertheless it was an accurate system. Ophthalmometric Nernst lamps with vertical slits were placed immediately above and below a horizontal telescope in front of the eye and the reflection from the corneal surfaces was observed. Using a moveable fixation target the eye was positioned so that the reflection from the slits was seen from both the corneal surfaces which had been aligned through the telescope. A theodolite type instrument was then set with its zero line against the endothelial focus, then the posterior reflex was located which lay at the basepoint of the perpendicular between the surfaces. A moveable linear light source was adjusted so that the anterior reflex was seen in line with the posterior reflex, thus the angle between the zero line and the moveable linear light source was ascertained with the theodolite and from these readings the apparent corneal thickness was measured.

Hartinger in 1921 was the first person to use a slit lamp biomicroscope beam to measure corneal thickness. The

light beam was passed obliquely through the area of cornea to be measured and an Ulbrich's measuring drum was used to calculate directly the difference in position between the images of the anterior and posterior corneal surfaces. This therefore was the first method to be devised which gave a direct measurement of the apparent corneal thickness.

Juillerat and Koby (1928) in their method of measuring apparent corneal thickness also made use of a slit lamp biomicroscope but with the addition of a micrometer eye-piece. They found that the best method was to set the axis of the microscope parallel with the optical axis of the eye and the light beam at an angle of 45° to the microscope axis. Measurement in twenty subjects gave a mean value of 0.590 millimeters with a standard deviation of 0.014. According to Ehlers and Hansen (1971) the large value for the corneal thickness was partly due to the fact that 1.4 was used as the value for the refractive index of the cornea in the calculation of the real thickness from the apparent measurement, there were also errors due to the use of the eye-piece micrometer which required two successive readings to be taken.

In 1948 Von Bahr introduced his new method of measurement of apparent corneal thickness of the cornea, which

was based on the same principles as those of Blix, but instead of using succesive adjusments of the point of convergence of the illumination system, the new system allowed simultateous observation and adjustment of the images. The instrument consisted of two rotating glass plates which were symetrically moveable by a gearing system; these plates allowed the passage of the light rays to the lower half only, thus by rotation of these glass plates the specular refection of the epithelial corneal surface becomes coincident with that of the endothelial surface, this angle of rotation of the glass plates gave an indirect measurement of the corneal thickness. Von Bahr produced a graph which simplified the calculation.

Maurice and Giardini (1951) used Von Bahr's principle, but instead of two thin glass plates they used a plastic plate approximately four millimeters in thickness which was mounted within a Haag- Streit slit lamp biomicroscope, between the lens and the slit. A thin horizontal strip of coloured celluloid coverd the central area of the plate. The plastic plate was mounted so that it could be rotated by means of a lever which moved over a fixed measuring scale. The plate was rotated until the white endothelial reflex was brought into alignment with the coloured epithelial reflex. This angle of rotation was a measure of apparent thickness of the cornea; the apparatus

was empirically calibrated to give actual corneal thickness. Maurice and Gardini found in forty four subjects a mean corneal thickness of 0.507millimeters with a standard deviation of 0.011.

Jaeger (1952) made an attachment which fitted the Zeiss Oberkochen slit lamp biomicroscope and measured apparent corneal thickness. The optical section of the incident light perpendicular to the corneal surface was observed at an angle of 40°. The image of the optical section was observed in the microscope and the thickness was measured by aligning the anterior and posterior corneal refections by means of rotating a plane parallel glass plate covering the lower half of the image. The calculation of the real thickness was found from a given formula. Jaeger stated that the corneal thickness could be measured to an accuracy of ± 0.02 millimeters.

Donaldson (1965) made an image splitting eyepiece, which produced a doubling of the image seen through the eyepiece, and thus only one half of the image is seen. The slit lamp biomicroscope beam image was positioned on the apex of the cornea in order to measure central apparent corneal thickness. Donaldson took measurements of two hundred and sixty eight eyes, using an average of five readings, he found a mean central corneal thickness of 0.522 millimeters

with a standard deviation of 0.006. Donaldson also used a graph to convert the apparent to the real corneal thickness.

Using Jaegers principle Mishima and Hedbys (1968) introduced a new attachment for the Haag Streit slit lamp biomicroscope. This attachment ensured that the slit lamp beam was directed perpendiculary to the centre of the cornea. The apparatus makes use of the Donaldson biprism eyepiece. The main attachment consists of two glass plates the upper one rotatable about the vertical axis, whilst the lower one remains fixed. A metal diaphragm with a narrow vertical aperture extends from the main attachment, the extension of the diaphragm has two pinlights attached at the same distance from the vertical aperture as the distance between the centre of the glass plates to the vertical aperture. The pinlights are the same distance apart as the length of the vertical aperture. When the attachment is in place the vertical aperture of the diaphragm makes an angle of 40° with the microscope.

The patient is instructed to look at a target which can be moved so that any position of the cornea can be measured. The slit lamp biomicroscope is adjusted so that the light beam is incident on the cornea and the blurred

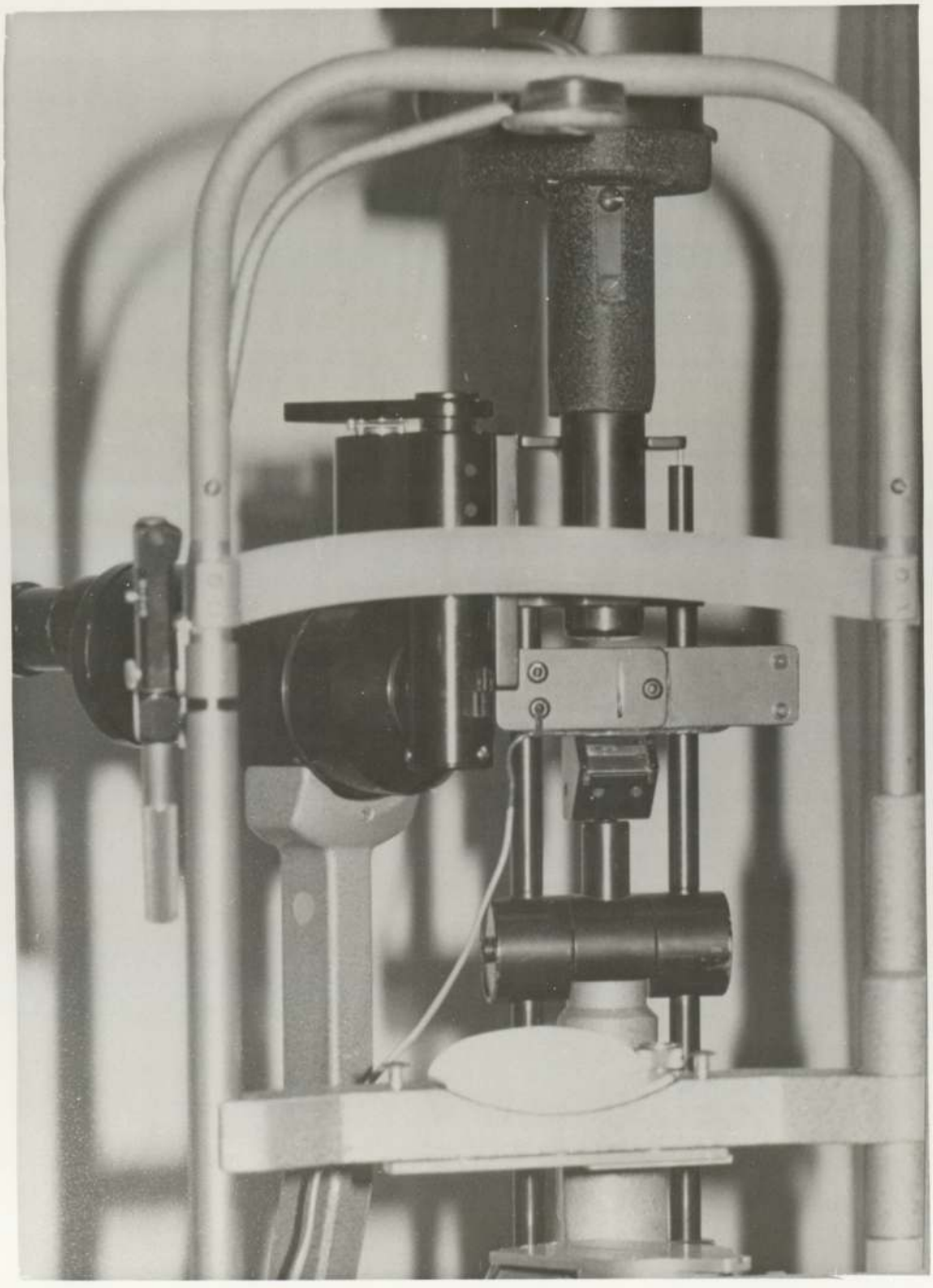
images of the pinlights are seen equidistant from the horizontal dividing line of the visual field. The microscope is moved until the blurred images of the pinlights are seen on the corneal epithelium to ascertain the perpendicular direction of the beam. The upper glass plate is rotated so that the image of the endothelium seen in the upper field is in alignment with the image from the epithelial surface. The apparent corneal thickness can be calculated from the angle of rotation of the upper glass plate. There is a table available which converts apparent corneal thickness to real corneal thickness for specific central anterior corneal radii, and an assumed refractive index of the cornea. Mishima and Hedbys found an average corneal thickness of 0.518 millimeters with a standard deviation of 0.02.

This pachometer is the most widely available, however, various more sophisicated attachments have been described by Ehlers and Sperling (1977) and Hirji and Larke (1978) Other methods using laser light, interferometry, photography and ultrasound have been used, however, all these techniques require complex equipment which is not readily available for clinical use.

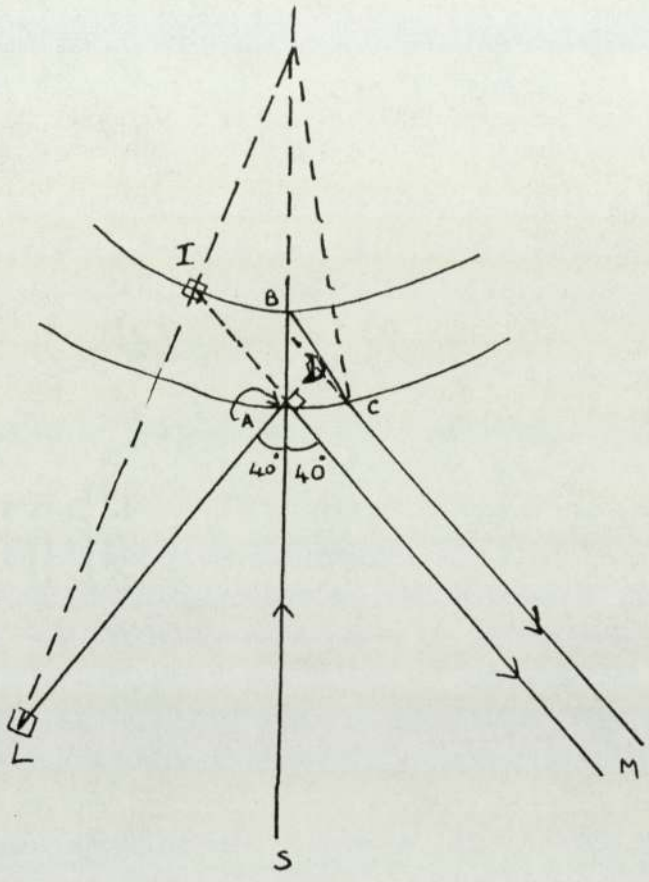
As apparent corneal thickness is to be used to estimate

PLATE 4.1

Haag Streit pachometer showing extension tube with pinlights



OPTICAL SYSTEM FOR THE HAAG-STREIT PACHOMETER
AFTER MISHIMA AND HEDBYS 1968



S = SLIT LAMP
A-B = CORNEAL THICKNESS
A-D = APPARENT CORNEAL THICKNESS
M = MICROSCOPE
L = PINLIGHTS ATTACHED TO EXTENDED DIAPHRAGM
I = IMAGE OF PINLIGHTS

Figure 4.1

DIAGRAM SHOWING ALIGNMENT OF THE IMAGE AS SEEN THROUGH THE SPILT OCULAR OF THE HAAG-STREIT PACHOMETER

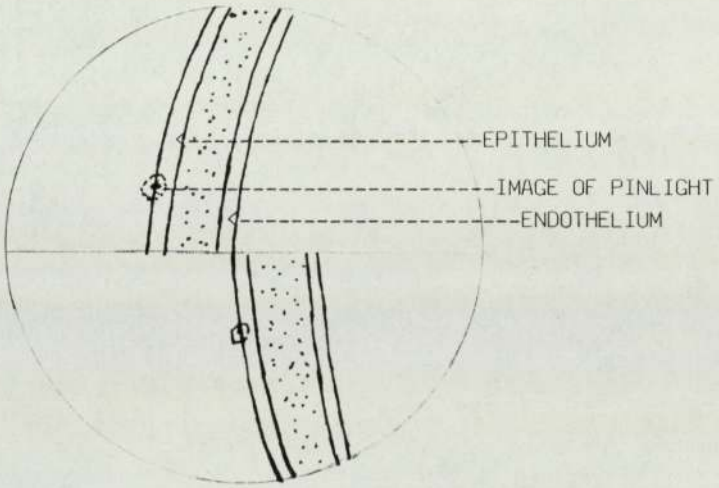


Figure 4.2

corneal hydration it is particularly important that the accuracy of the instrument should be known. The two greatest causes of inaccuracy of the instrument are:-

(1) Focus of the slit lamp.

(2) Position of the slit beam in relation to the cornea.

The second problem has been overcome to a certain extent by using the Mishima and Hedbys modification. The first can never be totally elliminated, however, the error is greatly reduced by taking an average of five readings on each occassion. The instrument, and observer, accuracy was tested using glass plates of various known thicknesses and refractive indices.

Three different glass plates were used and an average of five readings taken on ten different occasions. The results are shown in tabular form overleaf, as can be seen in all cases the pachometer readings were slightly thicker than the calculated value. There was an inherent instrument and observer error of between six and a half, and eight percent. In all probability this is due solely to inaccurate focussing and observer proximal accommodation. The error is totally unchanged by calculating the real thickness, therefore it would seem advisable

RESULTS OF PACHYMETRY MEASUREMENTS ON GLASS PLATES OF VARIOUS THICKNESS

Glass plate stated thickness	Measured thickness with micrometer	Theoretical apparent thickness	Measured thickness pachometer units	Calculated thickness
1.00mm	0.99 mm	0.65mm	0.655 $\pm$ 0.043	1.01 $\pm$ 0.065
0.75mm	0.79 mm	0.52mm	0.53 $\pm$ 0.042	0.81 $\pm$ 0.064
0.50mm	0.48 mm	0.32mm	0.33 $\pm$ 0.026	0.50 $\pm$ 0.04

to leave any readings that are purely for comparative purposes in pachometer units, because in the human eye there is the added complication of needing to know the radius of curvature of the surface at the point where the thickness is measured, also there is no way of measuring the in- vivo refractive index of the cornea.

A table showing the corneal thickness measurements obtained by various investigators is shown overpage.

TABLE SHOWING THE CORNEAL THICKNESS MEASUREMENTS OBTAINED BY VARIOUS INVESTIGATORS

AUTHOR	DATE	CORNEAL THICKNESS	NUMBER OF EYES
Blix	1880	0.482 to 0.576	10
Gullstrand	1909	0.46 to 0.51	2
Juilleral and Koby	1928	0.466 to 0.703	20
Von Bahr	1948	0.565 $\pm$ 0.035	224
Maurice and Giardini	1951	0.507 $\pm$ 0.028	44
Donaldson	1965	0.522 $\pm$ 0.041	268
Martola and Baum	1968	0.523 $\pm$ 0.039	209
Mishima and Hedbys	1968	0.518 $\pm$ 0.02	Not Known
Lowe	1969	0.517 $\pm$ 0.034	157

Section 4.2

Methods of Measuring Intraocular Pressure

There are basically two ways of measuring the intraocular pressure either directly by manometric means or more usually indirectly by tonometric means.

Manometry is by far the most accurate method, but it is unrealistic to use in the clinical situation because it requires the insertion of a cannula, and therefore the patient needs a general aneasthetic.

Tonometry gives an indirect method of measuring the intraocular pressure, the principle involves applying a force to the eye and measuring the resultant deformation.

The first person to recognise the relationship between 'hard eyes' and loss of vision in glaucoma was Mackenzie in 1830. Very high or very low intraocular pressure can be detected by applying finger pressure to the tunics of the eye. This method gives an indication of how 'hard' or 'soft' the eye is, but does not give reliable or measureable results.

Von Graefe probably produced the first working tonometer in 1863, using the general principle of a plunger of known

weight being applied to the cornea, and the amount of corneal indentation measured. Cocaine was used as the topical anaesthetic with the Von Graefe tonometer, the effects of which could be the reason why the tonometer never gained popularity. The most widely used impression tonometer is that of Schiotz which was first introduced in 1905 and subsequently modified in 1924 and 1926. The Schiotz tonometer consists of a base plate which is curved to rest on the average cornea, a weighted plunger runs through the axis of the tonometer which activates a pointer on a scale. This scale reading is converted into measurements of intraocular pressure by use of a table. Over the last twenty years this instrument has become less popular since the introduction of the applanation tonometer which has several advantages.

The fundamental principle of applanation tonometry is that a known area of cornea is flattened by a variable weight. The earliest applanation tonometer was the Maklakoff (1885) which consisted of several flat based weighted cylinders of five to fifteen grams. A dye solution was spread over the base of the cylinder which was then placed onto the eye, it was immediately removed and put on a piece of paper so that a print of the area of contact could be obtained. The early types of applanation tonometer

were not very accurate because of the problems of surface tension at the eyes surface. It was not until 1955 when Goldmann introduced his tonometer that this problem was overcome. It is based on measuring the pressure necessary to cause a fixed diameter (3.06 millimeters) of applanation. The instrument is attached to the Haag Streit slit lamp bimicroscope usually, although there is a hand held model available. The probe that contacts the eye is shaped in the form of a truncated cone with a transparent plastic tip having a surface end diameter of seven millimeters. The cone consists of two prisms with their apices in contact this means that the field of view is doubled and the two images can be compared. Fluorescein solution is used to enable the applanation zone to be seen easily, which lies just within the innermost borders of the fluorescein ring. The doubled image causes the fluorescein ring to divide optically into two equal semicircular halves, whose respective centers are separated by a fixed amount. With increasing applanation the area of measurable size is reached when the inside edge of one semicircle relates to that of the other as an 'S' shaped curve. The amount of fluid displaced is only half a microlitre compared to some fifteen or twenty for the schiotz instrument. This means that there is no necessity to account for scleral or ocular ridgity. All the original Goldmann calcutions for calibrating the

instrument were made assuming a standard corneal thickness of half a millimeter.

To estimate the errors due to the observer when the Goldmann applanation tonometer is used, one volunteer was subjected to intraocular pressure readings being taken for twenty days at the same time of day. The volunteer was a male so that menstral variations were eliminated. This resulted in a mean intraocular pressure of 17.95mm Hg with a standard deviation of 0.66. This indicates that there is an inherent error of four percent with this particular instrument and observer. The most feasible causes of the error are, the innacuracy in aligning the image, and the effect of the ocular pulse.

Section 4.3

Ophthalmometry using the Zeiss Ophthalmometer

The Zeiss ophthlmometer measures the radius of curvature of the anterior corneal surface using the basic principle of Helmholz (1854). The Zeiss ophthalmometer differs from many other keratometers in that it has a telecentric system thus avoiding the problems of observers proximal accommodation. The fundamental optical principle is that the cornea acts as a convex mirror to the two ophthalmometer mires which are situated within the instrument and illuminated by a common source are refected from the central portion of the cornea. The mires lie in the focal planes of two collimater objectives so that they are imaged at infinity, thus observer accommodation problems are eliminated.

It is necessary to ascertain the accuracy of the instrument before using it for measurement purposes. Two volunteer subjects (both male) had the radius of their anterior corneal surfaces measured ten times and averaged at fifteen minute intervals.

These results indicated that the Zeiss ophthalmometer is an extremely accurate method of measuring the central corneal radius the maximum error found being 0.2 percent.

Section 4.4

CMT 10 Chloride Ion Titrator

Standard laboratory equipment was used to estimate the tonicity of the tears, a CMT 10 chloride titrator was donated by Messers Bausch and Lomb. The instrument is designed to evaluate the chloride content in micro samples. The CMT 10 works on the principle of columetric titrations that is titrations in which the titrating agent is produced in solution by electrolysis, and the number of coulombs expended by the electrolytic reaction is measured. During a titration a current is passed through the solution from a silver anode to the cathode which consists of a silver wire immersed in sulphuric acid. This current liberates silver ions at the anode and hydrogen ions at the cathode. The system is designed in such a way that free silver is not formed at the cathode. The silver released from the cathode reacts with the chloride ion in solution and forms silver chloride. Thus the amount of chloride removed from the solution is equal to the amount of silver chloride formed which in turn is equivalent to the quantity of silver produced by the process. It is therefore possible to measure the time required to produce a known quantity of silver and thus this can become a measure of the chloride ions in the solution.

It is imperative that the sample is of an exactly known quantity; when dealing with the tears it is very difficult to obtain large samples. A one microlitre micro pipette was used to collect the unstimulated tears from the lower conjunctival cul de sac. The CMT 10 was being used to the limit of its accuracy with such small samples; it was therefore most important to discover just how accurate the values obtained were, because it was impractical for the reasons already stated in section 3.5 to obtain more than three samples per eye. It was decided to use freshly made sodium chloride solutions of known tonicities to test the accuracy of the instrument and sampling technique. The results showed that there was a maximum error of five percent. The other factor which it was necessary to ascertain was how repeatable the results would be in the human eye. Two volunteer male subjects were used, samples of tears being collected every half hour over a three hour period. The method of taking the samples has already been described in section 3.5. in each case sufficient tears were collected to enable three samples to be analysed. Again there was a five percent error in the technique. No matter how carefully the samples are collected there will inevitably be some reflex tearing. It would seem reasonable to assume that any errors greater than five percent could be attributable to the treatment levels, whereas those under five percent are technique errors.

RESULTS OF TESTING THE ACCURACY OF THE CHLORIDE ION TITRATOR

ACTUAL TONICITY	0.7%	0.8%	0.9%	1.0%	1.1%	1.2%
MEASURED Cl^-	119 ± 6	137 ± 6	161 ± 6	177 ± 6	188 ± 7	206 ± 10
MEASURED TONICITY	0.696 ± 0.035	0.801 ± 0.032	0.942 ± 0.038	1.035 ± 0.031	1.0998 ± 0.044	1.205 ± 0.06

Section 4.5

Slit Lamp Biomicroscopy

The slit lamp is one of the most important diagnostic instruments for examination of the anterior and posterior segments of the eye. Alivar Gullstand won the nobel prize in medicine and physiology in 1911 for his work on the dioptrics of the eye and the development of the biomicroscope. Since then there have been various improvements in the mechanical operation and illumination system however, the basic principle of all present day slit lamps is the same as the original developed by Gullstrand.

There are six basic illumination techniques which are used to observe the various aspects of the eyes structure.

(1) Direct illumination, this method allows direct viewing of the structure being examined, it is necessary for the microscope to be coincident with the illumination system at and angle of 40° to 50° with this technique.

(2) Indirect illumination; this method allows an opaque area to be examined with the light source focussed in an adjacent area of the cornea. A beam of light is shone on one side of the area under observation, then the slit lamp is rotated 30° to 60° to either side of the microscope.

(3) Direct retro illumination; this method of illumination allows a transparent or semi- transparent object to be seen by reflecting light from tissue posterior to the media. The tissue is observed in the direct path of the reflected beam.

(4) Indirect retro illumination; this method is similar to direct retro illumination except in this case the tissue under observation is seen in the indirect path of the reflected light.

(5) Sclerotic scatter; the light beam is focussed at the limbus, whilst the slit source is placed at an angle of 40° to 60° so that there is total internal reflection from the corneal surfaces. Since the light is being internally reflected no light emerges directly towards the examiner. If there is an area of reduced light transmission within the cornea such as an area of corneal oedema it will appear either grey or brighter than the background depending upon the degree of translucency.

(6) Specular reflection this method of slit lamp examination is used to inspect the smooth surfaces of the eye. To enable specular reflection to occur it is essential that the angles of incidence and reflection are equal. When this method of illumination is set up correctly the

examiner sees a bright light refected from the optical surface. This refection is known as the zone of specular reflection.

As the corneal parallelepiped beam is brought closer to the catoptric image of the filament, the stromal layer of the parallelepiped beam changes in appearance from a dull whitish grey to a brighter grey with many highly luminous spots. This increased brightness of the reflected light has been called luminous specularity by Walker 1977. The bright reflection from the interior corneal surface is whitish and rather uniform in appearance, but the reflection from the corneal endothelium has a dull golden mosaic pattern. This honeycomb pattern is caused by the flat corneal endothelial cells. Specular reflection is the only technique by which the endothelial cells can be seen using a slit lamp.

Section 4.6

Method of Observing the Corneal Endothelium

Vogt in 1920 developed a slit lamp technique for observing the edothelium by specular illumination, however, the magnification was insufficient for a detailed study of the cellular structure. In 1968 Maurice introduced a new specular microscope suitable for photographing the magnified endothelium in situ. The microscope consisted essentially of a light source which is passed through a slit aperture and condensing lens. The slit beam is directed through the objective lens of the microscope and onto the cornea. Modifications were made by Liang et al (1975) so that it was possible to examine and photograph the corneal endothelium at high magnification in vivo. Further changes were introduced by Bourne and Kaufman (1976[2]) and then by Sherrard (1977). The optical principles of the clinical specular microscope have been fully expained by Laing et al (1979). The greatest disadvantage of this technique is that it requires applanation of the cornea with the dipping cone lens, which necessitates using a topical aneasthetic. Sherrard has used an hydrogel contact lens as part of the dipping cone, cornea, optical system so that it would have been possible to use this method of observing the corneal endothelium,

Roper-Hall (1983) has indicated that a soft lens makes photographing the corneal endothelium a much less reliable technique.

Bron and Brown (1974), seem to be the first authors to describe a photographic method for viewing the endothelium of the in vivo cornea. This method required no physical contact with the eye and gave high magnification of the corneal endothelium. They used the macrophotography unit constructed by Brown (1970); the equipment consisted of a macrophotographic objective fitted to a reflex camera by means of an extension tube, the whole apparatus was mounted onto a Zeiss photo slit lamp which provided illumination for observation and also a synchronised flash exposure. A more successful attempt has been reported by Holm (1978) who used a specially fitted microscope supplied with an objective with a long working distance. The camera was mounted horizontally on a bracket attached to a photo slit lamp. This instrument was made by Preisler Instruments Sweden after a suggestion by Dr Olle Holm. Photographs obtained with a modified slit lamp have also been reported by Laule et al (1978), they added a beam splitter, a two times negative lens and a camera arm for stereophotography. The photographs were projected and a total magnification of two hundred times was obtained. Holden and Zantos (1979) used a standard photo slit

lamp to obtain photographs of the corneal endothelium, and rephotographed part of the original slide in order to obtain a sufficiently large magnification to enable inspection of the individual cells.

McCarey (1979) introduced some modification to the macro-photography unit described by Brown (1970) so that it was possible to increase the magnification and resolution of the endothelial cell image.

Koester et al (1980) used both a contact and a non-contact specular microscope to photograph the corneal endothelium, through the use of a scanning mirror system the field of view with this system is expanded to nearly one millimeter in diameter.

Barr and Schoessler (1980) used the Holden and Zantos (1979) technique with modifications of the fixation system of the Nikon slit lamp, they concluded that similar central areas of the endothelium could be photographed at different times by different observers.

The system used in this project to obtain endothelial photographs has been described previously by Belisario-Reyes, Kempster, and Sabell (1980). The system consists

of a light weight reflex camera body with an eighty five millimeter extension tube attached to one of the eye pieces of the Zeiss Jena photo slit lamp. Minor electrical modifications were made to the slit lamp to divert the flash beam so that it synchronized with the camera in the new position. It is necessary to focus the slit lamp eyepiece so that a clear image is obtained in the view finder of the camera. In order to observe the corneal endothelial cells a completely clear viewfinder is used, which gives rise to a slight difficulty, that of variation in the observers accommodation. Providing the usual focussing precautions are taken this did not present too much of a problem. To obtain the specular reflection a medium width slit beam was used and the illumination system was set at 60° to the observation system. A magnification of forty times gave the most acceptable results for examining the indivdual cells of the endothelium. By varying the subjects direction of gaze the specular image could be viewed at different parts of the corneal endothelium. It was found that the same portion of the cornea could be examined and photographed by keeping the position of the fixation light in a constant position. In order to reduce the micro nystagmus of gaze, and also give a critical fixation target a 0.75 millimeter red spot light was used. Photographs were taken using slide film of a relatively low photographic

speed, it was found that 50 ASA gave very acceptable results.

The estimation of cell density was made by first photographing a graticule which was marked at ten micron intervals, through the photographic set up making sure that the same magnification was used for both the graticule and the subject. This calibration was then measured and an accurate mask made that was equivalent to a one millimeter square. This was held in contact with the slide of the endothelial cells, then projected, and the cells counted within the square. The other method which was found to be viable was to project the graticule and mark a matt paper screen, and then to project the slide of the endothelial cells and count the cells within the marked square. The main disadvantage of this system is that each time the projector screen distance is altered it is necessary to recalibrate the paper screen.

The reproducability of the photographic technique was estimated by taking twenty photographs on separate occasions of the same eye at the same time of day. The results was a mean of 2238 cells per square millimeter with a standard deviation of 158. This would indicate that errors of up to seven percent must be attributable to technique errors. The main problems are difficulty in

focussing the instrument accurately, and also the complication of finding exactly the same point on the endothelium on successive occasions.

PLATE 4.2

Corneal endothelial cells

CHAPTER 5

Type of Carrier Used for Treatment

Ever since the introduction of hydrogel contact lenses, by Wichterle and Lim of Czechoslavakia in 1960, they have become increasingly popular, this has been particularly noticeable in the hospital eye service, where contact lenses are used for therapeutic purposes. At the Birmingham and Midland Eye Hospital in 1970 hydrogel contact lenses accounted for two percent of all contact lenses prescribed, however by 1982 the percentage of hydrogel contact lenses had risen to sixty percent, of which twenty five percent were daily wear low water content lenses, the remainder being extended wear high water content lenses.

Hydrogel contact lenses have some advantages over conventional hard corneal and scleral contact lenses.

(1) Their greater comfort in wear.

(2) There is little or no adaptive period required.

(3) There is no significant spectacle blur following the wearing of these lenses

(4) Certain lenses can be used for extended periods of wear, and as bandage lenses, also as drug carriers.

There have been conflicting reports about the exchange of fluid through these lenses Gasset and Kaufman (1970) have reported that there is little exchange of fluid, and Hill and Augsberger (1971) have shown that oxygen transmission through hydrophilic lenses of reasonable thickness is not sufficient to allow for normal corneal metabolism. Farris and Donn (1972) concluded that no contact lens lets sufficient oxygen through to enable the cornea to breathe normally.

It is well known that if a solution of fluorescein should be inadvertently introduced into an eye wearing a soft lens then the hydrogel lens will be dyed yellow almost immediately, and yet after twenty four hours, if the lens is worn continuosly, the fluorescein will have been dispersed to such an extent that the lens is clear, and fluorescein cannot be detected even with the use of a colbalt blue light. Thus it would seem that an hydrogel contact lens in wear in the eye does have some exchange of fluid. This may well be due to the action of the eyelids.

Soft lenses are subdivided into two main groups those

which are worn on a daily basis, and those which may be worn for extended periods.

The original Czechoslavakian soft lenses were made of poly (2 - hydroxyethyl mathacrlate) H.E.M.A. and the manufacturing process was that of spin casting as described by Wichterle et al (1961). Since then numerous polymers and copolymers have been used, some of which have produced lenses of different water content and oxygen permeability, making some suitable for wearing for extended periods of time and during sleep.

H.E.M.A. is an extremely stable polymer and is not effected by using solu tions of different tonicities according to Tighe 1980. Bausch and Lomb soflens are made by spin casting H.E.M.A. (Gasson; 1980) this method of manufacture produces very uniforn lenses which have constant overall size and thickness as well as back and front curves. Thus for any work where it is important to have a constant reservoir of saline these lenses are most useful. They have a 38.6 percent water content and an oxygen permeability of 8×10^{-11} (cm^2/ sec))ml O_2/ml.mm.Hg.) according to Morris and Fatt (1977); thus this lens is only suitable as a daily wear hydrogel lens. The particular lenses used were the Bausch and Lomb Soflens Series N which has a back optic radius of 7.90 mm and an overall

size of twelve and a half millimeters and a thickness of 0.15 millimeters (Gasson ; 1980) A series N soflens cannot be worn as an extended wear lens because it does not have sufficient oxygen permeability. If a H.E.M.A. lens is to be used in this way then it must be made much thinner to enable sufficient oxygen to be transmitted to the cornea, (Holden ; 1983), Bausch and Lomb now produce these lenses as plano therapuetic lenses, at the time that the experimental work was being undertaken these lenses were not freely available. It was therefore decided that lenses from another family of polymers would have to be used. Duragel 60 and 75 lenses were donated by Peter Madden of Madden contact lenses ltd, and were made to specific specifications under the direct supervision of Randolph Layman, because of the different water contents and therefore the different oxygen charachteristics these lenses could be used as daily and extended wear lenses respectively. According to Gasson (1980) Duragel is an amido - amino copolymer with teriary amines. The material is made by placing monomers in a vacuum system and exposing then to the effects of a low pressure gas discharge, this system produces low energy electrons which interact with the mixture of monomers producing active chemical sites which form cross linked polymers, the polymerisation process can be closely controlled, the method of manufacture is by lathe cutting.

According to Morris and Fatt (1977) the sixty percent water content Duragel lens has an oxygen permeability of 13.9×10^{-11} (cm^2/sec)($ml.O_2/ ml.mm.Hg.$) whereas the seventy five percent Duragel lens has an oxygen permeability of 39.4×10^{-11} (cm^2/sec)($ml.O_2/ ml. mm. Hg$) thus making it suitable for wearing over extended periods and during sleep. The lenses were all made to be of thirteen millimeters overall size; for the initial experimental work the lenses all had the same back optic design and radius of 8.10 millimeters, they were all made to a standard thickness. This was done to ensure that each eye had the same osmotic reservoir of saline present.

The animal and initial human work used the Bausch and Lomb Series N soflenses, because it was known that these lenses would not be effected by using saline solutions of different tonicities. It was then realised that it was important to find the effect different saline solutions have on the cornea when lenses of higher water content are used. Therefore it was decided that it was essential to use a lens that could be made from the same polymer but have differing water contents at the time the only lens freely available was the Duragel.

In all cases the lenses were presoaked for twenty four hours in the required solution and then autoclaved at

120° C for twenty minutes. They were then left a further twenty four hours before being used for either the animals or the humans. Each treatment level had a new set of lenses so that in no cases could the lenses by contaminated with different solutions.

CHAPTER 6

Relationship between Intracoular Pressure and Corneal Thickness

Section 6.1. Introduction

The basic premise of this work is that the cornea will react to a contact lens as if it were a foreign body. It seems that the only likely response the cornea will make will be that of changing its hydration, which is directly related to corneal thickness. It has been established by Friedman (1973) that the cornea has similar properties to a semi-permeable membrane and therefore it should be possible to regulate corneal thickness by osmotic forces.

There are various established causes of corneal swelling:-

(1) Temperature below 10° C (Mishima and Hayakawa ; 1972)

(2) Application of ouabain (Brown and Hedbys ; 1965)

(3) Exclusion of oxygen (Langham and Taylor; 1965)

(4) Endothelial damage (Dikstein; 1973)

(5) Increase in introcular pressure as

I.P. = I.O.P. - S.P.

Where I.P. is imbibation pressure; I.O.P. is intraocular pressure; and S.P. is swelling pressure (Ehlers; 1966[2])

(6) Hypotonic saline or aqueous solution (Friedman; 1972, 1972[2])

It is highly unlikely that the cornea in the living body would be at a temperature of below 10 ^{o}C, therefore as far as this particular project is concerned it can be ruled out as a factor.

Again no situation can be foreseen where ouabain would be applied knowingly to the in vivo eye, so this factor is not applicable.

Any contact lens will exclude the natural oxygen supply to the corneal epithelium there have been exhaustive and very complicated studies on this aspect of contact lens wear such as those of Hill and Fatt (1963); Hill and Fatt (1963[2]); Fatt et al (1964); Hill and Fatt (1964[2]) Fatt (1969); Fatt and Hill (1970); Fatt and St. Helen (1971); Fatt and Lin (1976). Any studies of

uptake of oxygen would require an oxygen probe being placed on the unanaethatised eye, and in the opinion of the writer using the currently available instruments this would cause unwarranted discomfort to the subject, and is not without danger of damaging the intact corneal epithelium. After considerable thought it was decided that if all eyes were subjected to the same amount of oxygen deprivation that is by using contact lenses of exactly the same size this would give a situation where all the eyes were having the same treatment; this assumption is not without its problems because obviously all eyes are not the same size and all subjects have a different rate of metabolism. It was thought that this approximation was preferable to the rather unethical practice of using oxygen probes on normal eyes, although now Larke (1980) has developed an oxygen sensor which can be used clinically, however, it is understood that it does give a variability of eight percent, and it was not developed until after the experimental work on this project had been completed. The method used does have the merit that it simulates the clinical situation acurately.

In the normal eye it is very unlikely that there will be damage of the corneal endothelium, however it is not

known if lack of oxygen and other factors of wearing an hydrogel contact lens could cause changes within the endothelial layer and the damaged endothelium produce corneal oedema. It was therefore decided to estimate endothelial cell density by photographing the cornea using the method already described in Section 4.6.

It is not really well established how corneal thickness and intraocular pressure are related or if there is an equivalent change in swelling pressure with any change in intraocular pressure. As it is desirable to use a topical aneasthetic when intraocular pressure is measured obviously it is not reasonable to use the subjects who were going to use contact lenses, because the local aneasthetic will cause changes within the corneal epithelium and this in turn could cause changes in the osmolarity of the cornea. It was therefore decided to use pathological eyes in an endeavour to see if there is any correlation between corneal thickness (hydration) and intraocular pressure. It is realised that this in no way mimics the normal eye with raised pressure, but it is not possible for a non medical practitioner, in this country, to increase intraocular pressure artificially in vivo in humans, and it is extremely doubtful if it would be an ethical procedure. Therefore, any conclusions drawn must be within the limits of the path-

ological eyes available. It was thought that animal eyes could have been used, but the only experimental animals available were rabbits, and they do not give an adequate model of the human eye for measuring intraocular pressure, because the instruments available were designed for use in humans and are not calibrated for the rabbit cornea or the dimensions of the rabbit eye.

There are various types of glaucoma, some of which cause a raised intraocular pressure such as acute glaucoma, and chronic simple glaucoma. Low tension glaucoma has all the attributes of glaucoma without the raised intraocular pressure, whilst ocular hypertension has the raised intraocular pressure without the other manifestations of glaucoma. Therefore it would seem reasonably justified to state that in eyes which are glaucomatous then any changes in corneal thickness can be related to raised intraocular pressure, and the low tension glaucoma group taken as a control group. Similarly for the ocular hypertensive group the changes in corneal thickness can be taken as due to the raised intraocular pressure and a normal gruop taken as the controls Thus it should be possible to establish what effect if any intraocular pressure has on the control of corneal deturgesence.

To see what effect tonicity has on osmosis and thus on corneal thickness it was decided after initial experiments on the investigator, when a H.E.M.A. hydrogel contact lenses were soaked in half normal saline, that an animal model should be used first in order to set safe limits for the human work. It was quickly discovered that the cornea is very sensitive to small changes in tonicity, and animal eyes were sacrificed to discover the microscopic nature of the disturbance. When hypotonic soaking solutions were used the changes in the rabbit eye were irreversible. After the results of this work it was obvious that if human in vivo eyes were going to be used that the tolerance of the tonicity of the soaking solution for the hydrogel lenses was very narrow indeed, and that it would be reasonable to expect changes in corneal thickness with tonicities of 0.7 percent saline and also changes with 1.2 percent saline.

It was important to discover the changes that occur with the different treatment levels which are within the physiological variation, which are likely to occur, therefore before any conclusions could be drawn from the results it was essential that a base line of diurnal variations was found. There are also likely to be menstral variations

but as these are very difficult to compensate for, and very time consuming, it was decided that it was better to use male volunteers. In the case of the pathological eyes where it was difficult to find sufficient numbers all the female patients were post menapausal.

Section 6.2.

Variation of intraocular pressure with corneal hydration

In the normal cornea the total swelling is controlled by a variety of restraints. Maurice (1969) has described the cornea as being like a rubber sponge trapped between two glass plates, this description indicates that the corneal limiting membranes tend to compress the stroma which will absorb water like a sponge and act as a mechanical force against the superficial corneal layers. When the stroma swells the collagen fibres are pushed away from one another by the mucoid. The mechanical forces added to the tissue pressure within the cornea are equivalent to the intraocular pressure and thus it would seem that a change in intraocular pressure may be correlated to corneal thickness. Yettborg and Dohlman (1965) have shown that there is no increase in corneal thickness with increased intraocular pressure whilst Hansen (1971) noted that there is an increasing corneal thickness with an increase in intraocular pressure, and Ehlers and Riise (1967) have shown that there is a decreasing thickness with increasing intraocular pressure. De Cavellos et al (1976) found no statistically significant correlation between intraocular pressure and corneal thickness. However, it is known in the clinical situation of acute glaucoma where there

is a sudden rise in intraocular pressure that there is inevitably corneal oedema and associated increase in corneal thickness. Typically these patients are seen with a steamy cornea which returns to its normal transparency when the intraocular pressure is reduced either medically or surgically. In the rabbit, however, according to Laverne and Kelecom (1962), and Maurice et al (1966) the grossly swollen cornea is clearly divided into anterior and posterior sections, and there is a suggestion that the lamellae separate into alternate sheets of greater and lesser cloudiness thus causing irreversible changes within the cornea.

Glaucoma is a disease entity which usually has as one of its manifestations a raised intraocular pressure, the other clinical siuation in which the intraocular pressure is raised is ocular hypertension in this condition the patient has an intraocular pressure which is above the normal range, but does not have any of the other clinical signs of glaucoma. There is also low tension glaucoma in which the intraocular pressure is within the normal range and yet all the other clinical manifestations of glaucoma are present. If a raised intraocular pressure does cause an increase in corneal thickness due to mechanical pressure then it would be expected in ocular hypertension and chronic simple

glaucoma groups that the corneal thickness would be greater than in the control group or in the patients who were suffering from low tension glaucoma. As ocular hypertension presents no signs that are apparent to the patient these patients are only seen when the intraocular pressure is taken as a routine investiagtion in an apparently normal eye. Therefore they are relatively rarely seen, the chronic simple glaucoma and the low tension glaucoma are seen more frequently because the visual signs are sometimes noticed by the patient or they are noted in routine eye examinations by ophthalmic opticians.

Section 6.2.i.

Experimental procedure

The patients were all seen at the Birmingham and Midland Eye Hospital, and the investigations were carried out at the initial visit of the patient, that is before commencement of any treatment, so that this could not have any effect on the results.

As the ocular hypertensives are rarely seen it was decided to match the other groups to the first twenty four ocular hypertensive eyes seen. The age range was sixty to seventy years, therefore there was no likelyhood of menstral variations being involved and all the readings were taken between 14.00 and 15.00 hours so that diurnal variation was standardised as far as possible. The first twenty four hypertensive eyes belonged to thirty six patients twelve of whom were men, the chronic simple glaucoma, low tension glaucoma and control groups also had thirty six patients and twenty four women. The diagnosis of the disease was made independently by ophthalmologists at the hospital and this was unknown to the investigator until after the readings had been completed. The writer took all the readings, and in the case of the central corneal thickness an average of three readings were taken, which was recorded

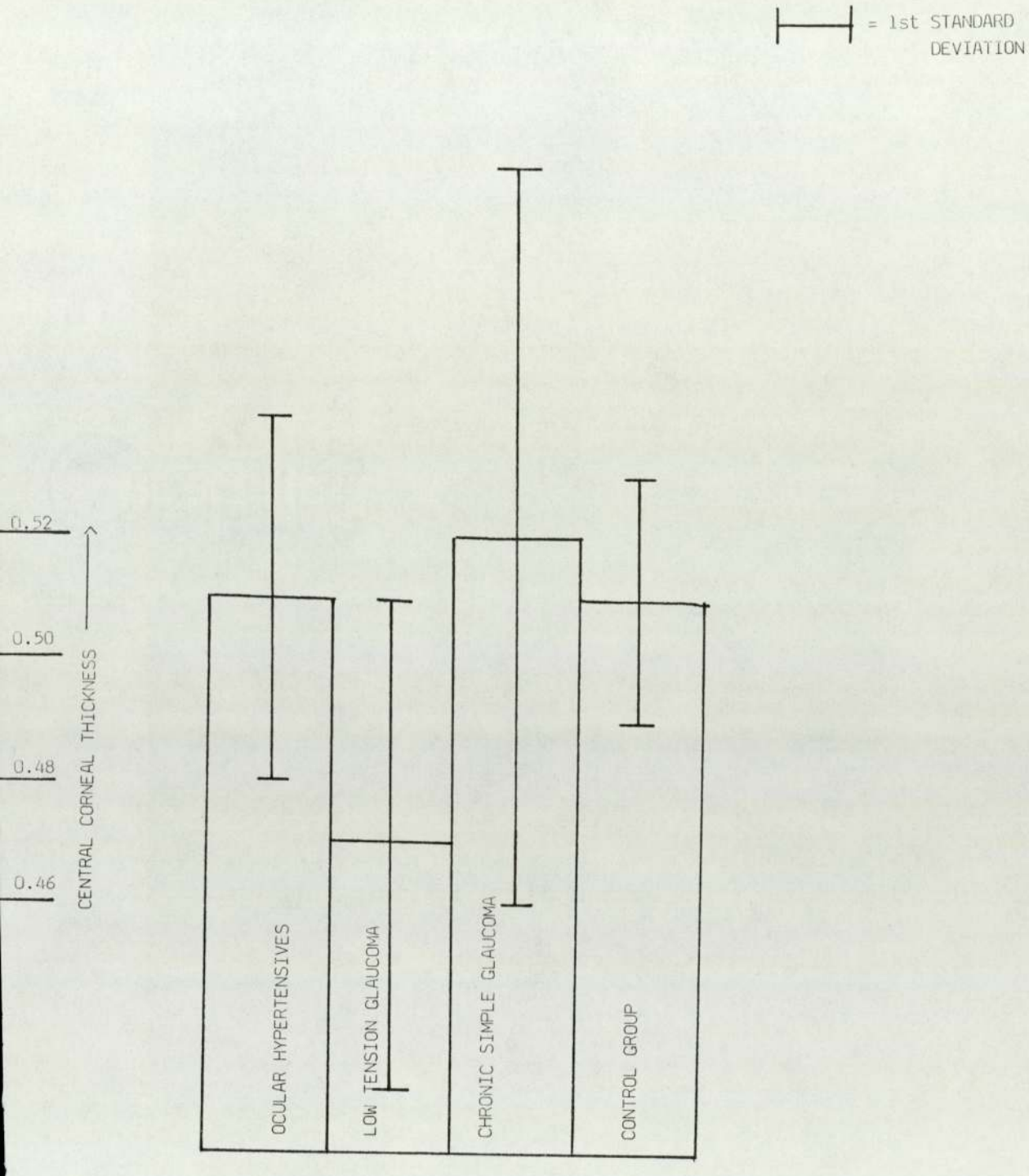
by an assistant so that the investigator was unaware of the results. For this particular group of results it was essential to correct the apparent corneal thickness into actual corneal thickness in order that tonometry readings could be corrected to hydrostatic pressure readings. Therefore the central anterior corneal radius was recorded, and the average apparent central corneal thickness corrected so that the central corneal thickness was recorded, all this was done by an assistant. A similar procedure was used with the intraocular pressure, which was recorded using the Goldmann applanation tonometer, however in this case the lowest reading was recorded by the assistant as the final value so that the effect of apprehension was minimised.

Section 6.2.ii

Results of variation in intraocular pressure with corneal thickness.

The histograms show that the low tension glaucoma (L.T.G.) has the lowest mean central corneal thickness, whilst that of the control group (C.G.), chronic simple glaucoma (C.S.G.) and ocular hypertensives (O.H.) Have very similar mean central corneal thickness. The low tension glaucoma group, central corneal thickness, shows by 't' test a statistically significant difference to that of any of the other groups at the p= 0.01 level. There is no statistical difference between means of the chronic simple glaucoma, ocular hypertensives, and the control group. It should be noted that the chronic simple glaucoma group has a considerably greater standard deviation to that of the other groups which indicates that there is more variation within the group, but the means certainly do not suggest that the central corneal thickness is correlated to intra ocular pressure.

Ehlers et al (1975) have shown conclusively that the intraocular pressure as measured indirectly with the Goldmann applanation tonometer only equals the hydrostatic pressure in the eye when the corneal thickness is 0.52 millimeters and the tonometer reading is 20 mm. Hg..



HISTOGRAM OF CENTRAL CORNEAL THICKNESS USING TONOMETRIC INTRAOCULAR PRESSURE

Figure 6.1

HISTOGRAM FOR TONOMETRIC INTRAOCULAR PRESSURE FOR VARIOUS TYPES OF GLAUCOMA

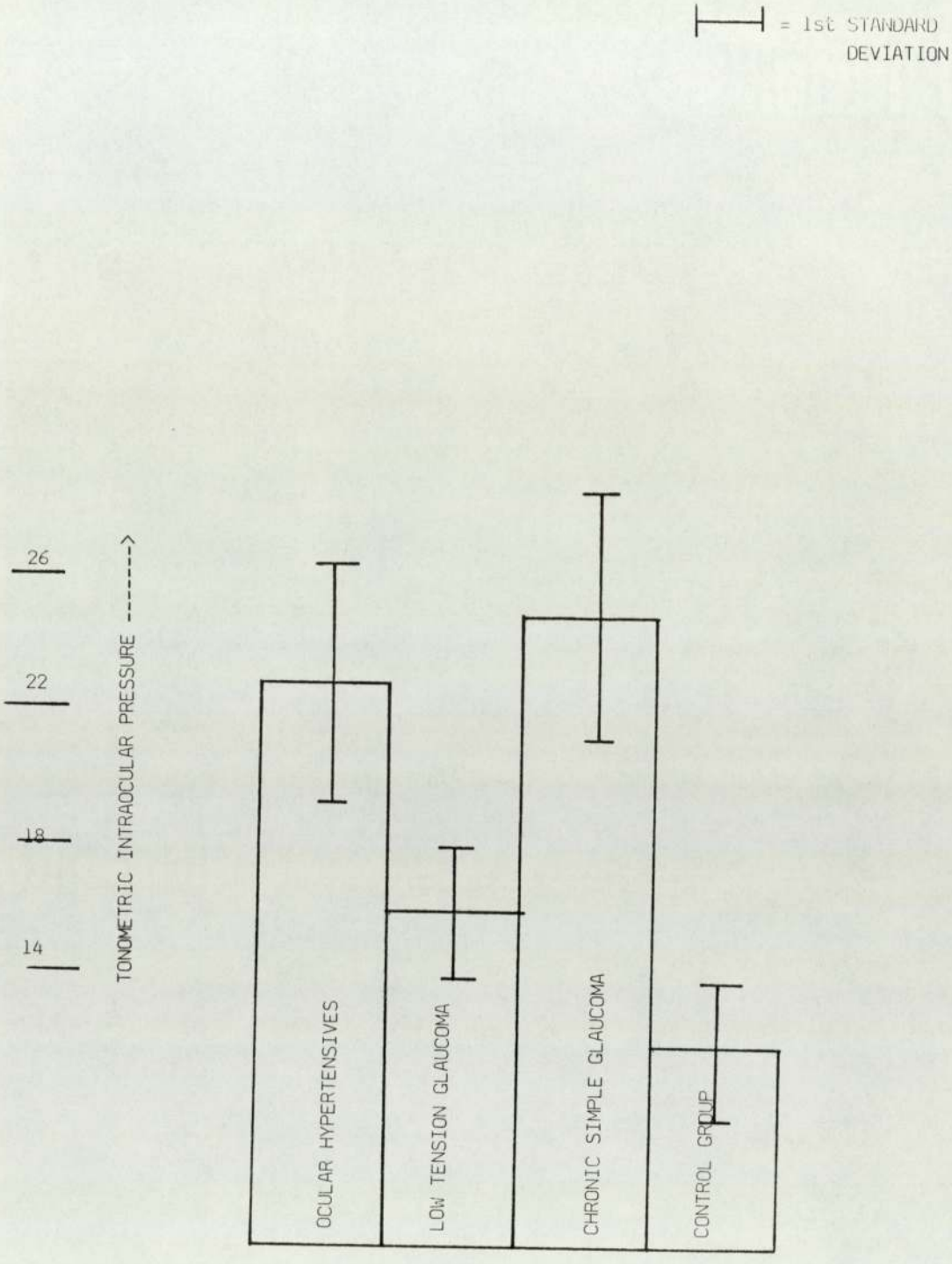


FIGURE 6.2

They found a considerable error in applanation tonometry due to corneal thickness variations. For example they found that if the corneal thickness was 0.45 millimeters and the measured intraocular pressure 20 mm. Hg. the actual hydrostatic pressure would be 25.2 mm. Hg. with this type of variation between tonometric results and the hydrostatic pressure it could be quite possible that the diagnosis of low tension glaucoma may be in the incorrect category. Therefore it would seem reasonable that when a true hydrostatic pressure is required, as for example in distinguishing between normal and pathological eyes as in the case of glaucoma that at the very least corneal thickness is recorded and ideally a correction factor is incorporated with the recorded values.

If the tonometer results are corrected so that they are the hydrostatic pressure measurement, using the Ehlers correction factor then the diagnosis in several cases would require adjusting. Six of the ocular hypertensives become normal and are therefore transferred to the normal control group, thirteen of the low tension glaucomas would have a raised intraocular pressure thus they would have to be placed in the chronic simple glaucoma group, and two of the chronic simple glaucomas would have a clinically normal intraocular pressure thus making

them into low tension glaucomas. The only group which remained unchanged was the control group. It can be seen from the histogram of hydrostatic pressure that the mean central corneal thickness for the various groups changes when the Ehlers factor is incorporated and the patients redistributed according to the hydrostatic pressure. A 't' test between means shows that there is a significant difference between means for the chronic simple glaucoma at $p = 0.001$ and for the ocular hypertensives at $p = 0.01$ level, however there is no significant difference between the low tension and the control group. This puts a very different complection on the correlation that there might be between hydrostatic pressure and central corneal thickness. These results although limited in number would indicate that when the intraocular pressure is raised that the cornea is thinner than av - erage assuming 0.52 millimeters to be the average thickness. It would not seem unreasonable to suggest that all the outer coats of the eye become thinner with increased intraocular tension due to being stretched rather like a balloon the greater the pressure the thinner the walls this is not a very good example because the eye does not have a closed system, but one with an outflow mechanism for the aqueous. Thus it cannot be a straightforward situation of the greater the pressure the thinner the cornea. Also there is no reason to assume that because

HISTOGRAM OF CENTRAL CORNEAL THICKNESS USING HYDROSTATIC INTRAOCULAR PRESSURE

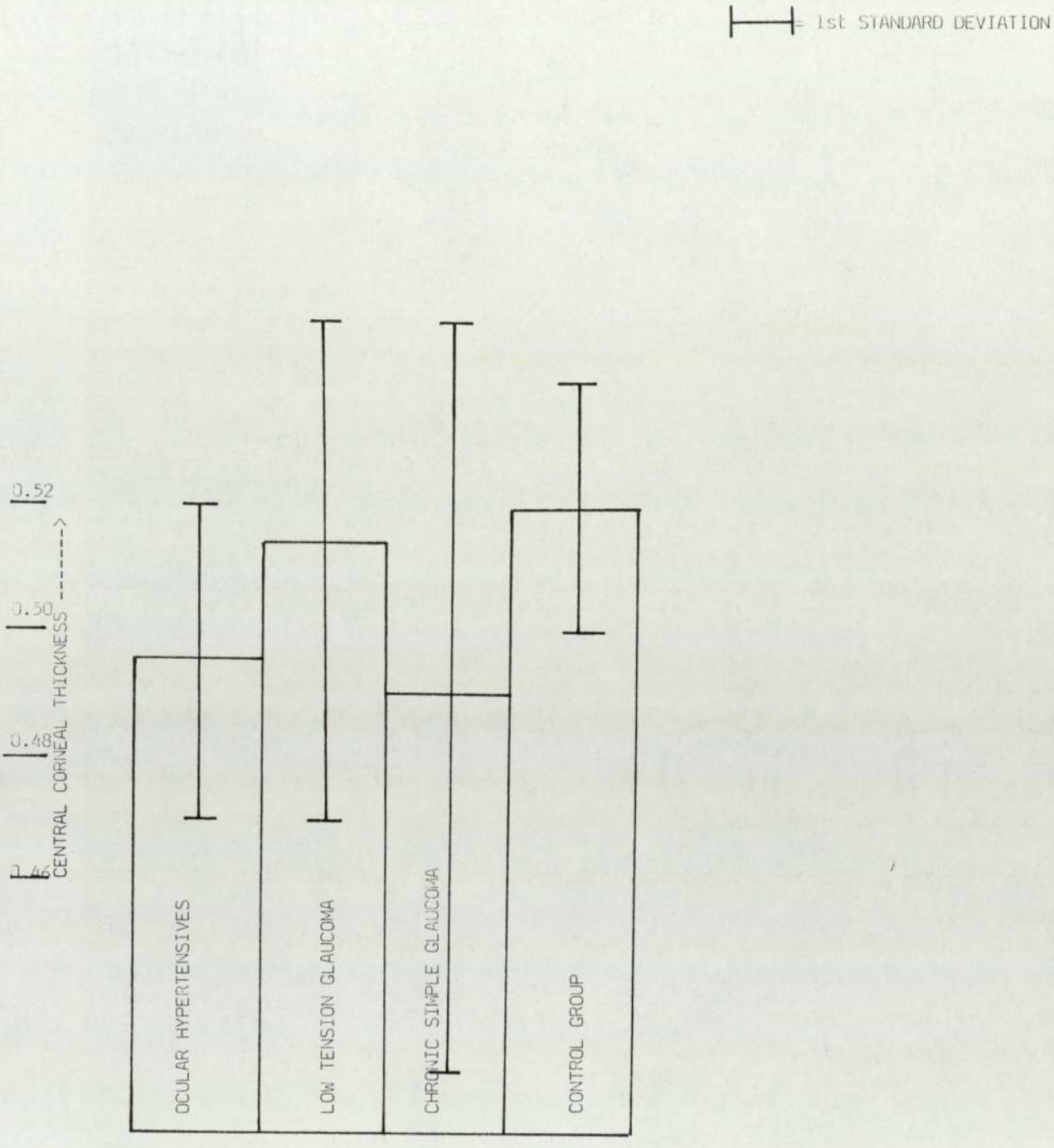


Figure 6.3

HISTOGRAM FOR HYDROSTATIC INTRAOCULAR PRESSURE FOR VARIOUS TYPES OF GLAUCOMA

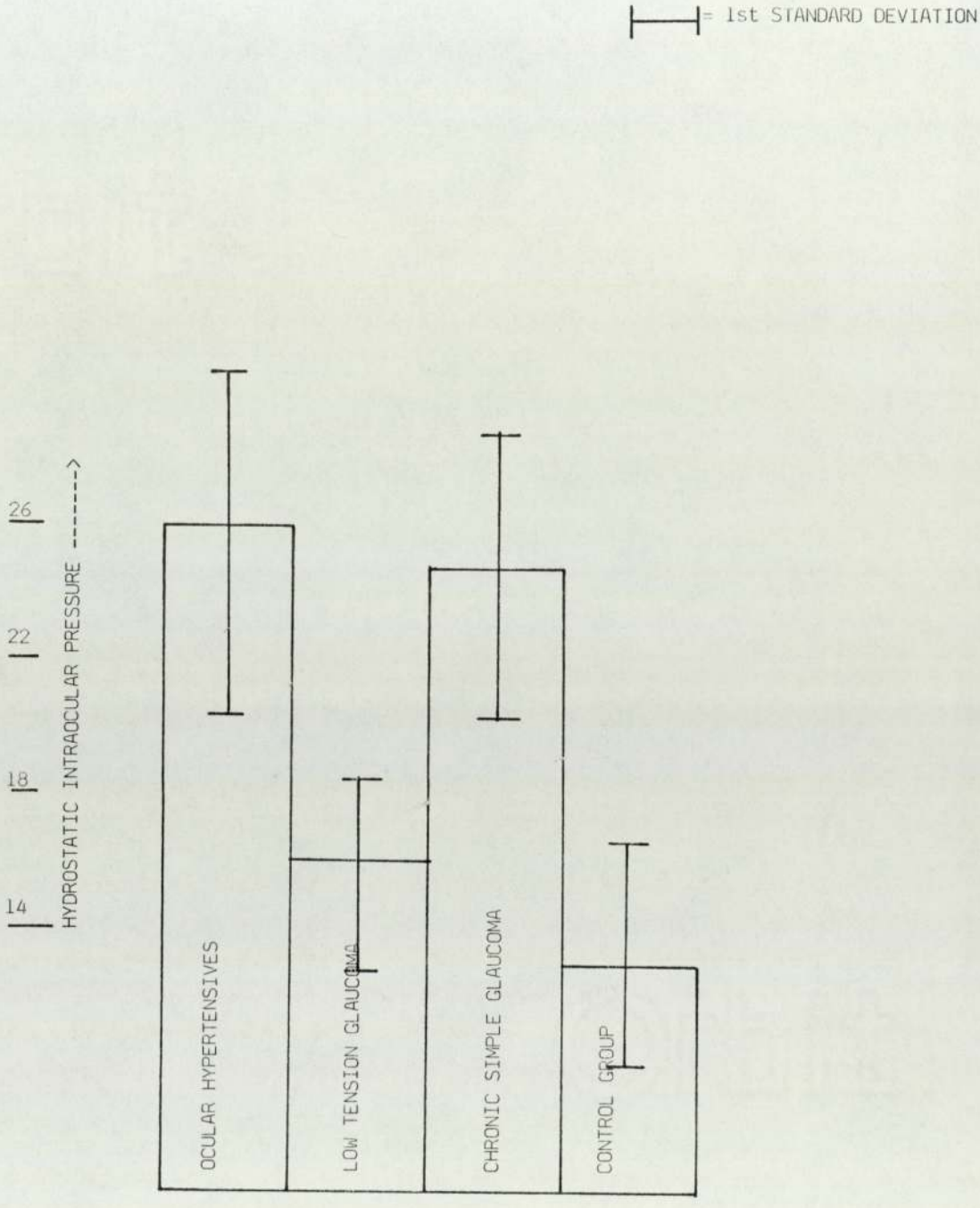


Figure 6.4

the central corneal thickness is attenuated that the average corneal thickness is also thinner. Ehlers et al (1975) used a Haag Streit keratometer to measure the central anterior corneal radius, whereas in this study a Zeiss ophthalmometer was used, these instruments use different refractive indices to calculate the radius of the cornea this could also be a cause of error in the results.

Could it be that because certain eyes have a thinner than average cornea they require a greater hydrostatic pressure in order to maintain the eyes shape? Could the reason be that there is an increased inflow of aqueous and the outflow mechanism is normal, or the reverse, in which case it is feasible that the coats of the eye will stretch. Whatever the reasons the results unquestionably indicate that when the intraocular hydrostatic pressure is raised the cornea is attenuated which agrees with the results of Ehlers and Riise (1967) but does not agree with De Cevallos et al (1976) or Ytteborg and Dohlman (1965).

It is not known if any of the other writers used the Ehlers factor, but it is reasonably safe to assume that they did not in any work published before 1975; as can be seen from this study if this factor is not taken into

account very different conclusions would be drawn from the results. As early as 1957 Goldmann and Schmidt stated that applanation tonometry could not be used for measuring intraocular pressure in rabbits because the results were always lower than the hydrostatic pressure due to the different dimensions of the rabbit eye, they did not state specifically because of the difference in the thickness of the cornea. Thus it appears that tonometry is dependant upon corneal thickness, and although it would be interesting to know if patients with a thinner than average cornea have an intraocular pressure on the high side of normal it is outside the scope of this particular work.

Suffice it to say that it would appear that hydrostatic pressure is dependant upon tonometry and corneal thickness and therefore it would be inadvisable to use this parameter when estimating changes in the hydration of the cornea by measuring changes in corneal thickness. There is also the added problem that although Goldmann tonometry is the standard method of measuring intraocular pressure it is usual to use a topical aneasthetic and it has been well documented by Pfister and Burstein (1976) that topical aneasthesia causes changes in the corneal epithelial barrier functions, thus this again would mitigate against using the Goldmann applanation tonometer in this study.

None of the patients in this study showed any reduction in visual acuity, therfore there was no gross loss of corneal transparency, thus it would seem that in the case of closed angle acute glaucoma where there is a sudden rise in intraocular pressure and a reduction of outflow the increase in corneal thickness and gross oedema is due to a collapse of the corneal pump mechanism and cannot be construed as being of the same situation as any form of open angled glaucoma.

It would seem that although there is an inter relationship between intraocular pressure and central corneal thickness these results do not suggest that there is a necessary correlation between increased intraocular pressure and lack of corneal transparency. Berkeley (1971) has shown theoretically and mathematically that under certain conditions an increase in intraocular pressure leads to tissue compression on the posterior side of the stroma and tissue expansion on the anterior side. He predicts that a continuation of raised intraocular pressure will produce corneal swelling. As all these patients were seen at a very early stage of their conditions it could be postulated that the intraocular pressure had not been increased for a sufficient length of time to reach the swelling stage.

There are many questions left unanswered at this stage, however, without doubt there is an inter relationship between applanation tonometry, corneal thickness and hydrostatic pressure. It would seem reasonable to postulate that there is no real correlation between raised hydrostatic pressure and loss of corneal transparency within the usual clinical range. Therefore applanation tonometry is not a good predictor of changes in corneal hydration.

Section 6.3

Diurnal Variation in the human eye of, corneal thickness, ohthalmometer readings, and intra ocular pressure.

It has been known for many years that the intraocular pressure in humans shows a marked diurnal variation. It is generally accepted after the work of Kollner (1916). that the pressure is highest in the early morning and lowest at midnight. Although more recent studies have shown that there are considerable variations within subjects with respect to high and low pressures. Drance (1960) found that forty two percent of subjects peak at 06.00 hours and yet sixteen percent of subjects had their lowest pressure reading in the early morning. Neither of these papers took into account the Ehlers factor as far as intraocular tonometric pressure and hydrostatic pressure are concerned. Ehlers first showed in (1966[3]) that there is a relationship between intraocular pressure and corneal thickness, but it was not until 1975 that Ehlers, Bramsen and Sperling published a table so that intraocular pressure could be corrected for corneal thickness and converted into true hydrostatic pressure.

Mandell and Fatt (1965) have shown that there is a diurnal variation in corneal thickness, when readings were taken on one subject on four consecutive days.

They found that the thickness of the corneal was increased by three and a half percent on initial uncovering of the eye. Hirji (1978) found that there was a minimal variation in corneal thickness throughout the day, however, he also used the method of taping the lids shut on initial waking and then the subjects made there own way to the laboratory.

According to Mishima (1968) when the corneal surface is bathed in an hypertonic saline solution an osmotic flow of water takes place out of the cornea across the epithelium, the cornea then becomes hypertonic and extracts water from the aqueous humour. As a result a flow of water takes place from the anterior chamber to the tears, because of the tonicity changes the tissue becomes attenuated. He also indicated that as a result of evaporation the cornea becomes slightly thinner on opening and thicker on closing the eye lids.

The results of Gerstmann (1972) on three adults two females and one male, do not entirely agree with those of Mandell and Fatt he found that the cornea thinned approximately five percent during the first three hours after waking and a further two and a half percent during the rest of the day.

The extensive work of Kikkawa (1973) on diurnal variation

of corneal thickness in rabbits does not agree with the work of Gerstmann, Mandell and Fatt, nor Hirji. He could not find any definite changes which could be correlated to the hour of the day, although he did find thickness variation. The differences in corneal thickness were at the outside limits of the normal range. The general trend was for the cornea to be thickest in the morning and thinnest in the afternoon. The reverse occured during the night hours. He could not find any apparent difference due to lid closure.

The conflicting reports of changes in corneal thickness, and the manner in which these experiments have been carried out in humans, also because in the past tonometry readings have not been corrected for corneal thickness, it was decided to investigate diurnal changes in greater depth. At the same time ophthalmometer readings were recorded to see if there were any marked changes in corneal radius on a daily basis. The readings were all taken as previously described in section 6.2.i again making use of an assistant to record the readings taken by the writer. The measurements were all taken on a non contact lens wearing population, so that contact lenses could not be a cause of corneal changes.

Section 6.3.i

Experimental procedure

Eleven normal non contact lens wearing adults were investigated at the Birmingham and Midland Eye Hospital. Five females and six males with an age range of thirty six to seventy six years and a mean age of sixty one and a half years. All the females were post menapausal so the menstral cycle was not a factor which could cause variation.

All the subjects were volunteers and were admitted to hospital for one night. A preliminary reading was taken at 16.00 hours to give the subjects some idea of the routine that would subsequently be used, these results were discarded because it was thought that the subjects might be a little tense about the proceedings, and it is well known that apprehension tends to cause unreliable tonometry readings, frequently causing an apparent increase in intraocular pressure, which theoretically could have an effect on corneal thickness, therefore these results could well have been spurious and lead to incorrect conclusions. Subsequent readings were taken at 20.00, 24.00, 08.00, 10.00, 12.00, and 16.00 hours. Each time the readings were taken an assistant recorded the results, the ophthalmometer readings were subsequently approximated to being vertical and horizontal to make the analysis

of the results a little less complicated. The order of the measurements was, corneal thickness, corneal radius, and finally intraocular pressure. The reason for this was so that any slight corneal disturbance caused by using the tonometer would not distort the other readings.

Subjects were asked not to sleep between the 20.00 and 24.00 hour readings, as far as is known none did fall asleep, however, it is impossible to be totally sure of this because the investigator did not stay in the room with the subjects. Equally it is not possible to be certain that all the volunteers slept for the required eight hours between midnight and 08.00 hours on the following morning. All the subjects had to be awakened so that the 08.00 hours reading could be recorded, this of course only means that the subjects were asleep just prior to the early morning result, not that they had been asleep all night. There is also no guarantee that the subjects did not have a 'cat nap' at anytime during the day.

The slit lamp and the ophthalmometer were taken to the bedside of the volunteers to ensure as far as possible that the first reading of the day was taken as soon as the subjects eyes were open. The lids were not taped for any individual, as it was felt that a more natural

result would be obtained if the eyes were not kept forcibly closed, by the unnatural process of having tape on the eye lids.

Section 6.3.ii

Results of the diurnal variation in the human eye of, corneal thickness, corneal radius, and intraocular pressure.

The percentage change in the measured parameters, taking the 08.00 hours reading as the zero, are shown in tabular form overleaf.

Several interesting facts are demonstared by these results corneal thickness is certainly greatest on waking, and in fact had not totally settled down two hours after waking. Depending on whether tonometric pressure readings or hydrostatic pressure readings are used the conclusions drawn from the results will be very different. It the results are expressed as tonometric pressure readings then it would appear that the intraocular pressure is greatest at 08.00 hours and least at 20.00 hours, whereas if the results are expressed as hydrostatic pressure readings it would seem that there is a twelve hour cycle rather than a twenty four hour cycle, the readings are lowest at 08.00 hours and 20.00 hours and highest at 16.00 hours, this could explain some of the differences that have been found by other authors. There was no significant diurnal variation in the ophthalmometer readings the percentage changes being less than 0.6 percent. As has already been described, section 4.3., the error of the Zeiss

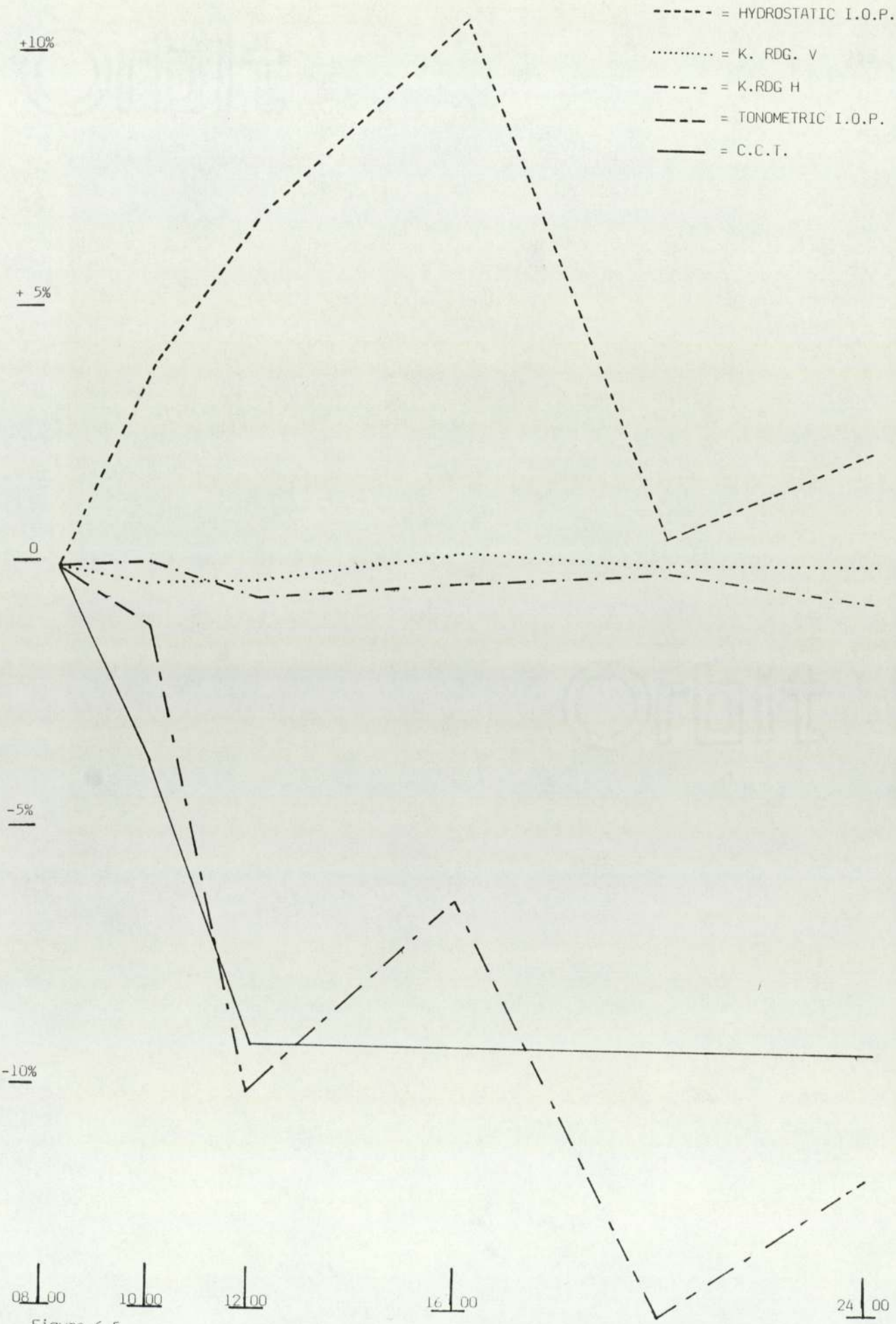
PERCENTAGE DIURNAL CHANGE IN, CENTRAL CORNEAL THICKNESS, INTRAOCULAR PRESSURE, AND ANTERIOR CORNEAL RADII TAKING 08.00 HOURS AS ZERO

TIME	10.00	12.00	16.00	20.00	24.00
CENTRAL CORNEAL THICKNESS	-3.7%	-9.3%	-9.3%	-9.3%	-9.3%
TONOMETRIC PRESSURE	-1.1%	-10.0%	-6.4%	-14.4%	-11.7%
HYDROSTATIC PRESSURE	+3.9%	+6.8%	+10.7%	+0.6%	+2.3%
VERTICAL CORNEAL RADIUS	-0.3%	-0.3%	+0.3%	+0.1%	+0/1%
HORIZONTAL CORNEAL RADIUS	0	-0.6%	-0.4%	-0.1%	-0.6%

ophthalmometer is 0.2 percent. Therefore the diurnal differences in the readings are greater than the instrument errors but nevertheless were statistically insignificant.

A one way analysis of variance of all the diurnal variations is shown in the tables on the following pages. In the statistical analysis the 10.00 hour readings were ignored thus leaving a standard difference of four hours between readings.

The statistical results indicate that there is a significant difference in the central corneal thickness with the time of day, but there is no such suggestion for anterior central corneal radius, thus it may be postulated that the cornea thickens in an antero- posterior direction only, and that the increase is across the complete cornea not solely in the central portion of the cornea. This explains why there is no noticeable visual disturbances, because an increase in thickness across the complete breadth will not cause disruption to the refracting ability of the cornea. The results show that there is no correlation between changes in corneal thickness and changes in intraocular pressure, both have a diurnal variation but they do not seem to have any link with one another. The Pearsons 'r' correlation coefficient for thickness


PERCENTAGE CHANGES DUE TO DIURNAL VARIATIONS
HYDROSTATIC I.O.P.
K. RDG. V
K.RDG H
TONOMETRIC I.O.P.
C.C.T.
+10%
+ 5%
0
-5%
-10%
08 00
10 00
12 00
16 00
24 00
HOURS ------->
Figure 6.5

and tonometric pressure readings is r = 0.01 and for thickness and hydrostatic pressure r = 0.03. It might be expected that there would be a correlation between the thickness of the eyes coats and the pressure within the system, if a very simple example is taken; it obviously requires more pressure to inflate a football compared to a balloon of the same size but with thinner walls. This is not an appropriate example for the eye because the football and the balloon are both closed systems, whereas the eye has an outflow mechanism. It can be postulated that the canal of Sclemn and the aqueous veins keep the balance of the intraocular pressure, and there is no need for there to be any correlation between intra ocular pressure and the thickness of the centre of the cornea. These results agree with De Cevallos at al (1976) but totally disagree with the work of Ehlers et al (1975) and Ehlers and Hansen (1976) who have shown that there is a correlation between central corneal thickness and intraocular pressure. Again the corneal thickness readings as corrected from the apparent corneal thickness may be different from those of Ehlers because of the different refractive indices used by the different manufacturers. There is also the possibility that the refractive index of the cornea will change with increasing thickness, however Fatt and Harris (1973) have shown that within the clinically observed range of corneal thickness there is

no significant error in the measurement as made by the pachometer. It could be that a far better measurement of corneal thickness would have been the average thickness using a similar method to that being used to express average thickness of hydrogel contact lenses. Unfortunately this is not a practical proposition with the limited information obtained for these results, it would necessitate the use of a topographic system for both corneal thickness and corneal radius, also it would be necessary to know the posterior radii of the cornea.

These results show that:-

(1) There is a statistically significant diurnal variation in central corneal thickness ($p = 0.05$)

(2) There is no statistically significant diurnal variation in central anterior radius of the cornea.

(3) There is a statistiacally significant diurnal variation in intraocular pressure if it is expressed as hydrostatic pressure.

(4) There is no statistically significant diurnal variation in intra ocular pressure when it is expressed as

tonometric pressure, but the means show that there is a tendency for the tonometric pressure to be lowest at 20.00 hours and highest at 08.00 hours.

It would seem therefore that any further experimental work where corneal thickness was going to be taken into account the measurements must not commence until the volunteers have been awake for at least four hours. There is no point in trying to correlate changes in corneal thickness with intraocular pressure because no significant correlation could be found between these two measurements.

SUMMARY TABLES FOR ANALYSIS OF VARIANCE FOR DIURNAL VARIATIONS

SUMMARY TABLE FOR ANALYSIS OF VARIANCE FOR DIURNAL VARIATION OF CENTRAL CORNEAL THICKNESS

Source	df	S.S.	Var Est	F	p
Between hours	4	0.0362	0.00905	2.54	0.05
Within hours	109	0.38829	0.00356		
Total	113	0.42449			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR DIURNAL VARIATION OF INTRAOCULAR TONOMETRIC PRESSURE

Source	df	S.S.	Var Est	F	p
Between hours	4	76.818	19.2045	0.77	not significant
Within hours	109	2715.773	24.9153		
Total	113	2792.591			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR DIURNAL VARIATION OF INTRAOCULAR HYDROSTATIC PRESSURE

Source	df	S.S.	Var Est	F	p
Between hours	4	59	14.75	2.569	0.05
Within hours	109	626	5.74		
Total	113	685			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR DIURNAL VARIATION OF VERTICAL CORNEAL RADII

Source	df	S.S.	Var Est	F	p
Between hours	4	0.0483	0.012075	0.208	Not significant
Within hours	109	6.3223	0.0580028		
Total	113				

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR DIURNAL VARIATION OF HORIZONTAL CORNEAL RADII

Source	df	S.S.	Var Est	F	p
Between hours	4	0.0526	0.01315	0.26	Not significant
Within hours	109	5.5086	0.05054		
Total	113	5.5612			

CHAPTER 7

A study of changes in rabbit cornea, when contact lenses presoaked in hypotonic saline are worn.

Section 7.1
Introduction

Human patients wearing hydrogel contact lenses may prepare their own saline storage solutions from distilled water and commercially available salt tablets. Boyd (1975) has shown that such patient prepared saline solutions are not always made up to the recommended strength.

Work already published by Kempster at al (1975) has shown that there is an evoked corneal thickness change when a H.E.M.A. soft contact lens is presoaked in hypertonic saline solutions, it would seem that there may also be similar changes with hypotonic soaking solutions. Knowing the type of changes that occured with the hypertonic solutions it was thought advisable to use animals for the initial studies before using the human model.

Section 7.1.i

Experimental procedure

Twelve Bausch and Lomb N series soflenses were presoaked, six in 0.7 percent saline and the other six in normal saline. The lenses were treated as previously described in chapter 5, and were placed on the eyes of six albino male New Zealand rabbits of approximately one and a half kilograms. The experimental eye was fitted with the lens presoaked in 0.7 percent saline , whilst the contralateral control eye was fitted with a lens presoaked in normal saline. Apparent corneal thickness was measured using the pachometer as described in section 4.1 at one hour intervals, after five hours the lenses were removed. The animals were observed for a further five days, after which time they were killed and the corneae subjected to histological examinations by Dr R. Barry consultant pathologist Birmingham and Midland Eye Hospital.

Section 7.1.ii

Results - Changes in the cornea produced by wearing contact lenses presoaked in hypotonic saline.

The table overpage shows the percentage changes in central corneal thickness of the rabbits. The experimental eye showed a marked increase in central corneal thickness after the initial hour of wear by the fourth hour of wear the cornea had doubled in thickness. Kaye et al (1973) have shown that corneal thickness changes in rabbit are reversible up to one hundred and fifty percent, and between one hundred and fifty and two hundred percent, the swelling could not be reversed. These results agreee with Kaye et al., as can be seen from the graph there was in fact an increase of central apparent corneal thickness in the experimental eye nineteen hours after the lenses had been removed, but there had been an attenuation in the control eye. It took three days before the experimental eye was showing a reduction in thickness and even then it was still one hundred percent thicker than the initial measurement.

The histological report, overleaf, on the rabbit corneae was undertaken by Dr R, Barry consultant pathologist at Birmingham and Midland Eye Hospital. The photographs

TABLE SHOWING PERCENTAGE CHANGE IN RABBIT CENTRAL CORNEAL THICKNESS

HOURS	1	2	3	4	5	6	24	48	72	96	120
EXPERIMENTAL EYE	+50%	+57.1%	+83.3%	+97.6%	+121.4%	+166.7%	+161.9%	+185.7%	+185.7%	+102.4%	+92.8%
CONTROL EYE	+7.14%	+11.9%	+14.3%	+14.3%	+9.53%	+11.9%	+2.38%	-4.76%	-4.76%	-4.76%	-4.76%

PLATE 7.1

Photomicrograph of rabbit cornea showing thinning of the corneal epithelium with the formation of subepithelial bullae and a spongy appearance of the stroma

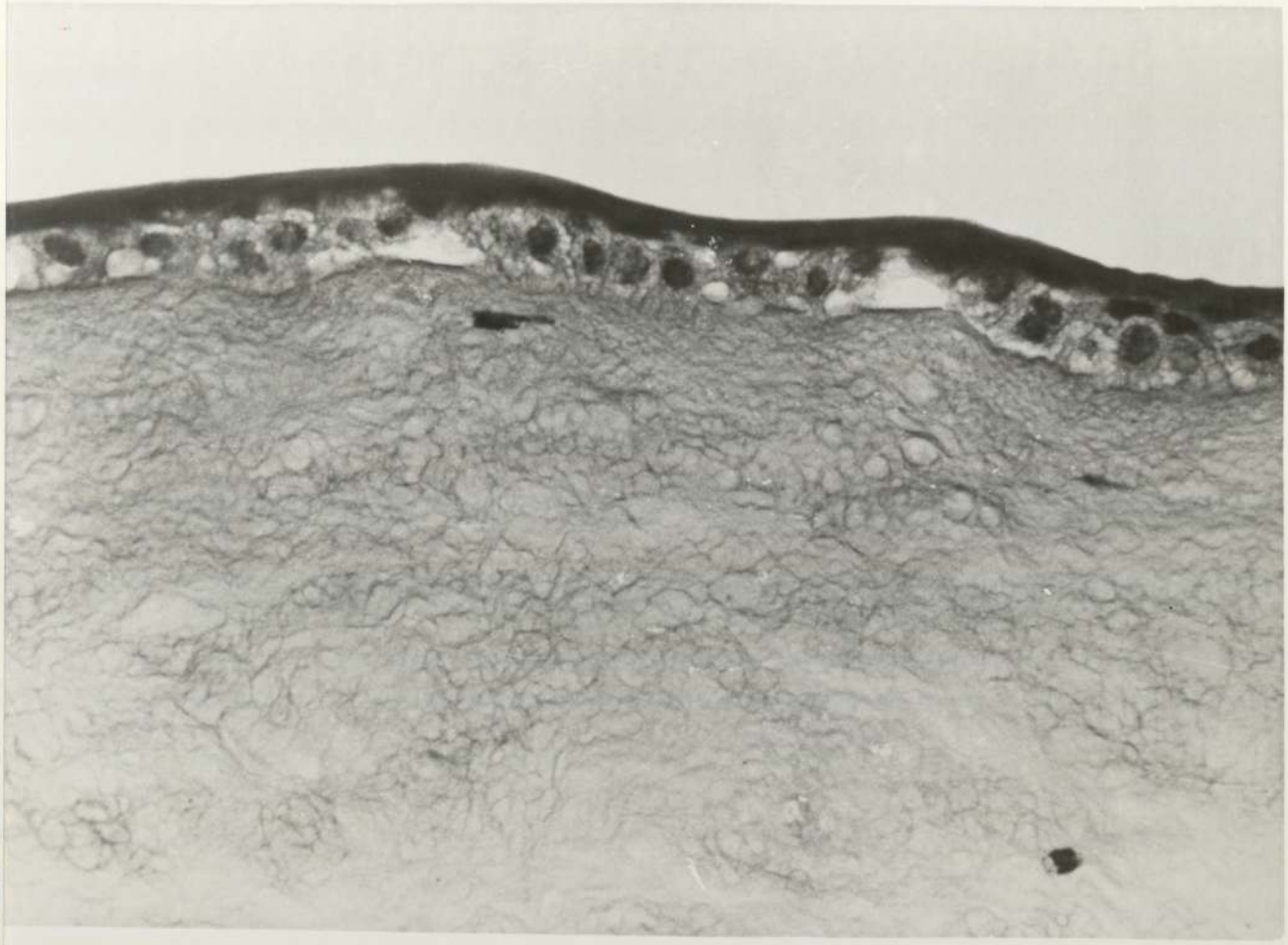


PLATE 7.2

Photomicrograph of rabbit cornea showing grossly disturbed stroma with some evidence of stromal vesicles

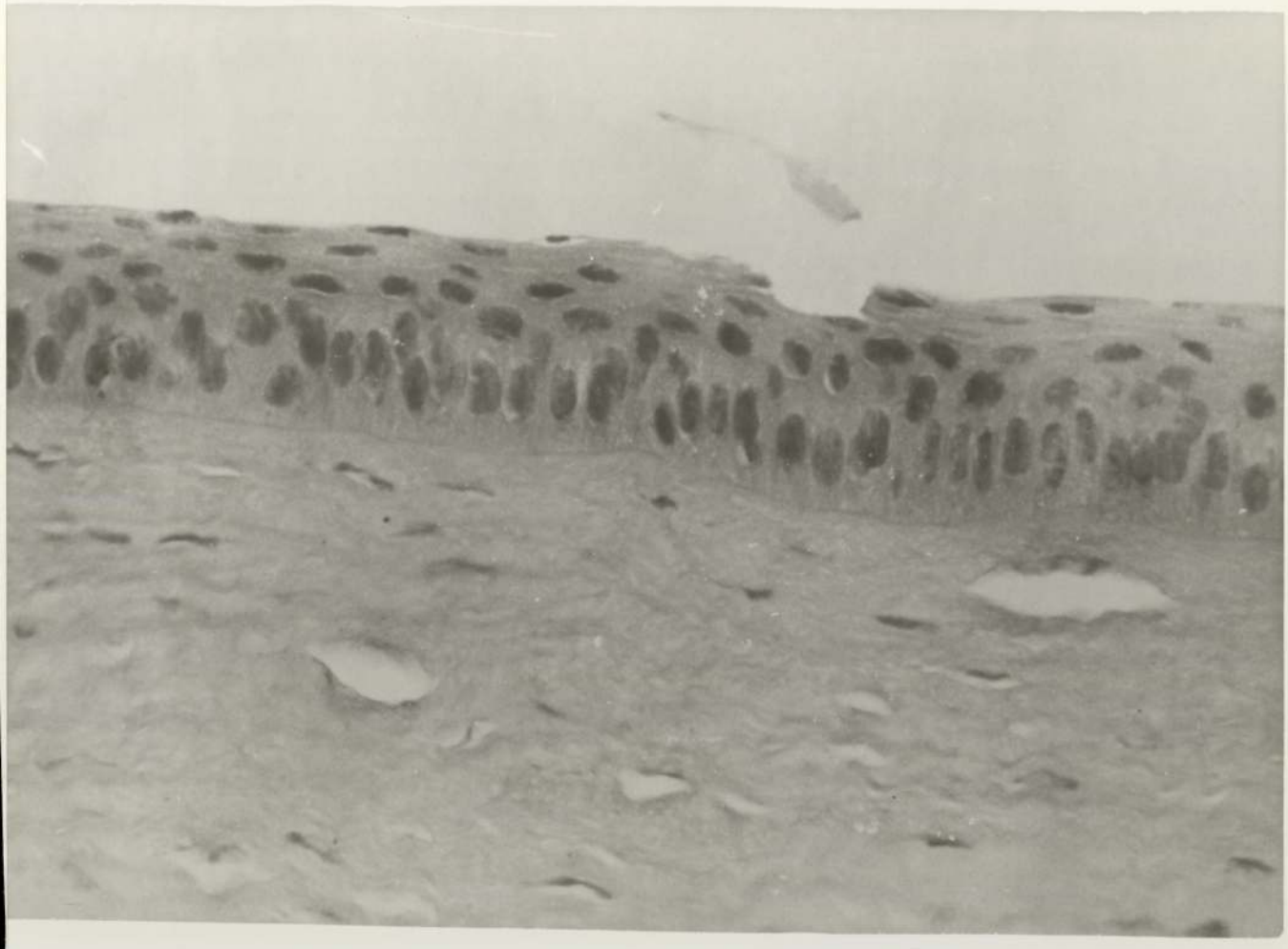


PLATE 7.3

Photomicrograph of rabbit cornea showing formation of fluid filled bullae at the epithelial/stroma interface and also evidence of stromal disruption.

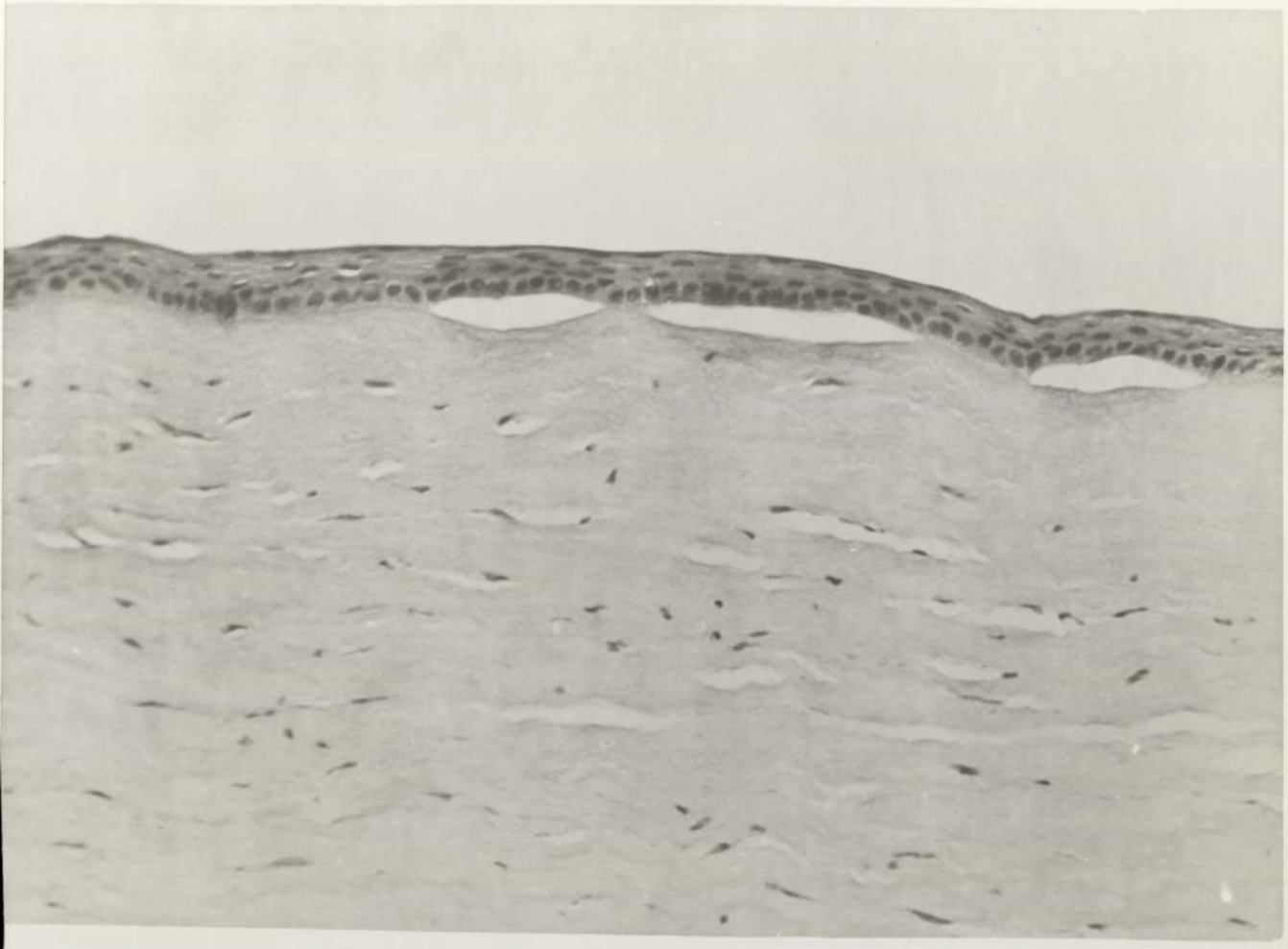


PLATE 7.4

Photomicrograph of rabbit cornea showing bullae under higher magnification. The appearance being consistent with the slit lamp view of the bullae.

PLATE 7.5

Slit lamp view of rabbit cornea, experimental eye.

Immediately following removal of contact lens.

PLATE 7.6

Slit lamp view of rabbit cornea, control eye.

Immediately following removal of contact lens.

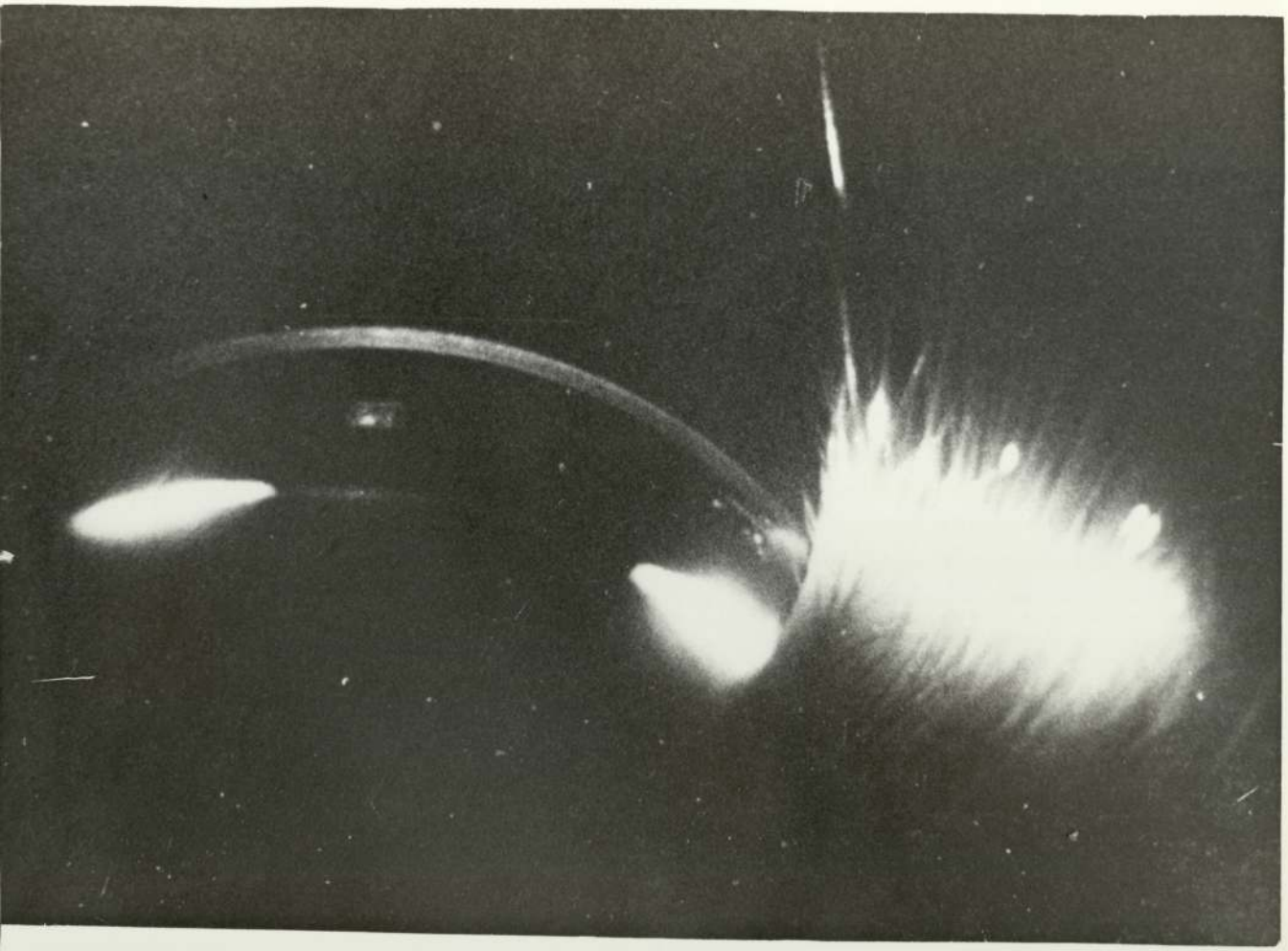
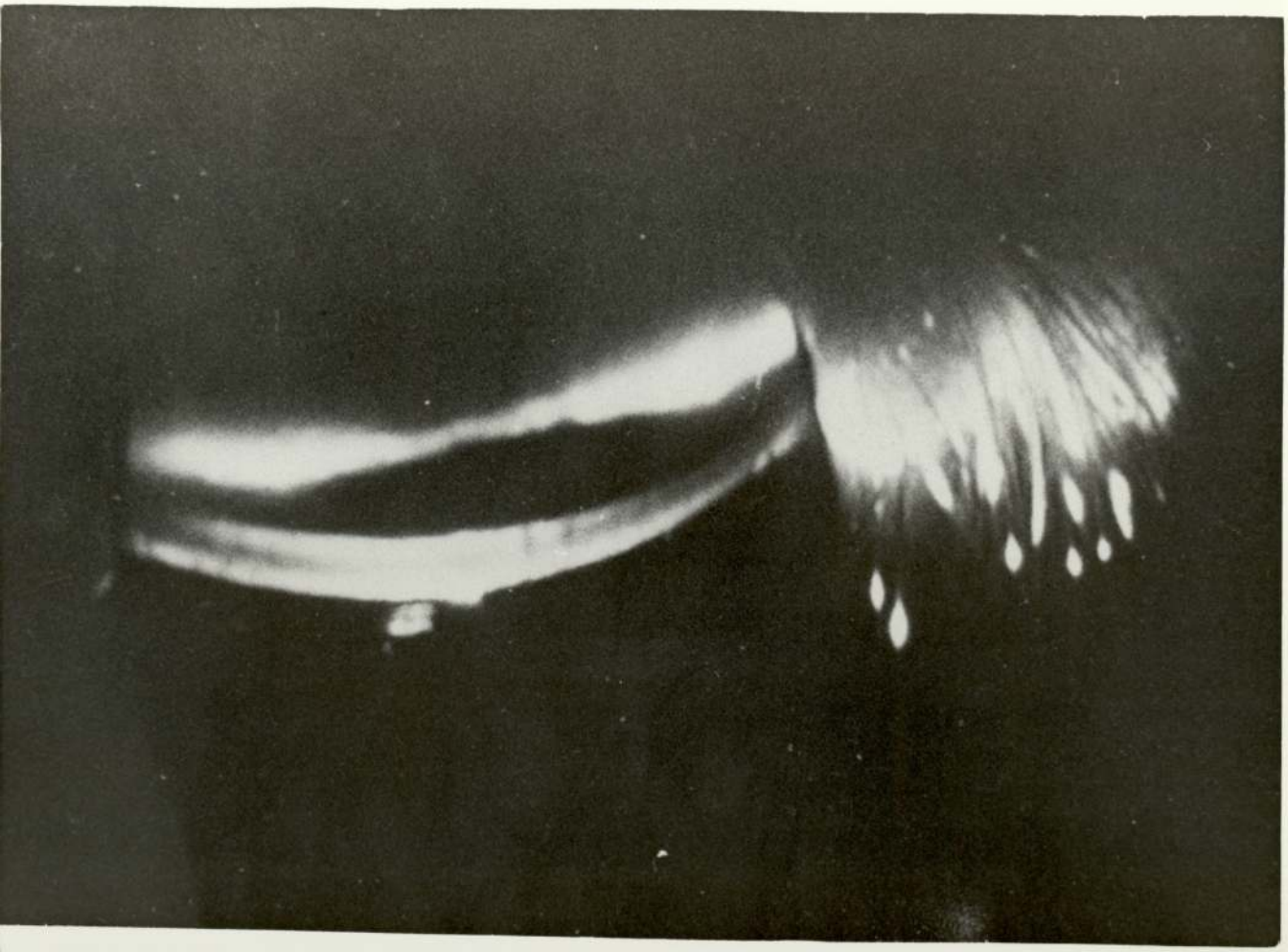


PLATE 7.7

Slit lamp view of rabbit cornea, experimental eye.
Twenty four hours after removal of contact lens.



BIRMINGHAM AREA HEALTH AUTHORITY (TEACHING)
WEST BIRMINGHAM HEALTH DISTRICT

REGIONAL OPHTHALMIC PATHOLOGICAL SERVICE

BIRMINGHAM AND MIDLAND EYE HOSPITAL

Church Street, Birmingham B3 2NS

Name RABBITS Age - Date 6th Nov. 1975.

Hospital Aston University. Specimen No.

Hospital No. - Surgeon Miss J. Lonnston Slide No. 300/75.

REPORT

HISTOLOGY NOTES ON 6 EXPERIMENTAL RABBITS.

2 of the 6 rabbits (Nos. 4 & 6) showed similar changes in the eyes submitted to the experimental procedure, i.e. the presence of thinning of the corneal epithelium, combined with intercellular oedema of the epithelium, with the formation of occasional subepithelial bullae, and a spongy appearance of the stroma. A 3rd experimental eye (3E) showed subepithelial bullae, and very slight oedema of the epithelium only. In two of the rabbits the findings were inconclusive, in spite of a good tissue representation. In one other animal (No.5.) insufficient tissue was available for a valid interpretation of the corneal changes.

D. R. Barry.
Consultant Pathologist.

EYE 113 RP 7895

show the subepithelial bullae as described in the report.

The reason for the different results may be because it was impossible to stop some of the rabbits from eye closure and this could have produced a better ' healing' process than if the eyes were open.

A one way analysis of variance showed that there was a statistically significant variation in central corneal thickness in both the experimental and the control eye. For both eyes the value of p was at the 0.001 level.

The graphs show why there is a statistical difference for both the control and the experimental eyes with the two treatments used. The control eye mimics the experimental eye but to a much lesser extent. The reason why this occurs is not known; it could be due to the sympathetic relationship between the eyes or it could be because there is an inevitable effect on the rabbit eye from wearing any contact lens, whatever the soaking solution. Parrish and Larke (1981) have shown that there is a sympathetic response in the human eye when a contact lens is worn on one eye and the contralateral eye acts as the control.

The graph also shows that the wearing of a lens presoaked

CENTRAL CORNEAL THICKNESS CHANGES IN RABBIT CORNEAE IN THE EXPERIMENTAL AND CONTROL EYE

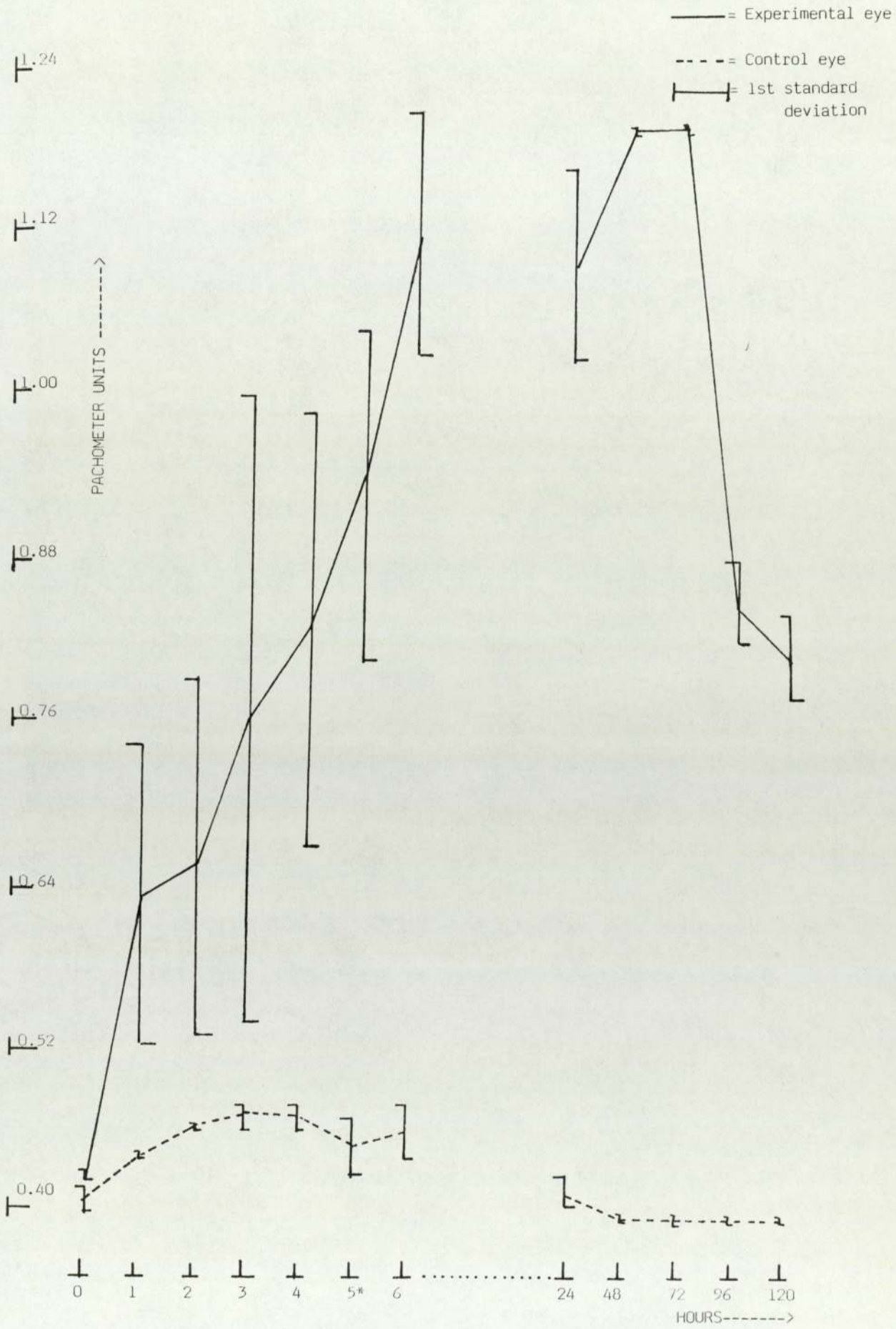


Figure 7.1

in 0.7 percent saline has a far more marked effect on the rabbit corneae than the one soaked in normal saline. Thus it would seem that the hypotonic saline was instrumental in producing the epithelial bullae and also the gross stromal disturbance in the rabbits.

The corneal swelling in the rabbit corneae was far in excess of that anticipated and posed ethical problems when human experimentation was considered. Some of the problems could have been caused by the material being used and the relatively low oxygen permeability of the Bausch and Lomb series 'N' soflens. It was therefore decided that as far as the human work was concerned it would be advisable to use a lens with a slightly higher oxygen permeability. As explained in chapter 5 the lens selected was the Duragel 60, although this lens is still classifed as a daily wear lens it has a greater water content and oxygen transmission than the Bausch and Lomb series 'N' soflens.

SUMMARY TABLES FOR ANALYSIS OF VARIANCE FOR RABBIT STUDIES

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

EXPERIMENTAL EYE SOFLENS PRESOAKED IN 0.7% SALINE

SOURCE	df	S.S.	Var Est	F	p
BETWEEN HOURS	6	0.18314	0.3052	11.56	0.001
WITHIN HOURS	30	0.7920	0.0264		
TOTAL	36	2.6234			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

CONTROL EYE SOFLENS PRESOAKED IN NORMAL SALINE

SOURCE	df	S.S.	Var Est	F	p
BETWEEN HOURS	6	0.0155	0.002583	11.5687	0.001
WITHIN HOURS	30	0.0067	0.0002233		
TOTAL	36	0.0222			

Control eye for analysis of experimental eye on previous page

CHAPTER 8

Changes in human corneal thickness produced by Duragel 60 hydrogel contact lenses soaked in non isotonic saline.

Section 8.1

Initial studies using Duragel 60 contact lenses soaked in 0.7 percent saline.

In view of the results of the animal work it was decided that extreme caution should be exercised as far as the human work was concerned, before volunteers were subjected to the treatment, the writer and the then project supervisor submitted themselves to three hours of lens wear, when the Duragel 60 had been presoaked in 0.7 percent saline using the same format as in the animal studies already explained in section 7.1.i. with the exception that the readings were taken every forty five minutes, and the lenses were only worn for three hours.

The graph shows the results as can be seen after two hours wear the cornea had increased by fifty three and a half percent, and it took a further three hours for the cornea to regain its original thickness. The control eye wearing the lens soaked in normal saline showed some unexpected results, they showed a small increase in thickness with lens wear, which agrees with many other authors such as

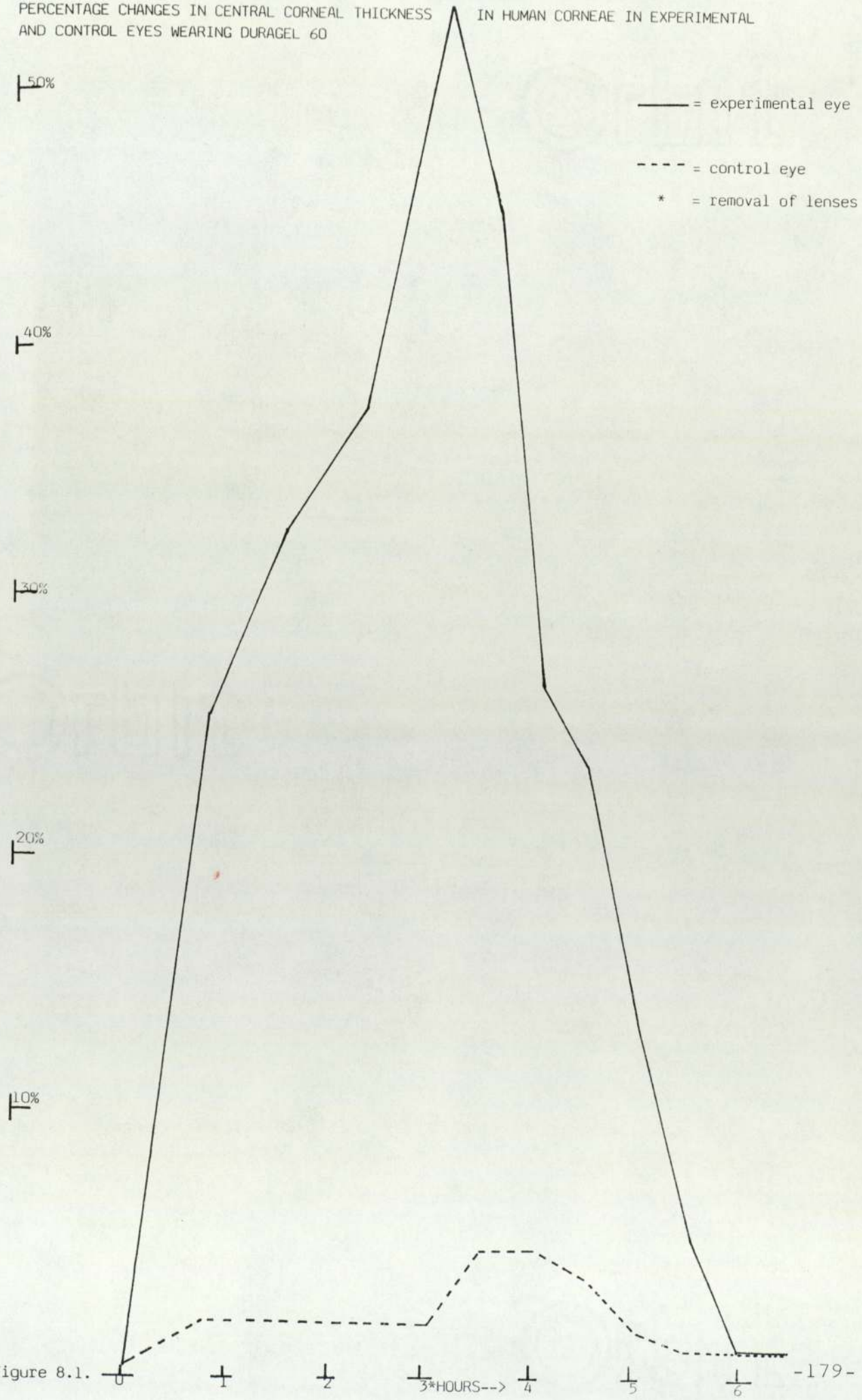

PERCENTAGE CHANGES IN CENTRAL CORNEAL THICKNESS IN HUMAN CORNEAE IN EXPERIMENTAL AND CONTROL EYES WEARING DURAGEL 60
50%
40%
30%
20%
10%
= experimental eye
= control eye
* = removal of lenses
0
1
2
3*HOURS-->
4
5
6

Figure 8.1.

Bailey and Carney (1973) , Carney (1975), (1975[2]), Kikkawa (1975), Sanders et al (1975), Carney (1976), and Rasson and Fatt (1982); however, when the lenses were removed the cornea continued to increase in thickness and it was not until a further two and a half hours later that the corneae had returned to their original values. A table overleaf shows a summary of a one way analysis of variance of the first three hours wear this shows in the experimental eye that there is strong statistical evidence that the changes in the corneal thickness are due to the wearing of the contact lens soaked in 0.7 percent saline with p= 0.001, however in the control eye the analysis of variance showed that there was no significant change in the corneal thickness due to wearing the Duragel 60 soaked in normal saline.

If the recovery time is taken into account the statistical evidence is completely different as can be seen from the summary tables of the one way analysis of variance. The recovery period in the control eye produces a statistically significant change in central corneal thickness. It can be postulated that this is due to the sympathetic response of the eyes, or it could be that the cornea was just beginning to reach the point where anoxia due to lens wear was begining to have an effect on the cornea, and if the lens had continued to be worn the thickness would still have

increased.

These results indicated that it was a safe procedure to use 0.7 percent saline to soak the Duragel 60 lens providing that it was not worn for more than three hours.

SUMMARY TABLES FOR ANALYSIS OF VARIANCE FOR INITIAL STUDIES WITH DURAGEL 60

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

EXPERIMENTAL EYE FOR FIRST THREE HOURS

Source	df	S.S.	Var Est	F	p
Between hours	4	0.07824	0.01956	37.6154	0.001
Within Hours	5	0.0026	0.00052		
Total	9	0.08084			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

CONTROL EYE FOR FIRST THREE HOURS

Source	df	S.S.	Var Est	F	p
Between Hours	4	0.00016	0.00004	0.8	Not significant
Within Hours	5	0.00025	0.00005		
Total	9	0.00041			

Control eye for analysis of experimental eye on previous page

SUMMARY TABLE OF ANALYSIS OF VARIANCE

EXPERIMENTAL EYE INCLUDING RECOVERY TIME

Source	df	S.S.	Var Est	F	p
Between Hours	11	0.18525	0.0168409	37.424	0.001
Within Hours	12	0.0054	0.00045		
Total	23	0.19065			

SUMMARY TABLE OF ANALYSIS OF VARIANCE

CONTROL EYE INCLUDING RECOVERY TIME

Source	df	S.S.	Var Est	F	p
Between Hours	11	0.00141	0.0001282	2.799	0.05
Within Hours	12	0.00055	0.0000458		
Total	23	0.00196			

Control eye for analysis of experimental eye on previous page

Section 8.1.i

Further studies using Duragel 60 contact lenses presoaked in 0.7.percent saline.

In order to obtain statistically viable results it is necessary to use more than two subjects, and as the previous results described in section 8.1. had shown that the procedure was safe it was decided to use six volunteers, ensuring that the eyes were not exposed to more than three hours of non isotonic lens wear. In addition to recording changes in corneal thickness it was decided that changes in tear tonicity should be monitored in order to see if it was possible to ascribe how much of the change in corneal thickness was due to anoxic effects of wearing a contact lens. All of the volunteers were told of the results of the animal study and the human study and all were trained observers being either final year students, pre registered, or registered ophthalmic opticians. Male volunteers were chosen so that menstral variations were excluded. The average age was twenty four years with a range of twenty to thirty years, none had previously worn contact lenses. The range of refractive errors, best sphere, was +2.00 D . to - 3.00 D with a mean of -1.50 D. Ideally only emmetropes would have been used, but it was impractical to find six emmetropic willing male volunteers.

Section 8.1.ii

Results of the further study with Duragel 60 contact lens presoaked in 0.7 percent saline.

The graph shows that there is an almost linear increase in corneal thickness in the treated eye, however there is also a smaller increase in central corneal thickness in the control eye. The chloride ion content of the tears does not show any such regular change. On initial insertion of the lenses there was a fall in the chloride ion content of the tears, which is in agreement with Hill (1975), this fall in concentration occured in both the experimental and control eye, then there was a large increase in chloride ion content of the tears in the first forty five minutes. After that, in the experimental eye there was a steady increase in apparent central corneal thickness, and a steady decrease in chloride ion content of the tears, whereas, in the case of the control eye both the central corneal thickness and the chloride ion content of the tears stay in far greater equilibrium.

Summary tables of the analysis of variance calculations are overleaf, these show that the experimental eye had a strongly statistically significant ($p = 0.001$) change in central corneal thickness due to the wearing of the Duragel 60 contact lens presoaked in 0.7 percent

PERCENTAGE CHANGE IN CENTRAL CORNEAL THICKNESS FOR EYES WEARING DURAGEL 60 PRESOAKED IN 0.7% SALINE SOLUTION

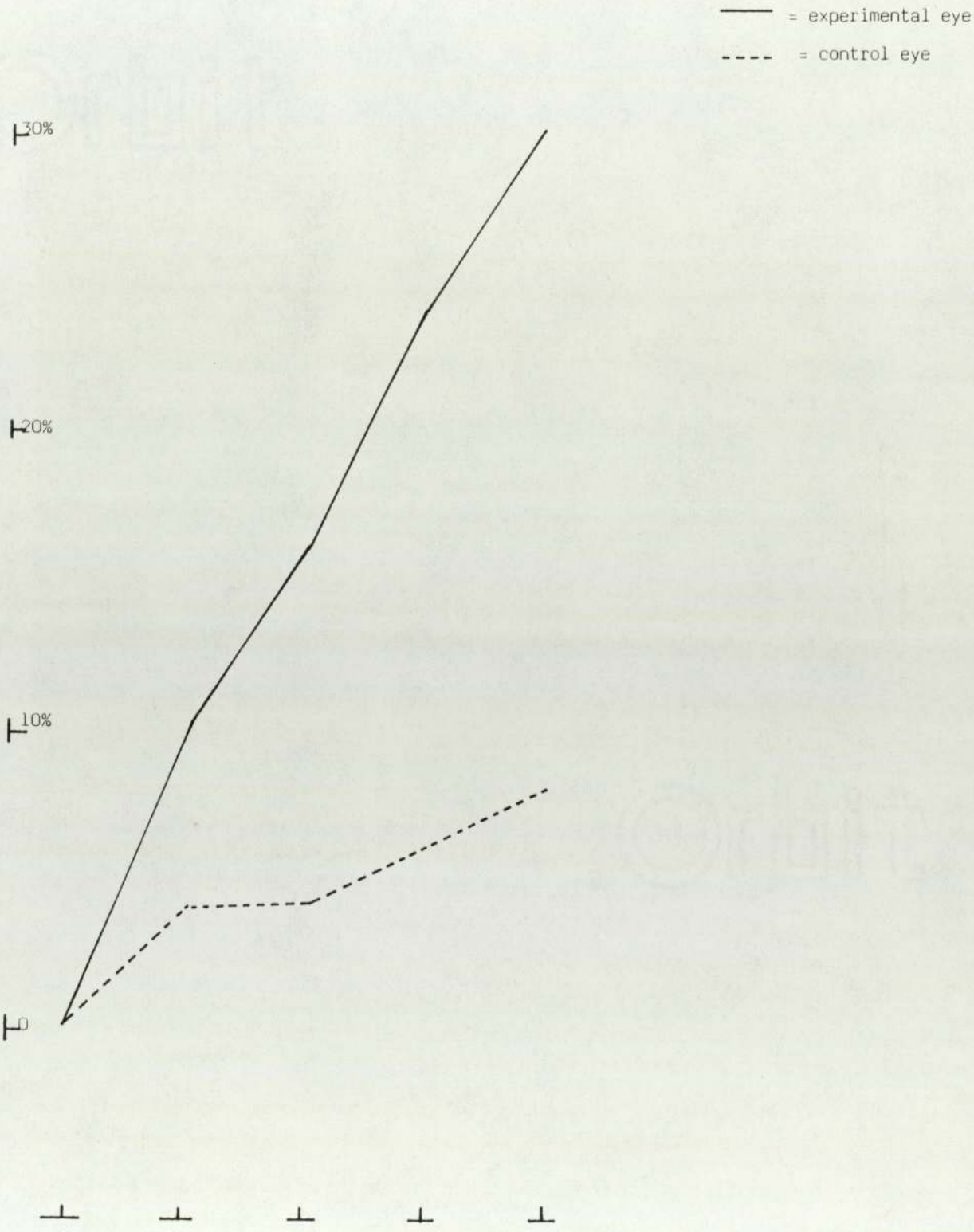


Figure 8.2

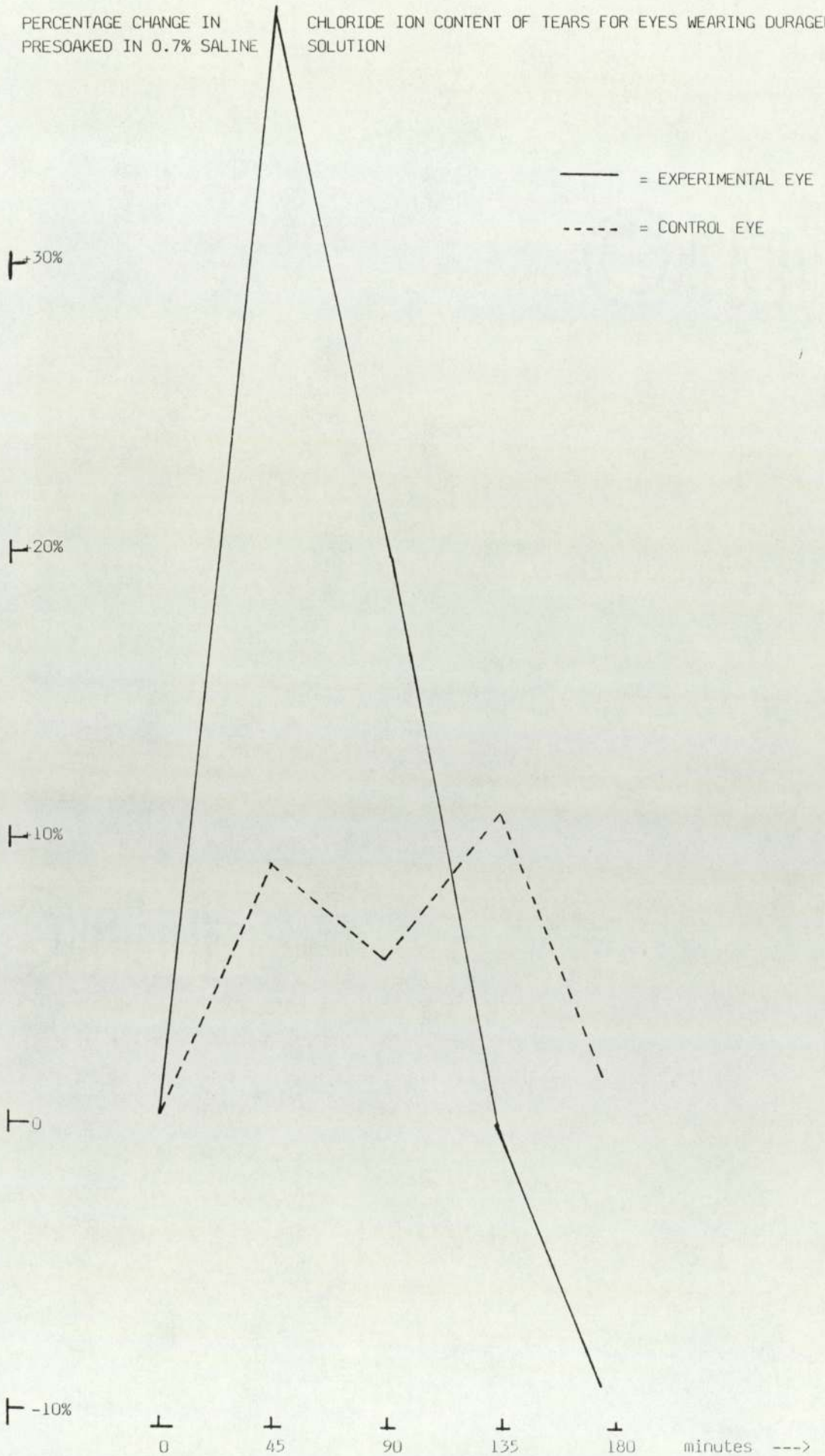

PERCENTAGE CHANGE IN CHLORIDE ION CONTENT OF TEARS FOR EYES WEARING DURAGEL 60 PRESOAKED IN 0.7% SALINE SOLUTION
= EXPERIMENTAL EYE
= CONTROL EYE
30%
20%
10%
0
-10%
0
45
90
135
180
minutes --->

Figure 8.3

saline, the change in the chloride ion content of the tears over the same period showed a significant change however this was not such a marked effect (p = 0,025) as the change in apparent corneal thickness.

The control eye in each case did not show any statistically significant result, however a 't' test between means of initial and final corneal thickness readings showed that there was a significant difference at the 0.1 level, whereas when a similar calculation was made for the control group of the chloride ion content of tears there was no statistical difference.

These results indicate that :-

(1) If a Duragel 60 soft contact lens is soaked in 0.7 percent saline there is a statistically significant change in both the central corneal thickness and the chloride ion content of the tears.

(2) If a Duragel 60 soft contact lens is soaked in 0.9 percent (normal) saline, when the lens has been worn for three hours there is a statistically significant difference between means for central corneal thickness, but not for the chloride ion content of the tears.

These findings would indicate that although the corneal changes are greater when the lens is soaked in the hypotonic saline there are still some changes when it is soaked in normal saline. It seems that the ionic difference in the soaking solutions is not the only factor that effects the corneal changes. As said before it could be due to the sympathetic response of the eyes, however it could be because the particular soft lenses are of sixty percent water content, overall size thirteen millimeters and have a standard back optic radius. No attempt had been made to fit the volunteers with the lenses so there could well have been an effect due to the lenses fitting incorrectly this would agree with the results of Polse (1972), who found that changing the fit of an hydrogel contact lens could stabilise the corneal fluctuations that sometimes occur when contact lens wear ceases. The reason that the fitting relationship had been ignored was because it was thought important that all the eyes were getting the same ' dose ' of solution supplied by the lenses, that is all the lenses had been treated in exactly the same manner and all had been very carefully made to ensure that they were the same specification, so all the volunteers were having the same amount of non-iso tonic saline, and polymers, placed on the experimental eye.

Isolating the variable originally seemed to be the best approach to the problem, but when the changes were occuring in the control eye it was realised that this may not be the case. It was therefore decided that different tonicities of saline should be used to soak the soft contact lenses to see if there was one particular tonicity which did not produce changes in corneal thickness and chloride ion content of tears.

SUMMARY TABLES FOR ANALYSIS OF VARIANCE FOR FURTHER STUDIES USING DURAGEL 60

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 0.7% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	0.079387	0.0198468	6.72	0.001
Within Hours	25	0.0733	0.002952		
Total	29	0.153187			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF CONTROL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	0.0045533	0.0011383	0.82	Not significant
Within Hours	25	0.0345227	0.0013809		
Total	29	0.039076			

Control eye for analysis of experimental eye on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 0.7% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	4	12912.867	3228.2168	4.07	0.025
Within Hours	25	19823.833	792.95332		
Total	29	32736.7			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN CONTROL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	784.33666	196.08417	0.967	Not significant
Within Hours	25	5067.8333	202.7133		
Total	29	5852.16996			

Control eye for analysis of experimental eye on previous page

FINAL PERCENTAGE CHANGES IN CENTRAL CORNEAL THICKNESS AFTER THREE HOURS OF WEAR OF DURAGEL60

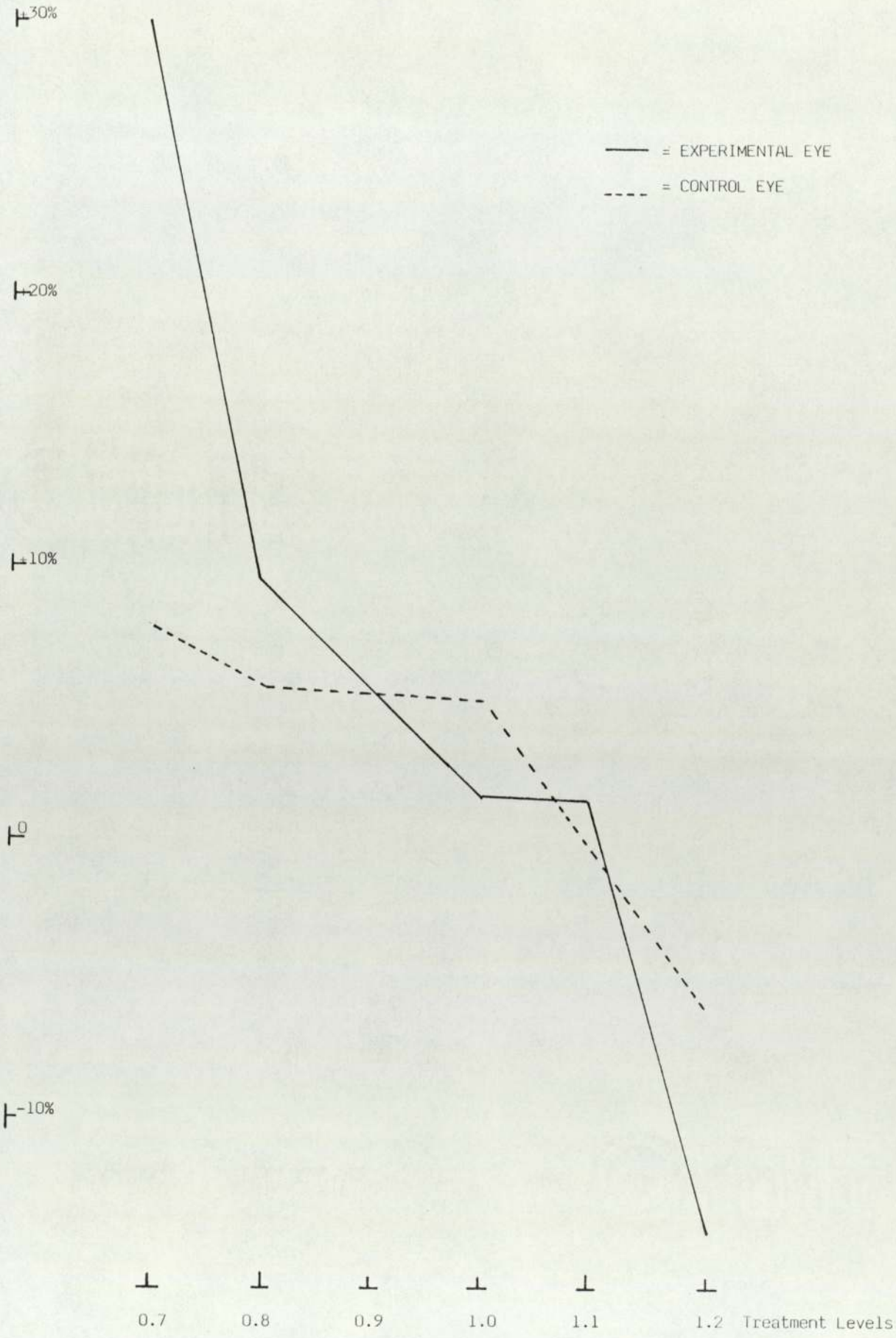


Figure 8.4

Section 8.2.

Study of changes produced in the cornea and the tears by wearing a Duragel 60 soft contact lens pre-soaked in hypotonic and hypertonic saline.

The same six volunteers were used, the Duragel 60 contact lenses were soaked in saline of different tonicities from 0.7 percent to 1.2 percent in 0.1 percentage steps. The lens for the control eye still being saoked in 0.9 percent (normal) saline. The tear samples were taken as previously described in section 4.4. The tears were sampled just prior to insertion of the lenses, then as soon as the lens had settled, and subsequently just prior to the corneal thickness being recorded. The reason that the tear samples were taken before the corneal thickness was measured was in case the slit lamp illumination caused sufficient photophobic reaction to induce reflex lacrimation.

Section 8.2.i

Results of the study of changes in the cornea and the tears induced by wearing a Duragel 60 soft contact lens pre-soaked in hypotonic and hypertonic saline solutions

The results of an analysis of variance and a 't' test between the initial and final apparent central corneal thickness after treatment are shown in tabular form on the following pages.

The differences in these results is not unexpected if the 'F' value of the analysis of variance is studied, because in each of the cases where the 't' test has been shown to be significant the 'F' value in the analysis of variance was at a number which meant that it was almost significant.

The 't' test between initial and final means indicates that if the lens in presoaked in 1.1 percent saline it produced no effect on the apparent central corneal thickness of both the experimental and the control eye.

The graph showing the percentage change in apparent corneal thickness after wearing the lenses for three hours shows that the control eye mimics the change in thickness shown by the experimental eye.

SUMMARY TABLE OF 't' TEST BETWEEN INITIAL AND FINAL MEANS

CENTRAL CORNEAL THICKNESS

Treatment Level	0.7%	0.8%	0.9%	1.0%	1.1%	1.2%
Experimental Eye	0.001	0.001	0.02	0.001	N.S.	0.001
Control Eye	0.01	0.05	0.05	0.001	N.S.	0.001

Note N.S. = Not significant

SUMMARY TABLE OF SIGNIFICANCE VALUES FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS

Treatment Level	0.7%	0.8%	0.9%	1.0%	1.1%	1.2%
Experimental Eye	0.001	0.01	N.S.	N.S.	N.S.	0.001
Control Eye	N.S.	N.S.	N.S.	N.S.	N.S.	0.001

Note N.S. = Not significant

The analysis of variance for the chloride ion content of the tears and a 't' test between means of pre-insertion and final results are shown in tabular form overleaf.

The chloride ion content of the tears does not seem to follow the same pattern as that of central corneal thickness. The graphs show the pattern of percentage change in chloride ion content induced by the wearing of the Duragel 60 soft contact lens. The chloride ion content changed dramatically on insertion of the lens in every case. This could have been due to the effect of reflex lacrimation, especially in the cases where the tonicity of the tears was reduced, or it could be due to excess saline on the lenses mixing with the tears. This would explain why in the case of the hypertonic solutions the tonicity of the tears was apparently increased.

From the graph which shows the effect of lens insertion on the tear concentration, it can be seen that there is a far greater change in the experimental eye than in the control eye. However it would have been expected that the change for the control eye would have been constant this was not the case. The mean for all the control eyes on insertion of the Duragel 60 soft contact lens was 0.74 ± 0.06 percent saline and pre-insertion the mean

PERCENTAGE CHANGE IN CHLORIDE ION CONTENT OF TEARS ON INITIAL INSERTION OF DURAGEL 60 FOR DIFFERENT TREATMENT LEVELS

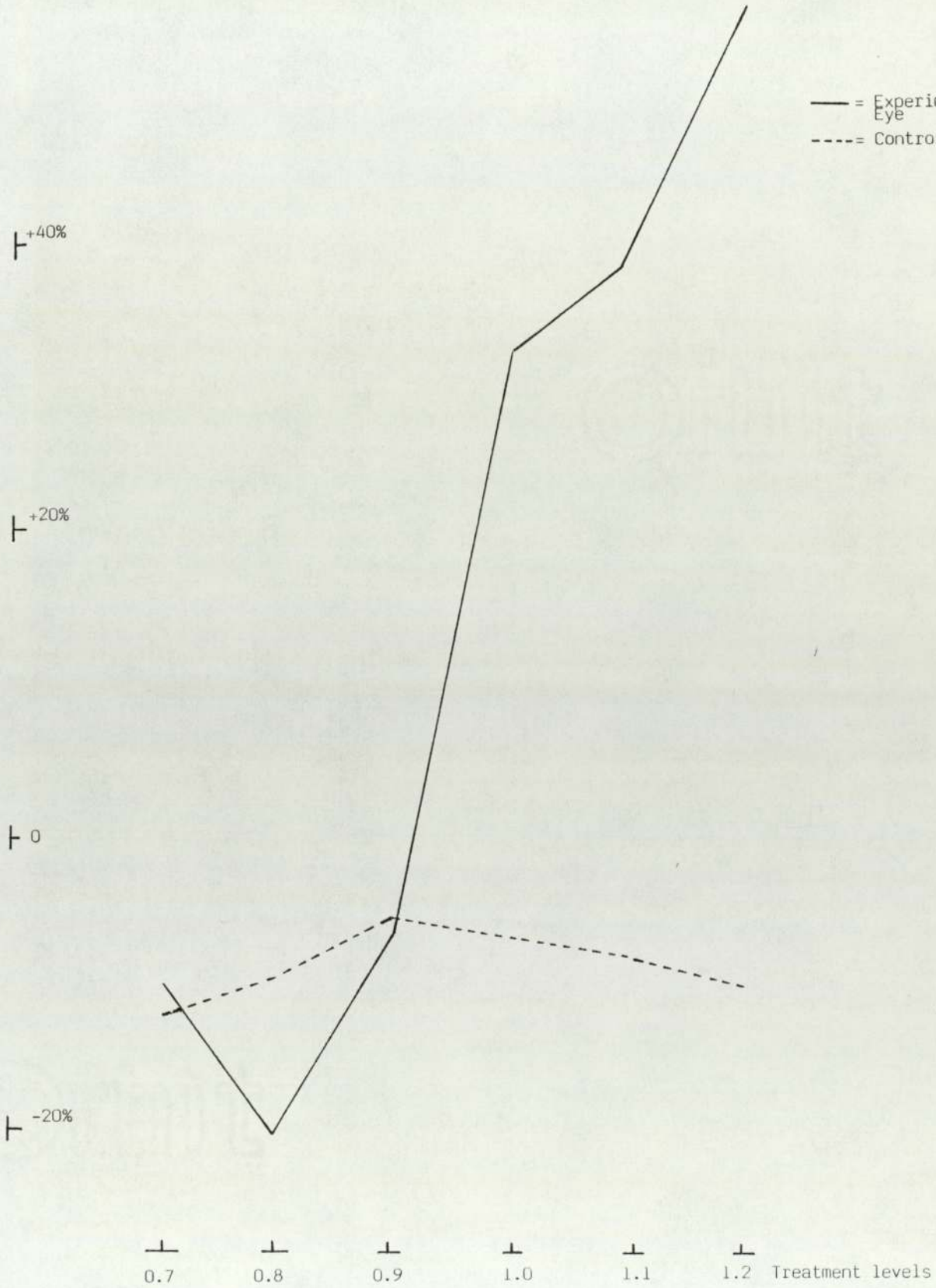


Figure 8.5

FINAL PERCENTAGE CHANGE IN CHLORIDE ION CONTENT OF TEARS AFTER THREE HOURS OF WEAR OF DURAGEL 60

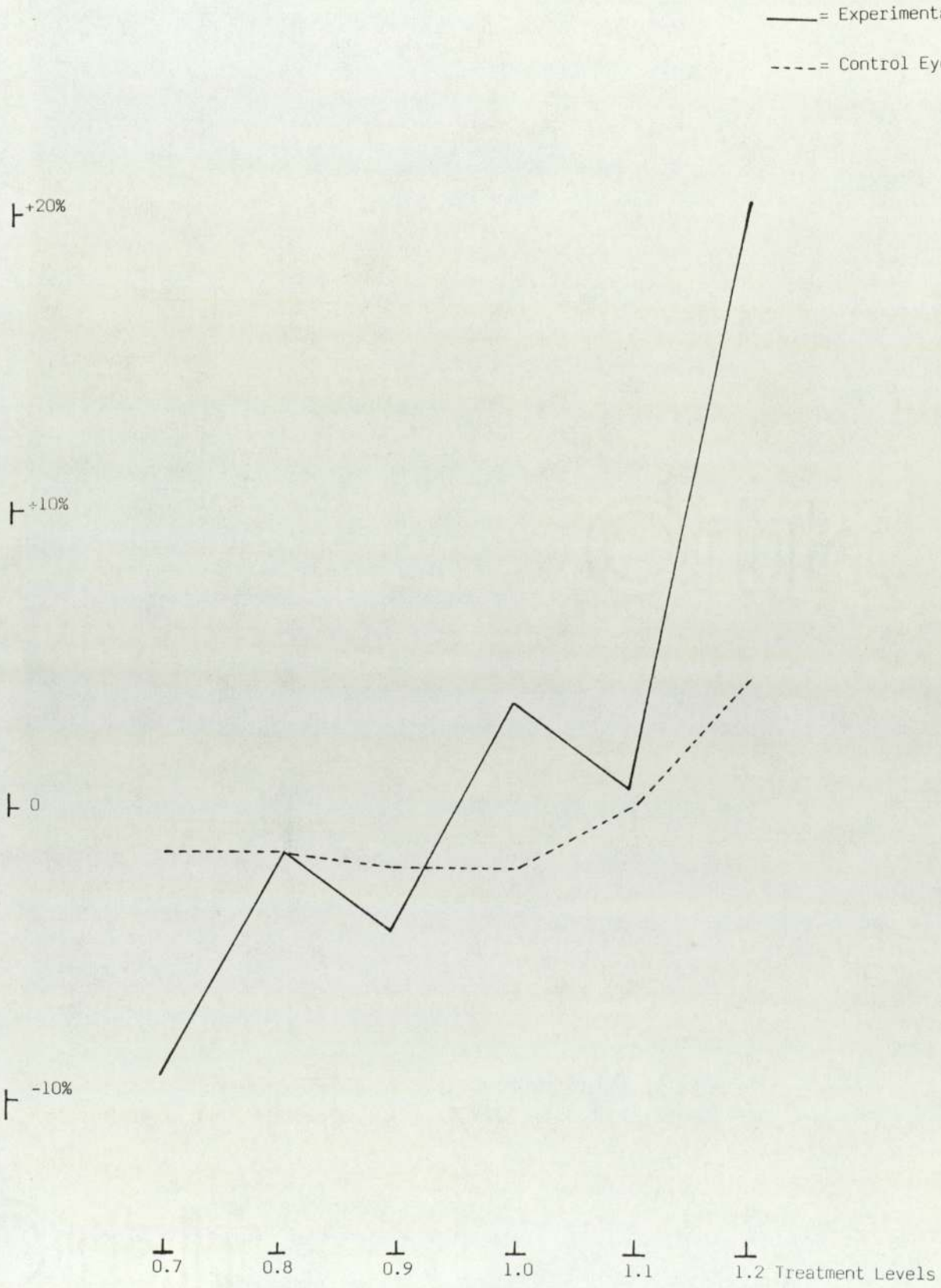


Figure 8.6

SUMMARY TABLE OF SIGNIFICANCE VALUES FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS

Treatment Level	0.7%	0.8%	0.9%	1.0%	1.1%	1.2%
Experimental Eye	0.025	0.001	N.S.	N.S.	N.S.	0.001
Control Eye	N.S.	N.S.	N.S.	N.S.	N.S.	0.01

Note N.S. = Not significant

SUMMARY TABLE OF 't' TEST BETWEEN INITIAL AND FINAL MEANS CHLORIDE ION CONTENT/

Treatment Level	0.7%	0.8%	0.9%	1.0%	1.1%	1.2%
Experimental Eye	0.01	N.S.	0.001	0.001	N.S.	0.001
Control Eye	0.1	N.S.	0.05	N.S.	N.S.	0.001

Note N.S.= Not significant

value was 0.81 $\pm$ 0.07 percent, this would indicate why the 't' test for the 0.8 percent treatment level was insignificant.

The problems of taking tear samples were great, it being very difficult to avoid stimulation of the tears. This is the most likely cause of the large standard deviation and also why the analysis of variance showed so many insignificant results.

The graph shows the individual variation in treatment levels for central corneal thickness and the tonicity variations in the tears, there does not seem to be any similarity in the shape of the graphs.

The results of the study of changes induced in the cornea and the tears by wearing a Duragel 60 soft contact lens for three hours which had previously been pre- soaked in hypotonic or hypertonic saline indicate that:-

(1) The tonicity of the soaking solution causes changes in the central corneal thickness. The hypotonic solutions causing corneal swelling and the hypertonic solution causing attenuation. When the lenses were soaked in a solution of 1.1 percent saline the least change in corneal thickness occured.

PERCENTAGE CHANGE IN CENTRAL CORNEAL THICKNESS WITH DURAGEL 60 PRESOAKED IN DIFFERENT TONICITIES OF SALINE SOLUTION

EXPERIMENTAL EYE

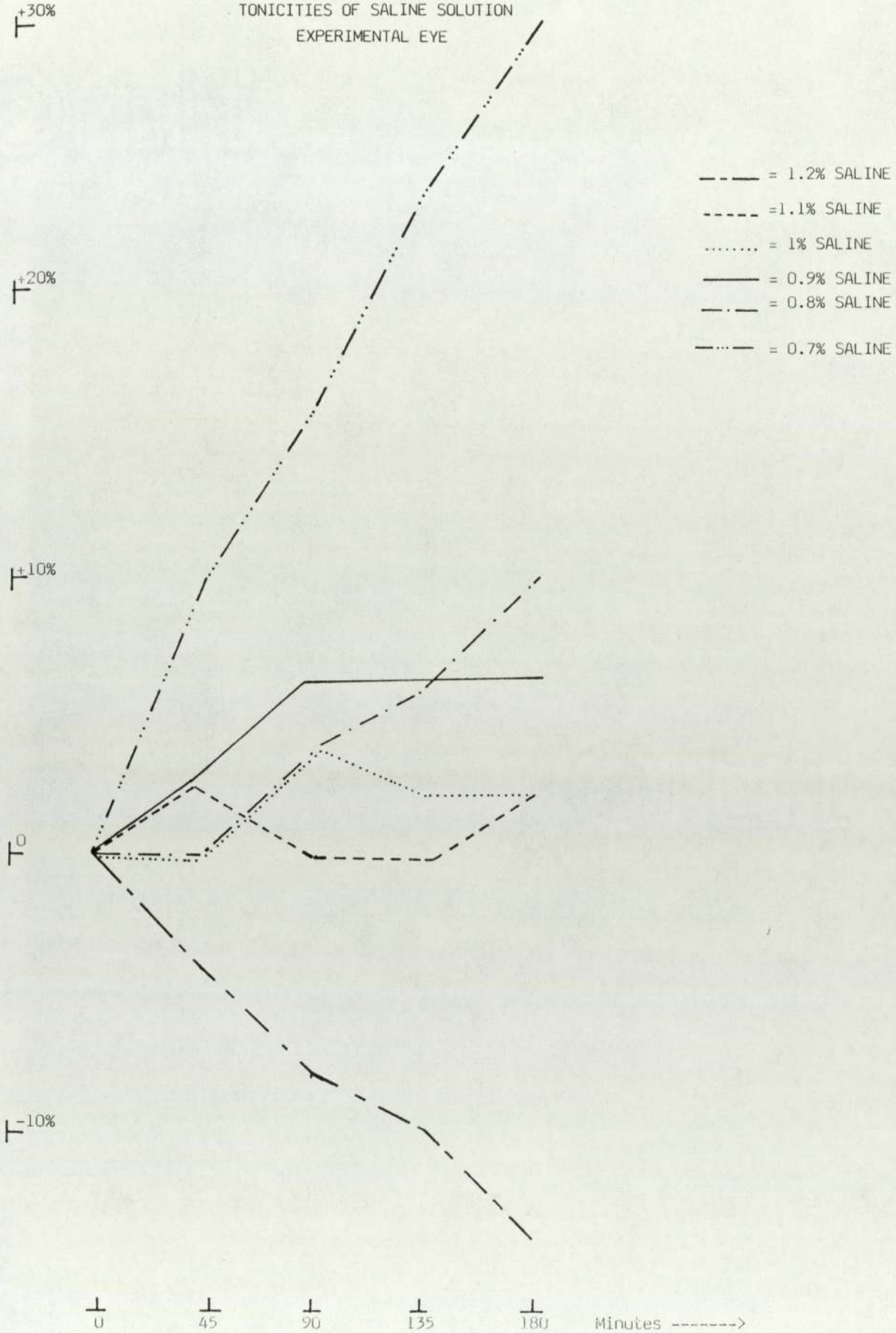


Figure 8.7

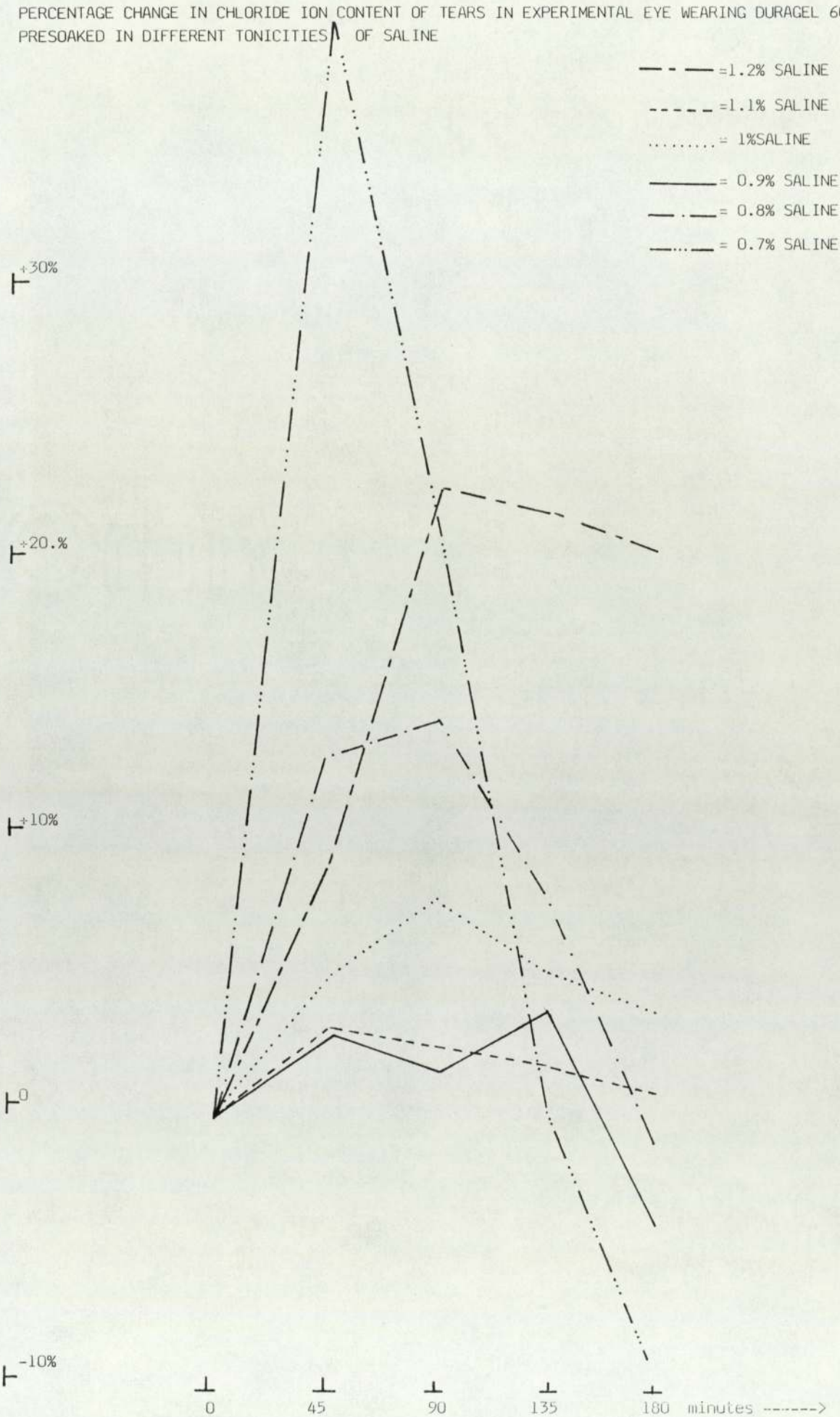

PERCENTAGE CHANGE IN CHLORIDE ION CONTENT OF TEARS IN EXPERIMENTAL EYE WEARING DURAGEL 60 PRESOAKED IN DIFFERENT TONICITIES OF SALINE
=1.2% SALINE
=1.1% SALINE
= 1%SALINE
= 0.9% SALINE
= 0.8% SALINE
= 0.7% SALINE
+30%
+20.%
+10%
0
-10%
0
45
90
135
180
minutes

Figure 8.8

PERCENTAGE CHANGE IN CENTRAL CORNEAL THICKNESS IN CONTROL EYE WEARING DURAGEL 60 IN 0.9% SALINE EXPERIMENTAL EYE WEARING DURAGEL 60 PRESOAKED IN DIFFERENT TONICITIES OF SALINE.

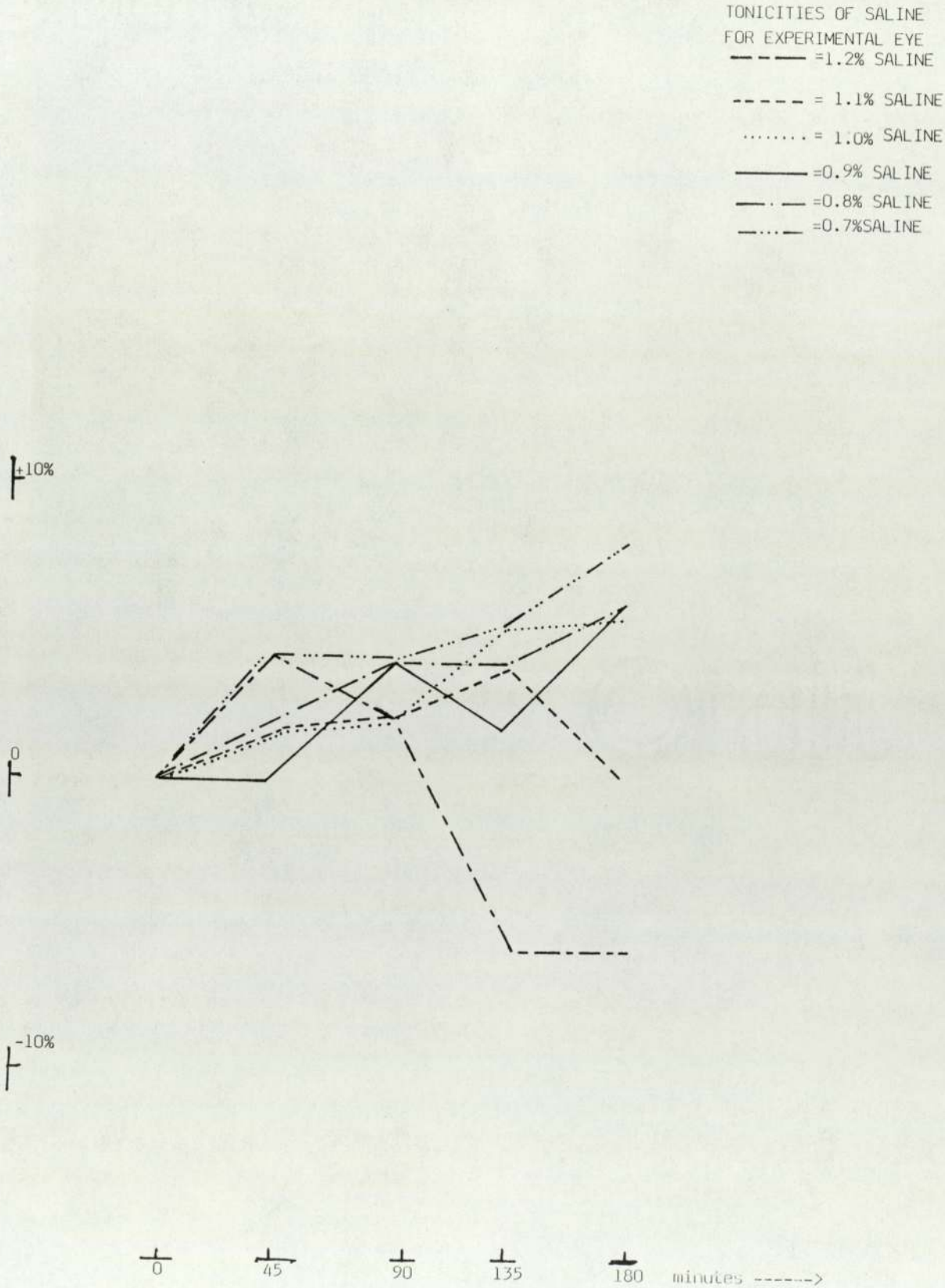


Figure 8.9

PERCENTAGE CHANGE IN CHLORIED ION CONTENT OF TEARS IN CONTROL EYE WEARING DURAGEL 60 IN 0.9% SALINE. EXPERIMENTAL EYE WEARING DURAGEL 60 PRESOAKED IN DIFFERENT TONICITIES OF SALINE SOLUTION.

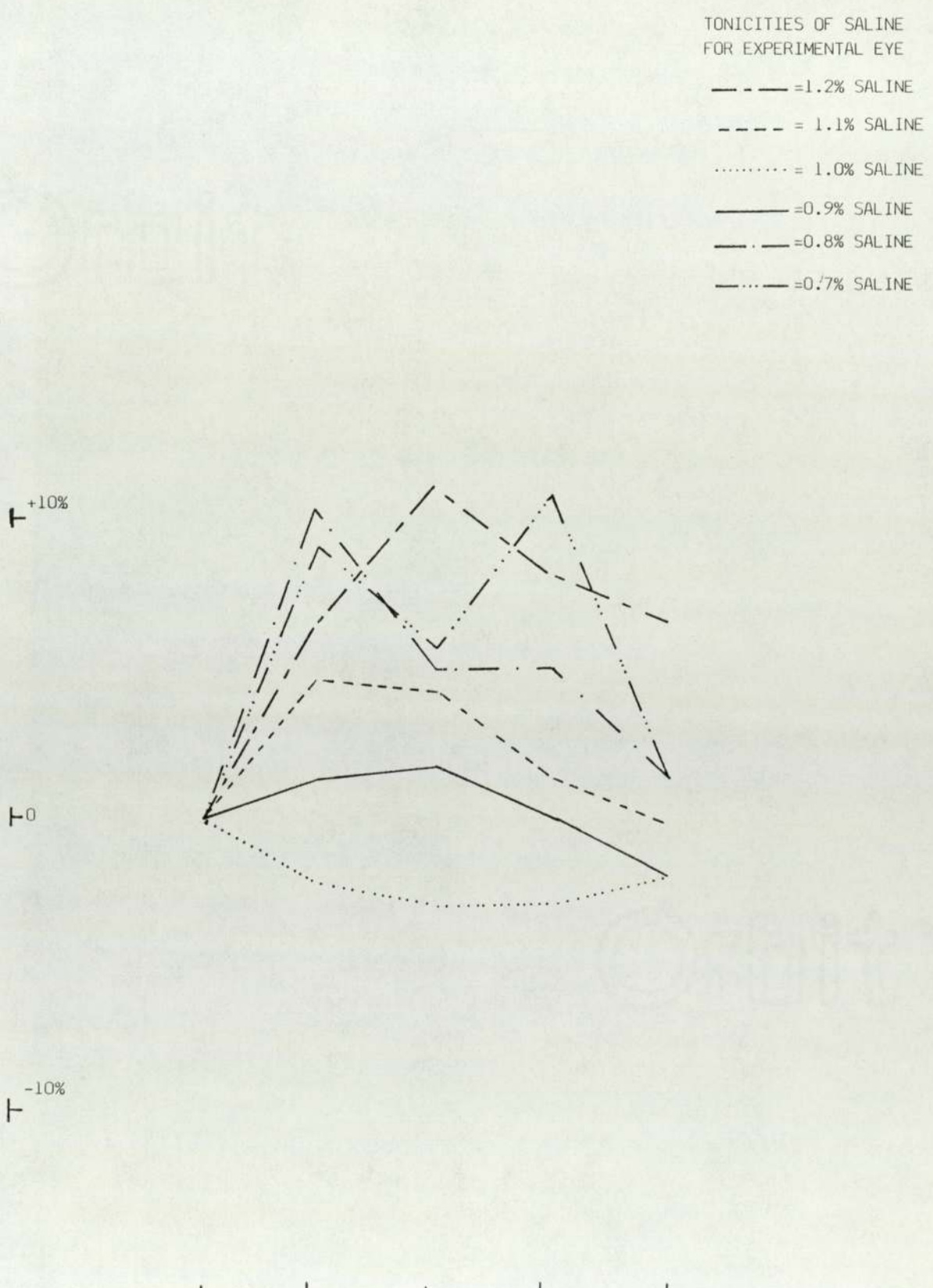


Figure 8.10

(2) The eye that was used as a control showed similar changes to those of the experimental eye, although to a much lesser extent. This would indicate that the changes are probably due to the sympathetic response of the eye.

(3) The changes in the chloride ion content of the tears, on initial insertion of the contact lenses, in the control eye, the tonicity of the tears was reduced by 0.7 percent from the pre- insertion level. This was probably due to a mixture of reflex tearing due to the introduction of a foreign body, and poor technique.

(4) When a Duragel 60 soft contact lens is presoaked in an hypertonic solution, and then introduced into an eye there is an initial increase in the tonicity of the tears, however when a contact lens which has been presoaked in an hypotonic solution is first worn there is an initial decrease in the chloride ion content of the tears.

(5) There was not a gradual change in the tonicity of the tears with increasing wear of the lenses soaked in the non-isotonic solution, as can be seen from the graphs, however the graph showing changes in the ionic content of tears with treatment levels does show that with in-

creasing hypertonicity of soaking solution there is an increase in the chloride ion content of the tears.

(6) The control eye shows similar, but smaller changes in tear tonicity, after forty five minutes of wearing the lenses, it can only be supposed that this is due to the inervation of the lacrimal glands, because the eyes are usually in a situation where they have identical tear tonicities.

SUMMARY TABLES FOR ANALYSIS OF VARIANCE FOR FURTHER STUDIES USING DURAGEL 60 CENTRAL CORNEAL THICKNESS

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 0.7% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	0.079387	0.0198468	6.72	0.001
Within Hours	25	0.0738	0.002952		
Total	29	0.153187			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	0.0041533	0.0010383	0.948	Not significant
Within Hours	25	0.0273667	0.0010947		
Total	29	0.03152			

Control eye for analysis of experimental eye (0.7% Saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 0.8% SALINE

Source	df	S.S	Var Est	F	p
Between hours	4	0.012586	0.0031467	4.916	0.01
Within hours	25	0.016	0.00064		
Total	29	0.0285867			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF CONTROL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	0.00528	0.00132	1.896	Not significant
Within Hours	25	0.0174	0.000696		
Total	29	0.02268			

Control eye for analysis of experimental eye (0.8% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	4	0.00542	0.001355	2.3577	Not significant
Within Hours	25	0.0143777	0.0005747		
Total	29	0.019867			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF CONTROL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	0.0027467	0.0006867	1.0468	Not significant
Within Hours	25	0.0164	0.000656		
Total	29	0.0191467			

Control eye for analysis of experimental eye (0.9% saline) on previous page

SUMMARY TABLE FOR ANAYLSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 1.0% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	0.0016867	0.0004217	1.5098	Not significant
Within Hours	25	0.0069833	0.0002795		
Total	29	0.0086703			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF CONTROL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	0.003	0.00075	1.6422	Not significant
Within Hours	25	0.0114167	0.0004567		
Total	29	0.0144167			

Control eye for analysis of experimental eye (1% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 1.1% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	0.00072	0.00018	0.4218	Not significant
Within Hours	25	0.010667	0.0004267		
Total	29	0.011387			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF CONTROL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	0.0017133	0.0004283	1.1430	Not significant
Within Hours	25	0.0093667	0.0003747		
Total	29	0.01108			

Control eye for analysis of experimental ey (1.1% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 1.2% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	0.0158334	0.0039583	7.7114	0.001
Within Hours	25	0.0128333	0.0005133		
Total	29	0.286667			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF CONTROL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	0.0119	0.002975	9.1623	0.001
Within Hours	25	0.0081167	0.0003247		
Total	29	0.0200167			

Control eye for analysis of experimental eye (1.2% saline) on previous page ,

SUMMARY TABLES FOR ANALYSIS OF VARIANCE FOR FURTHER STUDIES USING DURAGEL 60 CHLORIDE ION CONTENT OF TEARS

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 0.7% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	12912.867	3228.2168	4.07113	0.025
Within Hours	25	19823.833	792.95332		
Total	29	32736.7			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN CONTROL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	784.33666	196.08417	0.967	Not significant
Within Hours	25	5067.8333	202.7133		
Total	29	5852.17			

Control eye for analysis of experimental eye (0.7% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTNET OF TEARS IN EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 0.8% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	4	2411.5333	602.8833	6.4699	0.001
Within Hours	25	2329.65	93.186		
Total	29	4741.2			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN CONTROL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	4	807.53666	201.88417	2.498	Not significant
Within hours	25	2020.33	80.8132		
Total	29	2827.87			

Control eye for analysis of experimental eye (0.8% saline) on previou page.

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	444.46666	111.11667	1.3818	Not significant
Within Hours	25	2010.33	80.4132		
Total	29	2454.79666			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN CONTROL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	4	123.0033	30.750833	0.616	Not significant
Within hours	25	1247.67	49.9068		
Total	29	1370.6733			

Control eye for analysis of experimental eye (0.9% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 1.0% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	4	253.0	63.25	0.389	Not significant
Within hours	25	4066.5	162.66		
Total	29	4319.5			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN CONTROL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	67.13333	16.78333	0.1239	Not significant
Within Hours	25	3385.17	135.4068		
Total	29	3452.3			

Control eye for analysis of experimental eye (1% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED IN 1.1% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	4	82.6666	20.6666	0.4769	Not signifiacnt
Within hours	25	1083.33	43.3332		
Total	29	1165.99666			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN CONTROL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	289.00333	74.7	0.6287	Not significant
Within Hours	25	2970.17	118.8		
Total	29	3268.17333			

Control eye for analysis of variance of experimental eye (1-1% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN EXPERIMENTAL EYE

DURAGEL 60 PRESOAKED in 1.2% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	4	5071.8033	1267.9508	17.3059	0.001
Within Hours	25	1831.67	73.2668		
Total	29	6903.4733			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN CONTROL EYE

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	4	836.6666	209.16667	4.774	0.01
Within hours	25	1095.33	43.8132		
Total	29	1932.09666			

Control eye for analysis of experimental eye (1.2% saline) on previous page

CHAPTER 9

Section 9.1.

Study of changes produced in the cornea and the tears by wearing Duragel 75 soft contact lenses pre-soaked in hypotonic and hypertonic saline solutions.

The fact that presoaking Duragel 60 contact lenses in 1.1 percent saline produced the least disturbance to the corneal thickness was interesting, it was decided to see if changing the water content of the contact lens carrier would alter the results in any way. This should indicate if the size of the osmotic reservoir made any difference. Duragel 75 lenses were used, and made to exactly the same specifiaction as the Duragel 60.

It was decided that a corneal endothelial cell count would be made to see if there were any noticeable changes in endothelial cells with changes of the saline soaking solutions. The same volunteers were used as when using the Duragel 60 contact lenses, and the same procedure was followed except that following the measurement of central corneal thickness the endothelial cells were photoghraphed. Measurements were taken at half hourly intervals, and the lenses were worn for four and a half hours.

Section 9.1.i.

Results of the study of corneal changes and tear tonicity differences produced by Duragel 75 contact lenses soaked in hypotonic and hypertonic saline solutions before wear.

Summary tables of the analysis of variance of all of the results are shown on the following pages, also a summary of a 't' test between initial and final means.

The graphs show that the changes in apparent central corneal thickness follow a similar pattern to those seen when the Duragel 60 contact lenses were used. Again the treatment level that produced the least change in apparent central corneal thickness was the one where the hydrogel contact lens had been soaked in a slightly hypertonic solution (one percent saline).

The graphs indicate that once again the control eye tends to follow the changes that occur in the experimental eye. The changes that occur with the Duragel 75 contact lenses (in the control eye) were greater than those found with the daily wear Duragel 60 soft contact lenses, however there are greater changes with the experimental eye as well, therefore this could be simply a further manifestation of a sympathetic response of the control eye with the experimental eye, or again due to the greater osmotic reservoir contained in the higher water content lenses.

PERCENTAGE CHANGE IN THE CORNEA OF THE EXPERIMENTAL EYE DUE TO WEARING DURAGEL 75 PRESOAKED IN DIFFERENT TONICITIES OF SALINE

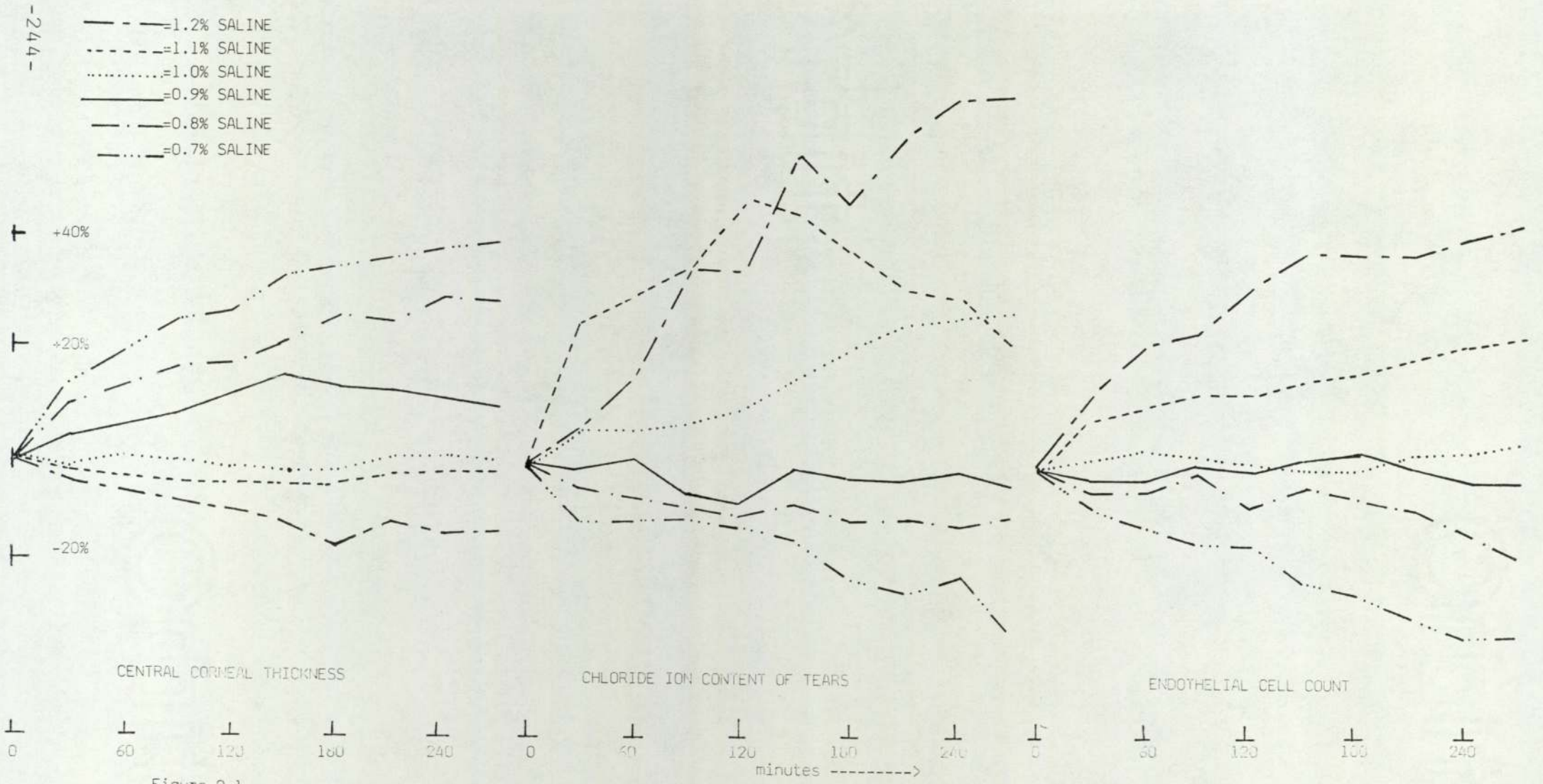


Figure 9.1

PERCENTAGE CHANGE IN THE CORNEA OF THE CONTROL EYE WEARING DURAGEL 75 PRESOAKED IN 0.9% SALINE WHEN EXPERIMENTAL EYE WEARING DURAGEL 75 PRESAOKED IN DIFFERENT TONICITIES OF SALINE SOLUTION

— — — =1.2% SALINE IN EXPERIMENTAL EYE
- - - - - =1.1% SALINE IN EXPERIMENTAL EYE
..... =1.0% SALINE IN EXPERIMENTAL EYE
——— =0.9% SALINE IN EXPERIMENTAL EYE
—·— =0.8% SALINE IN EXPERIMENTAL EYE
—···— =0.7% SALINE IN EXPERIMENTAL EYE

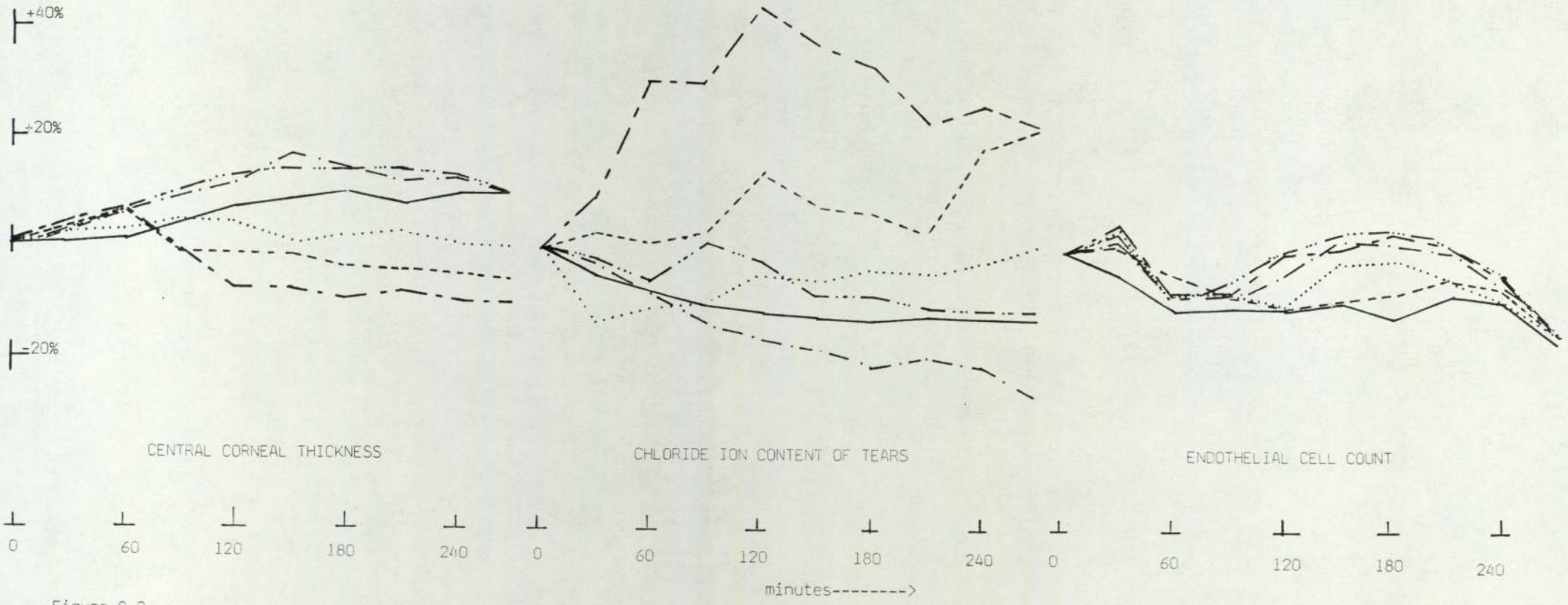


Figure 9.2

SUMMARY TABLE OF SIGNIFICANCE VALUES FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS

Treatment Level	0.7%	0.8%	0.9%	1.0%	1.1%	1.2%
Experimental Eye	0.001	0.001	0.001	N.S.	N.S.	0.001
Control Eye	0.001	0.001	0.001	N.S.	0.01	0.001

Note N.S.= Not significant

SUMMARY TABLE OF 't' TEST BETWEEN INITIAL AND FINAL MEANS

CENTRAL CORNEAL THICKNESS

Treatment Level	0.7%	0.8%	0.9%	1.0%	1.1%	1.2%
Experimental Eye	0.001	0.001	0.001	N.S.	N.S.	0.001
Control Eye	0.001	0.001	0.001	N.S.	0.001	0.001

Note N.S.= Not significant

The statistical analysis indicates that the one percent and 1.1 percent treatment levels produced the least change in the apparent central corneal thickness, a 't' test between the initial and final means also show that there is no significant difference. This would suggest that either one percent or 1.1 percent saline could be used to soak these lenses without causing changes in the apparent central corneal thickness.

The chloride ion content of the tears does not show any clearly defined pattern with differences in treatment level. The analysis of variance is significant at all levels. The 't' test between initial and final means does show that there was an insignificant difference for the Duragel 75 soft contact lens which had been presoaked in one percent saline. The reason for these somewhat irratic results could be because of the problems of collecting the samples, as has been seen when collecting samples in the initial trial of the instrument there was an inherent four percent error. Nevertheless these errors were greater than the inherent instrument error, so it would seem that any contact lens introduced into the eye will cause changes in the chloride ion content of the tears, which seem to be almost random changes. The graph does indicate that with increasing corneal thickness the tears tend to become more hypotonic and

SUMMARY TABLE OF SIGNIFICANCE VALUES FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS

Treatment Level	0.7%	0.8%	0.9%	1.0%	1.1%	1.2%
Experimental eye	0.001	0.001	0.01	0.001	0.01	0.001
Control eye	0.001	0.001	0.001	0.001	0.01	0.001

SUMMARY TABLE OF 't' TEST BETWEEN INITIAL AND FINAL MEANS CHLORIDE ION CONTENT

Treatment Level	0.7%	0.8%	0.9%	1.0%	1.1%	1.2%
Experimental Eye	0.001	0.001	0.20	0.001	0.001	0.001
Control Eye	0.001	0.001	0.001	N.S.	0.001	0.001

note N.S. = Not significant

vice versa, this suggests that if osmosis is partly responsible for maintaining corneal deturgesence that the tears could be partly responsible for some of the changes that occur. However this cannot be the complete reason as can be seen from the graph which shows percentage changes all drawn in the positive direction. These graphs indicate that the changes that occur in the tonicity of the tears are in excess of those taking place in the apparent corneal thickness, thus it would seem that osmosis can only be a contributory factor to corneal thickness changes due to the wearing of soft contact lenses.

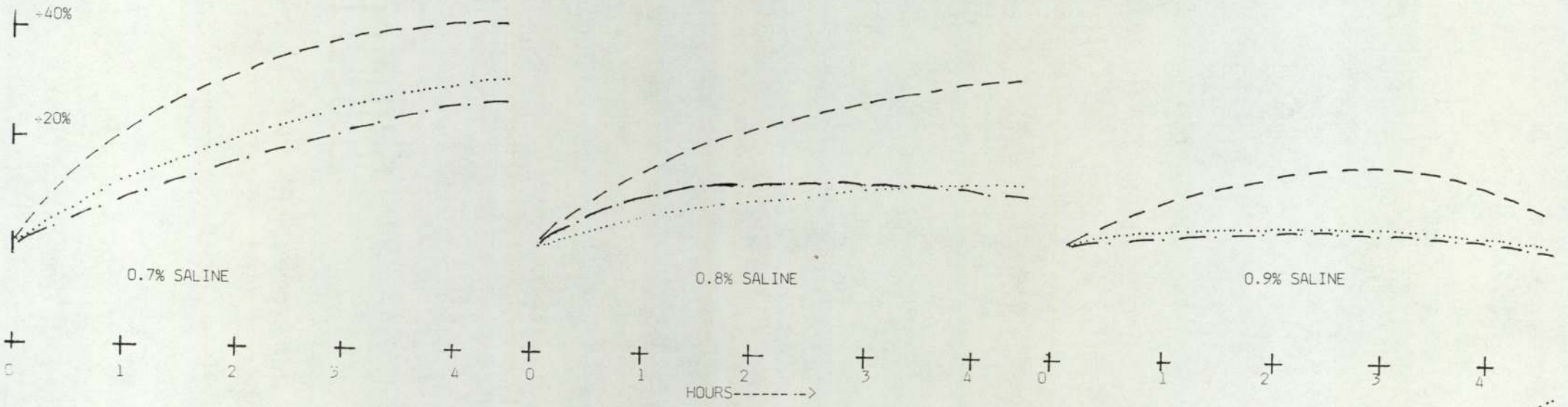
The changes that occur in the endothelial cell count are similar, but opposite, to those that occur in corneal thickness. The graph drawn showing all the changes that occur in a positive direction indicate that when the treatment levels were hypotonic the endothelial changes that occured were less than those of the apparent corneal thickness, and when the treatment levels were hypertonic the endothelial changes were greater than those occuring in the apparent corneal thickness. In the hypotonic range of treatments the endothelial cell count and the changes in the tonicity of the tears were very similar indeed, however in the hypertonic range of treatments they bore no resemblence to one another at all.

GRAPHS SHOWING COMPARATIVE PERCENTAGE CORNEAL CHANGE FOR DIFFERENT TREATMENT LEVELS

= CENTRAL CORNEAL THICKNESS

= CHLORIDE ION CONTENT OF TEARS

= ENDOTHELIAL CELL COUNT



SUMMARY TABLE OF SIGNIFICANCE VALUES FOR ANALYSIS OF VARIANCE

FOR ENDOTHELIAL CELL COUNT

Treatment Level	0.7%	0.8%	0.9%	1.0%	1.1%	1.2%
Experimental Eye	0.001	0.01	N.S.	N.S.	0.001	0.001
Control Eye	0.001	0.001	N.S.	N.S.	0.01	0.025

Note N.S.= Not significant

SUMMARY TABLE OF 't' TEST BETWEEN INITIAL AND FINAL MEANS ENDOTHELIAL CELL COUNT

Treatment Level	0.7%	0.8%	0.9%	1.0%	1.1%	1.2%
Experimental Eye	0.001	0.001	N.S.	N.S.	0.001	0.001
Control Eye	0.001	0.001	0.01	0.01	0.01	0.001

Note N.S. = Not significant

The analysis of these results indicate that the one percent treatment level produces the least changes in apparent corneal thickness, and endothelial cell count, whereas the 0.9 percent treatment level produces the least change in the tear tonicity.

If the results of the Duragel 60 and 75 are compared for the one percent and 1.1 percent level, it can be seen that the Duragel 75 tends to keep the cornea at the pre insertion level of apparent corneal thickness and then attenuate the cornea, whilst the Duragel 60 tends to increase the corneal thickness.

The results of the study of changes produced in the cornea and the tears by wearing lenses pre-soaked in both hypotonic and hypertonic saline solutions show:-

(1) The central apparent corneal thickness, and the endothelial cell count are maintained at or nearest to their preinsertion levels by presoaking the Duragel 75 soft contact lens in one percent saline solution.

(2) The chloride ion levels of the tears showed the least change when the Duragel 75 soft contact lens was presoaked in normal saline.

GRAPH SHOWING COMPARISON OF PERCENTAGE CHANGE IN CENTRAL CORNEAL THICKNESS FOR DURAGEL 60 AND 75 PRESOAKED IN 1% AND 1.1% SALINE

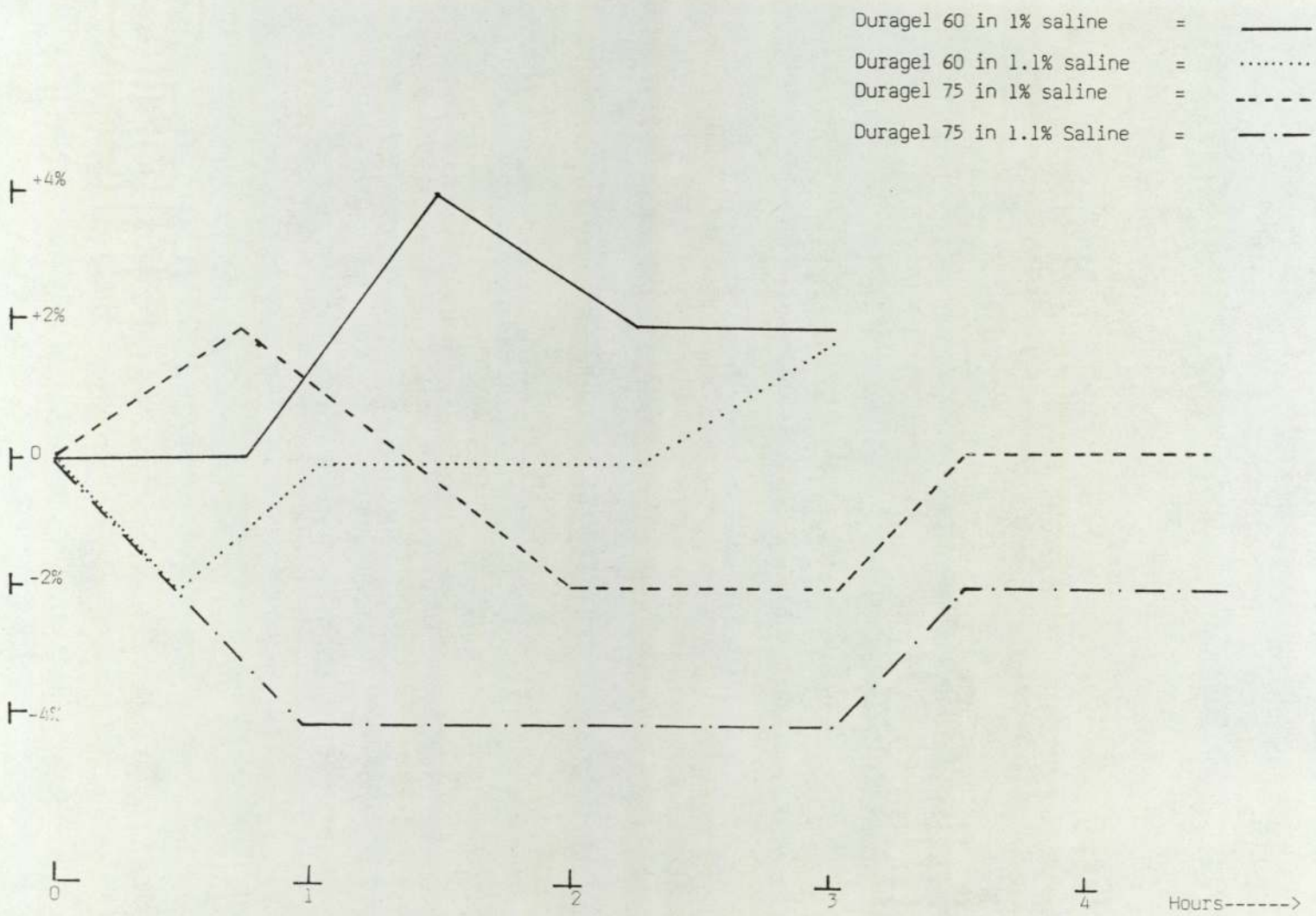


Figure 9.4

(3) The control eye mimics the changes that occur in the experimental eye as far as apparent corneal thickness and tonicity of the tears is concerned, but does not mimic the experimental eye for changes in the endothelial cell count.

(4) The apparent corneal thickness, tonicity of tears, and endothelial cell count all tend to change to a similar extent in the hypotonic treatment range.

(5) The corneal thickness and endothelial cell count change to a similar extent in the hypertonic treatment range.

(6) The tonicity of the tears changes to a far greater extent than either the endothelial cell count or the central apparent corneal thickness in the hypertonic range.

These results indicate that if hydrogel contact lenses were presoaked in a slightly hypertonic saline solution there should be less changes within the cornea, than if they are soaked in normal saline. It is interesting to note that the manufactures of Perma lens soft contact lenses have produced a solution for wetting the lenses which is stated to be hypertonic.

It would seem that the eye is sensitive to relatively small changes in ionic concentration, particularly in the hypotonic range. It was therefore concluded that it would be safe to use one percent saline for soaking extended wear high water content gel lenses and 1.1 percent saline solution for soaking daily wear lower water content soft lenses.

SUMMARY TABLES FOR ANALYSIS OF VARIANCE DURAGEL 75

CENTRAL CORNEAL THICKNESS

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 0.7% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	9	0.2316013	0.0258443	29.49	0.001
Within Hours	50	0.043817	0.0008743		
Total	59	0.2754183			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS FOR CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between Hours	9	0.0295067	0.0032785	14.33	0.001
Within Hours	50	0.0011433	0.0002287		
Total	59	0.04094			

Control eye for analysis of experimental eye (0.7% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 0.8% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	0.124147	0.0137905	8.57	0.001
Within hours	50	0.080383	0.0016077		
Total	59	0.2044977			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	0.027268	0.0030298	14.63	0.001
Within hours	50	0.080383	0.0016077		
Total	59	0.037618			

control eye for analysis of experimental eye (0.8% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	0.0295067	0.0032785	14.33	0.001
Within hours	50	0.011433	0.0002287		
Total	59	0.0409397			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	0.01976	0.0021956	18.61	0.001
Within hours	50	0.0059	0.000118		
Total	59	0.02566			

Control eye for analysis of experimental eye (0.9% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 1.0% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	0.0004813	0.0000535	0.28	Not significant
Within Hours	50	0.009417	0.0001883		
Total	59	0.0098983			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	0.0027813	0.000309	1.695	Not significant
Within hours	50	0.009117	0.0001823		
Total	59	0.0118983			

Control eye for analysis of experimental eye (1% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 1.1% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	0.001373	0.000156	0.877	Not significant
Within hours	50	0.0087	0.000174		
Total	59	0.010073			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	0.022393	0.0004479	3.245	0.01
Within hours	50	0.0069	0.000138		
Total	59	0.029293			

Control eye for analysis of experimental eye (1.1% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 1.2% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	0.0350663	0.0038963	14.04	0.001
Within hours	50	0.01387	0.0002774		
Total	59	0.2089363			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CENTRAL CORNEAL THICKNESS OF CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	0.0244147	0.0027127	18.61	0.001
Within hours	50	0.007283	0.0001457		
Total	59	0.0316977			

Control eye for analysis of experimental eye (1.2% saline) on previous page

SUMMARY TABLES FOR ANALYSIS OF VARIANCE DRUAGEL 75

CHLORIDE ION CONTENT OF TEARS

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 0.7% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	9373.08	1041.4533	11.35	0.001
Within hours	50	4585.50	91.71		
Total	59	13958.58			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	2128.9	236.544	4.33	0.001
Within hours	50	2726	54,52		
Total	59	4854.9			

Control eye for analysis of experimental eye (0.7% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 0.8% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	7781.68	864.6311	6.74	0.001
Within hours	50	6408.5	128.17		
Total	59	14190.18			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	1290.9	143.43	4.83	0.001
Within hours	50	1485	29.7		
Total	59	2775.9			

control eye for analysis of experimental eye (0.8% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	862.8333	95.87	3.03	0.01
Within hours	50	1582.2	31.64		
Total	59	2445.0333			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	1950.6666	216.74073	6.434	0.001
Within hours	50	1684.3	33.686		
Total	59	3634.96			

Control eye for analysis of experimental eye (0.9% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 1.0% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	12656.6	1406.2889	11.63	0.001
Within hours	50	6371	127.42		
Total	59	19027.6			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	2326.0333	258.448114	4,54	0.001
Within hours	50	2845.7	56.914		
Total	59				

Control eye for analysis of experimental ey (1% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 1.1% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	20488.7	2276.52	2.97	0.01
Within hours	50	38244.2	764.9		
Total	59	58732.2			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	15542.433	1727.937	3.69	0.01
Within hours	50	23383.2	467.664		
Total	59	38925.633			

Control eye for analysis of experimental eye (1.1% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 1.2% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	70619.2	7846.5778	6.2	0.001
Within hours	50	63274	1265.48		
Total	59	133893.2			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR CHLORIDE ION CONTENT OF TEARS IN CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	18619.867	2068.87	6.61	0.001
Within hours	50	15648	312.96		
Total	59	34267.87			

Control eye for analysis of experimental eye (1.2% saline) on previous page

SUMMARY TABLES FOR ANALYSIS OF VARIANCE DURAGEL 75

ENDOTHELIAL CELL COUNT

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR ENDOTHELIAL CELL COUNT OF EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 0.7% SALINE

Source	df	S.S.	Var Est	F	p
Betweeen hours	9	308198	34244.22	20.56	0.001
Within hours	50	83250	1665		
Total	59	391448			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR ENDOTHELIAL CELL COUNT FOR CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	96514.93	10723.88	3.9	0.001
Within hours	50	137281	2745.62		
Total	59	233795.93			

Control eye for analysis of experimental eye (0.7% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR ENDOTHELIAL CELL COUNT FOR EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 0.8% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	112311.733	12479.08	3.72	0.01
Within hours	50	167932	3358.64		
Total	59	280243.73			

SUMMARY FOR ANALYSIS OF VARIANCE

FOR ENDOTHELIAL CELL COUNT FOR CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	107503.23	11945.41	4.75	0.001
Within hours	50	125738	2514.76		
Total	59	233241.73			

Control eye for analysis of experimental eye (0.8% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR ENDOTHELIAL CELL COUNT OF EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	10397.13	1155.24	0.26	Not significant
Within hours	50	219671	4394.42		
Total	59	230068.13			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR ENDOTHELIAL CELL COUNT FOR CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	40150.33	4461.15	1.54	Not significant
Within hours	50	144391	2887.82		
Total	59	184541.33			

Control eye for analysis of experimental eye (0.9% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR ENDOTHELIAL CELL COUNT FOR EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 1.0% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	18082.76	2009.19	0.89	Not significant
Within hours	50	111818	2236.36		
Total	59	129900.76			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR ENDOTHELIAL CELL COUNT OF CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	39015.4	4335.04	1.32	Not significant
Within hours	50	164502	3290.04		
Total	59	203517.4			

Control eye for analysis of experimental eye (1% saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR ENDOTHELIAL CELL COUNT FOR EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 1.1% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	156476.27	17386.25	4.64	0.001
Within hours	50	186919	3738.38		
Total	59	343395.27			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR ENDOTHELIAL CELL COUNT OF CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	84231	9359	2.96	0.01
Within hours	50	158074	3161.48		
Total	59	242305			

Control eye for analysis of experimental eye (1.1 saline) on previous page

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR ENDOTHELIAL CELL COUNT OF EXPERIMENTAL EYE

DURAGEL 75 PRESOAKED IN 1.2% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	657901.93	73100.21	19.31	0.001
Within hours	50	189301	3786.02		
Total	59	847202.93			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

FOR ENDOTHELIAL CELL COUNT OF CONTROL EYE

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Source	df	S.S.	Var Est	F	p
Between hours	9	72643.53	8071.5	2.43	0.025
Within hours	50	166061	3321.22		
Total	59	238704.53			

Control eye for analysis of experimental eye (1.2 saline) on previous page

CHAPTER 10

Section 10.1

Patient studies using an hypertonic saline solution to soak Duragel 60 and Duragel 75 soft contact lenses.

A group of five patients were selected with sufficiently similar eyes to enable lenses of the same specification to be fitted to each eye, after being aquainted with all of the previous results of the studies with hypertonic saline solutions and the Duragel 60 and 75 soft contact lenses they were asked if they wished to volunteer as patients to enable further studies on these lenses and solutions to be carried out. At the end of the experiments they were all supplied with two pairs of free contact lenses, by Peter Madden, of Madden Contact Lenses Ltd.

It was decided to keep the pattern of patient visits to the well tried methods that have been in use for many years, always with the proviso that if there were any unforseen problems that the patient could come back at any time. The only difference from the normal routine followed for soft conatct lens patients was that a few extra measurements were taken at each visit.

The patients were fitted with a pair of Duragel 60 and

75 soft contact lenses according to the manufacturers instructions.

After the patients had achieved all day wear with a Duragel 60 soft contact lens they wore the lenses for nineteen weeks, and then had two weeks of non contact lens wear before they came back and were supplied with the Duragel 75 extended wear lenses. These lenses were worn for nineteen weeks without a break, then there was a further two weeks of non contact lens wear, and finally the patients were supplied with one Duragel 60 and one Duragel 75 lens the later being worn continuously the former on a daily wear basis, again for a nineteen week period. During the two week non contact lens wear periods the patients lenses were kept with their notes to ensure that there was no contact lens wear.

The first part of the experimental procedure involved the fitting and wearing of the daily wear Duragel 60 soft contact lenses using a 1.1 percent saline solution to soak and wet the lenses. The patients used a standard wearing schedule; of three hours increasing by one hour a day until twelve hours continuous wear was achieved, this was considered as wearing the lenses on a daily basis.

The chloride ion content of the tears, central apparent

corneal thickness, and endothelial cell count were recorded at the initial visit, and then when the patient had attained all day wear and worn the lenses for one week, the next visit was after a further two weeks of wear, then after a further four weeks of wear, and finally after a further twelve weeks of wear.

A similar pattern of readings was followed for the extended wear lenses, and the daily wear/ extended wear regime. It is realised that it is unusual to use such a slow build up of wearing time for the extended wear lenses but it was essential to use a similar pattern for similarity of treatment to the cornea. With the extended wear lenses once a twelve hour wearing time had been achieved the patients were allowed to leave the lenses in for extended periods. The saline soaking solution used for the Duragel 75 lenses was one percent, and for the Duragel 60/75 soft contact lenses the saline was 1.05 percent.

Unfortunately it was not possible to find five male patients who required contact lenses and fulfilled the other necessary conditions. The patients consisted of two females and three males with an age range of fifteen to forty one years with a mean of twenty five years. The refractive error range (best sphere) was -1.25 D

to -6.75D with a mean of -3.50 D. The ophthalmometer readings had a range, in the horizontal direction, of 7.45 to 7.95 millimeters with a mean of 7.74; in the vertical meridian the range was 7.35 to 7.90 millimeters with a mean of 7.68. The average difference between ophthalmometer readings was 0.09 millimeters with a range of 0.05 to 0.20 millimeters. The extended wear lenses were fitted on flattest ophthalmometer reading or the nearest 0.05 millimeter flatter as the lenses could only be made in 0.10 millimeter steps. The daily wear lenses were fitted 0.9 millimeters flatter than the flatest ophthalmometer readings or again the nearest 0.05 millimeters flatter. All the lenses were a standard thirteen millimeters in diameter. All the readings were taken after the patient had been awake for six hours.

Section 10.1.i.

Results of patient studies wearing Duragel 60 and 75 soft contact lenses soaked in an hypertonic saline solution.

A summary of the statistical analysis of the results is shown in tabular form overleaf. These results seem to indicate that by soaking the daily wear lens in one percent saline, or 1.05 percent saline produced insignificant changes in the three parameters measured, similarly for the extended wear lens if it is soaked in 1.05 or 1.1 percent saline solution. Thus it would seem that for a very small change in the ionic concentration of the soaking solution that some of the corneal changes described as being attributable to the wearing of hydrogel contact lenses could be elliminated. Patients did not notice any discomfort from wearing these lenses . The visual acuity remained the same throughout the experimental period in all the patients, on no occasion when the eyes were examined was there any noticeable corneal oedema by slit lamp examination, nor was there anysignificant corneal staining. The changes that occured when wearing these lenses soaked in the hypertonic saline were so small that none of them gave a statistically significant result and all were within the errors of the measuring techniques used. It is interesting to consider why there were not greater changes in the tonicity of the

tear film, when the previous experimental results are investigated.

The main difference with these experimental proceedings and those described in the previous chapters, are first that both the patients eyes had the same treatment level, it could be that this produces a more stable effect and does not put the system out of balance in tha same way as using different solutions for each eye. Second, in the earlier experiments the samples were taken every forty five minutes, and although only three microlitres were removed at each sampling this could be sufficient to cause the normal tear equilibrium to be upset. In the patient experiments the tears were only sampled once at each patient visit, thus causing a minimal disruption to the normal tear production.

It seems that the 1.05 percent saline soaking solution did not produce any more changes than the one percent for the high water content lenses, and the 1.1 percent for the lower water content lenses. If all hydrophilic contact lenses were hydrated, soaked and wetted with 1.05 percent saline there would be far less disturbance to the cornea as indicated by these results.

The results of the corneal changes found in patients

wearing Duragel 60 and 75 soft contact lenses soaked in an hypertonic saline solution show that:-

(1) In the normal wearing situation if Duragel 75, daily wear soft contact lenses are soaked in one or 1.05 percent saline solution, there are no significant changes in the chloride ion content of the tears, in the central apparent corneal thickness, and the endothelial cell count.

(2) If a Duragel 60 soft contact lens is soaked, and stored in 1.05 or 1.1 percent saline solution, and worn in the normal fashion then there are no significant changes in the tonicity of the tears. Also there are no changes of significance in the central apparent corneal thickness and the endothelial cell count of the cornea.

(3) A solution of 1.05 percent saline would be a better soaking, storing and wetting solution for Duragel 60 and Duragel 75 soft contact lenses when worn in the normal non pathological eye.

GRAPH SHOWING PERCENTAGE CORNEAL CHANGE IN PATIENTS WEARING DURAGEL 60 AND DURAGEL 75 SOFT CONTACT LENSES PRESOAKED IN HYPERTONIC SALINE

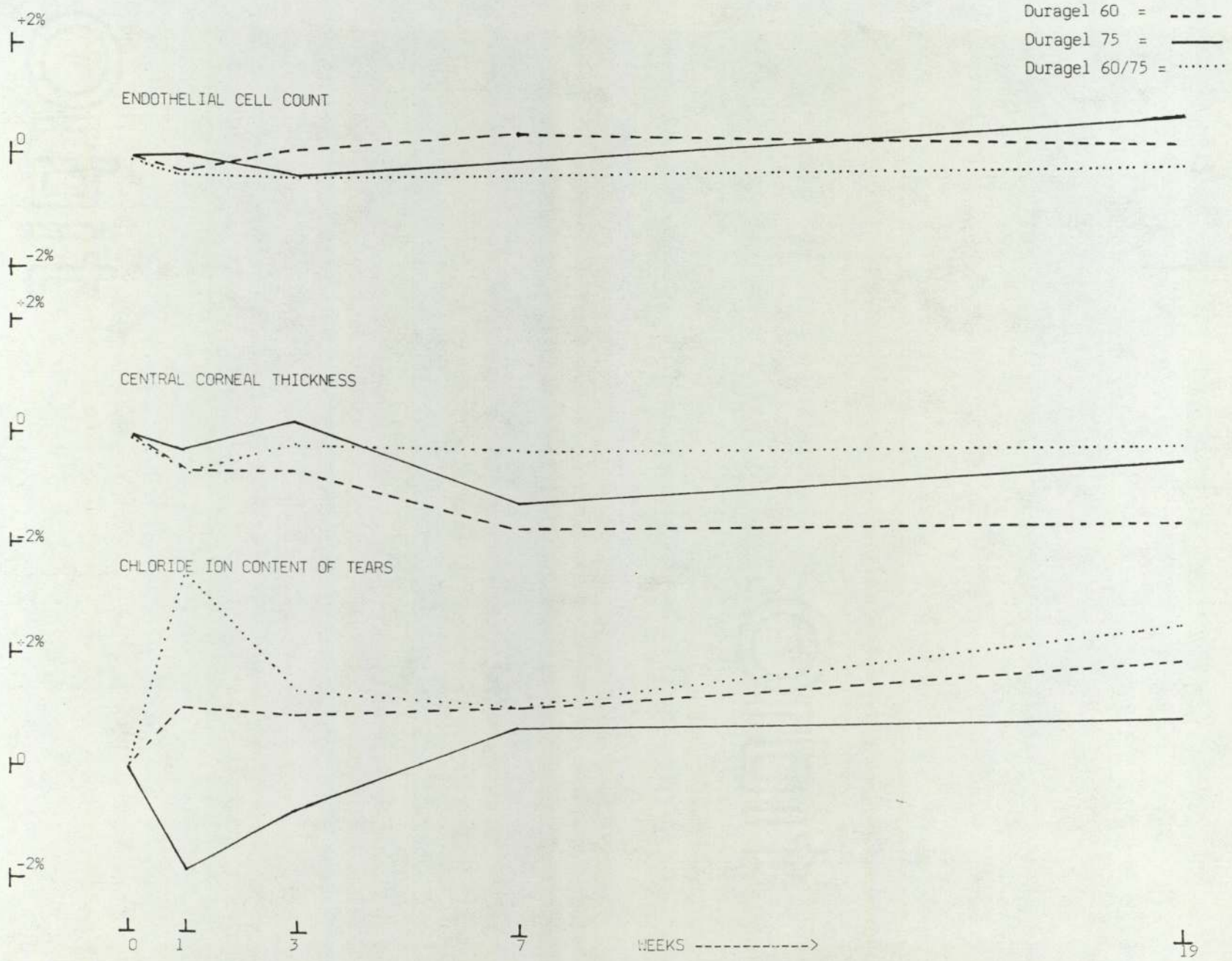


Figure 10.1

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

DURAGEL 60 PRESOAKED IN 1.1% SALINE

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

DURAGEL 60 PRESOAKED IN 1.1% SALINE

CENTRAL CORNEAL THICKNESS

Source	df	S.S.	Var Est	F	p
Between hours	4	0.000288	0.000072	0.36	Not significant
Within hours	45	0.009071	0.0002016		
Total	49	0.009359			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

DURAGEL 60 PRESOAKED IN 1.1% SALINE

CHLORIDE ION CONTENT OF TEARS

Source	df	S.S.	Var Est	F	p
Between hours	4	90.1	22.525	0.31	Not significant
Within hours	45	3232.6	71.835536		
Total	49	3322.7			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

DURAGEL 60 PRESOAKED IN 1.1% SALINE

ENDOTHELIAL CELL COUNT

Source	df	S.S.	Var Est	F	p
Between hours	4	365	91.25	0.11	Not significant
Within hours	45	37008	822.4		
Total	49	37373			

SUMMARY TABLES FOR ANALYSIS OF VARIANCE

DURAGEL 75 PRESOAKED IN 1.0% SALINE

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

DURAGEL 75 PRESOAKED IN 1.0% SALINE

CENTRAL CORNEAL THICKNESS

Source	df	S.S.	Var Est	F	p
Between hours	4	0.00052	0.00013	0.82	Not significant
Within hours	45	0.00713	0.0001584		
Total	49	0.00765			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

DURAGEL 75 PRESOAKED IN 1.0% SALINE

CHLORIDE ION CONTENT OF TEARS

Source	df	S.S.	Var Est	F	p
Between hours	4	58.9	14.725	0.867	Not significant
Within hours	45	749.1	16.646667		
Total	49	808			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

DURAGEL 75 PRESOAKED IN 1.1% SALINE

ENDOTHELIAL CELL COUNT

Source	df	S.S.	Var Est	F	p
Between hours	4	218.64	54.66	0.07	Not significant
Within hours	45	34576	768.36		
Total	49	34794.64			

SUMMARY TABLES FOR ANALYSIS OF VARIANCE

DURAGEL 60/75 PRESOAKED IN 1.05% SALINE

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

DURAGEL 60/75 PRESOAKED IN 1.05% SALINE

CENTRAL CORNEAL THICKNESS

Source	df	S.S.	Var Est	F	p
Between hours	4	0.000052	0.000013	0.048	Not significant
Within Hours	45	0.0121	0.0002689		
Total	49	0.012152			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

DURAGEL 60/75 PRESOAKED IN 1.05% SALINE

CHLORIDE ION CONTENT OF TEARS

Source	df	S.S.	Var Est	F	p
Between hours	4	167.3	41.825	0.76	Not significant
Within hours	45	2481.9	55.153333		
Total	49	2649.2			

SUMMARY TABLE FOR ANALYSIS OF VARIANCE

DURAGEL 60/75 PRESOAKED IN 1.05% SALINE

ENDOTHELIAL CELL COUNT

Source	df	S.S.	Var Est	F	p
Between hours	4	62.76	15.69	0.023	Not significant
Within hours	45	30315	673.67		
Total	49	30377.76			

CHAPTER 11

CONCLUSIONS

The body will react to any introduced foreign body with rejection symptoms, the eye is no exception. The only changes that can occur in the cornea are either thickening or attenuation, the usual reaction being that of swelling and resultant corneal oedema. The reason why the cornea becomes oedematous when a contact lens is worn is not completely understood, it could be due to anoxia, and yet Throft and Friend (1972) have shown that the application of a plastic disc to the cornea, even in the prescence of a fully oxygenated cornea will lead to corneal oedema. They concluded that the corneal oedema caused by the wearing of contact lenses could be due to the mechanical stimulus to glycogen breakdown, or a limit to the amount of enzymes that are available for glucose metabolism; also O'Leary et al (1981) have shown that after six hours of oxygen deprivation the human cornea did not swell, and they concluded that there were changes in the intercellular spaces. Whereas Carney (1975[3]; 1975[4]) has shown that if a gas of a hundred percent oxygen tension is passed over the anterior corneal surface, in patients wearing hydrogel contact lenses, then both the central and peripheral corneal thickness

increases which were induced by wearing contact lenses were elliminated.

Farris and Donn (1972) and Holly and Rofojo (1972) have stated that no hydrogel contact lens is sufficiently permeable to oxygen to allow normal corneal respiration. Takanashi et al (1966) have also shown that no contact lens will allow sufficent oxygen to get through to the cornea, and they also suggested that oxygen cannot come from the aqueous to allow corneal respiration. Leibowitz and Laing (1973) found a thirty percent increase in corneal thickness which persisted with continuous wear of extended wear contact lenses. Effron and Carney (1982) have reported contary findings to those of O'Leary et al they found that the human cornea responds rapidly to anoxia after five minutes of total oxygen deprivation, the cornea reaches a maximum state of demand and after longer periods of anoxia the oxygen requirement is slightly reduced. Kikkawa (1975) found in rabbits that there was a significant increase in corneal thickness and change in oxygen consumption with hydrogel wear, this supports the view of Fatt (1972) who indicated that the individual oxygen requirement of of hydrogel lenses made the difference between patients being able or unable to wear extended wear lenses. Earlier Hill and Fatt (1964) and Hill (1967) had

suggested that if hydrophilic lenses were fitted so that the eyelids could cause an adequate tear exchange then sufficient oxygen would be available for corneal respiration. Rasson and Fatt (1982) showed that the wearing of a Bausch and Lomb H.E.M.A. Soflens, which has an oxygen tension of twelve millimeters of mercury under the lens causes an increase in central corneal thickness of two percent whereas a polyvinyl pyrolidone methyl methacrylate lens of sixty percent water content and an oxygen tension of seventy four millimeters of mercury caused no swelling in the central region of the cornea. In 1979 Hirji and Larke found that only corneal sensitivity was reduced in extended wear contact lenses, there being no other side effects.

It can be seen from the above that there is no concensus of opinion as to whether anoxia is the main cause of oedema associated with contact lens wear.

It has been shown by Stevenson et al (1983) that bathing the eye in hypotonic solutions will produce oedema, they also described some corneal attenuation when the eye was subjected to one and a half percent saline. They showed that there is an absolute linear relationship between the tonicity of the solution and the increase in corneal thickness. This would indicate that the cornea can be

altered due to changes in osmotic pressure. This effect has been known for many years Von Bahr (1948[2]) found that rabbit cornea increased in thickness after ten minutes exposure to hypotonic solutions. Chan and Mandell (1975) bathed the cornea in saline solutions of various tonicities and found that the bathing solution that caused the least change in the cornea were the normal and one percent saline solutions. For solutions of 1.5 and two percent there was corneal attenuation and for 0.6 and 0.3 percent saline and distilled water the cornea became swollen. Remole (1981) has shown that immersing the cornea in distilled water and 0.3 percent saline produced a substantial change in the cornea, whereas for two subjects the least disturbance was with normal saline and for one subject the mimimal change was with the 0.6 percent solution. They discontinued the trials with 1.2 percent solution because of patient discomfort. Green and Donn (1973) have shown in rabbits that a two percent saline solution reduced the corneal thickness by eight percent and five percent saline attenuated the cornea by ten percent. There does seem to be a concensus of opinion in these works with the exception of Remole (1981) that hypotonic solutions tend to cause corneal swelling and hypertonic solutions cause corneal attenuation.

The results of the experimental work have shown that the

cornea is nine percent thicker on waking compared to mid-day. However there is a fairly rapid attenuation of the cornea after the initial measurement had been recorded. After two hours the initial swelling had been decreased by almost half to 5.6 percent swelling. Gerstmann (1972) found a seven percent thinning of the cornea throughout the waking hours, whereas Mandell and Fatt (1965) showed that the cornea was 3.6 percent thicker on waking than normal. The technique they used was of taping the eye lids closed rather than waking the subject so that the readings could be taken as soon as the eyes opened. Also all the readings were taken on one subject. In this work there was a 5.6 percentage decrease in thickness between the 08.00 and 10.00 hour reading, it could be that the 10.00 hours reading was giving a nearer result to that of Mandell and Fatt than the 08.00 Hour reading, because in this work the normal waking metabolism had been eliminated, also it is quite possible that some of the patients had a 'cat nap' between the 08.00 and 10.00 hours thus giving less attenuation than would normally be expected.

It would have been useful if the readings had been taken at more frequent intervals than four hourly, but unfortunately this was not realised until after the results had been analysed, and it was impractical to repeat

these results.

The anterior corneal radius would seem to be totally independent of any changes that occured in corneal thickness or intraocular pressure this is a very useful finding because it means that changes in ophthalmometer readings are not necessarily indicative of changes in corneal thickness, and in fact changes can be occuring in the cornea that will not be detected by using this instrument, this is a fact that many experienced contact lens practitioners have realised for some time, and it became increasingly obvious with the introduction and use of soft contact lenses. This means that it is most important when contact lens after care patients are seen that, if the radii of the curvature have not changed, that corneal changes are looked for with alternative instrumentation.

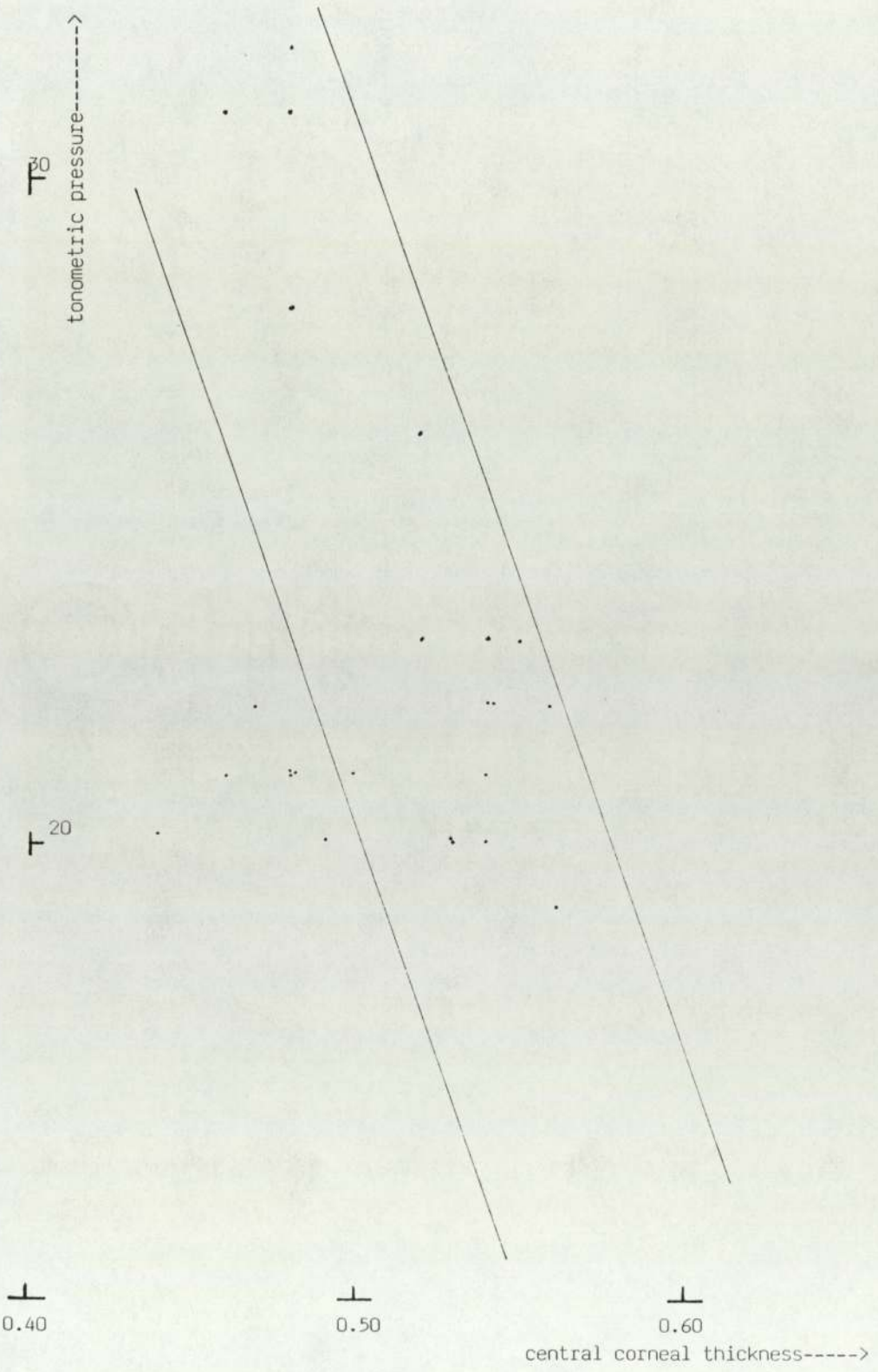
The results with the intraocular pressure and corneal thickness are interesting. If the standard Goldmann tonometric readings are taken as the intraocular pressure readings then the corneal thickness follows a similar pattern, however if applanation readings are converted into hydration pressure , by taking the corneal thickness into account and using the Ehlers factor then there does not seem to be any correlation between the

intraocular pressure and the thickness. This would suggests that intraocular pressure cannot be taken as any indication of corneal hydration changes. The control group has the smallest change in mean intraocular pressure when the Ehlers factor is taken into account. The greatest difference in the mean was in the low tension glaucoma group. Therefore it seems that corneal thickness is an important factor in determining intraocular pressure, but is independent of it as a parameter of the eye. This is in agreement with Ehlers and Hansen (1976) and Ehlers and Hansen (1974) who found that in seven patients suffering fron low tension glaucoma that the central corneal thickness was significantly reduced. The results of this survey indicated that in low tension glaucoma the corneal thickness was lower than in the other groups, however when the results had been modified to being hydrostatic intraocular pressure then the group with the lowest mean corneal thickness was the chronic simple gaucoma. The scattergrams overleaf show that there is a tendency for a correlation between central corneal thickness and hydrostatic intraocular pressure. The pearsons 'r' correlation coefficient for the results is shown in tabular form in the following pages. As can be seen from these tables there is no correlation between tonometric intraocular pressure and central corneal thickness, but for hydrostatic intraocular pressure

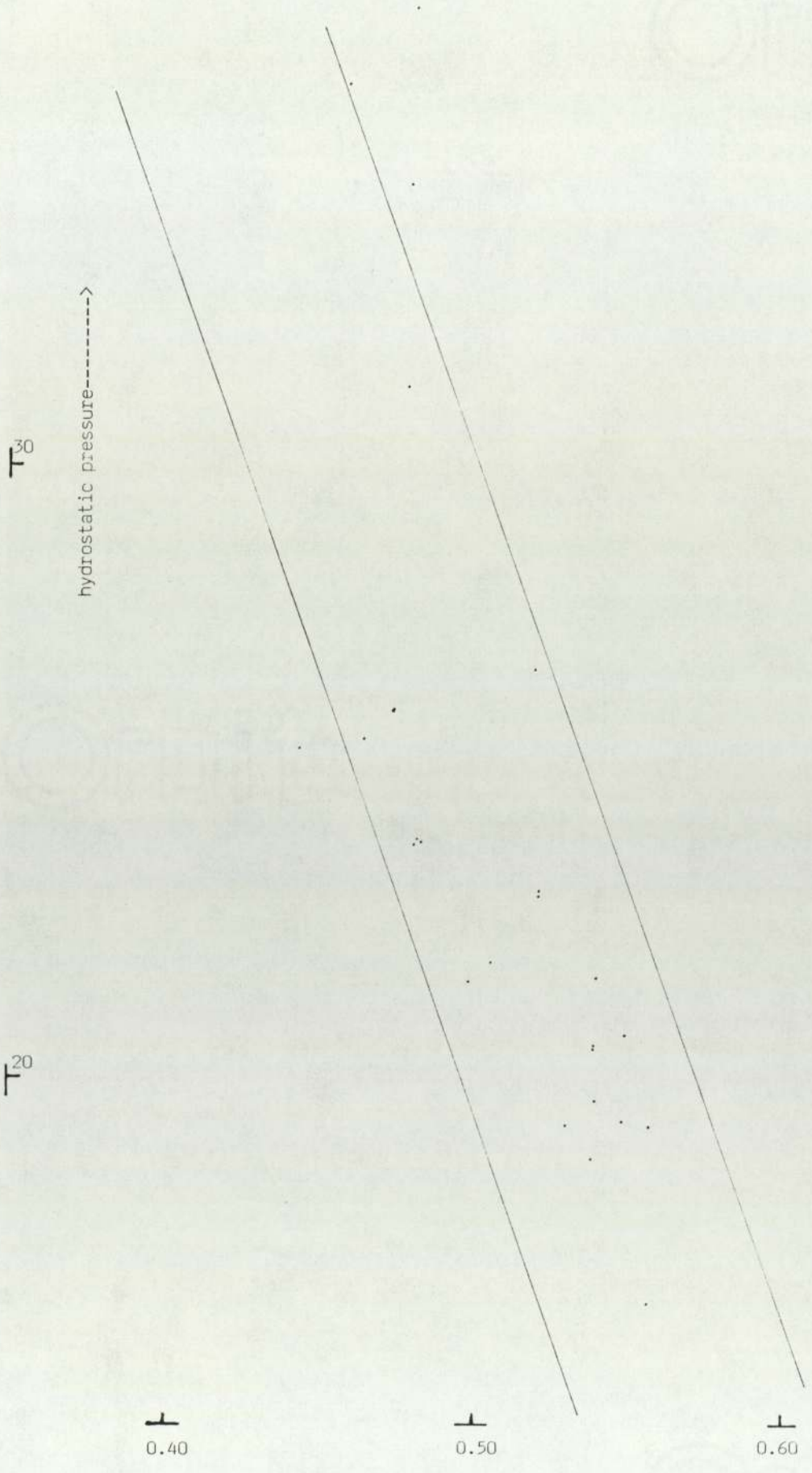
SCATTERGRAMS FOR OCULAR HYPERTENSIVES

SCATTERGRAM FOR OCULAR HYPERTENSIVE FOR TONOMETRIC INTRAOCULAR PRESSURE

AND CENTRAL CORNEAL THICKNESS



SCATTERGRAM FOR OCULAR HYPERTENSIVES FOR HYDROSTATIC INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS IN ORIGINAL GROUPS



SCATTERGRAM FOR OCULAR HYPERTENSIVES FOR HYDROSTATIC INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS AFTER REGROUPING

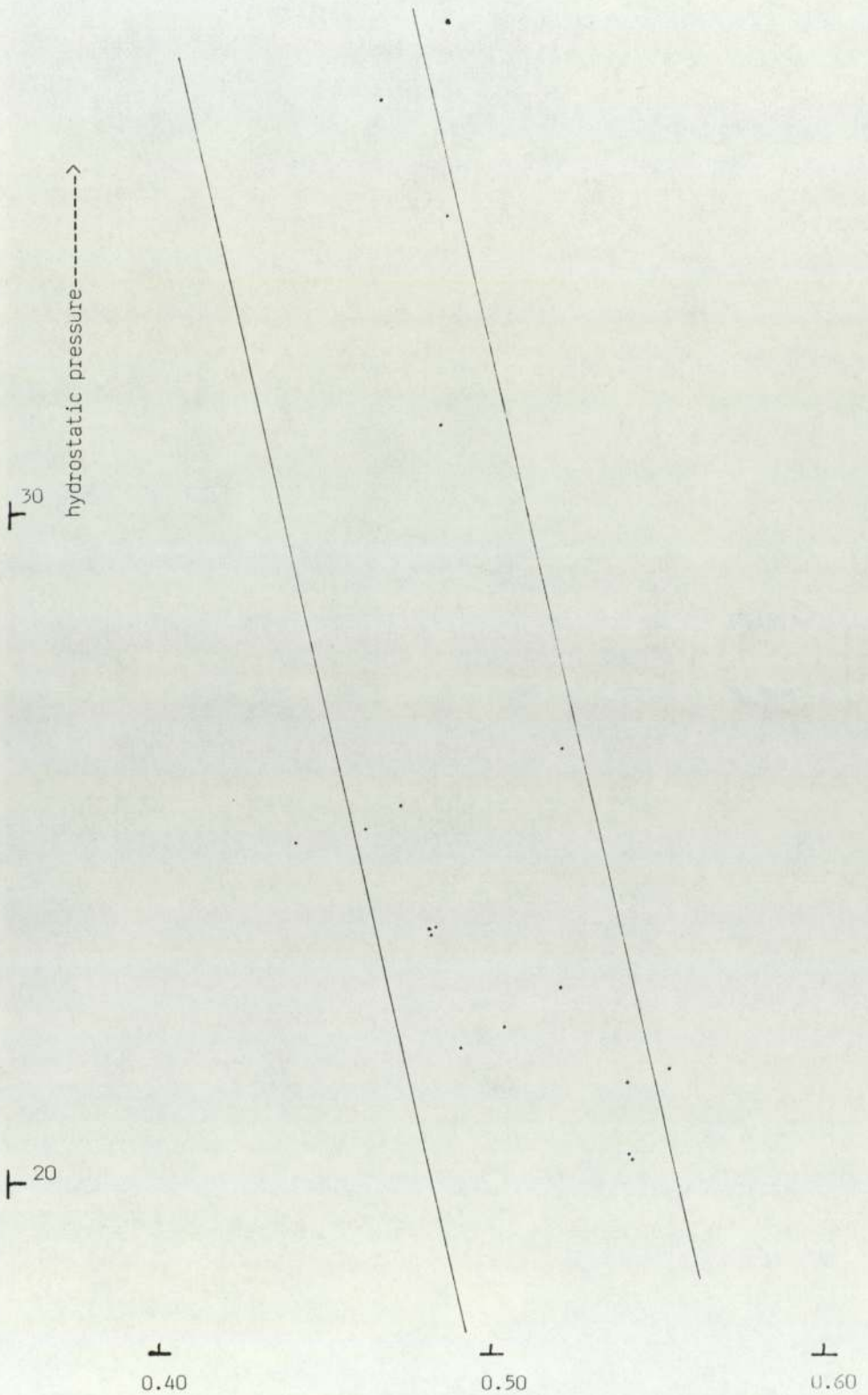


Figure 11.3

SCATTERGRAMS FOR LOW TENSION GLAUCOMA

SCATTERGRAM FOR LOW TENSION GLAUCOMA FOR TONOMETRIC INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS

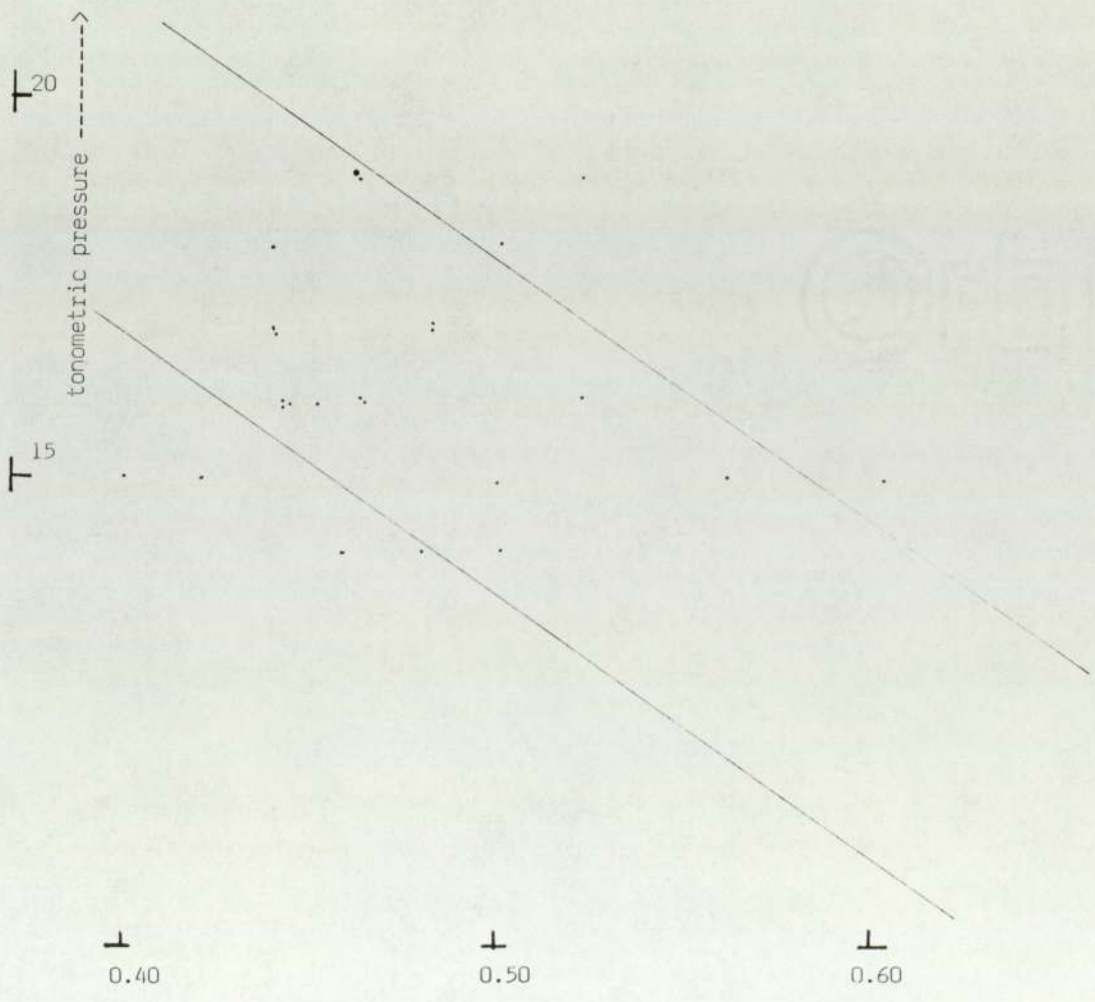


Figure 11.4

SCATTERGRAM FOR LOW TENSION GLAUCOMA FOR HYDROSTATIC INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS IN ORIGINAL GROUPS

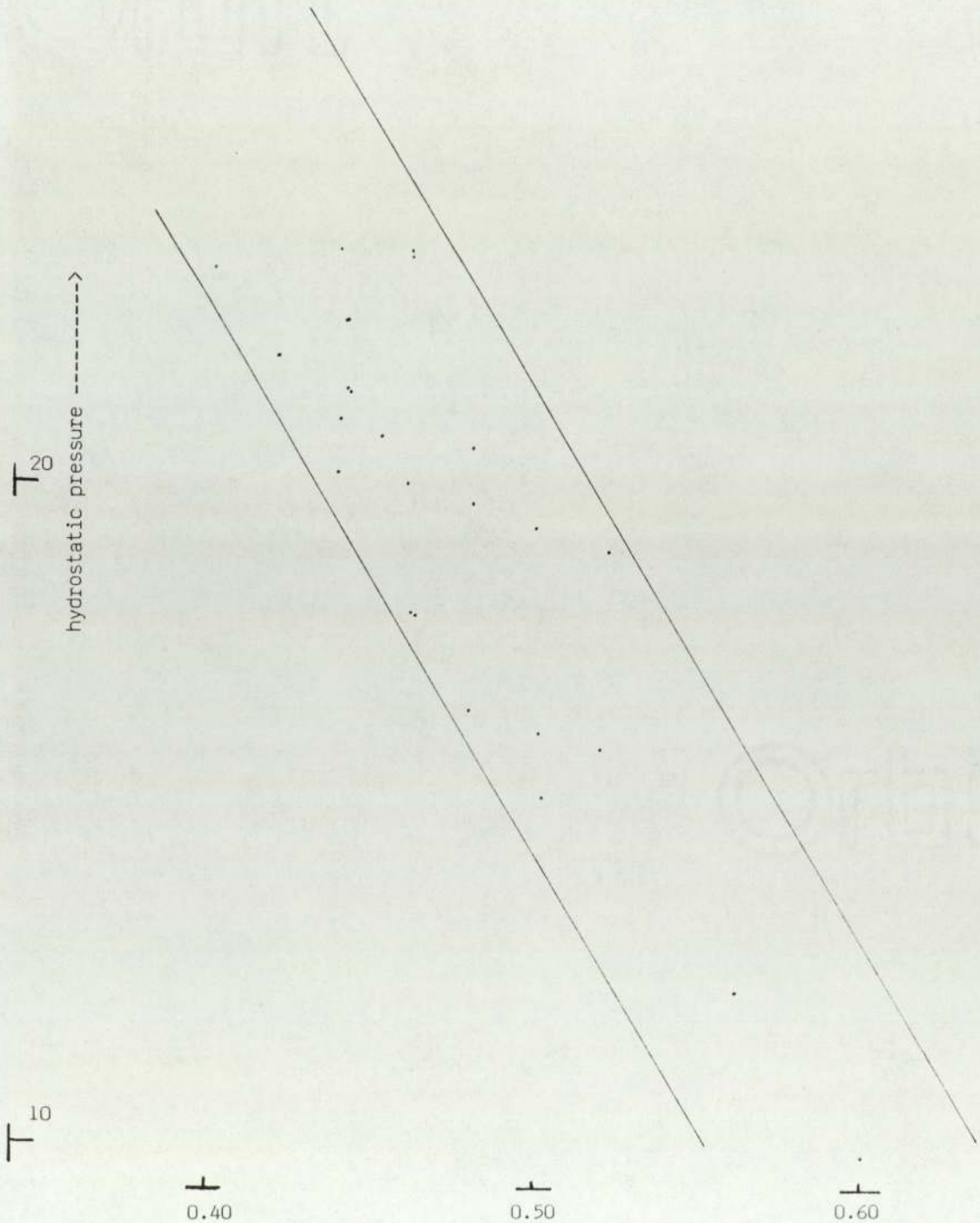


Figure11.5

SCATTERGRAM FOR LOW TENSION GLAUCOMA FOR HYDROSTATIC INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS AFTER REGROUPING

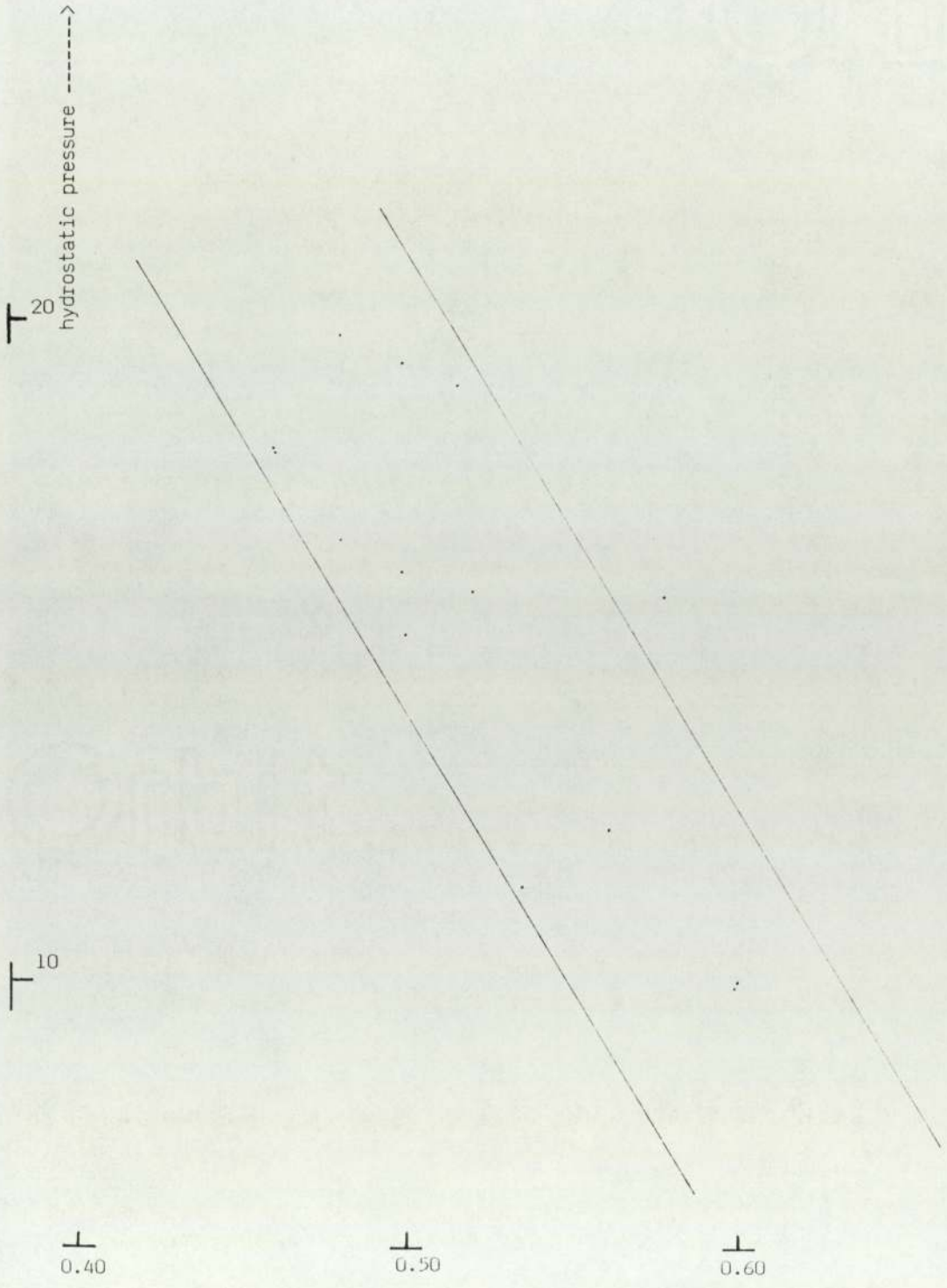


Figure 11 6

SCATTERGRAMS FOR CHRONIC SIMPLE GLAUCOMA

SCATTERGRAM FOR CHRONIC SIMPLE GLAUCOMA FOR TONOMETRIC INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS

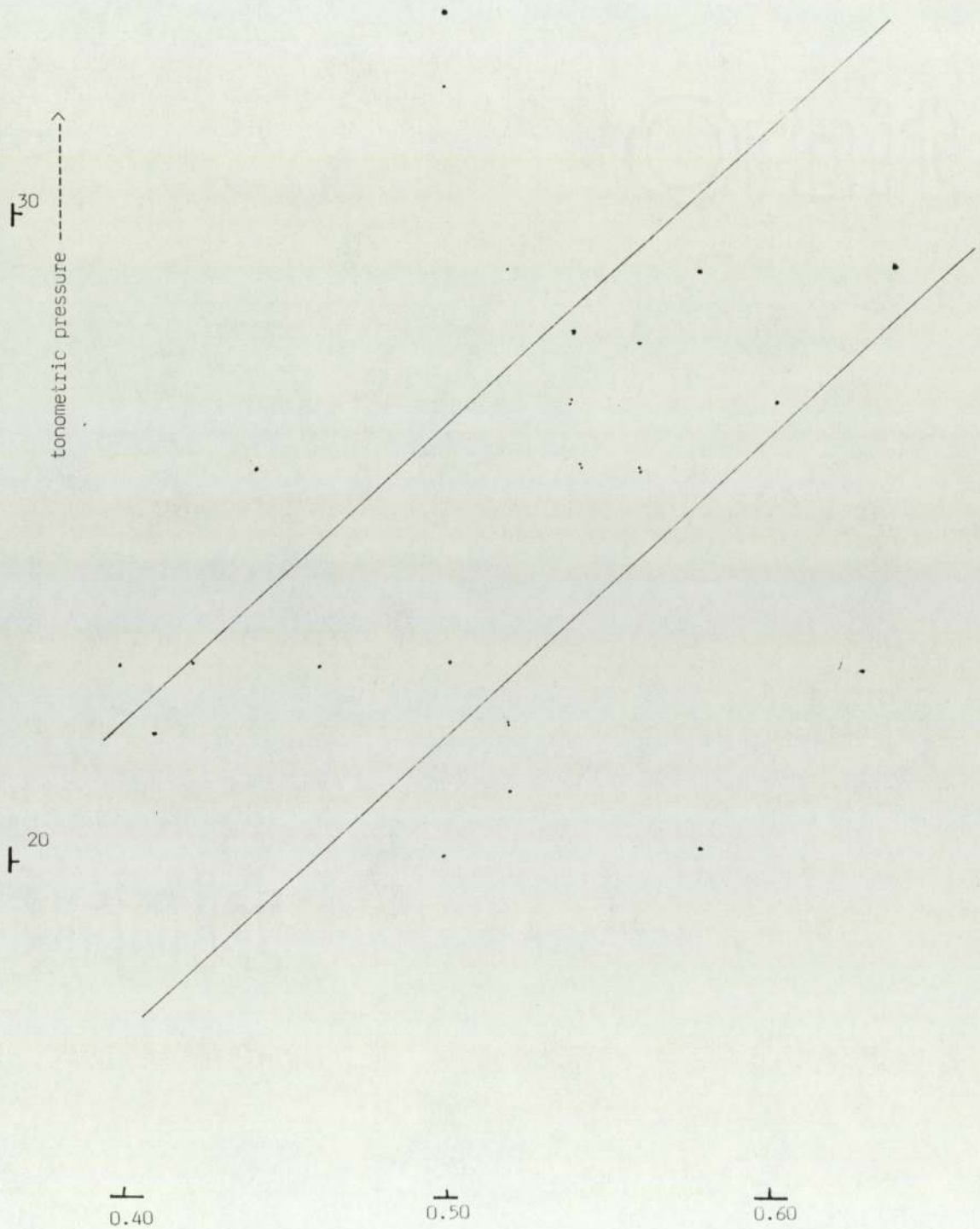


Figure 11.7

SCATTERGRAM FOR CHRONIC SIMPLE GLAUCOMA FOR HYDROSTATIC INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS IN ORIGINAL GROUPS

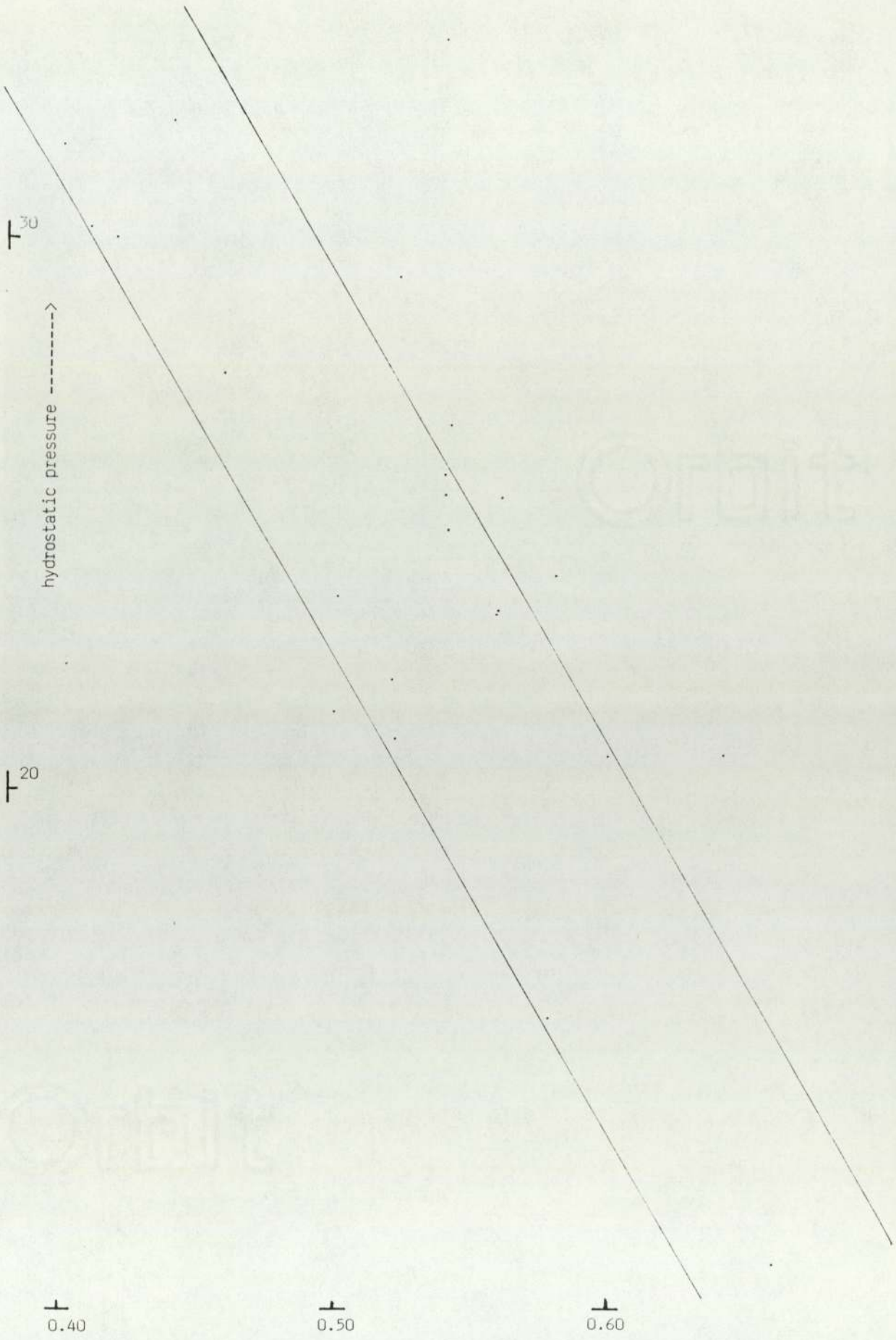


Figure 11.8

SCATTERGRAM FOR CHRONIC SIMPLE GLAUCOMA FOR HYDROSTATIC INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS AFTER REGROUPING

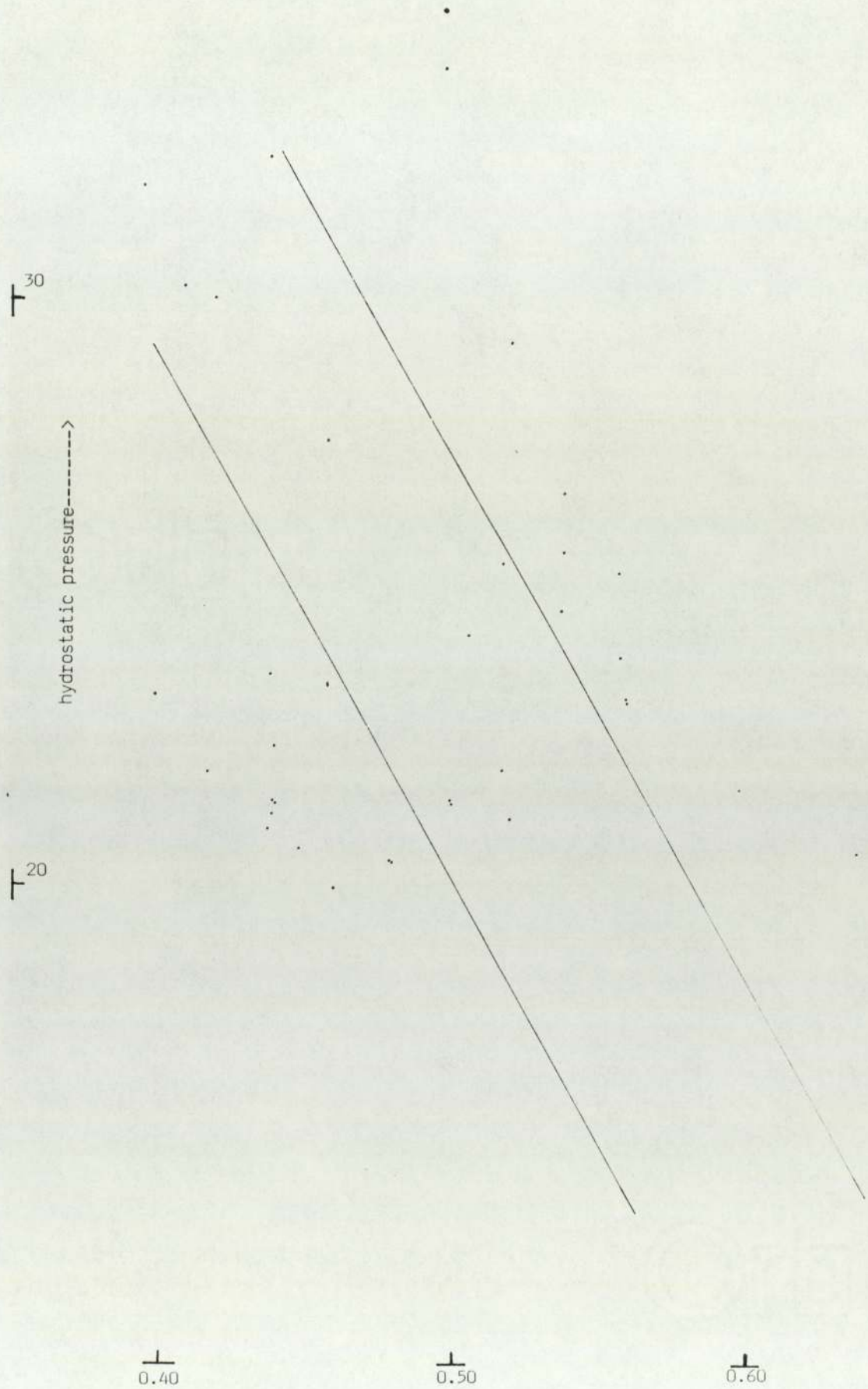


Figure11.9

SCATTERGRAMS FOR CONTROL GROUP

SCATTERGRAM FOR CONTROL GROUP FOR TONOMETRIC INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS

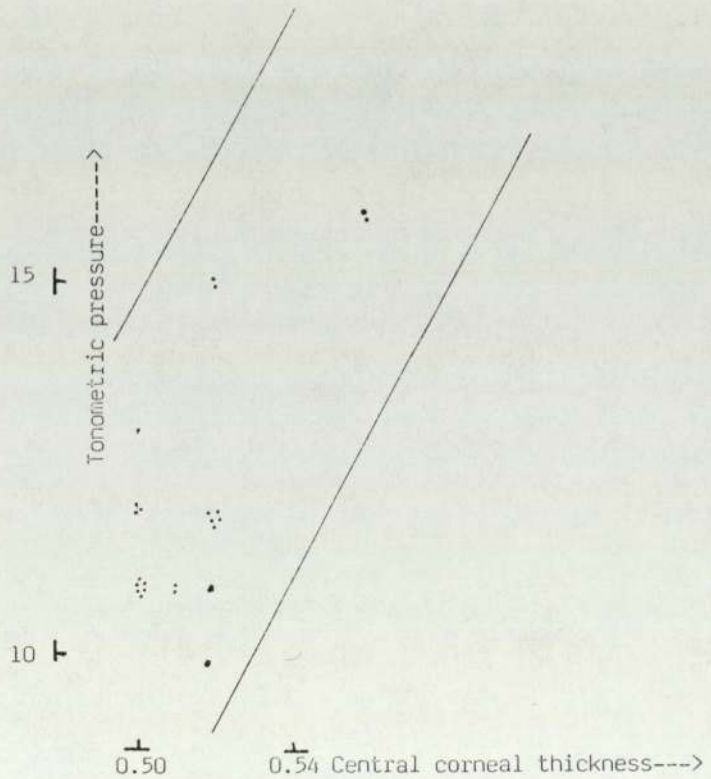


Figure 11.10

SCATTERGRAM FOR CONTROL GROUP FOR HYDROSTATIC INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS IN ORIGINAL GROUPS

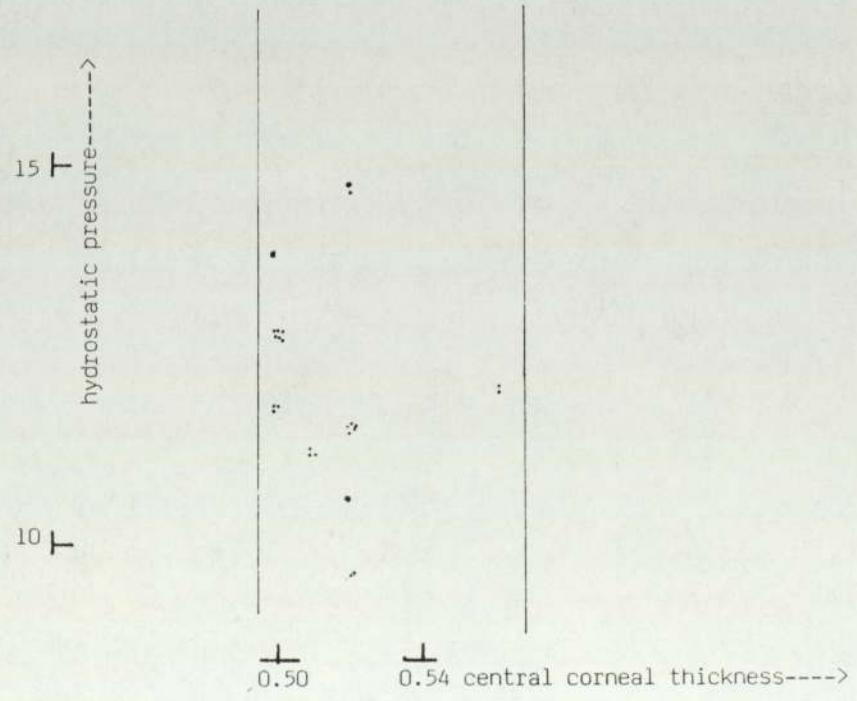


Figure 11.11

SCATTERGRAM FOR CONTROL GROUP FOR HYDROSTATIC INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS AFTER REGROUPING

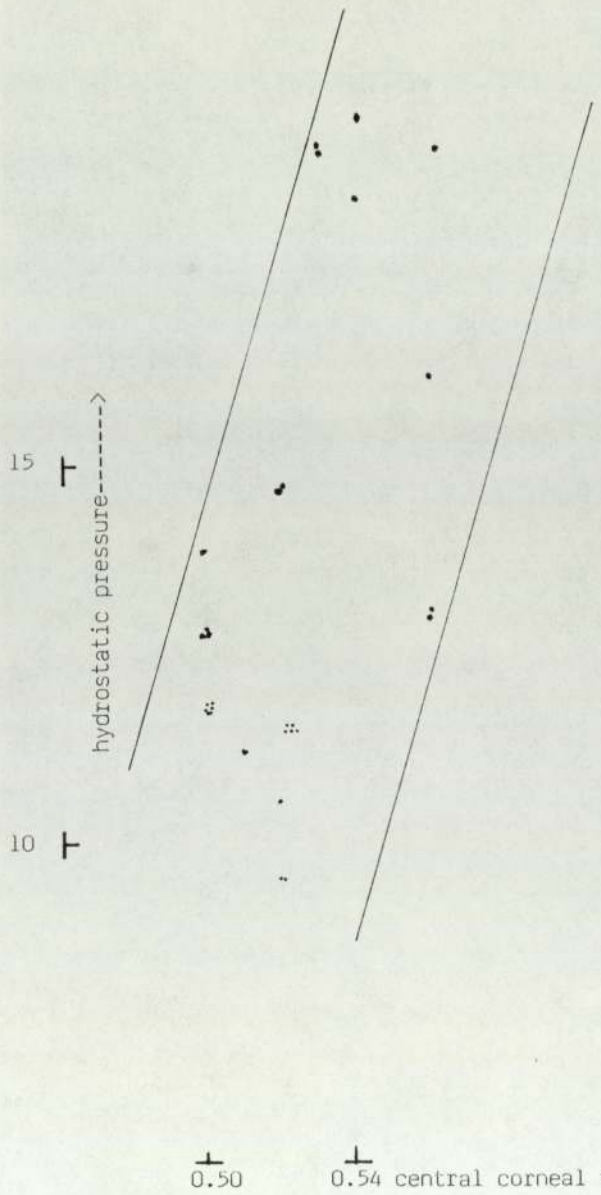


Figure 11.12

PEARSON 'r' CORRELATION COEFFICIENT FOR INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS IN VARIOUS GLAUCOMAS

Type of Glaucoma	Ocular Hypertensives	Low Tension Glaucoma	Chronic Simple Glaucoma	Control Group
Tonometric intraocular pressure	0.3	0.06	0.18	0.0005
Hydrostatic intraocular pressure	0.7	0.9	0.8	0.1
Hydrostatic intraocular pressure and group redistributed	0.5	0.7	0.1	0.5

and central corneal thickness there is a strong correlation in all the groups except the control group. Whereas when the results are redistributed so that they are in the correct categories the low tension glaucoma shows the strongest correlation and yet the group has a mean central corneal thickness of 0.51 $\pm$ 0.4 mm which is certainly well within the normal limits for corneal thickness.

A summary table of the slope of the correlation coefficient is given on the following pages, from these it can be seen that in the ocular hypertensive group there is a tendency for the intraocular pressure to be higher with a thinner cornea, this is the case for the low tension glaucoma, whereas the control group is the reverse situation. The chronic simple glaucoma is unusual because in the tonometric intraocular pressure case the lower intraocular pressure has the thicker cornea, whereas when the Ehlers' factor has been applied the reverse occurs. This is a somewhat misleading statement because in all the groups marked with an asterisk the correlation is so poor that there is almost a random distribution this can be clearly seen in the scattergrams. In all the groups that showed any reasonable correlation coefficient the intraocular pressure was higher when the cornea was thinner. This is contary to the findings of Ehlers et.

al (1975). The lack of correlation between the intraocular pressure, both hydrostatic and tonometric, and the central corneal thickness, in the control group would again indicate that there is no value in using the intraocular pressure as a guide to corneal thickness changes in the in-vivo eye.

The animal studies and the human studies all indicated that the contralateral eye cannot be taken as a true control eye because in all cases there were changes in the control eye that mimiced those of the experimental eye. In retrospect it would have been a far better experimental design to have used both eyes on all the volunteers for all the different treatment levels. Nevertheless it is an important finding that the contralateral eye does not make an adequate control eye; this is in agreement with the findings of Parrish and Larke (1981).

These results indicate that soaking both low and high water content soft lenses in hypotonic saline solution increase the corneal swelling compared to using normal saline, this would agree with Von Bahr (1948), Chan and Mandell (1975) and Stevenson et al (1983) who all found an increase in central corneal thickness when the cornea was bathed in hypotonic solution, but it disagrees with Remole (1981). The central corneal

A SUMMARY TABLE OF THE SLOPE OF THE CORRELATION COEFFICIENT

Type of Glaucoma	Ocular Hypertensives	Low Tension Glaucoma	Chronic Simple Glaucoma	Control Group
Tonometric intraocular pressure	-34*	-2*	+10*	0*
Hydrostatic intraocular pressure	-108	-69	-63	+86*
Hydrostatic intraocular pressure and redistributed groups	-87*	-49	-10*	+79*

thickness was attenuated when the lenses were soaked in saline of 1.2 percent tonocity. It has already been shown that soaking H.E.M.A. lenses in 1.35; 1.8; and two percent saline caused marked attenuation and then reflex swelling of the cornea (Kempster and Larke 1978). It is interesting to note that Remole (1981) discontinued the use of 1.2 percent saline due to the discomfort the solution caused to the volunteer subjects.

The interesting results as far as corneal hydration (as measured by central corneal thickness) is concerned were those of the one and 1.1 percent saline soaking solutions as these indicated minimal changes in the central corneal thickness and thus in corneal hydration this was true for both the daily and extended wear lenses. Mishima and Maurice (1961) found that the rabbit cornea thinned four percent due to evaporation from the eyes surface when the eye was open, and they also found that if a one percent solution was used to bathe the eye then the corneal hydration was unaltered. Stevenson et al (1983) found that bathing the cornea for half an hour in normal saline produced a swelling of 2.88 percent whilst bathing it in 1.5 percent saline caused a reduction in thickness of 0.18 percent. Thus it would seem that it is not unrealistic to suggest that a 1.05 percent saline soaking solution would produce a greater stability in the central corneal thickness.

It seems that for the lower water content lenses that the saline solution needs to be slightly more hypertonic than with the higher water content lenses, and yet the patient studies were particularly rewarding as they indicated that the changes in central corneal thickness when the slightly hypertonic solutions were used to soak and store the lenses were very minimal indeed and in fact a 1.05 percent solution could be used for both the daily and extended wear Duragel soft contact lenses. It is realised that nineteen weeks is a comparatively limited time for a trial of this nature, and it would be advisable to use these solutions for a much longer time on patient trials before they are used for all hydrogel lenses and the general soft contact lens public. The results of this study would seem to be very encouraging, and as stated before it is interesting to note that the manufactureres of Perma lens (extended wear lenses) have produced a wetting solution (Clerz) which is stated to be hypertonic.

The chloride ion content of the tears in the experimental situation showed a random distribution. It can only be assumed that this can be mainly attributed to poor experimental design and the fact that there was an interaction between the control and experimental eye. The results in the patient trails were far more encouraging as far

as tear tonicity was concerned. In all probability this was due to the fact that the eyes were both receiveing lenses soaked in solutions with the same tonicity. No statistically significant variation could be found in this case.

The endothelial cell count showed a marked change when the hypotonic and the 1.2 percent hypertonic saline soaking solutions were used, this could have been partly inherent in the method used, because the cells were photo-raphed through the cornea at a slighlty oblique angle and if the cornea was swollen or attenuated this could have produced either an increased or decreased field of view, and there could have been a distortion due to the differ-ences in the corneal hydration.

In conclusion it would appear from this study that the following results have been obtained:-

(1) There is a diurnal variation in central corneal thickness.

(2) There is a correlation between central corneal thickness and intraocular pressure.

(3) Intraocular pressure is an independent variable as far

as corneal hydration is concerned.

(4) There is no diurnal variation in central anterior corneal radius.

(5) Soaking hydrogel contact lenses in both hypotonic and normal saline produces corneal swelling.

(6) Soaking hydrogel contact lenses in hypertonic saline of 1.2 percent or greater produces corneal attenuation.

(7) Soaking Duragel 60 daily wear soft contact lenses in 1.1 and 1.05 percent saline produces minimal corneal changes.

(8) Soaking Duragel 75 extended wear soft contact lenses in 1.05 and 1.0 percent saline produces minimal corneal changes.

(9) Soaking Duragel 60 daily wear soft contact lenses and Duragel 75 extended wear lenses in 1.05 percent saline produces minimal changes in the tonicity of the tears in the normal patient wearing situation.

(10) The contralateral eye cannot be used as a control eye in the type of study described because it tends to imitate the experimental eye.

These results would seem to indiacte that hydrogel daily wear contact lenses should not be worn immediately on waking, the patient should wait until the central corneal swelling has subsided, this is probably even more important for the hard lens wearer.

The contact lens solution manufacturers should be encouraged to investigate the use of the hypertonic saline solutions with all types of hydrogel contact lenses, initially using 1.05 percent for all lenses. If this did not prove suitable for the daily wear lenses after longer patient trails then it would be suggested that a 1.1 percent solution should be tried. It would be far easier from the marketing situation if one tonicity solution could be used for all types of contact lenses.

It is obviously very wrong that patients should be allowed to make up their own saline solutions for use with soft contact lenses. It is inevitable if they use salt tablets and distilled water that one day they will get the mixture incorrect, it has been known for patients to either forget to put the salt tablet into the distilled water, or sometimes inadvertently to put two tablets rather than one. These sort of mistakes if repeated could cause problems. Any patient who is still using this method for making saline should be actively disuaded,and

advised to use commercially available normal saline.

This study has shown that the cornea is very sensitive to differences in saline tonicity, and that the changes that occur may be overlooked unless a very careful slit lamp examination is carried out, or alternatively corneal thickness measurements recorded.

CHAPTER 12

Critique of the study

There are various problems in this study which in retrospect could have been avoided.

The diurnal variations should have been repeated on the same group of patients and readings recorded at a minimum of once an hour. This would have given a far better idea of the rate of change in the measured parameters. This was not done because originally it was very difficult to set up such a group of volunteers, it necessitated using a four bedded (glaucoma) ward at the Birmingham and Midland Eye Hospital. This could only be used because the glaucoma technician was not able to use the ward for a week. This opportunity has not arisen again at a convenient time.

The intraocular pressure measurements should have been taken on a far greater number of patients, and the studies should have been repeated in animals using modified tonometry equipment. The reason more patients were not used was because of the difficulty in matching patients, and finding patients with ocular hypertension and low tension glaucoma is not easy. Animal studies could have been

carried out, but the writer did not have the necessary qualifications to perform tha manometry work and also it was thought to be too far from the original concept of the study. However this would be required in order that substa ntive conclusions could be drawn.

The experimental design for the rabbit study was very poor indeed, and should have been redesigned so that matched rabbits were used one of the pair being supplied with lenses soaked in normal saline the other pair being given lenses soaked in hypotonic saline, this would have enabled far more reliable statistical results to have been obtained. However the use of the contralateral eye as a control did show that in rabbits the one eye imitates the other. No information in the literature had been found that would have suggested that this situation would arise.

The human studies could be equally criticied for poor experimental design, because again the contralateral eye should not have been selected as the control eye. It was thought, incorrectly, that using both eyes in the same patient would give more reliable results, because the experimental conditions for each were exactly the same. For example it has been shown by Haeringen and Glasius (1975) that cholesterol levels vary in tears

with differing food intake, which could alter the response of the eye to the lens. It was assumed that if cholesteral levels varied then so could other constituents, and therefore it would be a better if control eye and experimental eye were used simultaneously.

Another basic error in the work is that the lenses should have been fitted to the individual volunteers, as an incorrectly fitted lens could have been some of the cause of the corneal swelling. It was assumed that because the same fit was used that this would give less discrepancy in analysing the results, because all patients were being subjected to the same level of treatment, also because comparative results were required rather than absolute values it was erroneously thought that this was a better system.

A subjective method of accessing corneal hydration changes should have been used such as that employed by Wilson and Stevenson (1981). There was no clinical or laboratory technique available until these authors described a method of measuring halo brightness, and unfortunately the majority of the practical work for this study had been completed by 1981.

The tear tonicity and endothelial cell count should have

used throughout all the experiments, but it was not until some of the results were scrutenized that it was realised that it would be necessary to have further information in order to make reasonable assumptions about the corneal changes that were occuring.

The patient studies should have lasted for at least a year, and then the corneae studied for a further year to ensure that no untoward effects occured. This was impractical simply because of the time involved. The patients should have been seen at more frequent intervals and many different types of lenses and polymer combinations should have been used. It would have been useful to have a weekly record of the measurements, this was not a practical proposition because of the time involved for the patients, as it was in fact ten patients started on the trial and only five stayed the full course.

CHAPTER 13

Suggestions for further experimental work

The three main facts which emerge from this very limited study are:-

(1) That there is a diurnal variation in the central corneal thickness, and the cornea is thicker on waking. This is not an unknown fact.

(2) Corneal thickness may make a difference to the diagnosis of certain glaucomas, again this is not a new concept.

(3) That soaking certain soft contact lenses in 1.05 percent saline reduces the deleterious effect that these lenses have on the corneal thickness and perhaps corneal hydration control. As far as can be ascertained this is the first time this effect has been described, although the work of other writers such as Mishima and Maurice as long ago as 1961 would suggest that this should be the case.

There should be further investigations into the effect

that wearing hydrogel contact lenses, hydrated, soaked, and stored in 1.05 percent saline solution have on the soft contact lens wearing population. The effect on other polymers should be explored, as well as the effect of using hard lenses with this slightly hypertonic saline. All these investigations need to be in much greater depth than this preliminary study and would need to include such techniques as measuring halo brightness, as described by Wilson and Stevenson (1981), and micropachometry as described by O'Leary et al (1981). Changes in average rather than central corneal thickness should be investigated, if this is practical, because it is only by showing the full extent of the corneal thickness changes that it can be proven that hypertonic solutions are better for the cornea.

The patient trials should last for a minimum of one year to see what effects the lenses have ultimately on the cornea. In the nineteen week studies no cellular corneal changes could be seen using the slit lamp biomicroscope, but it could be that after prolonged wearing of soft lenses with the hypertonic saline that the fit may be altered, and cause corneal changes which so far have not been envisaged.

The effects of wearing daily wear hydrogel contact lenses, hard lenses, and scleral lenses in the first few hours of waking should be further investigated in much greater detail. Also the effect that different amounts and types of sleep have on corneal hydration require further experimental work. This study was extremely limited in this respect and it is quite reasonable to postulate that the quantity of REM sleep could make a difference to the corneal hydration characteristics, patient age could also cause differences. In this study the age group was elderly and it could be that in the child and young adult because of the differences in metabolic rate that the corneal changes are also different.

Much greater study of tears and their effect on the contact lens wearing population is required, why the results were so different in this study is very difficult to explain.

The endothelial cell studies require better equipment to be developed for use in the clinical situation so that further in depth work can be carried out in the consulting rooms of contact lens practitioners.

The majority of these suggestions require time, money and expertise which are not available to the writer. It is therefore hoped that the ideas will attract the necessary

sponsers and students to continue this work, which may be of great importance to future generations of contact lens wearers.

If it is accepted that man originally evolved from a saline aquatic enviroment, then it is not unexpected that a slightly hypertonic solution should be the natural corneal enviroment.

APPENDICES

APPENDIX 1

VERIFICATION OF INSTRUMENTS USED IN STUDY (CHAPTER 4)

VERIFICATION OF PACHYMETRY READINGS

USING CROWN GLASS PLATES OF REFRACTIVE INDEX 1.523

1 millimeter plate, measured thickness with micrometer 0.99millimeters

Reading	Apparent thickness measured with pachymeter	Real thickness calculated
1	0.65	0.99
2	0.71	1.08
3	0.62	0.94
4	0.72	1.09
5	0.60	0.91
6	0.70	1.07
7	0.65	0.99
8	0.68	1.04
9	0.71	1.08
10	0.61	0.93
Mean	0.665	1.01
S.D.	0.043	0.065
% error	6.5%	6.5%

0.75 millimeter plate, measured thickness with micrometer 0.79 millimeters

1	0.50	0.76
2	0.60	0.92
3	0.53	0.81
4	0.61	0.93
5	0.49	0.75
6	0.52	0.79
7	0.50	0.76
8	0.53	0.81
9	0.54	0.82
10	0.48	0.73
Mean	0.53	0.81
S.D.	0.042	0.064
% error	7.9%	7.9%

VERIFICATION OF PACHYMETRY READINGS (continued)

0.5 millimeter plate, measured thickness with micrometer 0.48 millimeters

Reading	Apparent thickness measured with pachymeter	Real thickness calculated
1	0.38	0.58
2	0.34	0.52
3	0.30	0.46
4	0.32	0.49
5	0.32	0.49
6	0.36	0.55
7	0.30	0.46
8	0.35	0.53
9	0.30	0.46
10	0.31	0.47
Mean	0.33	0.50
S.D.	0.026	0.04
% error	7.9%	8%

VERIFICATION OF GOLDMANN APPLANATION TONOMETER

Day	Intraocular pressure
1	17
2	18
3	17
4	18
5	19
6	18
7	18
8	18
9	18
10	18
11	17
12	19
13	17
14	17
15	18
16	19
17	18
18	19
19	18
20	18
mean	17.95
S.D.	0.6689
% error	3.7%

VERIFICATION OF ZEISS OPHTHALMOMETER READINGS

Subject 1

	RIGHT EYE		LEFT EYE	
Reading	Vertical	Horizontal	Vertical	Horizontal
1	7.85	8.00	7.95	8.05
2	7.83	8.03	7.90	8.07
3	7.85	8.00	7.95	8.05
4	7.87	8.00	7.93	8.05
5	7.85	8.05	7.95	8.05
6	7.85	8.05	7.95	8.05
7	7.85	8.00	7.95	8.07
8	7.83	8.00	7.93	8.05
9	7.85	8.00	7.95	8.05
10	7.85	8.00	7.93	8.03
Mean	7.848	8.008	7.939	8.052
S.D.	0.01	0.017	0.0157	0.0107
% error	0.127%	0.212%	0.197%	0.1328%

Subject 2

1	7.40	7.20	7.35	7.25
2	7.40	7.20	7.37	7.25
3	7.43	7.23	7.37	7.25
4	7.40	7.20	7.35	7.23
5	7.40	7.20	7.35	7.25
6	7.43	7.20	7.35	7.25
7	7.40	7.20	7.35	7.23
8	7.43	7.20	7.35	7.25
9	7.40	7.23	7.37	7.25
10	7.40	7.20	7.35	7.25
Mean	7.409	7.206	7.356	7.246
S.D.	0.0137	0.012	0.0091	0.008
% error	0.1849%	0.1665%	0.1237%	0.1104%

VERIFICATION OF CMT 10 USING KNOWN TONICITIES OF SALINE SOLUTION

Reading	0.7%	0.8%	0.9%	1.0%	1.1%	1.2%
1	129	133	161	177	181	195
2	120	142	152	163	190	194
3	116	131	164	188	189	212
4	112	141	166	181	182	218
5	122	143	167	177	208	196
6	127	127	155	175	186	199
7	119	144	159	179	188	193
8	119	135	164	176	184	219
9	112	133	154	177	185	215
10	113	143	169	173	185	214
Mean	119	137	161	177	188	206
S.D.	6	6	6	6	7	10
% error	5%	4%	4%	3%	4%	5%

VERIFICATION OF CMT 10 FOR HUMAN TEARS

Reading	Subject one	Subject two
Initial	136	149
½ hour	138	136
1 hour	150	148
1½ hours	140	145
2 hours	148	151
2½ hours	156	145
3 hours	145	139
Mean	144.7	144.7
S.D.	6.65	5.03
% error	4.59%	3.47%

VERIFICATION OF ENDOTHELIAL CELL PHOTOGRAPHY

Reading	Cell Count
1	2440
2	2024
3	2024
4	2024
5	2024
6	2280
7	2344
8	2248
9	2440
10	2440
11	2024
12	2296
13	2296
14	2156
15	2224
16	2280
17	2440
18	2368
19	2368
20	2024
Mean	2238
S.D.	158
% error	7.06%

APPENDIX 2

DATA FOR RELATIONSHIP BETWEEN INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS (CHAPTER 6.2)

RELATIONSHIP BETWEEN INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS

Subject	Ocular Hypertension		Low Tension Glaucoma		Chronic Simple Glaucoma		Control Group	
	Central corneal thickness	Intraocular pressure	Central Corneal thickness	Intraocular pressure	Central Corneal thickness	Intraocular pressure	Central corneal thickness	Intraocular pressure
1	0.50	21	0.56	15	0.50	23	0.52	10
2	0.47	22	0.60	15	0.54	26	0.52	11
3	0.56	19	0.50	15	0.58	28	0.50	11
4	0.53	20	0.50	14	0.56	26	0.50	11
5	0.48	21	0.44	16	0.42	23	0.50	11
6	0.48	21	0.44	17	0.41	22	0.51	11
7	0.49	20	0.50	18	0.50	20	0.56	16
8	0.48	21	0.52	19	0.52	29	0.56	16
9	0.48	28	0.46	16	0.46	23	0.52	15
10	0.48	32	0.46	19	0.54	27	0.52	15
11	0.54	20	0.44	16	0.58	20	0.50	12
12	0.53	20	0.44	18	0.60	27	0.50	12
13	0.44	20	0.52	16	0.64	29	0.52	12
14	0.46	21	0.48	17	0.66	21	0.52	12
15	0.56	22	0.46	19	0.54	26	0.50	12
16	0.55	23	0.44	16	0.52	22	0.50	13
17	0.52	23	0.46	14	0.56	28	0.52	12
18	0.52	26	0.48	17	0.56	26	0.52	12
19	0.48	31	0.42	15	0.40	23	0.52	10
20	0.46	31	0.40	15	0.44	26	0.50	11
21	0.54	21	0.48	14	0.52	21	0.50	11
22	0.54	22	0.46	14	0.54	28	0.50	11
23	0.54	22	0.45	16	0.50	33	0.51	11
24	0.54	23	0.44	16	0.50	32	0.52	12
Mean	0.51	23	0.47	16	0.52	25	0.51	12
S.D.	0.03	3.7	0.04	1.6	0.06	3.5	0.02	1.7

TONOMETRIC AND HYDROSTATIC INTRAOCULAR PRESSURE

Subject	Ocular Hypertension		Low Tension Glaucoma		Chronic Simple Glaucoma		Control Group	
	Tonometric pressure	Hydrostatic pressure	Tonometric pressure	Hydrostatic pressure	Tonometric pressure	Hydrostatic pressure	Tonometric pressure	Hydrostatic pressure
1	21	22.4	15	12.2	23	24.5	10	9.6
2	22	25.7	15	9.8	26	25.4	11	10.6
3	19	16.2*	15	16.2	28	23.8	11	11.9
4	20	19.3*	14	15.2	26	23.2	11	11.9
5	21	23.9	16	21.4Δ	23	30.1	11	11.9
6	21	23.9	17	22.4Δ	22	30.3	11	11.3
7	20	22.2	18	19.3	20	21.4	16	13.2
8	21	23.9	19	19	29	29.3	16	13.2
9	28	31.5	16	20 Δ	23	27.6	15	14.8
10	32	37.5	19	23.4Δ	27	25.7	15	14.8
11	20	18.6*	16	21.4Δ	20	15.9¥	12	12.9
12	20	19.3*	18	23.5Δ	27	21.6	12	12.9
13	20	25.2	16	15.9	29	20.6	12	11.6
14	21	25.4	17	19.7	21	11.4¥	12	11.6
15	22	19.2*	19	23.4Δ	26	24.7	12	12.9
16	23	21.7	16	21Δ	22	22	13	13.9
17	23	23	14	18	28	25.3	12	11.6
18	26	26.6	17	20.5Δ	26	23.2	12	11.6
19	31	34.6	15	21.9Δ	23	32	10	9.6
20	31	36.3	15	23.2Δ	26	32.4	11	11.9
21	21	19.6*	14	16.6	21	21	11	11.9
22	22	20.6	14	18	28	26.7	11	11.9
23	22	20.6	16	20.7Δ	33	34.9	11	11.3
24	23	21.6	15	21.2Δ	32	33.9	12	11.6

Subjects marked * have a normal intraocular pressure that is transfer to the control group
Subjects marked Δ have an increased intraocular pressure that is transfer to the chronic simple glaucoma group
Subjects marked ¥ have a reduced intraocular pressure that is transfer to the low tension glaucoma group

SUBJECTS REGROUPED ACCORDING TO HYDROSTATIC PRESSURE

Subjects	Ocular Hypertensives		Low Tension Glaucoma		Chronic Simple Glaucoma		Control group	
	Central corneal Thickness	Hydrostatic Pressure	Central corneal Thickness	Hydrostatic Pressure	Central corneal Thickness	Hydrostatic Pressure	Central Corneal Thickness	Hydrostatic Pressure
1	0.50	22.4	0.56	12.2	0.50	24.5	0.52	9.6
2	0.47	25.7	0.60	9.8	0.54	25.4	0.52	10.6
3	0.48	23.9	0.50	16.2	0.58	23.8	0.50	11.9
4	0.48	23.9	0.50	15.2	0.56	23.2	0.50	11.9
5	0.49	22.2	0.50	19.3	0.42	30.1	0.50	11.9
6	0.48	23.9	0.52	19	0.41	30.3	0.51	11.3
7	0.48	31.5	0.52	15.9	0.50	21.4	0.56	13.2
8	0.48	37.5	0.48	19.7	0.52	29.3	0.56	13.2
9	0.44	25.2	0.46	18	0.46	27.6	0.52	14.8
10	0.46	25.4	0.48	16.6	0.54	25.7	0.52	14.8
11	0.55	21.7	0.46	18	0.60	21.6	0.50	12.9
12	0.52	23	0.58	15.9	0.64	20.6	0.50	12.9
13	0.52	26.6	0.52	11.4	0.54	24.7	0.52	11.6
14	0.48	34.6	Mean 0.514	15.9	0.52	22	0.52	11.6
15	0.46	36.3	S.D. 0.04	2.99	0.56	25.3	0.50	12.9
16	0.54	20.6			0.56	23.2	0.50	13.9
17	0.54	20.6			0.40	32	0.52	11.6
18	0.54	21.6			0.44	32.4	0.52	11.6
19	Mean 0.495	25.9			0.52	21	0.52	9.6
20	S.D. 0.03	5.09			0.54	26.7	0.50	11.9
21					0.50	34.9	0.50	11.9
22					0.50	33.9	0.50	11.9
23					0.44	21.4	0.51	11.3
24					0.44	22.4	0.52	11.6
25					0.46	20	0.56	16.2
26					0.46	23.4	0.53	19.3
27					0.44	21.4	0.54	18.6
28					0.44	23.5	0.53	19.3
29					0.46	23.4	0.56	19.2
30					0.44	21	0.54	19.6
31					0.48	20.5	Mean 0.52	13.4
32					0.42	21.9	S.D. 0.02	2.9
33					0.40	23.2		
34					0.45	20.7		
35					0.44	21.2		
				Mean	0.489	24.7		
				S.D.	0.06	4.08		

APPENDIX 3

DATA FOR DIURNAL VARIATION IN, CENTRAL CORNEAL THICKNESS OPHTHALMOMETER READINGS, AND INTRAOCULAR PRESSURE

(CHAPTER 6.3)

DIURNAL VARIATIONS CENTRAL CORNEAL THICKNESS

Subject	08.00	10.00	12.00	16.00	20.00	24.00
1	0.60	0.58	0.58	0.58	0.64	0.58
2	0.60	0.58	0.50	0.58	0.58	0.59
3	0.50	0.48	0.46	0.44	0.40	0.42
4	0.56	0.47	0.46	0.44	0.44	0.43
5	0.48	0.43	0.46	0.52	0.42	0.45
6	0.52	0.43	0.45	0.46	0.45	0.46
7	0.46	0.52	0.48	0.42	0.53	0.53
8	0.44	0.43	0.42	0.42	0.42	0.43
9	0.52	0.50	0.50	0.56	0.45	0.48
10	0.52	0.50	0.50	0.52	0.50	0.49
11	0.55	0.56	0.50	0.49	0.50	0.50
12	0.55	0.56	0.49	0.54	0.52	0.50
13	0.69	0.69	0.68	0.62	0.64	0.63
14	0.47	0.49	0.49	0.42	0.44	0.46
15	0.44	0.48	0.48	0.50	0.44	0.46
16	0.52	0.48	0.46	0.49	0.58	0.41
17	0.56	0.55	0.48	0.46	0.52	0.54
18	0.56	0.55	0.48	0.48	0.50	0.49
19	0.52	0.50	0.52	0.46	0.40	0.55
20	0.66	0.64	0.58	0.44	0.48	0.42
21	0.55	0.49	0.48	0.48	0.47	0.46
22	0.53	0.49	0.48	0.48	0.47	0.46
Mean	0.54	0.52	0.49	0.49	0.49	0.49
S.D.	0.06	0.06	0.06	0.06	0.07	0.06

DIURNAL VARIATIONS OPHTHALMOMETER READINGS

	08.00		10.00		12.00		16.00		20.00		24.00	
Subject	Vertical	Horizontal	Vertical	Horizontal	Vertical	Horizontal	Vertical	Horizontal	Vertical	Horizontal	Vertical	Horizontal
1	7.80	7.80	7.75	7.80	7.80	7.80	7.90	7.60	7.85	7.90	7.80	7.85
2	7.75	7.75	7.70	7.70	7.70	7.70	7.75	7.75	7.73	7.80	7.70	7.75
3	7.75	7.80	7.80	7.90	7.80	7.88	7.85	7.90	7.80	7.85	7.85	7.85
4	7.85	7.95	7.88	7.90	7.88	7.88	7.90	7.90	7.88	7.88	7.90	7.90
5	7.95	7.70	7.88	7.80	7.88	7.75	7.85	7.85	7.85	7.90	7.85	7.75
6	7.85	7.80	7.80	7.83	7.80	7.80	7.95	7.80	7.85	7.75	7.85	7.75
7	7.35	7.60	7.45	7.51	7.45	7.55	7.65	7.35	7.38	7.45	7.38	7.45
8	7.80	7.80	7,50	7.75	7.50	7.55	7.65	7.70	7.50	7.65	7.65	7.75
9	7.47	7.45	7.43	7.52	7.43	7.45	7.50	7.70	7.45	7.40	7.45	7.40
10	7.37	7.40	7,37	7.42	7.37	7.42	7.33	7.43	7.35	7.40	7.40	7.35
11	7.35	7.40	7.35	7.40	7.35	7.37	7.35	7.40	7.40	7.43	7.35	7.33
12	7.35	7.40	7.28	7.42	7.28	7.45	7.33	7.45	7.30	7.45	7.35	7.40
13	7.50	7.45	7.35	7.41	7.35	7.41	7.35	7.45	7.50	7.45	7.45	7.37
14	7.45	7.40	7.50	7.40	7.50	7.47	7.55	7.50	7.53	7.47	7.45	7.50
15	7.45	7.60	7.50	7.75	7.50	7.40	7.37	7.45	7.50	7.50	7.55	7.40
16	7.55	7.90	7.55	8.15	7.55	7.50	7.47	7.50	7.50	7.55	7.50	7.50
17	7.85	7.95	7.95	7.87	7.95	7.85	7.90	7.85	7.87	7.93	7.90	7.87
18	7.93	8.00	7.97	7.97	7.97	7.95	8.00	8.03	7.97	7.95	8.00	7.97
19	8.17	8.03	8.05	7.92	8.05	7.97	8.07	7.90	8.05	7.90	8.15	7.90
20	7.93	8.05	8.00	7.90	8.00	7.95	8.00	7.90	8.05	7.95	8.05	7.95
21	8.00	7.95	8.05	7.92	8.05	7.94	8.00	7.90	8.00	7.90	8.00	7.95
22	7.93	7.87	7.91	7.90	7.91	7.90	7.90	7.90	7.95	7.90	7.95	7.90
Mean	7.70	7.73	7.68	7.73	7.68	7.68	7.72	7.70	7.69	7.72	7.71	7.68
S.D.	0.25	0.22	0.25	0.22	0.25	0.22	0.26	0.24	0.25	0.21	0.25	0.23

DIURNAL VARIATIONS TONOMETRIC INTRAOCULAR PRESSURE

Subject	08.00	10.00	12.00	16.00	20.00	24.00
1	27	26	24	25	28	22
2	24	24	21	25	22	23
3	17	16	18	17	12	13
4	16	15	16	16	17	12
5	11	12	14	18	8	10
6	15	14	11	10	10	12
7	13	14	16	11	20	19
8	11	12	10	9	12	11
9	19	20	21	26	16	17
10	19	20	20	22	16	18
11	24	24	21	21	18	22
12	24	23	21	24	22	20
13	32	31	30	28	30	30
14	15	14	15	14	10	13
15	14	15	15	20	12	22
16	18	17	12	16	24	12
17	19	18	15	14	16	18
18	19	18	18	14	16	18
19	15	15	11	15	8	18
20	29	30	24	14	16	12
21	18	17	14	15	12	12
22	16	15	11	14	14	12
Mean	18.8	18.6	16.9	17.6	16.1	16.6
S.D.	5.5	5.4	5	5.3	6.1	5.1

DIURNAL VARIATION HYDROSTATIC INTRAOCULAR PRESSURE

Subject	08.00	10.00	12.00	16.00	20.00	24.00
1	21	22	20	22	20	22
2	18	20	23	22	18	18
3	17	19	22	21	20	19
4	17	19	20	20	17	16
5	14	18	18	19	14	14
6	15	14	16	14	14	16
7	17	20	19	17	20	18
8	16	18	16	15	17	17
9	19	20	23	24	21	20
10	19	20	20	22	18	19
11	22	21	23	23	20	23
12	22	20	23	23	22	21
13	19	18	18	20	21	22
14	18	16	17	20	19	17
15	18	18	18	22	18	19
16	18	19	16	19	19	18
17	18	16	18	18	16	17
18	16	16	18	19	16	17
19	15	16	18	19	14	16
20	19	21	20	18	18	17
21	16	17	17	19	15	16
22	15	17	14	17	16	17
Mean	17.7	18.4	18.9	19.6	17.8	18.1
S.D.	2	1.99	2.5	2.5	2.4	2.2

APPENDIX 4

DATA FOR RABBIT STUDIES (CHAPTER 7)

CENTRAL CORNEAL THICKNESS OF RABBIT EYE WEARING SOFLENS PRESOAKED IN 0.7% SALINE

Subject	Insertion	1 hour	2 hours	3 hours	4 hours	5 hours	6 hours	24 hours	48 hours	72 hours	96 hours	120 hours
1	0.40	0.50	0.70	0.80	0.90	1.00	1.20	1.20	1.20	1.20	0.82	0.80
2	0.42	0.60	0.80	1.10	0.90	1.00	1.00	1.00	1.20	1.20	0.84	0.80
3	0.42	0.50	0.50	0.70	0.80	0.90	1.20	1.04	1.20	1.20	0.82	0.78
4	0.42	0.70	0.48	0.50	0.58	0.70	1.00	1.10	1.20	1.20	0.90	0.86
5	0.42	0.80	0.70	1.00	1.10	1.10	1.20	1.18	1.20	1.20	0.88	0.84
6	0.42	0.70	0.80	0.50	0.70	0.90	1.10	1.08	1.20	1.20	0.88	0.84
Mean	0.42	0.63	0.66	0.77	0.83	0.93	1.12	1.10	1.20	1.20	0.85	0.81
S.D.	0.007	0.11	0.13	0.23	0.16	0.12	0.09	0.07	0	0	0.03	0.03

CENTRAL CORNEAL THICKNESS OF RABBIT EYE WEARING SOFLENS PRESOAKED IN 0.9% SALINE

Subject	Insertion	1 hour	2 hours	3 hours	4 hours	5 hours	6 hours	24 hours	48 hours	72 hours	96 hours	120 hours
1	0.42	0.44	0.46	0.46	0.46	0.44	0.46	0.40	0.40	0.40	0.40	0.40
2	0.42	0.44	0.46	0.48	0.46	0.43	0.44	0.42	0.40	0.40	0.40	0.40
3	0.40	0.44	0.46	0.46	0.48	0.42	0.44	0.42	0.40	0.40	0.40	0.40
4	0.40	0.44	0.46	0.46	0.46	0.45	0.48	0.42	0.40	0.40	0.40	0.40
5	0.42	0.44	0.46	0.48	0.48	0.46	0.46	0.42	0.40	0.40	0.40	0.40
6	0.40	0.44	0.46	0.48	0.46	0.48	0.48	0.42	0.40	0.40	0.40	0.40
Mean	0.41	0.44	0.46	0.47	0.47	0.45	0.46	0.42	0.40	0.40	0.40	0.40
S.D.	0.01	0	0	0.01	0.01	0.02	0.02	0.01	0	0	0	0

APPENDIX 5

DATA FOR INITIAL STUDIES WITH DURAGEL 60 (CHAPTER 8.1)

CENTRAL CORNEAL THICKNESS IN INITIAL STUDIES USING DURAGEL 60 PRESOAKED IN 0.7% SALINE

Subject	Initial	45 mins.	90 mins.	135 mins.	180 mins.	210 mins.	240 mins.	270 mins.	300 mins.	330 mins.	360 mins.	390 mins.
J.R.L.	0.51	0.65	0.69	0.72	0.78	0.72	0.65	0.62	0.60	0.55	0.52	0.52
A.J.K.	0.50	0.62	0.65	0.67	0.77	0.75	0.63	0.63	0.55	0.52	0.50	0.50
Mean	0.505	0.635	0.67	0.695	0.775	0.735	0.64	0.625	0.575	0.535	0.51	0.51

CENTRAL CORNEAL THICKNESS IN INITIAL STUDIES USING DURAGEL 60 PRESOAKED IN 0.9% SALINE

Subject	Initial	45 mins.	90 mins.	135 mins.	180 mins.	210 mins.	240 mins	270 mins.	300 mins.	330 mins.	360 mins.	390 mins.
J.R.L.	0.51	0.52	0.52	0.52	0.52	0.53	0.52	0.52	0.51	0.51	0.51	0.51
A.J.K.	0.50	0.51	0.51	0.51	0.51	0.53	0.54	0.53	0.52	0.51	0.51	0.51
Mean	0.505	0.515	0.515	0.515	0.515	0.53	0.53	0.525	0.515	0.51	0.51	0.51

APPENDIX 6

DATA FOR FURTHER STUDIES WITH DURAGEL 60 (CHAPTER 8.2)

DURAGEL 60 PRESOAKED IN 0.7% SALINE

Central corneal thickness

	Experimental eye					Control Eye				
Subject	Insertion	45 mins.	90 mins.	135 mins.	180 mins.	Insertion	45 mins.	90 mins.	135 mins.	180 mins.
1	0.54	0.58	0.60	0.60	0.62	0.56	0.58	0.58	0.60	0.60
2	0.52	0.54	0.54	0.56	0.58	0.50	0.52	0.52	0.52	0.54
3	0.50	0.58	0.64	0.68	0.72	0.50	0.54	0.54	0.53	0.54
4	0.48	0.50	0.58	0.62	0.70	0.48	0.49	0.50	0.52	0.54
5	0.48	0.50	0.52	0.54	0.54	0.48	0.50	0.50	0.50	0.49
6	0.50	0.58	0.60	0.70	0.74	0.50	0.51	0.50	0.52	0.52
Mean	0.50	0.55	0.58	0.62	0.65	0.50	0.52	0.52	0.53	0.54
S.D.	0.02	0.04	0.04	0.06	0.07	0.03	0.03	0.03	0.03	0.03

Chloride ion content of tears

Subject	Pre-insertion	insertion	45 mins	90 mins	135 mins	180 mins	Pre-insertion	insertion	45 mins	90 mins	135 mins	180 mins
1	110	102	155	136	123	103	115	111	122	120	167	114
2	105	101	131	120	115	101	110	100	124	122	121	113
3	120	103	226	162	122	112	125	102	135	132	129	128
4	132	121	228	206	129	115	132	115	151	150	141	133
5	105	105	137	126	108	110	110	101	121	110	110	109
6	135	104	115	103	109	103	136	108	140	136	139	140
Mean	135	106	164	142	118	107	121	106	132	128	134	123
S.D.	12	7	44	34	8	5	10	6	11	13	18	11

DURAGEL 60 PRESOAKED IN 0.8% SALINE

Central corneal thickness

Subject	Experimental eye					Control eye				
	Insertion	45 mins.	90 mins.	135 mins.	180 mins.	Insertion	45 mins.	90 mins.	135 mins.	180 mins.
1	0.54	0.54	0.56	0.56	0.58	0.54	0.54	0.56	0.58	0.58
2	0.52	0.52	0.56	0.58	0.60	0.52	0.52	0.54	0.54	0.56
3	0.50	0.52	0.54	0.54	0.56	0.50	0.50	0.52	0.52	0.52
4	0.48	0.48	0.50	0.52	0.54	0.48	0.48	0.50	0.50	0.52
5	0.48	0.50	0.50	0.52	0.54	0.48	0.48	0.50	0.50	0.52
6	0.52	0.48	0.54	0.52	0.54	0.52	0.52	0.56	0.52	0.54
Mean	0.51	0.51	0.53	0.54	0.56	0.51	0.51	0.53	0.53	0.54
S.D.	0.02	0.02	0.03	0.02	0.02	0.02	0.02	0.02	0.03	0.02

Chloride ion content of tears

Subject	Pre-insertion	Insertion	45 mins	90 mins	135 mins	180 mins	Pre-insertion	Insertion	45 mins	90 mins	135 mins	180 mins
1	146	101	152	150	167	141	143	131	153	149	150	141
2	140	102	150	148	155	140	139	122	148	145	142	135
3	134	109	171	166	144	125	136	127	149	143	139	131
4	139	118	153	162	152	149	141	133	156	152	148	143
5	153	127	169	172	147	152	150	132	171	154	157	152
6	146	128	171	181	156	141	146	129	169	157	161	168
Mean	143	114	161	163	154	141	143	129	158	150	150	145
S.D.	6	11	9	11	7	8	5	4	9	5	8	12

DURAGEL 60 PRESOAKED IN 0.9% SALINE

Central corneal thickness

Subject	Experimental Eye					Control Eye				
	Insertion	45 mins.	90 mins.	135 mins.	180 mins.	Insertion	45 mins.	90 mins.	135 mins.	180 mins.
1	0.54	0.56	0.56	0.57	0.56	0.53	0.54	0.54	0.56	0.56
2	0.52	0.54	0.56	0.56	0.58	0.54	0.54	0.56	0.55	0.58
3	0.50	0.50	0.50	0.52	0.54	0.52	0.54	0.54	0.52	0.54
4	0.49	0.53	0.54	0.52	0.52	0.48	0.50	0.50	0.49	0.52
5	0.48	0.48	0.52	0.52	0.52	0.51	0.52	0.53	0.52	0.54
6	0.51	0.52	0.54	0.54	0.54	0.48	0.50	0.49	0.50	0.50
Mean	0.51	0.52	0.54	0.54	0.54	0.51	0.52	0.53	0.52	0.54
S.D.	0.02	0.03	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.03

Chloride ion content of tears

Subject	Preinsertion	Insertion	45 mins	90 mins	135 mins	180 mins	Pre-insertion	Insertion	45 mins.	90 mins	135 mins	180 mins
1	150	142	155	158	157	154	155	143	153	152	151	153
2	145	143	142	141	148	133	142	137	143	147	140	139
3	135	128	142	135	131	121	131	121	143	139	138	127
4	138	122	148	135	148	139	141	139	142	139	140	138
5	144	123	148	146	149	138	144	141	146	146	144	141
6	152	145	152	159	159	142	150	132	151	155	153	147
Mean	144	134	148	146	149	138	144	136	146	146	144	141
S.D.	6	9	5	10	9	10	7	7	4	6	6	12

DURAGEL 60 PRESOAKED IN 1.0% SALINE

Central corneal thickness

	Experimental Eye					Control Eye				
Subject	Insertion	45 mins.	90 mins.	135 mins	180 mins.	Insertion	45 mins.	90 mins.	135 mins.	180 mins.
1	0.54	0.52	0.54	0.54	0.54	0.54	0.54	0.54	0.56	0.56
2	0.52	0.50	0.50	0.52	0.52	0.52	0.52	0.54	0.54	0.56
3	0.50	0.49	0.52	0.50	0.50	0.50	0.52	0.50	0.51	0.52
4	0.48	0.48	0.52	0.50	0.50	0.48	0.50	0.49	0.50	0.50
5	0.50	0.50	0.52	0.51	0.51	0.50	0.52	0.51	0.53	0.53
6	0.48	0.50	0.52	0.50	0.50	0.48	0.50	0.50	0.52	0.52
Mean	0.50	0.50	0.52	0.51	0.51	0.50	0.52	0.51	0.53	0.53
S.D.	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02

Chloride ion content of tears

	Experimental Eye						Control Eye					
Subject	Pre-insertion	Insertion	45 mins	90 mins	135 mins	180 mins	Pre-insertion	Insertion	45 mins	90 mins	135 mins	180 mins
1	157	207	167	169	173	161	156	146	157	157	155	159
2	141	193	159	163	158	153	140	132	135	130	139	132
3	139	187	148	142	145	143	138	129	124	125	120	122
4	134	194	129	127	123	137	132	119	137	136	131	137
5	144	191	151	159	151	152	143	138	141	139	139	151
6	149	176	153	152	157	149	147	129	153	145	149	140
Mean	144	191	151	152	151	149	143	132	141	139	139	140
S.D.	7	9	12	14	15	18	7	8	11	10	11	12

DURAGEL 60 PRESOAKED IN 1.1% SALINE

Central corneal thickness

	Experimental Eye					Control Eye				
Subject	Insertion	45 mins.	90 mins.	135 mins.	180 mins	Insertion	45 mins.	90 mins.	135 mins.	180 mins.
1	0.52	0.52	0.52	0.52	0.54	0.54	0.56	0.54	0.54	0.52
2	0.54	0.52	0.54	0.54	0.54	0.54	0.56	0.56	0.56	0.54
3	0.50	0.50	0.50	0.52	0.52	0.52	0.53	0.54	0.54	0.53
4	0.50	0.50	0.50	0.50	0.50	0.50	0.52	0.52	0.53	0.52
5	0.51	0.50	0.51	0.51	0.52	0.52	0.53	0.53	0.53	0.52
6	0.48	0.47	0.48	0.48	0.48	0.48	0.50	0.50	0.52	0.50
Mean	0.51	0.50	0.51	0.51	0.52	0.52	0.53	0.53	0.54	0.52
S.D.	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02

Chloride ion content of tears

	Experimental Eye						Control Eye					
Subject	Pre-insertion	Insertion	45 mins	90 mins	135 mins	180 mins	Pre-insertion	Insertion	45 mins	90 mins	135 mins	180 mins
1	152	201	150	152	151	150	153	144	157	166	163	161
2	147	199	149	148	147	147	146	131	158	148	142	135
3	141	205	147	146	142	143	137	123	149	145	134	127
4	133	218	148	139	142	137	129	117	136	132	135	139
5	146	204	150	149	148	147	144	132	151	150	146	144
6	155	197	158	161	157	159	151	142	153	161	157	156
Mean	146	204	150	149	148	147	144	131	151	150	146	144
S.D.	7	7	4	7	5	7	8	9	7	11	11	12

DURAGEL 60 PRESOAKED IN 1.2% SALINE

Central corneal thickness

	Experimental Eye					Control Eye				
Subject	Insertion	45 mins.	90 mins.	135 mins.	180 mins.	Insertion	45 mins.	90 mins.	135 mins.	180 mins
1	0.52	0.51	0.49	0.50	0.48	0.54	0.56	0.54	0.49	0.48
2	0.51	0.50	0.49	0.48	0.46	0.54	0.56	0.56	0.48	0.49
3	0.54	0.50	0.48	0.46	0.42	0.52	0.53	0.53	0.50	0.49
4	0.48	0.46	0.44	0.42	0.44	0.52	0.53	0.54	0.48	0.50
5	0.50	0.48	0.46	0.44	0.44	0.50	0.52	0.52	0.49	0.49
6	0.50	0.48	0.46	0.44	0.42	0.48	0.50	0.50	0.49	0.48
Mean	0.51	0.49	0.47	0.46	0.44	0.52	0.53	0.53	0.49	0.49
S.D.	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.01	0.01

Chloride ion content of tears

	Experimental Eye						Control Eye					
Subject	Pre-insertion	Insertion	45 mins	90 mins	135 mins	180 mins	Pre-insertion	Insertion	45 mins	90 mins	135 mins	180 mins
1	155	235	164	186	183	182	144	134	151	161	160	158
2	149	227	153	173	179	178	151	142	153	157	157	155
3	146	231	168	172	179	171	129	11	149	149	149	148
4	155	236	172	192	185	181	153	127	158	165	165	151
5	143	229	151	182	173	171	146	136	157	157	157	158
6	129	211	143	169	169	171	139	121	149	149	149	147
Mean	146	228	159	179	178	176	144	129	153	160	156	153
S.D.	9	8	10	8	5	5	8	10	3	7	6	4

APPENDIX 7

DATA FOR STUDIES WITH DURAGEL 75 (CHAPTER 9)

DURAGEL 75 PRESOAKED IN 0.7% SALINE

Experimental Eye

Central corneal thickness

Subject	Pre-insertion	Insertion	½ hour	1 hour	1½ hour	2 hour	2½ hour	3 hour	3½ hour	4 hour	4½ hour
1	0.50	0.52	0.58	0.58	0.64	0.64	0.68	0.68	0.68	0.70	0.70
2	0.50	0.50	0.54	0.60	0.62	0.66	0.66	0.67	0.68	0.68	0.66
3	0.48	0.48	0.52	0.58	0.60	0.62	0.62	0.64	0.64	0.62	0.64
4	0.50	0.50	0.58	0.64	0.66	0.65	0.66	0.66	0.68	0.72	0.70
5	0.50	0.50	0.60	0.62	0.64	0.65	0.71	0.70	0.73	0.72	0.74
6	0.50	0.50	0.58	0.59	0.60	0.63	0.68	0.70	0.72	0.74	0.76
Mean	0.50	0.50	0.57	0.60	0.63	0.64	0.67	0.68	0.69	0.70	0.70
S.D.	0.01	0.01	0.03	0.02	0.02	0.01	0.03	0.02	0.03	0.04	0.04

Chloride ion content of tears

1	135	120	122	125	125	130	120	115	100	95	95
2	150	147	150	143	128	118	123	98	103	108	100
3	140	135	138	132	129	117	112	102	104	110	95
4	139	136	124	132	128	117	102	100	98	115	95
5	138	137	129	127	133	123	139	131	119	121	112
6	145	142	139	135	133	131	131	137	115	121	102
Mean	141	136	134	132	129	123	121	114	107	112	100
S.D.	5	8	10	6	3	7	12	15	8	9	6

Endothelial cell count

1	2024	2020	1840	1900	1960	1980	1672	1576	1484	1484	1480
2	2368	2224	2292	1960	1900	2024	1840	1784	1676	1624	1672
3	2156	2296	2024	1960	1840	1784	1672	1728	1676	1624	1584
4	2440	2296	2156	1900	2024	1960	1784	1784	1728	1576	1480
5	2296	2024	1960	2292	2152	2156	1960	1784	1676	1528	1480
6	2440	2296	2152	2152	1960	1900	1896	1840	1728	1676	1672
Mean	2287	2193	2107	2027	1973	1967	1804	1749	1661	1585	1561
S.D.	153	123	185	146	98	113	118	84	83	64	86

DURAGEL 75 PRESOAKED IN 0.7% SALINE

Control Eye

Central corneal thickness

Subject	Pre-insertion	Insertion	½ hour	1 hour	1½ hour	2 hour	2½ hour	3 Hour	3½ hour	4 Hour	4½ hour
1	0.50	0.50	0.52	0.54	0.52	0.56	0.58	0.58	0.56	0.56	0.56
2	0.50	0.50	0.52	0.52	0.54	0.55	0.56	0.56	0.58	0.58	0.56
3	0.50	0.50	0.52	0.52	0.54	0.54	0.58	0.58	0.56	0.54	0.54
4	0.50	0.52	0.52	0.54	0.54	0.56	0.56	0.56	0.56	0.56	0.54
5	0.48	0.48	0.52	0.52	0.52	0.54	0.56	0.56	0.55	0.54	0.52
6	0.48	0.48	0.48	0.50	0.54	0.56	0.56	0.54	0.52	0.52	0.52
Mean	0.49	0.50	0.51	0.52	0.53	0.55	0.57	0.56	0.56	0.55	0.54
S.D.	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.02	0.02	0.01

Chloride ion content of tears

1	140	138	141	129	139	141	139	149	121	131	131
2	138	139	129	123	145	143	129	131	125	129	121
3	149	129	131	139	137	139	137	146	139	128	125
4	136	124	136	137	141	131	121	121	129	121	128
5	148	135	142	135	148	149	140	119	121	125	127
6	139	125	151	141	147	133	121	118	125	129	129
Mean	142	132	138	134	143	139	131	131	127	127	127
S.D.	5	6	7	6	4	6	8	13	6	3	3

Endothelial cell count

1	2024	2156	2152	2292	2296	2444	2024	2440	2444	2240	1960
2	2024	2296	2152	2156	1960	2020	2292	2152	2156	1960	1840
3	2280	2368	2444	2024	2152	2024	2296	2368	2444	1960	1900
4	2344	2292	2368	2444	1900	2440	2368	2292	2156	2024	1896
5	2248	2440	2444	1960	2024	2440	2444	2296	2024	2444	1900
6	2440	2520	2296	1900	1960	2024	2440	2368	2444	2240	1960
Mean	2227	2345	2309	2129	2049	2232	2311	2319	2278	2145	1909
S.D.	155	116	122	190	136	209	142	90	172	178	41

DURAGEL 75 PRESOAKED IN 0.8% SALINE

Experimental Eye

Central corneal thickness

Subject	Pre-insertion	Insertion	½ hour	1 hour	1½ hour	2 Hour	2½ hour	3 hour	3½ hour	4 hour	4½ hour
1	0.52	0.54	0.56	0.58	0.60	0.60	0.62	0.66	0.64	0.68	0.69
2	0.48	0.48	0.54	0.54	0.56	0.58	0.60	0.60	0.58	0.58	0.58
3	0.48	0.50	0.52	0.52	0.54	0.54	0.54	0.56	0.58	0.58	0.56
4	0.50	0.50	0.54	0.54	0.56	0.60	0.64	0.62	0.64	0.66	0.68
5	0.50	0.52	0.58	0.60	0.62	0.59	0.63	0.68	0.67	0.70	0.70
6	0.50	0.52	0.56	0.62	0.64	0.62	0.63	0.65	0.67	0.68	0.69
Mean	0.50	0.51	0.55	0.57	0.59	0.59	0.61	0.63	0.63	0.65	0.65
S.D.	0.01	0.02	0.02	0.03	0.03	0.02	0.03	0.04	0.04	0.04	0.05

Chloride ion content of tears

1	139	120	127	132	119	104	112	120	117	102	98
2	155	130	145	140	138	121	109	102	112	118	120
3	140	123	136	123	111	123	113	98	99	112	100
4	137	113	132	138	126	118	102	112	119	108	95
5	142	104	136	121	110	129	141	131	129	113	110
6	156	117	149	147	141	138	136	125	129	131	111
Mean	145	118	138	133	124	122	119	115	118	114	106
S.D.	8	8	7	9	12	10	14	12	10	9	9

Endothelial cell count

1	2344	2088	2280	2600	2688	2024	2368	2088	2520	2068	1900
2	2440	2088	2088	1900	2680	2024	2248	2024	1896	2048	1900
3	2156	2088	2368	2440	2088	2024	2248	2680	2024	2048	1896
4	2440	2520	1900	2248	2440	2248	2368	2024	1948	1948	2020
5	2024	2088	2296	2156	2292	2296	2600	1960	2020	2024	1948
6	2280	2020	2024	1840	2152	2024	2440	2020	2296	2044	1896
Mean	2281	2149	2159	2197	2290	2107	2379	2133	2117	2030	1926
S.D.	151	168	167	271	214	104	121	248	220	39	45

DURAGEL 75 PRESOAKED IN 0.8% SALINE

Control Eye

Central corneal thickness

Subject	Pre-insertion	Insertion	½ hour	1 hour	1½ hour	2 hour	2½ hour	3 hour	3½ hour	4 hour	4½ hour
1	0.50	0.50	0.52	0.52	0.54	0.55	0.56	0.56	0.58	0.58	0.56
2	0.50	0.50	0.52	0.52	0.54	0.54	0.58	0.58	0.56	0.54	0.54
3	0.50	0.52	0.52	0.54	0.54	0.56	0.56	0.56	0.56	0.56	0.54
4	0.48	0.48	0.52	0.52	0.52	0.54	0.56	0.56	0.55	0.54	0.52
5	0.48	0.48	0.48	0.50	0.54	0.56	0.56	0.54	0.52	0.52	0.52
6	0.50	0.52	0.52	0.52	0.54	0.54	0.56	0.56	0.55	0.56	0.56
Mean	0.49	0.50	0.51	0.52	0.54	0.55	0.56	0.56	0.55	0.55	0.54
S.D.	0.01	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.02	0.02	0.02

Chloride ion content of tears

1	138	135	129	129	121	118	123	125	129	131	137
2	149	135	127	127	131	129	129	127	129	130	125
3	136	129	131	121	137	127	137	121	123	121	129
4	148	131	121	133	129	131	135	119	124	125	131
5	139	121	129	121	127	136	133	137	131	127	126
6	148	121	128	129	123	138	139	134	137	129	129
Mean	143	129	128	127	128	130	133	127	129	127	130
S.D.	5	6	3	4	5	6	5	7	5	3	4

Endothelial cell count

1	2024	2296	2152	2156	1960	2020	2296	2152	2156	1960	1840
2	2280	2368	2444	2024	2152	2024	2292	2368	2444	1960	1900
3	2344	2292	2368	2444	1900	2440	2368	2292	2156	2024	1896
4	2248	2440	2444	1960	2024	2440	2444	2296	2024	2444	1900
5	2440	2520	2296	1900	1960	2024	2440	2368	2444	2240	2960
6	2440	2368	2296	2020	2368	2296	2156	2444	2024	2960	2020
Mean	2296	2381	2333	2084	2061	2207	2333	2320	2208	2098	1919
S.D.	142	80	101	179	158	191	99	91	175	184	57

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Experimental Eye

Central corneal thickness

Subject	Pre-insertion	Insertion	½ hour	1 hour	1½ hour	2 hour	2½ hour	3 hour	3½ hour	4 hour	4½ hour
1	0.50	0.50	0.52	0.54	0.52	0.56	0.58	0.58	0.56	0.56	0.56
2	0.50	0.50	0.52	0.52	0.54	0.55	0.56	0.56	0.58	0.58	0.56
3	0.50	0.50	0.52	0.52	0.54	0.54	0.58	0.58	0.56	0.54	0.54
4	0.50	0.52	0.52	0.54	0.54	0.56	0.56	0.56	0.56	0.56	0.54
5	0.48	0.48	0.52	0.52	0.52	0.54	0.56	0.56	0.55	0.54	0.52
6	0.48	0.48	0.48	0.50	0.54	0.56	0.56	0.54	0.52	0.52	0.52
Mean	0.49	0.50	0.51	0.52	0.53	0.55	0.57	0.56	0.56	0.55	0.54
S.D.	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.02	0.02	0.02

Chloride ion content of tears

1	138	129	132	136	131	139	138	137	136	140	141
2	136	126	139	138	130	132	136	133	135	142	143
3	150	138	149	150	126	127	138	136	143	136	132
4	148	142	148	148	133	131	142	139	146	138	130
5	140	150	138	140	143	129	150	146	132	148	141
6	145	145	136	145	139	126	145	148	139	146	143
Mean	143	138	140	143	134	131	142	140	139	142	138
S.D.	5	8	6	5	6	4	5	5	5	4	5

Endothelial cell count

1	2024	2024	2296	2152	2444	2444	2444	1896	2440	2440	2024
2	2156	2440	2152	2156	2024	1960	1900	2248	2444	2520	2248
3	2152	2444	2156	1960	2152	1900	2440	2440	2296	2296	2024
4	2292	2240	1960	1840	2024	2344	2368	2444	2024	1900	2896
5	2296	1960	2120	2280	2296	2292	2292	1960	2444	1960	1960
6	2444	2024	2292	2368	2368	2368	2156	2024	1900	2024	1960
Mean	2227	2189	2146	2126	2218	2218	2218	2267	2169	2258	2185
S.D.	134	199	125	179	163	209	191	222	219	241	332

DURAGEL 75 PRESOAKED IN 0.9% SALINE

Control Eye

Central corneal thickness

Subject	Pre-insertion	Insertion	½ hour	1 hour	1½ hour	2 hour	2½ hour	3 hour	3½ hour	4 hour	4½ hour
1	0.50	0.52	0.52	0.52	0.54	0.54	0.56	0.56	0.55	0.56	0.56
2	0.50	0.50	0.52	0.54	0.54	0.56	0.54	0.56	0.54	0.56	0.56
3	0.50	0.50	0.52	0.51	0.52	0.54	0.54	0.55	0.55	0.55	0.56
4	0.52	0.52	0.52	0.50	0.51	0.53	0.52	0.54	0.54	0.54	0.54
5	0.50	0.52	0.52	0.50	0.54	0.54	0.55	0.56	0.56	0.56	0.56
6	0.52	0.52	0.51	0.50	0.54	0.54	0.56	0.56	0.56	0.56	0.56
Mean	0.51	0.51	0.52	0.51	0.53	0.54	0.55	0.56	0.55	0.56	0.56
S.D.	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01

Chloride ion content of tears

1	148	131	133	143	133	123	122	137	135	139	135
2	151	132	136	133	135	132	133	131	121	121	135
3	156	142	121	136	136	139	129	121	133	130	128
4	145	130	123	133	123	123	131	123	129	125	125
5	145	133	131	127	132	131	123	125	137	126	123
6	139	121	122	132	136	136	123	126	126	136	129
Mean	147	132	128	134	133	131	127	127	130	130	129
S.D.	5	6	10	5	5	6	4	5	5	6	5

Endothelial cell count

1	2440	2368	2296	2020	2368	2296	2156	2444	2024	1960	2020
2	2024	2156	2368	2296	2444	2024	1960	2024	1960	2024	1960
3	2368	2024	2156	2024	1960	2152	2024	1960	2024	2444	2020
4	2444	2240	2024	2024	2152	2024	2368	1840	2368	2152	1960
5	2024	2248	2248	2020	1960	1896	2024	1960	2024	2020	1900
6	2368	2344	1960	1900	1896	1900	2024	2024	2248	1960	1896
Mean	2278	2230	2175	2047	2130	2049	2093	2042	2108	2093	1959
S.D.	182	116	145	120	211	141	136	190	147	169	50

DURAGEL 75 PRESOAKED In 1.0% SALINE

Experimental Eye

Central corneal thickness

Subject	Pre-insertion	Insertion	½ hour	1 hour	1½ hour	2 hour	2½ hour	3 hour	3½ hour	4 hour	4½ hour
1	0.48	0.48	0.48	0.48	0.48	0.48	0.49	0.49	0.50	0.50	0.50
2	0.48	0.48	0.48	0.48	0.46	0.47	0.48	0.48	0.48	0.48	0.48
3	0.50	0.49	0.48	0.50	0.51	0.50	0.49	0.48	0.49	0.50	0.50
4	0.52	0.51	0.50	0.51	0.52	0.51	0.50	0.51	0.52	0.51	0.51
5	0.50	0.49	0.50	0.51	0.49	0.49	0.50	0.51	0.50	0.50	0.50
6	0.50	0.49	0.50	0.50	0.51	0.50	0.49	0.49	0.50	0.50	0.49
Mean	0.50	0.49	0.49	0.50	0.50	0.49	0.49	0.49	0.50	0.50	0.50
S.D.	0.01	0.01	0.01	0.01	0.02	0.01	0.01	0.01	0.01	0.01	0.01

Chloride ion content of tears

1	135	121	131	142	149	138	151	162	165	173	175
2	145	129	149	138	142	140	149	156	176	179	182
3	151	132	156	162	160	172	177	179	183	186	189
4	153	126	161	165	152	161	179	185	189	190	192
5	142	118	159	161	168	179	181	189	190	195	191
6	146	119	158	149	159	162	173	181	196	189	186
Mean	145	124	152	153	155	159	168	175	183	185	186
S.D.	6	5	10	10	8	15	13	12	10	7	6

Endothelial cell count

1	2156	2344	2224	2024	2024	2368	2280	2156	2156	2024	2296
2	2296	2248	2280	2024	2296	2368	2344	2224	2296	2024	2156
3	2440	2020	2440	2296	2296	2024	2440	2440	2248	2344	2280
4	2156	2024	2280	2156	2296	2296	2024	2440	2440	2248	2024
5	2024	2368	2224	2224	2440	2024	2024	2024	2280	2344	2024
6	2368	2368	2156	2280	2440	2368	2368	2024	2440	2024	2024
Mean	2240	2229	2267	2167	2299	2241	2247	2218	2310	2168	2134
S.D.	142	152	88	111	139	156	164	172	102	148	119

DURAGEL 75 PRESOAKED IN 1.0% SALINE

Control Eye

Central corneal thickness

Subject	Pre-insertion	Insertion	½ hour	1 hour	1½ hour	2 hour	2½ hour	3 hour	3½ hour	4 hour	4½ hour
1	0.48	0.48	0.48	0.50	0.52	0.54	0.48	0.50	0.52	0.49	0.52
2	0.50	0.52	0.52	0.52	0.52	0.52	0.48	0.52	0.52	0.48	0.50
3	0.50	0.50	0.52	0.54	0.52	0.52	0.50	0.50	0.50	0.49	0.50
4	0.50	0.50	0.52	0.51	0.50	0.51	0.52	0.52	0.52	0.50	0.50
5	0.52	0.52	0.51	0.50	0.52	0.52	0.52	0.50	0.50	0.52	0.49
6	0.50	0.52	0.51	0.50	0.52	0.50	0.50	0.52	0.52	0.52	0.50
Mean	0.50	0.51	0.51	0.51	0.52	0.52	0.50	0.51	0.51	0.50	0.50
S.D.	0.01	0.01	0.01	0.01	0.01	0.01	0.02	0.01	0.01	0.01	0.01

Chloride ion content of tears

1	139	133	127	121	121	131	138	136	140	142	148
2	148	121	133	133	133	133	142	137	135	139	155
3	151	132	132	136	133	145	132	133	131	141	155
4	156	122	142	121	136	146	139	149	131	140	148
5	145	130	120	143	143	143	131	143	148	155	135
6	145	123	121	127	132	141	143	155	157	146	143
Mean	147	127	129	130	133	140	137	142	140	144	147
S.D.	5	5	7	8	6	6	5	8	10	5	7

Endothelial cell count

1	2440	2520	2296	1900	1960	2040	2444	2368	2444	2240	1960
2	2440	2368	2296	2020	2368	2296	2156	2444	2024	1960	2020
3	2024	2156	2368	2296	2444	2024	1960	2024	1960	2024	1960
4	2368	2024	2156	2024	1960	2152	1024	1960	2024	2444	2020
5	2444	2240	2024	2152	2028	2020	2020	1840	2368	2152	1960
6	2024	2248	2020	1960	1896	1900	1960	1960	2024	2020	1900
Mean	2290	2259	2193	2059	2109	2069	2094	2099	2141	2140	1970
S.D.	190	156	138	131	214	125	170	225	190	165	41

DURAGEL 75 PRESOAKED IN 1.1% SALINE

Experimental Eye

Central corneal thickness

Subject	Pre-insertion	Insertion	½ hour	1 hour	1½ hour	2 hour	2½ hour	3 hour	3½ hour	4 hour	4½ hour
1	0.50	0.50	0.50	0.48	0.50	0.48	0.48	0.46	0.46	0.46	0.46
2	0.50	0.48	0.48	0.46	0.47	0.48	0.48	0.48	0.46	0.46	0.46
3	0.48	0.48	0.47	0.46	0.47	0.48	0.48	0.48	0.48	0.48	0.50
4	0.48	0.48	0.48	0.48	0.48	0.46	0.48	0.48	0.50	0.50	0.50
5	0.48	0.48	0.48	0.48	0.48	0.46	0.46	0.46	0.47	0.48	0.48
6	0.48	0.47	0.46	0.46	0.46	0.46	0.46	0.48	0.48	0.48	0.48
Mean	0.49	0.48	0.48	0.47	0.47	0.47	0.47	0.47	0.48	0.48	0.48
S.D.	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.02

Chloride ion content of tears

1	140	142	156	139	156	172	185	196	176	145	165
2	138	150	172	183	196	205	207	195	178	182	160
3	149	163	183	190	206	215	219	199	185	193	179
4	136	129	196	207	199	211	199	179	187	212	181
5	148	141	202	189	190	225	221	213	195	196	185
6	139	153	167	193	211	235	218	198	207	185	175
Mean	142	146	179	184	193	211	208	197	188	186	174
S.D.	5	11	16	21	18	20	13	10	11	20	9

Endothelial cell count

1	2280	2296	2444	2596	2600	2600	2760	3112	3300	3116	3100
2	2344	2368	2600	2764	2848	2600	2596	2444	2764	2848	2896
3	2248	2292	2368	2520	2764	2680	2760	2932	2848	2932	2936
4	2440	2520	2680	2600	2764	2848	2764	2520	2600	2680	2848
5	2440	2444	2520	2368	2520	2600	2680	2596	2680	2764	2760
6	2024	2152	2368	2440	2156	2296	2444	2600	2520	2680	2600
Mean	2296	2345	2497	2548	2609	2604	2667	2701	2785	2837	2859
S.D.	142	118	116	127	230	163	117	239	253	154	154

DURAGEL 75 PRESOAKED IN 1.1% SALINE

Control Eye

Central corneal thickness

Subject	Pre-insertion	Insertion	½ hour	1 hour	1½ hour	2 hour	2½ hour	3 hour	3½ hour	4 hour	4½ hour
1	0.50	0.50	0.52	0.52	0.49	0.49	0.49	0.49	0.46	0.46	0.46
2	0.50	0.52	0.52	0.54	0.49	0.49	0.49	0.48	0.46	0.46	0.46
3	0.48	0.48	0.52	0.52	0.48	0.48	0.48	0.46	0.46	0.44	0.47
4	0.48	0.48	0.48	0.50	0.49	0.47	0.49	0.47	0.47	0.49	0.46
5	0.50	0.52	0.52	0.52	0.48	0.48	0.47	0.46	0.47	0.48	0.45
6	0.50	0.50	0.52	0.54	0.50	0.49	0.48	0.48	0.48	0.48	0.46
Mean	0.49	0.50	0.51	0.52	0.49	0.48	0.48	0.47	0.47	0.47	0.46
S.D.	0.01	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01

Chloride ion content of tears

1	149	163	183	191	207	215	219	196	181	193	173
2	136	129	196	206	198	210	197	183	181	202	179
3	148	141	202	189	193	220	211	203	190	197	180
4	139	153	167	191	211	231	208	196	200	182	178
5	148	161	153	163	173	193	212	197	185	199	185
6	151	132	156	153	155	172	163	161	156	181	185
Mean	145	147	176	182	190	207	202	189	182	192	180
S.D.	6	13	19	18	20	19	18	14	13	8	4

Endothelial cell count

1	2280	2368	2444	2024	2152	2024	2296	2368	2444	1960	1900
2	2344	2292	2368	2444	1900	2440	2368	2292	2156	2024	1896
3	2248	2440	2444	1960	2024	2440	2444	2296	2024	2444	1900
4	2440	2520	2296	1900	1960	2024	2440	2368	2444	2240	1960
5	2440	2368	2296	2020	2368	2296	2156	2444	2024	1960	2020
6	2024	2156	2368	2296	2444	2024	1900	2024	1960	2024	1960
Mean	2296	2357	2369	2107	2141	2208	2267	2299	2175	2109	1939
S.D.	142	114	60	195	203	190	191	133	199	177	45

DURAGEL 75 PRESOAKED IN 1.2% SALINE

Experimental Eye

Central corneal thickness

Subject	Pre-insertion	Insertion	½ hour	1 hour	1½ hour	2 hour	2½ hour	3 hour	3½ hour	4 hour	4½ hour
1	0.50	0.50	0.48	0.48	0.44	0.46	0.44	0.42	0.42	0.42	0.40
2	0.50	0.48	0.48	0.46	0.46	0.46	0.42	0.40	0.40	0.40	0.40
3	0.50	0.48	0.46	0.46	0.46	0.44	0.42	0.42	0.46	0.46	0.44
4	0.50	0.48	0.44	0.46	0.46	0.44	0.44	0.42	0.44	0.44	0.44
5	0.48	0.46	0.48	0.46	0.46	0.46	0.44	0.42	0.44	0.42	0.42
6	0.48	0.48	0.46	0.46	0.44	0.40	0.42	0.40	0.40	0.40	0.42
Mean	0.49	0.48	0.47	0.46	0.45	0.44	0.43	0.41	0.43	0.42	0.42
S.D.	0.01	0.01	0.01	0.01	0.01	0.02	0.01	0.01	0.02	0.02	0.02

Chloride ion content of tears

1	135	123	146	182	203	193	246	203	220	249	255
2	147	118	154	193	212	203	252	213	232	246	248
3	156	109	164	169	181	189	232	239	251	247	249
4	148	113	156	173	196	183	209	226	249	259	253
5	146	119	152	186	192	198	212	201	229	234	236
6	139	123	143	179	196	203	219	210	226	229	231
Mean	145	118	153	180	197	195	228	215	235	244	245
S.D.	7	5	7	8	10	7	16	13	12	10	9

Endothelial cell count

1	2156	2440	2596	2848	2444	3024	3024	3116	3208	3304	3280
2	2224	2296	2440	2600	2680	2848	3024	2936	3116	3024	3100
3	2280	2368	2764	2936	3112	3304	3400	3304	3500	3500	3550
4	2440	2520	2680	2848	3112	3024	3208	3600	3496	3496	3592
5	2368	2444	2680	2764	2848	3208	3400	3304	2936	3024	3112
6	2368	2596	2600	2736	3116	3208	3496	3304	3300	3400	3460
Mean	2306	2444	2640	2822	2885	3103	3259	3261	3259	3291	3349
S.D.	96	97	102	116	256	153	187	203	201	200	198

DURAGEL 75 PRESOAKED IN 1.2% SALINE

Control Eye

Central corneal thickness

Subject	Pre-insertion	Insertion	½ hour	1 hour	1½ hour	2 hour	2½ hour	3 hour	3½ hour	4 hour	4½ hour
1	0.52	0.52	0.50	0.48	0.48	0.47	0.44	0.46	0.44	0.46	0.46
2	0.50	0.50	0.50	0.48	0.48	0.48	0.48	0.46	0.46	0.46	0.46
3	0.50	0.50	0.49	0.49	0.49	0.46	0.46	0.46	0.46	0.44	0.46
4	0.50	0.50	0.50	0.48	0.50	0.44	0.48	0.44	0.46	0.44	0.44
5	0.50	0.52	0.48	0.50	0.50	0.45	0.46	0.46	0.46	0.45	0.44
6	0.48	0.48	0.50	0.50	0.50	0.44	0.46	0.44	0.45	0.44	0.42
Mean	0.50	0.50	0.50	0.49	0.49	0.46	0.46	0.45	0.46	0.45	0.45
S.D.	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01

Chloride ion content of tears

1	139	131	132	202	156	206	153	156	196	156	179
2	140	142	156	139	156	172	185	196	176	145	165
3	138	150	172	183	196	205	207	195	178	182	160
4	149	163	163	191	207	215	219	196	181	193	173
5	136	129	156	206	198	210	197	183	181	202	179
6	148	141	152	189	196	220	211	203	190	197	180
Mean	142	143	155	185	185	205	195	188	184	179	173
S.D.	5	11	12	22	21	15	22	16	7	21	8

Endothelial cell count

1	2368	2344	1960	1900	1960	1896	1900	2024	2248	1960	1896
2	2024	2156	2151	2292	2296	2444	2024	2440	2444	2240	1960
3	2024	2296	2152	2156	1960	2020	2292	2152	2156	1960	1840
4	2280	2368	2444	2024	2152	2024	2296	2368	2444	1960	1900
5	2344	2292	2368	2444	1900	2440	2368	2292	2156	2024	1896
6	2248	2440	2444	1960	2024	2440	2444	2296	2024	2444	1900
Mean	2215	2316	2253	2130	2049	2211	2221	2262	2245	2098	1899
S.D.	140	87	179	191	136	234	193	138	155	184	35

APPENDIX 8

DATA FOR PATIENT STUDIES (CHAPTER 10)

PATIENT CLINICAL INFORMATION

Patient C.H. Age 24 Right eye Subject 1 Left eye Subject 2

Refraction best sphere R -4.25D L -5.25D

Ophthalmometer Readings R 7.90 V / 7.75 H L 7.80 V / 7.75 H

Duragel 60 8.80 : 13.00 -4.75 Duragel 75 7.90 : 13.00 -4.75

Patient G.D. Age 21 Right eye Subject 3 Left eye Subject 4

Refraction best sphere R -6.25D L -6.75 D

Ophthalmometer Readings R 7.35 V / 7.50 H L 7.35 V / 7.45 H

Duragel 60 8.40 : 13.00 -6.50 Duragel 75 7.60 : 13.00 -6.50

Patient H.H. Age 41 Right eye Subject 5 Left eye Subject 6

Refraction best sphere R -1.75 D L -1.25 D

Ophthalmometer Readings R 7.55 V/ 7.60 H L 7.50 V/ 7.70 H

Duragel 60 8.50 : 13.00 -1.50 Duragel 75 7.70 : 13.00 -1.50

Patient G.H. Age 23 Right eye Subject 7 Left eye Subject 8

Refraction best sphere R-1.50 D L -1.50 D

Ophthalmometer Readings R 7.80 V / 7.90 H L 7.80 V / 7.87 H

Duragel 60 8.80 : 13.00 -1.75 Duragel 75 7.90 : 13.00 -1.75

Patient P.H. Age 15 Right eye Subject 9 Laft eye Subject 10

Refraction best sphere R - 3.25 D L -3.25 D

Ophthalmometer Readings R 7.90 V / 7.95 H L 7.80 V / 7.95 H

Duragel 60 8.90 : 13.00 - 3.50 Duragel 75 8.00 : 13.00 -3.50

PATIENT STUDY DURAGEL 60

Central corneal thickness

Subject	Initial	1 week	3 weeks	7 weeks	19 weeks
1	0.50	0.51	0.52	0.50	0.51
2	0.52	0.51	0.51	0.52	0.51
3	0.54	0.54	0.54	0.53	0.54
4	0.54	0.53	0.54	0.53	0.53
5	0.53	0.53	0.53	0.52	0.53
6	0.53	0.52	0.53	0.51	0.52
7	0.52	0.52	0.51	0.52	0.51
8	0.52	0.52	0.52	0.51	0.52
9	0.50	0.50	0.51	0.50	0.51
10	0.50	0.50	0.50	0.50	0.50
Mean	0.52	0.52	0.52	0.51	0.51
S.D.	0.01	0.01	0.01	0.01	0.01

Chloride ion content of tears

1	149	141	151	149	151
2	148	153	150	148	152
3	150	142	141	145	146
4	148	146	149	144	143
5	140	143	142	147	152
6	148	141	143	141	145
7	140	148	141	152	148
8	150	140	146	147	150
9	148	142	148	149	151
10	147	146	145	143	144
Mean	147	144	146	146	148
S.D.	4	4	4	3	3

Endothelial cell count

1	2440	2444	2468	2468	2484
2	2444	2448	2442	2476	2496
3	2256	2248	2240	2244	2276
4	2244	2256	2248	2276	2244
5	2456	2484	2468	2448	2480
6	2444	2496	2440	2444	2496
7	2488	2448	2440	2480	2444
8	2476	2468	2444	2496	2496
9	2468	2448	2456	2476	2476
10	2476	2448	2464	2468	2468
Mean	2419	2419	2411	2428	2436
S.D.	86	85	84	85	89

PATIENT STUDY DURAGEL 75

Central corneal thickness

Subject	Initial	1 week	3 weeks	7 weeks	19 weeks
1	0.52	0.52	0.50	0.50	0.50
2	0.52	0.52	0.52	0.50	0.52
3	0.54	0.52	0.53	0.53	0.53
4	0.54	0.53	0.54	0.53	0.53
5	0.53	0.52	0.53	0.53	0.51
6	0.53	0.53	0.52	0.52	0.50
7	0.52	0.51	0.52	0.51	0.51
8	0.52	0.52	0.52	0.51	0.52
9	0.50	0.51	0.50	0.50	0.50
10	0.50	0.50	0.50	0.50	0.52
Mean	0.52	0.52	0.52	0.51	0.51
S.D.	0.01	0.01	0.01	0.01	0.01

Chloride ion content of tears

1	140	149	143	144	145
2	138	136	149	145	148
3	145	150	142	140	143
4	145	153	146	150	152
5	142	141	151	141	143
6	145	143	141	150	149
7	148	140	145	148	151
8	146	152	148	144	146
9	142	145	143	145	147
10	142	139	138	142	143
Mean	143	145	145	145	147
S.D.	3	6	4	3	3

Endothelial cell count

1	2456	2452	2496	2476	2480
2	2496	2452	2468	2462	2456
3	2280	2240	2256	2276	2244
4	2244	2240	2296	2280	2248
5	2444	2482	2456	2484	2456
6	2440	2468	2444	2456	2476
7	2440	2440	2444	2476	2496
8	2456	2458	2448	2448	2480
9	2456	2448	2456	2468	2476
10	2496	2444	2476	2484	2480
Mean	2421	2412	2424	2431	2492
S.D.	82	87	76	77	92

PATIENT STUDY DURAGEL 60/75

Central corneal thickness

Subject	Initial	1 week	3 weeks	7 weeks	19 weeks
1	0.51	0.51	0.50	0.52	0.52
2	0.50	0.49	0.50	0.48	0.50
3	0.54	0.54	0.53	0.53	0.54
4	0.54	0.53	0.54	0.54	0.53
5	0.53	0.53	0.53	0.53	0.52
6	0.53	0.52	0.53	0.52	0.52
7	0.52	0.52	0.51	0.52	0.52
8	0.52	0.52	0.52	0.52	0.52
9	0.50	0.50	0.50	0.50	0.50
10	0.49	0.49	0.50	0.50	0.50
Mean	0.52	0.52	0.52	0.52	0.52
S.D.	0.02	0.02	0.02	0.02	0.01

Chloride ion content of tears

1	147	143	141	142	144
2	149	147	142	151	148
3	145	155	148	148	151
4	152	160	160	158	159
5	158	167	160	158	163
6	163	168	168	162	167
7	158	168	153	162	160
8	148	160	164	165	158
9	153	157	155	152	158
10	154	154	158	156	160
Mean	153	158	155	154	157
S.D.	5	8	9	6	7

Endothelial cell count

1	2464	2472	2468	2464	2476
2	2460	2468	2464	2468	2456
3	2296	2276	2276	2280	2296
4	2276	2256	2248	2256	2278
5	2496	2492	2476	2484	2480
6	2476	2472	2448	2468	2456
7	2468	2448	2468	2456	2464
8	2472	2456	2476	2476	2472
9	2464	2464	2456	2468	2460
10	2464	2460	2448	2456	2452
Mean	2434	2426	2423	2428	2429
S.D.	75	81	81	80	72

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