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PRESBYOPIA AND THE CHANGES WITH AGE IN THE HUMAN CRYSTALLINE LENS

BY R. F. FISHER

From the Department of Visual Science, Institute of Ophthalmology, Judd Street, London WC1H 9QS

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SUMMARY

1. A method of determining the distribution of capsular moulding pressure is described. This includes:

(*a*) measuring the decrease in polar depth of the lens from photographed lens profiles before and after the capsule has been cut around the entire equator of the lens,

(*b*) measuring the elastic properties of the lens substance by subjecting the lens to known centrifugal forces and photographing the polar strain so produced.

2. A method of determining the relationship between capsular and lenticular strain is described. This includes (*a*) measuring the elastic properties of the capsule (*b*) measuring the elastic properties of the lens substance and (*c*) measuring the profiles of the photographed lens.

The ratio of the strain of lens substance to capsule is expressed as a dimensionless parameter, the lens number.

3. The decrease in the amplitude of accommodation with increasing age is proportional to the lens number divided by the square of the radius of the accommodated lens, assuming that the movement of the capsulo-zonular attachments of the lens remains unimpaired in the ageing eye.

4. Ageing changes in the human crystalline lens are sufficient to account for a total loss of accommodation by the age of 61 years.

INTRODUCTION

Fincham (1937) showed that when the capsule of the human lens was removed, the decapsulated lens became flatter and more like its unaccommodated shape. Despite this important observation he still concluded that the lens substance was plastic in nature. Weale (1963), however, suggested that there was an interplay of forces between the capsule and the lens substance with both structures possessing inherent elasticity. Fisher (1969*a*, 1971) measured the elasticity of the capsule and lens substance and showed that the latter as well as the former was truly elastic provided the lens substance was subjected to centrifugal radial forces. Since these forces were accurately measured and the change in shape of the lens photographed, a further observation on the change in shape produced by reducing capsular moulding pressure to zero would enable the pressure distribution within the lens capsule to be deduced (Pl. 1).

The distribution of capsular moulding pressure forms the first part of this investigation while the second determines, by estimating Young's Modulus of Elasticity of the capsule, the degree of stretching of this capsule which extends around the intact and accommodated lens.

Thus it is possible to associate a given amount of capsular stretching with a measured change in the dimensions of the lens. If the capsular stretching and hence the movement of the capsulo-zonular attachments be assumed to remain constant with age, the relative movement of the lens substance can be estimated at every age. Fisher (1969*b*) showed that the accommodative power of the lens could be determined from its polar or equatorial movement, so the decrease in accommodative power with age could be deduced from the decrease in polar movement of the ageing lens. Thus an estimate of presbyopia from lenticular causes entails measurement of elasticity of the capsule and lens substance, and measurements of the profile on each of a series of lenses of different ages.

METHODS

Lens experiments

Lenses (fifty-eight) were obtained from human cadavers not more than 24 hr after death and in some cases as early as 4 hr after death (Fisher, 1971). Three separate experiments were performed on each of these lenses:

(i) determination of the elastic constants of the lens substance;

(ii) determination of the differences in capsular moulding pressure at the equator and anterior pole of the lens;

(iii) determination of the elastic constants of the lens capsule.

Each experiment was performed when possible in duplicate for every pair of cadaver lenses and the results averaged.

(*i*) *Determination of the elastic constants of the lens substance*

This has already been described (Fisher, 1971).

(*ii*) *Determination of the differences between capsular moulding pressure at the equator and pole of the lens*

This determination required measurements of the profile of the lens before and after the capsule was cut.

Procedure

The lens was mounted on the rotating lens support, and stationary photographs were taken (Fisher, 1971). Then the capsule was cut around the entire equator of the lens with microscissors under magnification, care being taken to avoid disturbing the capsule and under-lying lens substance. A further series of photographs were taken when the lens had been warmed again in isotonic saline to 37° C.

Storage experiments

All lenses were perfectly transparent at the time of testing, but to observe if storage within the cooled cadaver eye adversely affected the change in shape which occurred when the capsule was cut, two pairs of cadaver eyes were tested. The experiment of cutting the capsule was conducted within 4 hr of death on one eye, while the other was stored for a further 24 hr at 4° C. The lens was then removed from the second eyeball and the experiment repeated on this lens. The variation in the change of shape between the two lenses was not greater than 10 %.

Calculation of the differences in pressure within the capsule of the accommodated lens

The direct measurement *in vitro* of the capsular moulding pressure of the accommodated and extirpated lens has so far proved impossible. This is because cannulation of the delicate lens capsule has always resulted in rupture and loss of fluid. The present experiments were, therefore, designed to determine the differences of pressure indirectly for human lenses of varying ages.

It may be noted that it has only been possible to give some estimate of differences of pressure (Appendix), existing at the equator and pole of the lens, by a method which employs the measurement of changes in the profile of the lens substance when the capsule is cut. This is so, because the lens substance containing as it does a high proportion of water, is incompressible.

Thus the same change in shape would be produced regardless of the absolute magnitude of the respective capsular moulding pressures existing at the equator and pole of the lens provided the differences between them remained the same. This is true only within the limits of ultimate strength and the elastic yield point of the capsule. A further complication is that pressure differences are measured on the lens when the restraint exerted by the zonule has been abolished. However, Hess (1904) demonstrated that during maximum accommodation the zonule is so relaxed that the lens sinks owing to gravity. These pressure measurements, therefore, were made under conditions not greatly dissimilar to those occurring *in vivo* during maximum accommodation.

The difference in capsular moulding pressure and equator and pole of the lens was calculated from Appendix eqn. (1.3)

$$f_d = \delta b_c . E_p / b_a,$$

where

f_d = difference in capsular moulding pressure (Nm^{-2});

b_a = perpendicular distance of anterior pole from the equatorial plane of the accommodated lens (m);

δb_c = decrease in distance of anterior pole from the equatorial plane of the lens due to cutting the capsule (m);

E_p = Young's Modulus of polar elasticity (Nm^{-2}).

(*iii*) *Determination of the elastic constants of the lens capsule*

This has already been described (Fisher, 1969*a*).

Calculation of relative capsular strain when differences of pressure within the lens are equalized

In a previous paper Fisher (1969*b*) the concept of an equivalent spherical segment, representing the anterior portion of the lens, was employed to estimate the energy stored in the lens capsule. The change in radius (δR_m) of this theoretical sphere can in like manner be used to give a proportionate estimate of the capsular strain necessary to change pressure within the capsule. With a known difference in pressure between the equator and pole of a given lens the measure of the capsular strain necessary to equal this pressure change within the sphere is calculated from Appendix eqn. (2.2)

$$\delta R_m = f_d R_m^2/4t_e E_c,$$

where

δR_m = change in radius of the equivalent sphere of capsule (m);
f_d = difference in capsular moulding pressure between; pole and equator of the lens (Nm^{-2});
R_m = radius of equivalent sphere (m);
E_c = Young's Modulus of elasticity of the capsule (Nm^{-2});
t_e = equatorial thickness of the capsule (m).

Calculation of the polar movement of the lens substance for a constant movement of the capsulo-zonular attachments

In vivo the lenticular attachments of the zonule are inserted tangentially into an area of the capsule and thus a complex relationship exists between the movement of the zonule and capsular strain represented by a change in radius (δR_m) of the equivalent spherical capsule which theoretically surrounds the lens.

However, the shape of the lens does not alter greatly as it ages and there is no evidence that the mode of the insertion of the zonule into the capsule changes with age. Furthermore, any change in the shape of the lens substance *in vitro* (δb_c) and *in vivo* (δb) is directly comparable if intracapsular stresses in the two cases were known since both lens substance and capsule obey Hooke's Law within the limits of strain reversibility. This relationship may, therefore, be estimated by a dimensionless number, which contains all the factors which influence stress, namely thickness of capsule (t_e), the equivalent radius of the spherical segment of capsule (R_m), the ratio of elasticity of capsule and lens substance (E_c/E_p), and the anterior polar depth of the lens (δb_a). Thus the postulated constant movement of the capsulo-zonular attachments would then make changes in polar measurement of the lens proportional to this dimensionless parameter – the lens number (L_N) (see Appendix eqn. (3.2)).

Calculation of the change in dioptric power of the lens from the lens number and lens shape

It has been shown that changes in the dioptric power of the lens, provided it changes from one ellipsoidal profile to another during accommodation, could be related to changes in the shape of the lens (Fisher, 1969*b*). From the previous paragraphs the change in shape of the lens is proportional to the lens number while the change in dioptric power is calculated from Appendix eqn. (4.5).

$$\delta D = K' L_c,$$

where

L_c = lens coefficient (m^{-2}),
K' is a constant (m).

RESULTS

Changes in the anterior polar depth of the lens following cutting of the capsule

The decrease in polar depth of the lens when the capsule was cut around the equator was $-0{\cdot}17 \times 10^{-3}$ (m) $\pm 0{\cdot}05 \times 10^{-3}$ (m) (S.D.) over the whole series. There was no significant correlation of the change in polar depth with age ($r = 0{\cdot}09$).

Changes with age in the capsular moulding pressures

The difference between the capsular moulding pressures at the equator and anterior pole of the lens plotted against age ($n = 29$) is shown in Text-fig. 1. The disparity between equatorial and polar pressure appears to rise until at least the age of 60 yr. The most abrupt rise is seen after the age of 45 yr. It is difficult to measure pressure differences after 50 yr. of age, because of (*i*) difficulties in measuring small strains (see methods), (*ii*) pressure differences vary inversely as the spinning strain measurement, thus small changes in strain cause large changes in pressure. It is likely, however, that in a lens above 60 yr of age pressure differences decrease again since the elastic strength of the capsule declines markedly as age advances (Fisher, 1969*a*).

The amount of capsular strain required to produce the differences of moulding pressure observed within the lens

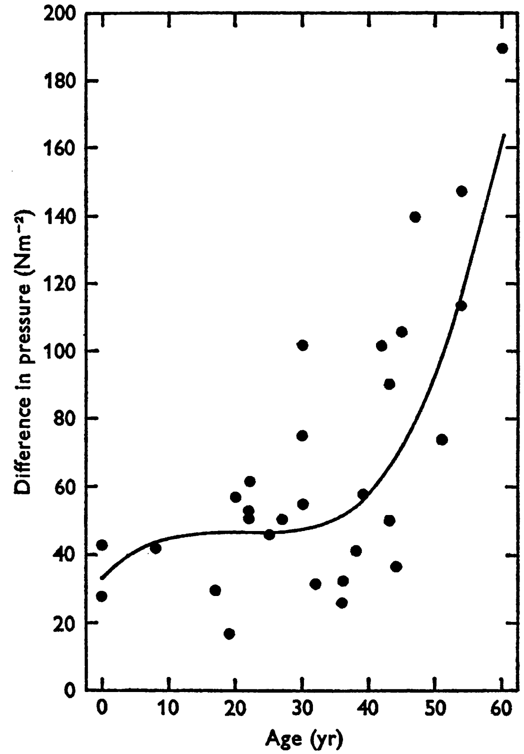
The relative magnitude of capsular strain in the accommodated lens expressed as the change in radius of an equivalent sphere of capsule plotted against age is shown in Text-fig. 2. There is a sevenfold increase of capsular strain at 60 yr of age to that observed at 15 yr of age. This strain or change in radius is the amount necessary to produce the same change of pressure within the capsule as the difference in pressure between the equator and pole of the lens observed at the respective ages.

When the same increase in the capsular radius is considered, from the accommodated to the unaccommodated state, this increase is proportional to the movement of the capsulo-zonular attachment to equalize pressure within the lens *in vivo* (see Methods).

The lens coefficient

Text-fig. 3 shows the lens coefficient plotted against age. The lens coefficient is a measure of the magnitude of the change in dioptric power of the lens for maximum accommodation (see Methods).

It will be seen that for a linear regression of the data the lens coefficient becomes zero at 61 yr of age indicating that lenticular changes with age are sufficient to abolish the accommodation by this age.



Text-fig. 1. Differences between the equatorial and polar moulding pressure of the capsule plotted against age ($n = 29$).

Pressure differences f_d ($\mathrm{Nm^{-2}}$) calculated from $f_d = \delta b_c E_p / b_a$ (see text) where δb_c = decrease in anterior polar depth due to cutting capsule around lens equator (m), b_a = distance of anterior pole from equatorial plane of accommodated lens (m), E_p = Young's Modulus of polar elasticity of lens ($\mathrm{Nm^{-2}}$).

$$f_d = a_d + b_d A + c_d A^2 + d_d A^3,$$

A = age (yr.)

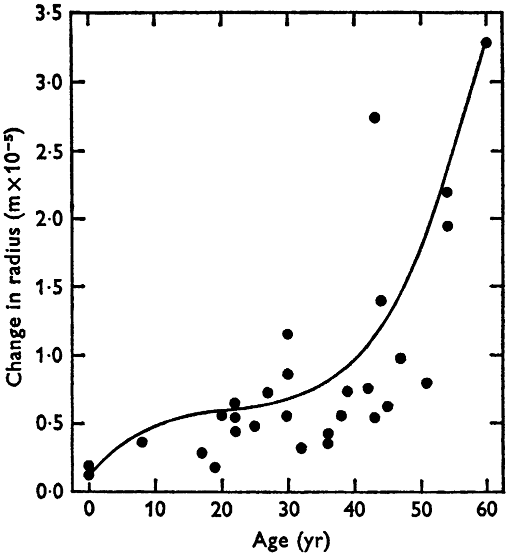
Constants

$$a_d = 32{\cdot}8, \qquad b_d = 2{\cdot}38,$$
$$c_d = -0{\cdot}123, \qquad d_d = 0{\cdot}0209.$$

Significance of changes in pressure with age

$$r = 0{\cdot}671 \quad (P < 0{\cdot}001).$$

Variance ratio 16·1 in excess of 0·1 % critical point.



Text-fig. 2. Change in the radius of capsular shell caused by a pressure difference equal to that occurring between the equator and pole of the lens plotted against age ($n = 29$).

Change in radius δR_m (m) calculated from $\delta R_m = f_d R_m^2 / 4 t_c E_c$ (see text) where f_d = difference between equatorial and polar capsular moulding pressure (Nm^{-2}), R_m = radius of equivalent sphere (m) t_e = thickness of equatorial capsule (m), E_c = Young's Modulus of capsular elasticity (Nm^{-2}).

$$\delta R_m = a_r + b_r A + c_r A^2 + d_r A^3,$$

$$A = \text{age (yr)}.$$

Constants

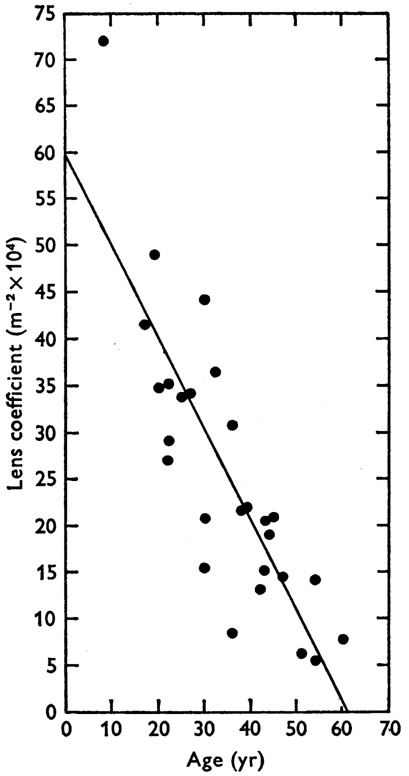
$$a_r = 0{\cdot}0815 \times 10^{-5}, \quad b_r = 0{\cdot}065 \times 10^{-5}$$

$$c_r = -0{\cdot}0028 \times 10^{-5}, \quad d_r = 0{\cdot}000045 \times 10^{-5}.$$

Significance of change in capsular radius with age: $r = 0{\cdot}626$, $P < 0{\cdot}001$. Variance ratio 9·79 in excess of 0·1 % critical point.

DISCUSSION

With the assumption that accommodation occurs upon constriction of the ciliary muscle with relaxation of the zonular fibres, the stresses produced by the lens capsule become the only active force to mould the lens substance into a more spherical shape, so increasing the dioptric power of the lens. The capsule may also overcome residual constraint of the ciliary muscle and frictional forces between the lens fibres. As it is an inherent property of the lens to become more spherical, forces available in the capsule may be equated solely with the elastic forces of the lens substance resisting movement. The error in such an assumption is to over-



Text-fig. 3. Lens coefficient representing factors which influence the amplitude of accommodation plotted against age ($n = 27$).

Lens coefficient (L_c) (m^{-2}) calculated from

$$L_c = \{L_N\}/a_a^2 = \{t_e b_a E_c/R_m^2 E_p\}/a_a^2 \quad \text{(see text)},$$

where

L_N = lens number;
E_c = Young's Modulus of capsular elasticity (Nm^{-2}),
E_p = Young's Modulus of polar elasticity of lens substance (Nm^{-2}),
t_e = thickness of capsule at the equator of the lens,
a_a = equatorial radius of the accommodated lens (m),
R_m = mean radius of curvature of anterior lens profile (m),
b_a = anterior polar depth of accommodated lens (m),
A = age (yr).

$$L_c = a_c + b_c A.$$

Constants

$$a_c = 59{\cdot}3, \quad b_c = -0{\cdot}97.$$

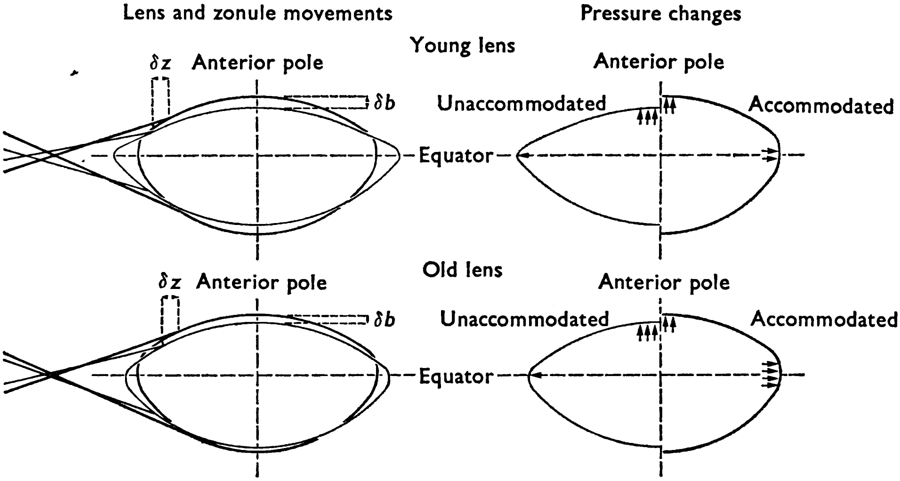
Significance of changes in lens coefficient with age

$$r = -0{\cdot}836, \quad P < 0{\cdot}001.$$

Variance ratio 58·2, in excess of 0·1 % critical point.

Note: the calculation of the lens coefficient assumes that there are no great differences in the shape of the lens so the two rounded neonatal lenses have been excluded.

estimate the capsular forces available to mould the lens. Thus at worst the formula proposed for the lens coefficient only underestimates the rôle of the lens in presbyopia.



Text-fig. 4. Diagrams of changes in the movement of the zonular attachments and intracapsular pressure occurring during accommodation

δz = movement of the capsulo-zonular attachments of the lens.

δb = anterior polar movement of the lens.

↑ = the resistance pressure of the lens substance.

Note: (i) the same movement (δz) of the zonular attachments is required to mould the lens substance in age as in youth despite the decreasing anterior polar movement of the lens (δb);

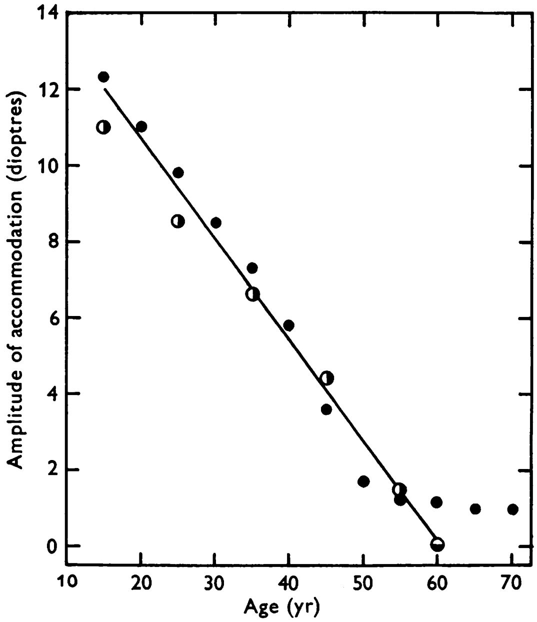
(ii) the relative pressure differences in the accommodated lens have been measured, while those of the unaccommodated lens are postulated from the radial attachment of the zonule at the lens periphery (see text).

Differences between the equatorial and polar moulding pressures within the capsule of the ageing lens

Cutting of the capsule of the lens produces markedly different changes in anterior polar movement of the lens substance from lens to lens without a significant relationship with age. However, if the lens substance elasticity is taken into account the ageing accommodated lens shows a highly significant increase with age of pressure differences within its capsule (Text-fig. 1).

In Text-fig. 4 the likely variations in the capsular moulding pressure are illustrated both in youthful and ageing lenses focused alternately upon distant and near objects. The Figure shows that when the eye is focused upon a distant object equatorial pressure is very low in both instances. This view is put forward by reason of the observation that tent-like elevations are produced in the capsule at the equator of the unaccommodated lens *in vivo* (Duke-Elder, 1961).

Since equatorial pressure is initially always greater than polar pressure (Text-fig. 1), as accommodation decreases following relaxation of the ciliary muscle, accompanied by increasing tension in the zonule, there is a point when they become equal. This is true whether the lens is old or young. However, in the ageing lens a greatly increased movement of the zonular attachments is required to decrease the stretched equatorial capsule and reach this point (Text-fig. 2).



Text-fig. 5. Presbyopic changes in the amplitude of accommodation due to changes with age in the lens

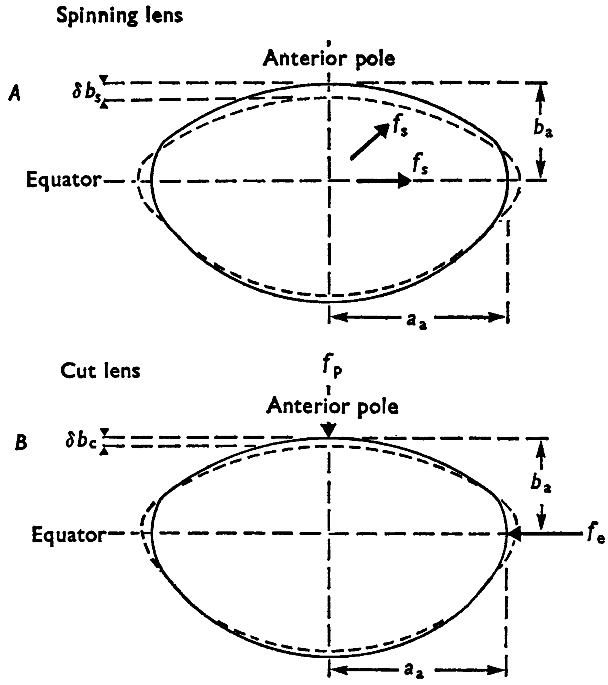
— Linear regression of lens coefficient (L_c) with age where

$$L_c = b_a t_e E_c / a_a^2 R_m^2 E_p$$

(see text), where

b_a = anterior polar depth of accommodated lens (m),
a_a = equatorial radius of accommodated lens (m),
t_e = equatorial thickness of lens capsule (m),
E_c = Young Modulus of elasticity lens capsule (Nm^{-2}),
E_p = Young's Modulus of polar elasticity of lens substance (Nm^{-2}),
R_m = radius of equivalent sphere of capsule (m).

● Duane's data, (1922), ◑ Brüchner's data (1959) (mean per decade); ◒ Hamasaki's data (Hamasaki, Org & Munz, 1956).



Text-fig. 6. Diagrams of the changes in the lens profile employed in the determination of differences in the capsular moulding pressure.

A Profile changes in a spinning lens: — Stationary lens profile. ----- Spinning lens profile. δb_s Polar strain of spinning lens (m).

B Profile changes in a stationary lens with capsule cut around the lens equator: — stationary lens profile with intact capsule; – – – stationary lens profile with cut capsule; δb_c Polar strain of lens with cut capsule (m).

Thus as the lens ages an ever increasing proportion of zonular movement is taken up in stretching or relaxing the weakening capsule while leaving the ever more resistant lens substance almost unmoved.

Ageing changes in the lens as a cause of presbyopia

Text-fig. 5 shows that the decrease in amplitude of accommodation with age can be well accounted for solely by lenticular factors. The effect of these factors is based on the assumption of a constant movement of the zonular insertion of the capsule during maximum accommodation, irrespective of the age of the subject. The lenticular factors are (i) a decrease in the elasticity modulus of the capsule (ii) an increase in the elasticity modulus of the lens substance and (iii) a flattening of the lens.

If other factors in accommodation occur and change with age they must for the most part be compensatory. For example increased contractability of the ciliary muscle may well be rendered ineffective by the stretching and weakening of the zonular fibres with age.

The importance of changes with age in the lens in decreasing the amplitude of accommodation as the prime cause of presbyopia is thus established. Moreover, the unimpaired shortening of the ciliary muscle as age advances is a necessary hypothesis to explain the amount of accommodation still remaining in the ageing eye. Recently the activity of the human ciliary muscle has been measured by Swegmark (1969). He recorded changes in the electrical resistance of the ciliary muscle during accommodation, and showed that the movement of the fibres as revealed by changes in their impedance remained unimpaired, at least until the age of 60 yrs.

It may be concluded therefore that (i) the equatorial capsule is stretched over the equator of the accommodated lens to an increasing extent as age advances; (ii) the ageing changes in the shape, capsule and substance of the lens are sufficient to explain the decrease in amplitude of accommodation at every age; (iii) the same excursion of the capsulo-zonular attachments of the lens in the ageing eye is necessary to produce the meagre amplitude of accommodation occurring in presbyopia as the maximum amplitude observed in youth.

I would like to acknowledge the encouragement given to me by Professor R. A. Weale, the technical assistance of Mrs B. E. Pettet, and the computer programming by Mr Brian Augier.

APPENDIX

1. *Pressure differences within the capsule of the accommodated lens* (Text-fig. 6)

ρ = density of lens substance (kg m^{-3}),
ω = speed of rotation of the lens (rad sec^{-1}),
f_d = difference in capsular moulding pressure (Nm^{-2}),
b_a = perpendicular distance of anterior pole from the equatorial plane of the accommodated lens (m),
δb_s = decrease in distance of anterior pole from equatorial plane due to spinning the lens about its polar axis (m),
δb_c = decrease in distance of anterior pole from equatorial plane of lens due to cutting the capsule (m),
a_a = equatorial radius of accommodated lens (m),
E_p = Young's Modulus of polar elasticity (Nm^{-2}),
σ = Poisson's ratio.

The anisometropic elasticity of the lens is neglected since it is almost isotropic both at 15 and 60 yr of age (Fisher, 1971, Fig. 12). For the stationary capsulated lens axial strain is caused by two forces at the equator (f_e) maintaining, and a force at the pole (f_p) opposing the accommodative shape of the lens. When the capsule is cut the strain ($\delta b_c/b_a$) is unmasked as all stresses are reduced to zero and the lens flattens.

Therefore

$$\delta b_c/b_a = (2\sigma f_e - f_p)/E_p. \tag{1.1}$$

Now σ for the incompressible lens substance is 0·5 and $f_a = (f_e - f_p)$. (1.2)
From (1.1) and (1.2)

$$f_d = \delta b_c E_p/b_a. \tag{1.3}$$

Note E_p is calculated from

$$E_p = \frac{7}{24} . a_a^2 b_a \rho \omega^2/\delta b_s \quad \text{(Fisher (1971) Appendix eqn. (3.6).}$$

2. *Calculation of relative capsular strain when differences of pressure within the lens are equalized*

R_m = radius of equivalent sphere of capsule (m),
R = radius of curvature on ellipsoidal profile at point $x.y$ (m),
E_c = Young's Modulus of elasticity of the capsule, (Nm^{-2}),
t_e = equatorial thickness of the capsule (m).

From Fisher (1969*a*, *b*).

$$R_m = \sum_1^{10} R.$$

$$\text{Circumferential strain} = \frac{2\pi\delta R_m}{2\pi R_m} = \frac{f_d R_m(1-\sigma)}{2t_e E_c}. \tag{2.1}$$

Thus as $\sigma = 0{\cdot}5$

$$\delta R_m = f_d R_m^2/4t_e E_c. \tag{2.2}$$

3. *Calculation of polar movement of lens substance relative to the movement of the capsulo-zonular attachment* (Text-fig. 4)

δ_z = radial movement of capsulo-zonular attachments (m),
L_N = lens number.

Combining eqns. (1.3) and (2.2)

$$\delta b_c = 4\{t_e b_a E_c/R_m^2 E_p\}\, \delta R_m. \tag{3.1}$$

Since there are (*i*) no gross changes in the shape of the lens or of the site of attachment of the zonule with ageing, and (*ii*) both capsule and lens substance obey Hooke's Law (Fisher, 1969*a*, 1971); δb_c and δR_m bear a constant relationship to δb and δz respectively from lens to lens.

Thus we may write

$$\delta b = K L_N \delta_z, \tag{3.2}$$

where

$$L_N = \{t_c b_a E_c/R_m^2 E_p\} \quad \text{and} \quad K \quad \text{is a constant.} \tag{3.3}$$

4. *Calculation of the change in dioptric power of the lens number and lens shape*

D = dioptric power of lens in dioptres,
R_1 = radius of curvature of the anterior pole of, the lens (m),
L_c = lens coefficient (m^{-2}),
V = volume of anterior segment of lens (m^3),
μ = mean refractive index of the lens in aqueous,
δb = change in anterior polar depth of the lens during maximum accommodation (m)

From Fisher (1969*a*) Appendix eqn. (5.2) and (5.3)

$$D = (\mu - 1)\left(\frac{1}{R_1} - k\right) \tag{4.1}$$

and

$$\frac{1}{R_1} = 2\pi b_a^2/3V. \tag{4.2}$$

Differentiating and combining eqns. (4.1) and (4.2), since there are no volume changes in the lens during accommodation, and $V = \frac{2}{3}\pi a_a^2 b_a$

$$\delta D = 2(\mu - 1)\,\delta b/a_a^2. \tag{4.3}$$

Again combining (4.3) and (3.2)

$$\delta D = 2(\mu - 1)L_N/a_a^2\}K'.\delta z. \tag{4.4}$$

If by definition $L_N/a_a^2 = L_c$, and if δz remains constant throughout life

$$\delta D = K'L_c \tag{4.5}$$

where K' is a constant.

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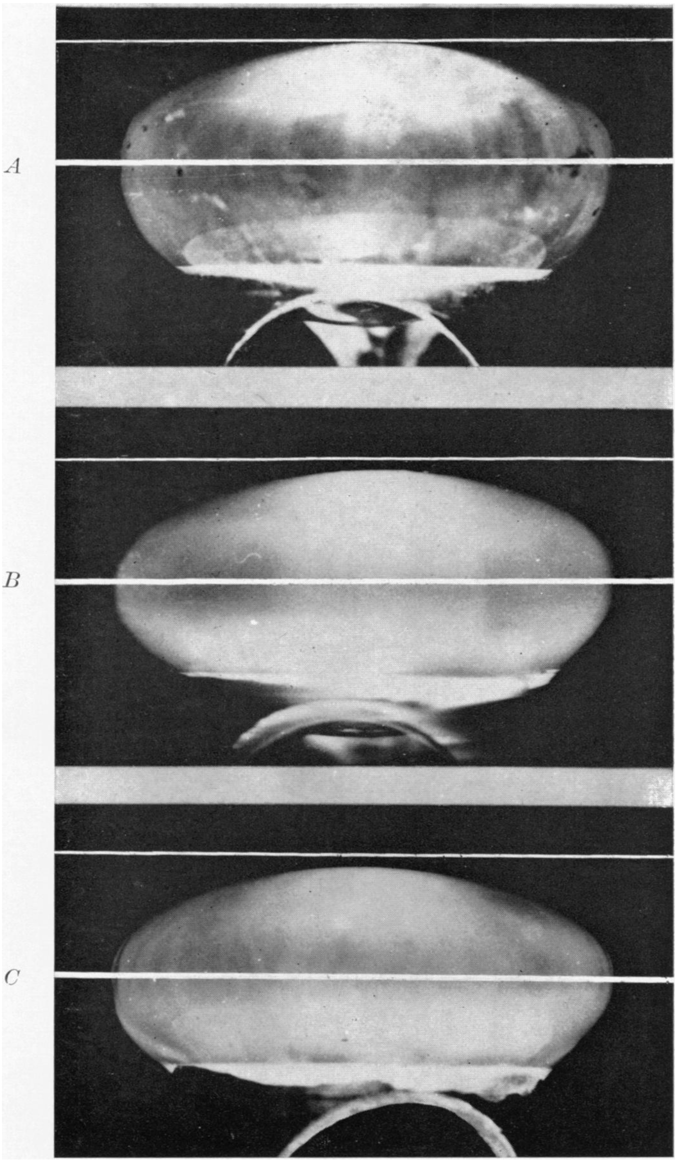

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EXPLANATION OF PLATE

Photographs of the anterior profile of a human lens (aged 21) with anterior pole uppermost. *A*: stationary lens. *B*: the same lens spinning at 1000 rev/min. *C*: the same lens stationary after the capsule was cut around the lens equator (equator shown in every case by a thick white line while a thin white line passes through the anterior pole of the lens shown in *A*).

Note: decrease in anterior polar thickness of the spinning and cut capsule profiles compared with the stationary profile.