11

THEORIES OF PRESBYOPIA

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Although the problems of near vision in the elderly provided the major impetus for the development of convex spectacle lenses in the 13th century, it was not until the 19th century that the characteristics of presbyopia were clearly differentiated from those of hyperopia. Reasonable speculation on the origins of presbyopia had to await the development of a basic understanding of the mechanism of accommodation. Nevertheless, it had long been suspected that lenticular change might be partly involved. In 1730, Petit[1] noted with respect to the lens: "The central part begins to become more firm in men of the age of 20 or 25 years; this firmness increases and extends little by little towards the circumference, which also becomes more rigid…" In 1793, Young[2] also remarked: "It has been observed that the central part of the crystalline becomes rigid with age, and this is sufficient to account for presbyopia…" Since this time, a variety of explanations for presbyopia have been reported; some were based on a single component of the accommodative mechanism, whereas others suggested that the origins of presbyopia are multifactorial. A number of reviews in the past 2 decades[3-9] have demonstrated that there currently is no complete agreement on which mechanisms are correct. This is unfortunate, as the effectiveness of surgical or other interventions designed to restore some active accommodation depends upon the correctness of the assumptions made about the factors that cause presbyopia.

Many aspects of our understanding of the accommodation mechanism and the age-dependent changes as components of presbyopia have been reviewed previously in Sections II and III, particularly in Chapter 8. Briefly, changes in the form of the ciliary muscle alter the forces imposed by the zonule on the lens and its capsule. These changing forces alter the shape of the lens and hence its power. Some have speculated that important roles might also be played by the elastic choroid, the vitreous, and, perhaps, the iris and pupil. How do these changes interact to lead to presbyopia?

GENERAL CONSIDERATIONS

Figure 11-1 shows some elements of the accommodative system that change with age and, as suggested by various authors, contribute to the development of presbyopia.

Over the years, 2 main theories regarding presbyopia development have been identified. In the first, commonly termed the *Hess-Gullstrand theory*, all responsibility is placed on the lens, with no contribution from changes in the ciliary muscle. It is assumed that the lens progressively loses its ability to change shape but that, within the "manifest" region where shape change is still possible, the ciliary-muscle force required to produce each diopter of accommodation remains unchanged. This means that, when the

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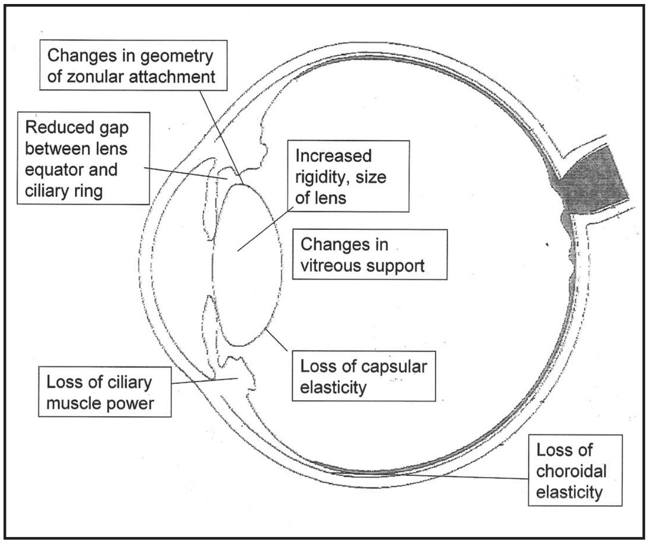

Figure 11-1. Factors of the accommodation system suggested by various authors as being implicated in the development of presbyopia.

dioptric limits of shape change are reached, a further latent region exists where, although the muscle is still capable of contracting, the stiffness of the lens prevents further changes in its optical power. In contrast to this concept, Duane[10] suggested that presbyopia results from a progressive weakening in the strength of the ciliary muscle and that the full, but diminishing, strength of the muscle is always being used to achieve the full amplitude of accommodation at all ages. Although his name is often coupled with that of Duane,[10] Fincham[11,12] suggested a somewhat different hypothesis. He suggested that the ciliary muscle retained its strength but that the force required per diopter of accommodation increased with age due to the increasing stiffness of the lens material. Thus, to achieve a given change in lens power, more force must be applied to the lens by the elastic capsule, thereby demanding a greater change in the ciliary muscle. Fincham[11,12] agreed with Duane[10] that all the available muscle strength was required to reach maximal amplitude but differed in noting that this maximal strength was essentially unchanged.

On the basis of these general ideas, we shall now consider in more detail the possible role played by the different structures that might contribute to presbyopia and the validity of the above and later theories. Studies involving pharmacological stimulation of accommodation are not discussed here, as they may not adequately simulate natural accommodation. When considering in vitro experiments, it is always necessary to remember the possibility of postmortem changes and the difficulty of adequately simulating the characteristics of the forces that act on the lens in the natural eye.

CRYSTALLINE LENS AND CAPSULE

As already noted, many authors have suggested that changes in these ocular components are the main, or perhaps the only, cause of presbyopia. Thus Gullstrand,[13] in an appendix to *Helmholtz's Treatise on Physiological Optics*, stated "…along with the steady increase of dimensions, there is found also a progressive sclerosis of the central portions and differentiating of the core. Functionally, this change in the lens is manifested by a progressive decrease of the amplitude of accommodation…" Several of the surgical interventions suggested in this book depend on the essential correctness of this view for their possible success.

While Gullstrand[13] talked only of "the lens," Fincham[11,12] recognized that it is the combined properties of the lens and capsule that are of importance because the capsule transmits the zonular forces to the lens substance. Thus, the elastic and other properties of both components affect the shape and index gradient changes, which provide the accommodative power change. The mechanical characteristics of the lens and its capsule have been extensively explored in vitro. Fisher[14-20] carried out a series of experiments, which, although they have been criticized for not accurately simulating the forces acting in vivo,[21] show that Young's modulus of elasticity for the capsule declines with age, reducing by a factor of approximately 2 between the ages of 20 and 60 years (Figure 11-2A). This suggests that the aging capsule becomes somewhat less effective at distributing the zonular forces across the lens. In contrast, an increase in Young's modulus occurs in the lens (Figure 11-2B; see also Augusteyn[22] for later data). Glasser and Campbell[23] found that the lenticular resistance to deformation increased markedly with age. In addition, when the lens capsule was removed, there was a substantial shape change and decrease in the power of younger lenses but little change in older lenses (Figure 11-3A), suggesting that the ability of capsular forces to mold the isolated lens substance had disappeared by approximately age 40 to 50 years. These changes were not due to a change in water content of the lens, which appears to be essentially constant with age.[24]

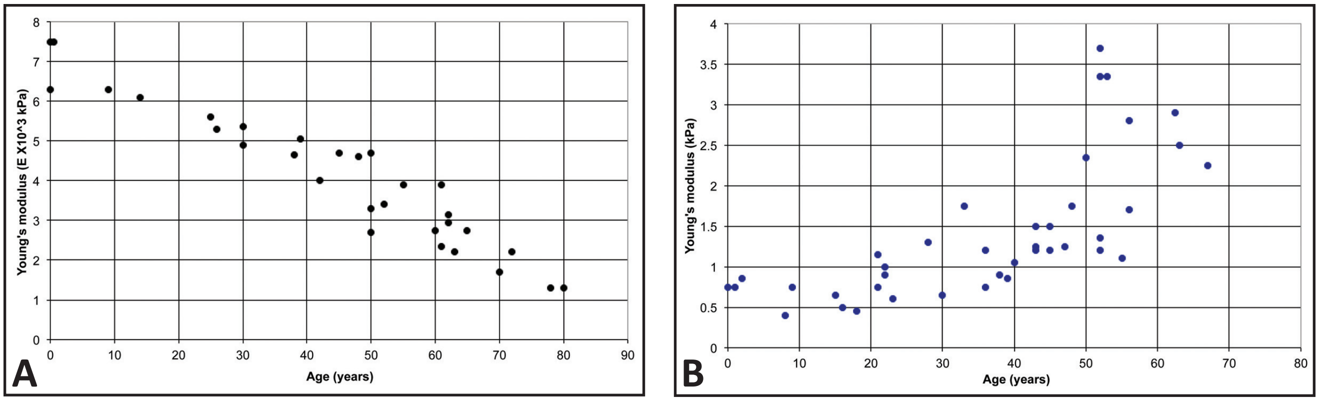

Figure 11-2. Change in Young's modulus with age for (A) the capsule and (B) the lens. Note that the capsular values are much higher than those for the lens. (Based on data compiled from Fisher RF. Elastic constants of the human lens capsule. *J Physiol (Lond).* 1969;201:1-19 and Fisher RF. The elastic constants of the human lens. *J Physiol (Lond).* 1971;212:147-180.)

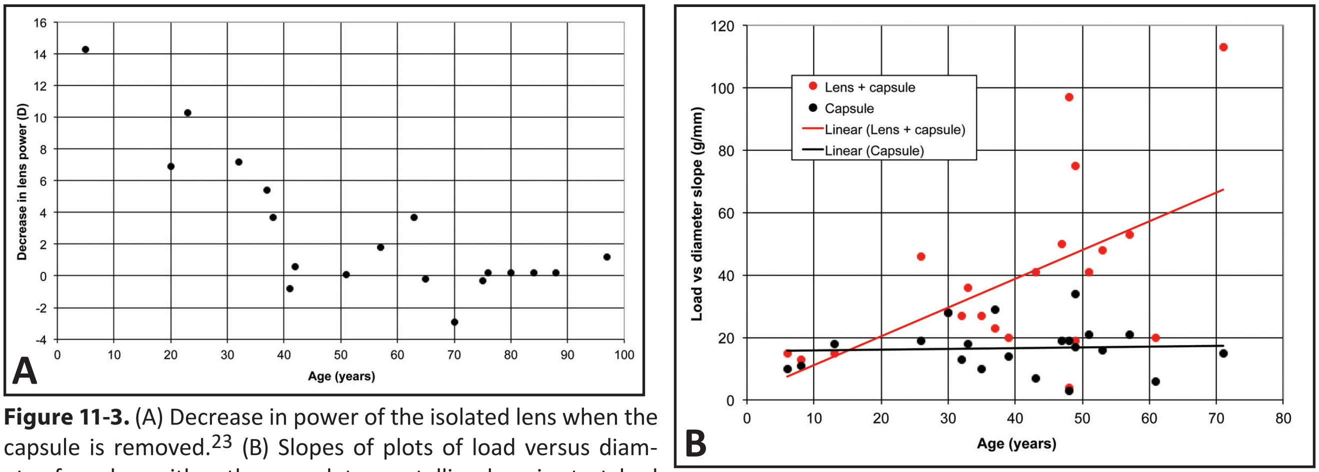

Figure 11-3. (A) Decrease in power of the isolated lens when the capsule is removed.[23] (B) Slopes of plots of load versus diameter for when either the complete crystalline lens is stretched (red symbols) or for the capsule alone after the contents had been removed through a mini-capsulorrhexis (black symbols) is stretched.[25] The lines are least-squares regression fits. As slope increases, the force required to stretch the lens increases.

Thus, the evidence broadly supports the idea that the lens substance may become progressively harder to deform, whereas the efficiency of the capsule, as a force distributor capable of changing lens shape, declines with age. Glasser and Campbell's[23] finding that the decrease in lens power that occurs on removal of its capsule (see Figure 11-3A) decreases almost linearly with age from approximately 5 years to 0 at the age of approximately 50 years is particularly persuasive. Also persuasive is the finding by Ziebarth et al[25] that, in vitro, the force required to radially stretch the natural lens increases through life, whereas the force required to stretch the empty capsule remains essentially constant (see Figure 11-3B). Note that, in youth, the stretch characteristics are dominated by the properties of the capsule, but the lens becomes progressively more important after the age of approximately 20 years. However, such in vitro changes may not reflect true accommodation, and doubt remains as to whether these lenticular/capsular changes alone are enough to account for the slow, progressive loss of accommodation up to the onset of its complete loss. For example, Figure 11-2B suggests that changes in lens elasticity are small until the age of approximately 40 years. Similarly, as the authors themselves admit, the data of Glasser and Campbell[23] for the force required to deform the lens only show substantial changes above the age of approximately 40 years, although the amplitude of accommodation will have declined steadily before this age; at best, the force increases exponentially rather than linearly. Thus, the implication is that other factors must contribute to the amplitude changes through life.

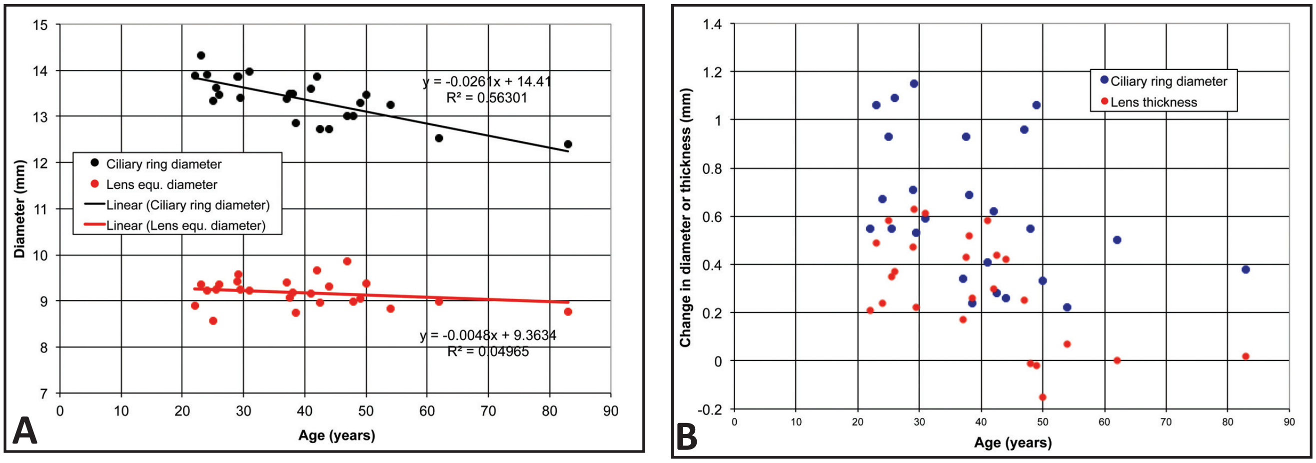

Figure 11-4. (A) The diameter of the ciliary ring and the equatorial diameter of the lens in the unaccommodated eye as a function of age, as determined by MRI. (B) The change in ciliary ring diameter and in lens central thickness in response to an 8.00-D accommodation demand, as a function of age. Although the ciliary muscle remains active into old age, there is no change in the lens shape beyond the age of approximately 50 years. (Based on data compiled and replotted from Strenk SA, Semmlow JL, Strenk LM, Munoz P, Gronlund-Jacob J, DeMarco JK. Age-related changes in human ciliary muscle and lens: a magnetic resonance imaging study. *Invest Ophthalmol Vis Sci.* 1999;40(6):1162-1169.)

CILIARY MUSCLE

As discussed previously, some early authors, such as Duane,[10] attributed accommodative decline to a loss in strength of the ciliary muscle. However, there is now plentiful evidence to suggest that the muscle remains active and retains its strength well beyond the onset of presbyopia and there is no support for a progressive weakening during prepresbyopic years. Notable are the impedance cyclography studies of Swegmark[26] and the early in vivo work of Fisher[18,20] on muscle strength, showing that the force of contraction of the ciliary muscle increases rather than decreases with age up to the onset of presbyopia. More recently, developments in magnetic resonance imaging (MRI) have allowed the dimensions of the accommodating ciliary body and lens to be directly studied in vivo.[27-29] Nevertheless, the form of the muscle does change with age,[30,31] and this affects the geometry of the relationship between the ciliary ring and the lens equator. This is illustrated in Figure 11-4, taken from the work of Strenk et al.[27] In the unaccommodated eye, the diameter of the ciliary ring shows a slow decline with age, whereas the equatorial diameter of the lens shows little change, leading to a decrease in the width of the circumlental space (Figure 11-4A), which is slightly wider nasally than temporally.[28] Nevertheless, the diameter of the ciliary ring continues to decrease with accommodative effort at ages long after the onset of presbyopia, when the lens has ceased to respond with changes in thickness and power (Figure 11-4B). Note that the decrease in the diameter of the ciliary ring with accommodative effort is in disagreement with Schachar's theory of accommodation (see Chapter 4),[32] although the progressive decrease in the width of the circumlental space is in agreement with his ideas.

ZONULE

With age, the forces imposed on the capsule and lens could potentially change as a result of changes in the ciliary body, as discussed above, changes in the zonular fibers themselves, or changes in the geometry of their attachment to the lens. Although Fisher[20] and van Alphen and Graebel[33] found that the extensile properties of the zonular fibers do not change over the age range of 15 to 45 years, using excised eyes, Farnsworth and Shyne[34] showed that the distance between the anterior zonular insertion and the lens equator increases steadily with age (Figure 11-5). This is in accord with the finding of Strenk et al[27] that most of the lens' increase in central thickness occurs anterior to the equator. Farnsworth and Shyne[34] therefore speculated that this finding may have a role in the development of presbyopia. This forms the basis of what is sometimes called the "geometric" theory of presbyopia, in which the underlying cause is attributed to the changing angle of insertion of the zonules, resulting in a progressively lower force being applied to the capsule. In Figure 11-5, note that although the

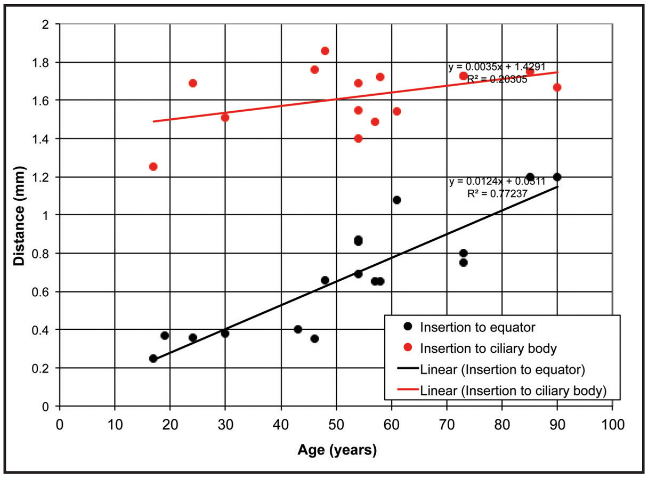

Figure 11-5. The distance between the zonular insertion and the lens equator, and the distance between the zonular insertion ring and the ciliary body as a function of age in excised lenses. (Based on data compiled from Farnsworth PN, Shyne SE. Anterior zonular shifts with age. *Exp Eye Res.* 1979;28:291-297.)

distance between the zonular insertions into the capsule and lens equator increases markedly, the distance between the insertion and the ciliary muscle does not; this would be expected if the lenses were fully accommodated and the zonular fibers were relaxed and of constant length.

Support for these results is provided by the finding of Sakabe et al[35] that the zonular-free zone of the anterior surface of the in vitro lens decreases in diameter. Moreover, Brown's[36] observations show that the shape of the lens equator changes with age and that the anterior and posterior zonular fibers become more divergent from each other. Thus, in the unaccommodated eye, the reduction in the width of the circumlental space (see Figure 11-4A), combined with the changes in the angle that the zonular fibers make with the capsule, may reduce the force that the zonule is capable of applying to the capsule and, through the latter's action as a force distributor, to the lens.[3,6] Therefore, it seems possible that these changes may at least supplement the changes in the mechanical characteristics of the lens and capsule in progressively reducing the amplitude of accommodation.

CHOROID AND IRIS

The uveal tract consists of the choroid, ciliary body, the iris and its opening, and the pupil. Thus, the age changes in the ciliary body should not be considered purely in isolation, as they are influenced by the other linked structures. From this, Bito and Miranda[5] suggested that, rather than presbyopia being caused by a lack of ability to accommodate, presbyopia is caused by a failure to adequately relax accommodation (the "disaccommodation" theory). It is hypothesized that this occurs because the elastic antagonist to the ciliary muscle provided by the choroid loses strength so that, with age, the lens assumes a permanently accommodated form with more steeply curved surfaces. In support of this hypothesis, there is some evidence that the elastic tendons, which form the posterior attachment of the ciliary muscle in rhesus monkeys, may thicken and become more rigid with age (see Chapter 8).[37,38]

In opposition to this idea is the apparent finding that retinal stretch, as a result of accommodative effort, can still occur in a 60-year-old presbyopic eye.[39] Moreover, recent MRI evidence of eyes in which the age-enlarged lens is removed and replaced by an IOL suggests that the human choroid maintains elasticity in the older eye because the ciliary body and iris are returned to their more posterior youthful positions after removal of the thickened crystalline lens.[9]

Weale has suggested that the iris root may play a role, with age-related miosis creating a pull on the iris root, which is transmitted to the ciliary tissue, causing a translation of the anchoring points of the zonule.[6]

OTHER STRUCTURES: VITREOUS

Following Tscherning[40] and others, Coleman[41,42] suggested a role for the vitreous in his "hydraulic" theory of accommodation. A major part of the hypothesis is that, during accommodation, the vitreous provides an obstacle that prevents backward movement of the posterior pole of the lens. Although the vitreous becomes more liquid with age and hence less able to prevent movement of the rear surface of the lens, in practice, such movement does not appear to occur as age advances and the properties of the vitreous change. Moreover, normal accommodation still occurs in eyes lacking a vitreous.[19] Therefore, it appears unlikely that vitreous changes play any major role in presbyopic change.

THE MODIFIED GEOMETRIC THEORY

Based largely on MRI observations, Strenk et al[9] integrated many earlier suggestions into an attractive overall theory of presbyopia. This theory proposes

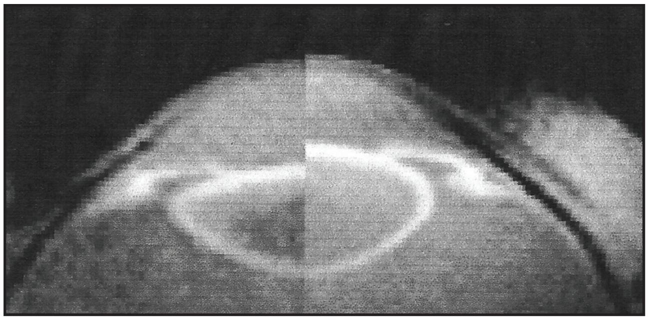

Figure 11-6. Composite of MRIs of the unaccommodated eye of (left) a 26 year old and (right) a 49 year old. Note the increased lens thickness, the reduced pupil diameter, and the anterior displacement of the uveal tract in the older eye. (Reprinted from *Prog Retin Eye Res*, vol 24(3), Strenk SA, Strenk LM, Koretz JF, The mechanism of presbyopia, pp 379-393, Copyright 2005, with permission from Elsevier.)

that lens growth, as shown in Figure 11-6, is the primary factor. The pupillary margin of the iris rests on the anterior lens surface, which creates a radial force on the iris that is transmitted to the iris root and ciliary muscle. As a result of scleral curvature, a tangential force is produced—the effect is to cause an inward and anterior displacement of the 2 structures, reducing pupil diameter. As the lens continues to age and grow, this inward and anterior displacement causes a progressive reduction in pupil diameter (senile miosis) and a decrease in ciliary ring diameter. The resultant reduction in zonular tension during resting accommodation leads to both increased lens curvature and a reduced amplitude of accommodation. Note, however, that these geometric changes do not preclude some contribution from the changing elastic characteristics of the lens to the progressive loss in amplitude.

SUMMARY

In general, the available evidence suggests that presbyopia is multifactorial in origin. Increasing lens stiffness is undoubtedly important, but a number of other factors may influence the steady reduction in accommodation with age. Many of these are related to the requirement that the zonule must remain taut in the face of significant age-related change in the geometry of the accommodative apparatus for accommodation to be fully relaxed. This may mean that, even under ideal circumstances, some proposed surgical remedies for presbyopia, which assume that only the stiffness of the lens prevents a functioning accommodation system, will be ineffective.

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