Accommodation and Presbyopia

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Accommodation is a dioptric change in power of the eye that occurs to allow near objects to be focused on the retina. The ability to accommodate is lost with increasing age in humans and monkeys. This phenomenon, called *presbyopia,* is the most common human ocular affliction, and its pathophysiology remains uncertain. The progressive loss of human accommodative amplitude begins early in life and results in a complete loss of accommodation by age 50 to 55 years. Presbyopia is correctable by various optical means and, although not a blinding condition, its cost in devices, lost productivity, and (more recently), for surgical interventions is considerable.

The classic theory of accommodation in humans proposes that the ciliary muscle moves forward and axially in the eye during contraction, releasing tension on the anterior zonular fibers and allowing the lens to become more spherical and thicken axially.[1] During disaccommodation, the ciliary muscle relaxes, allowing the elastic choroid to pull the ciliary muscle posteriorly, increasing the tension on the anterior zonules to flatten the lens. Alteration of every component of the accommodative apparatus has been proposed to explain presbyopia. Rhesus monkeys and humans exhibit a similar accommodative mechanism and lens growth throughout life and develop presbyopia with a similar relative age course.[2] Theories to explain the pathophysiology of presbyopia fall into two main categories, involving dysfunction of either the lens or the ciliary muscle. Another theory is based on a proposed mechanism of accommodation different from that which is classically accepted.[3] We summarize what is known about the anatomy and aging of the accommodative apparatus and how such changes might contribute to the loss of accommodative amplitude.

■ Anatomy

Anteriorly, the smooth ciliary muscle is attached to the scleral spur and trabecular meshwork by true tendons. Posteriorly, the muscle is attached to the elastic network of Bruch's membrane of the choroid, which ultimately, at its most posterior point, anchors to the scleral canal surrounding the optic nerve (Fig 1). A complex arrangement of elastic fibers (zonule of Zinn) forms a meridionally oriented meshwork extending forward from the ora serata (posterior zonule [PZ]) to the valleys between the ciliary processes and then continue anterocentripetally, attaching to the lens capsule (anterior zonule [AZ]). By scanning electron microscopy, the zonules appear to attach to the lens capsule in three distinct sets. The first set attaches along the lens equator itself and appears less numerous and finer than the two other sets, which attach 1.5 mm anterior and posterior to the lens equator. However, this apparent segregation may be artifactual, owing to clumping during tissue processing (perhaps based on differing chemical reaction to the fixative between different groups of fibers), and fresh tissues suggest a more uniform distribution along the lens equatorial region.[4] The zonular fibers anchor to the valleys of the pars plicata ciliary processes by a set of finer "tension" fibers,[5] which form a fulcrum.

■ Accommodation

Though the primate accommodative apparatus is very different from that of other species, the ocular anatomy and accommodative mechanism of the rhesus monkey are nearly identical to that of the human.[2,6,7] The

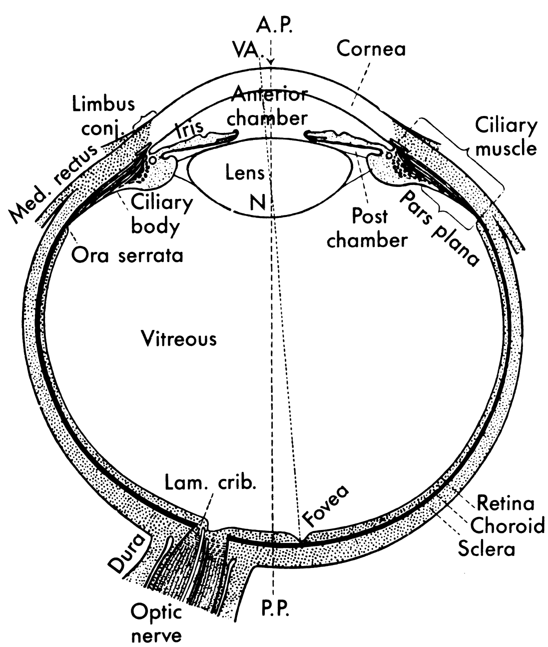

Figure 1. *Midsagittal section of the eye. P.P. = posterior pole; A.P. = anterior pole; VA = visual axis. (From RB Warwick, Eugene Wolff's anatomy of the eye and orbit. Philadelphia: Saunders, 1976:30 with permission.)*

following discussion of the primate mechanism encompasses both humans and monkeys, with differences indicated where appropriate.

During contraction of the ciliary muscle, the main muscle mass slides forward and toward the axis of the eye along the curved inner wall of the sclera. The ciliary ring formed by the inner apex of the muscle narrows, similar to the action of a true sphincter muscle. The fulcrum of the zonular fibers within the pars plicata of the ciliary body formed by the tension fibers moves forward and inward, and the pars plana zonules stretch while the AZ fibers attaching at the lens equatorial edge become flaccid. With release of the resting tension of the zonular fibers at the lens equator, the elastic capsule reshapes the lens; the lens becomes more sharply curved and thickens axially, and the equatorial diameter diminishes. Lens posterior movement is restricted by the vitreous humor and the anterior translation of the fulcrum formed by the zonular plexus. Though classically there has been thought to be no posterior movement of the posterior lens surface, partial coherence interferometry shows a posterior movement of the posterior surface, an anterior movement of the anterior surface, and a small forward translation of the center of mass of the lens.[8] The decrease in anterior chamber depth with accommodation is roughly 70% of the increase in lens thickness; 30% of the increase in lens thickness occurs as a posterior movement of the posterior lens surface.[8] The closer proximity of the cornea to the anterior lens refracting surface and increased lens convexity and thickness all increase the refracting power of the eye (Fig 2).

In the unaccommodated state, the anterior lens surface is less sharply curved than the posterior surface.[9,10] Although both surface curvatures sharpen during accommodation, the anterior does so more rapidly, but its steepness never exceeds that of the posterior surface. The internal curvatures mimic the behavior of the surface curvatures. As a whole, the lens thickens axially, and lens diameter decreases coronally during accommodation. In young adults (human), overall axial thickness may increase with accommodation from 3.5 to 5.0 mm, as measured by A-scan ultrasonography or Scheimpflug photography. This thickening occurs entirely in the nuclear region, with the axial dimensions of the anterior and posterior cortex remaining constant.[9–14]

Disaccommodation

During “disaccommodation,” when the ciliary muscle relaxes, the muscle is pulled posteriorly and outward along the inner scleral surface by the elastic Bruch’s membrane and by the PZ fibers.[15] The ciliary ring expands, restoring AZ tension and causing the zonules to stretch, pulling the elastic lens capsule centrifugally and posteriorly. Axial lens thickness decreases, equatorial lens diameter increases, and the internal, anterior, and posterior lens surfaces become less sharply curved. The anterior

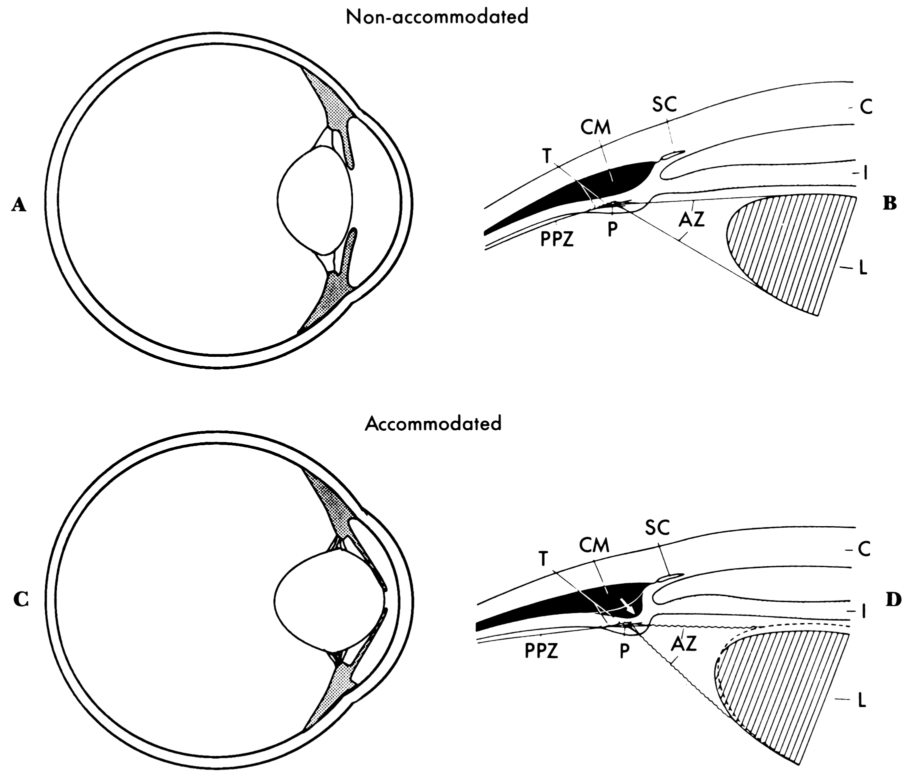

Figure 2. *Schematic representation of ocular geometry and ciliozonular mechanisms at rest (A, B) and during accommodation (C, D). Ciliary muscle (CM) contracted (D), forming an inner edge; the tension fiber system (T) is stretched, taking up the traction from posterior zonular fibers (PPZ) and the choroid. Thus the anterior zonular (AZ) fibers become relaxed and the lens (L) more spherical (dotted lines). P = zonular plexus; I = iris; C = cornea; SC = Schlemm's canal. Arrow indicates direction of ciliary muscle movement during accommodation. (Parts A and C reprinted with permission from KS Crawford, PL Kaufman, LZ Bito, The role of the iris in accommodation of rhesus monkeys. Invest Ophthalmol Vis Sci 1990 31:2185–2190. Parts B and D reprinted with permission from JW Rohen, Scanning electron microscopic studies of the zonular apparatus in human and monkey eyes. Invest Ophthalmol Vis Sci 1979 18:133–144. The Association for Research in Vision and Ophthalmology is the copyright holder for articles published in Investigative Ophthalmology and Visual Science.)*

chamber deepens as the lens flattens, the anterior lens surface moves away from the cornea, and the posterior lens surface moves forward toward the cornea to a lesser extent. The changes occurring on relaxation of the ciliary muscle result in a decrease of the refractive power of the eye, and the eye disaccommodates.

The ciliary muscle powers the accommodative effort, allowing release of AZ tension on the capsule; the capsule in turn molds the lens substance into the more spherical configuration. When the muscle relaxes, the extralenticular elastic forces (i.e., posterior choroid and PZ) pull the ciliary muscle back into the relaxed position, restoring tension to the AZ. The zonule anchored near the anterior end of the ciliary muscle in the valleys between the ciliary processes of the pars plicata[5] conveys the muscular and extralenticular elastic forces to the lens capsule.

Disaccommodation can be viewed as the active application of force to the lens by extralenticular elastic tissues, whereas accommodation represents an active neuromuscular process that releases or diverts such forces.[16] The vitreous may serve only as a support to stabilize the posterior surface of the lens or may serve a more "active" function by compressing the lens peripherally when the ciliary muscle contracts, thereby aiding its sphericization. However, a previous study found no difference in amplitude of accommodation after vitrectomy as compared to the contralateral eye.[17]

Extralenticular Accommodative Forces

The choroid and zonule comprise an elastic system. The pull of the elastic choroid and the relaxed ciliary muscle force-inertia are in equilibrium with the pull of the capsule. This resting equilibrium is altered when the ciliary muscle contracts and the balance shifts. A complex, dynamic interaction among muscle, zonule, capsule, and lens substance occurs to achieve accommodation. Owing to differences in capsular thickness and perhaps other properties, different magnitudes and vectors of forces are placed on the anterior and posterior aspects of the capsule. A putative anterior capsular component of lens reshaping and translation may produce specific changes in lenticular contour and position. Posteriorly, the PZ may allow for a smoother change and distribution of force on the capsule than would occur if AZ anchorage were solely to the ciliary processes. Additionally, because the entire choroid may slide forward and backward as the ciliary muscle contracts and relaxes, it may be advantageous to have a comparable pull on the internal aspect of the retina for unknown physiological reasons. The PZ, being continuous at the ora serrata with the internal limiting membrane of the retina, may accomplish this.

Variations on the Accommodative Mechanism

Variations on the generalized accommodative mechanism just described include a functional role for the vitreous.[18,19] This "hydraulic suspension" theory of accommodation includes an active contribution to changing the lens surface curvatures from the vitreous support together with the well-established capsular support. This theory is based on the observation of a differential pressure change in the eye with accommodation, causing a simultaneous increase in vitreous pressure and decrease in aqueous pressure. Observations of in vitro anterior and posterior polar movements of the lens argue against the need for vitreous support.[17] Similar accommodative amplitudes in the 2 eyes of a patient who had undergone a unilateral vitrectomy also argue that the vitreous is not essential for accommodation.[17]

An alternative accommodative theory proposed by Schachar[20] posits that the ciliary muscle increases rather than decreases equatorial zonular tension during accommodation, causing the equatorial edge of the lens to move toward rather than away from the sclera. Presbyopia is attributed to the continued equatorial growth of the lens and an inability of the ciliary muscle to tense the equatorial zonules. Surgical expansion of the sclera in the region of the ciliary body has been suggested to restore accommodation in presbyopes. However, the putative causes of presbyopia are not supported (see the chapter, "Aging of the Human Crystalline Lens and Presbyopia"). Goniovideography and ultrasound biomicroscopy (UBM) imaging in monkeys show that during accommodation, the lens equator moves away from the sclera in accordance with the Helmholtz accommodative mechanism and falls under the influence of gravity, suggesting release of zonular tension. Lens cross-sectional diameter was observed to decrease during accommodation in a young patient with ocular albinism in which retroillumination of the eye allows visualization of the lens equator[21] as it does in normal monkeys.[22] No independent support exists for Schachar's proposed accommodative mechanism, and no accommodation was observed when scleral expansion patients were assessed with an objective infrared optometer.[23] Thus, this accommodative mechanism is problematic, and if scleral expansion surgery does actually improve near vision, it may be through some mechanism other than restoration of dynamic accommodation, perhaps by inducing static lenticular multifocality.[22]

Neuromuscular Aspects

The ciliary muscle is a complex smooth muscle, atypical in structure and function (fast contraction-relaxation, large motor neurons at some distance from the muscle fibers, some ultrastructural features reminiscent of skeletal muscle). It has three regions, based on the orientation of the muscle fiber bundles—longitudinal, reticular, and circular.[24] The major innervation is parasympatheic, originating in the Edinger-Westphal nucleus, coursing with the third cranial nerve to synapse in the ciliary ganglion, and then traveling to the ciliary muscle via the short and possibly also long ciliary nerves.[25] The sympathetic supply to the ciliary muscle originates in the diencephalon and travels down the spinal chord. From there, second-order nerves leave the cord and run up the cervical sympathetic chain to synapse in the superior cervical ganglion. Third-order fibers continue up the sympathetic carotid plexus and enter the orbit with the first division of the trigeminal nerve or independently, joining the long and short ciliary nerve fibers. The sympathetics weakly relax the muscle, thus allowing functional antagonism to the parasympathetically induced comtraction and perhaps facilitating smooth tracking.

During accommodation, some muscle fibers reorient so that the area occupied by the circular portion enlarges, and the areas of the longitudinal and reticular portions decrease.[7,24] The entire muscle probably acts as a unified system to accomplish various aspects of complementary tasks related to accommodation and regulation of aqueous humor outflow.[26] Evidence suggests that (1) pharmacologic dissociation of accommodative and outflow responses to certain cholinergic drugs may be possible under some conditions[27,28]; (2) different subtypes of muscarinic receptors may predominate in different regions of the ciliary muscle,[29] and (3) ultrastructural and immunohistochemical-enzymatic differences exist between muscle cells in the different regions favoring different types of contractile dynamics.[30]

Through connections to the trabecular meshwork and inner wall of Schlemm's canal,[31,32] Ciliary muscle contraction expands the meshwork, widening the intertrabecular spaces and dilating the canal. At the same time, the lens thickens,[10,12] and the anterior chamber shallows (decreasing in volume). During sustained accommodation, these events result in reduced resistance to aqueous outflow from the anterior chamber into the canal and then into the general circulation.[33] This may help to maintain normal intraocular pressure during sustained accommodation and rid the eye of noncompressible fluid, providing "room" for the expanded lens.[19,34]

■ Aging of the Accommodative Mechanism: Presbyopia

Nearly every component of the accommodative mechanism has been proposed as a factor in the development of presbyopia. The similarities between the accommodative mechanisms and the time course of presbyopia relative to lifespan in rhesus monkeys and humans enable the rhesus to model human presbyopia, from which important information cannot be obtained directly because of the necessity for ocular invasion. We have studied real-time dynamics of the lens and ciliary muscle of the rhesus monkey. In the living, surgically iridectomized monkey, the lens can be imaged by Scheimpflug videography, whereas the lens equator, zonule, and ciliary process can be imaged by goniovideography (Fig 3).[6,35–37] By electrically stimulating the Edinger-Westphal nucleus,[38] the movements and spacings of these structures can be visualized, recorded, and analyzed in real time. Dynamic accommodation is measured using infrared photorefraction. Dynamic accommodation as measured by infrared photorefraction correlates well with ciliary muscle movement and movement of

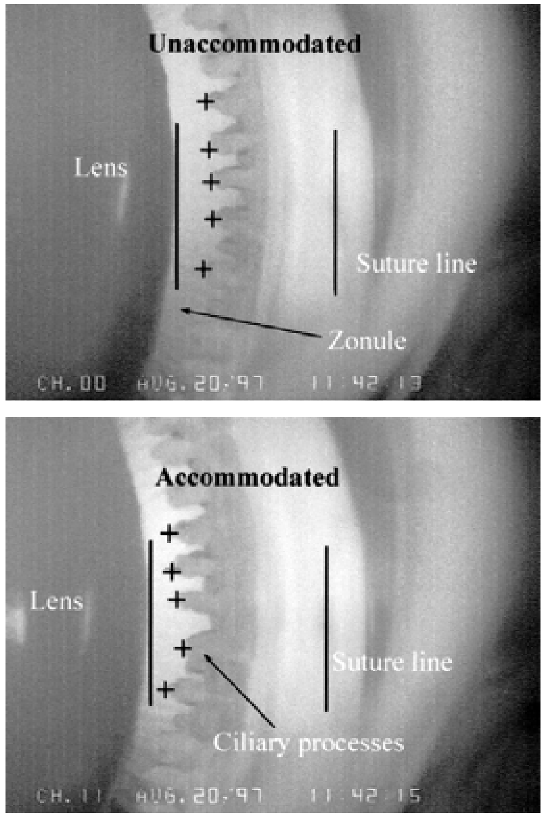

Figure 3. *Goniovideography of normal lens and ciliary process configuration. A 9-0 nylon suture placed at the limbus serves as a marking suture (right line) from which the distances to the lens equator (left line) and the ciliary processes (cross-hairs) are measured for each image during a 2-second-long stimulus.*

the equatorial edge of the lens (Fig 4).[22] Static and dynamic images obtained via UBM also give insights into age-related changes of the configuration of the ciliary muscle and PZ.[15]

Ciliary Muscle

Presbyopia has been attributed to ciliary muscle dysfunction, possibly caused by a loss of elasticity of the posterior muscle tendons, PZ fibers, or choroid,[39] or by age-related neuromuscular[40] or configurational changes.[7] The reduced mobility of the aged rhesus monkey ciliary muscle in situ[6] cannot be explained by only the subtle age-related degenerative changes observed on histological or ultrastructural examination of ciliary muscle from elderly rhesus monkeys.[7,40] The number and binding affinity of the muscarinic receptors do not change with age; no age-related changes

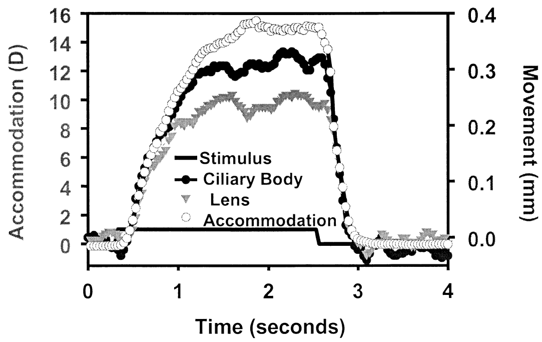

Figure 4. *Lens and ciliary body movements and refractive changes in eye of 6-year-old rhesus monkey during centrally stimulated accommodation. Physical movements measured from goniovideography; refractive change subsequently measured by infared photorefraction. Accommodation (solid symbols; left axis) of approximately 15.5 D and movements of ciliary processes and lens equator (open symbols; right axis) are plotted together. Solid line shows onset, duration, and end of stimulus. Ciliary process tips and lens equator move away from sclera, and accommodative amplitude increases after stimulus onset. A relatively steady state then is reached, during which minor fluctuations in refractive state and maximally accommodated positions of lens equator and ciliary body occur. When stimulus ends, refractive state rapidly returns to baseline as lens and ciliary body move back toward the sclera. (Reprinted with permission from A Glasser, PL Kaufman, Mechanism of accomodation in primates. Ophthalmology 1999;106:863–872.)*

are found in the activity of the biosynthetic and degradative enzymes for the cholinergic neurotransmitter acetylcholine that mediates ciliary muscle contraction,[41] and excised rhesus ciliary muscle shows no age-dependent loss of the contractile response to muscarinic agonists.[42] Thus, the parasympathetic neuromuscular mechanism remains normal. However, the anteroaxial muscle movement provides the geometrical alterations needed for accommodation, not the force of muscle contraction.[43]

In humans, magnetic resonance imaging (MRI) studies also show that the decrease in ciliary ring diameter that occurs with accommodative effort is reduced in older eyes.[44] However, the residual muscle movement is not accompanied by increasing lens thickness or decreasing lens equatorial diameter in the presbyopes.[44] This may reflect differences between humans and monkeys in the extent to which presbyopia affects the various intraocular accommodative structures. The MRI studies also show alterations in the configuration of the unaccommodated ciliary muscle. The ciliary body ring diameter and the circumlental space are reduced with increasing age. This result is in accordance with histological studies showing that the inner apex of the ciliary muscle moves forward and inward to appear more like a young accommodated ciliary muscle.[45] This configurational change could, in part, be due to the combined effects of an inward pull of the zonular fibers from the lens equator on the apex of the ciliary muscle and a loss of tension of the posterior attachment of the ciliary muscle. Whether this is a cause or a consequence of presbyopia is uncertain, but it represents an age change that could affect accommodative amplitude. Since the youngest eye in the histological study by Tamm and coworkers[45] was 34 years old—an age by which two-thirds of the accommodative ability is already lost—the anatomic correlates for the younger ages where the "action" really is are not available.

The loss of ciliary body movement with age in rhesus monkeys is not due to restriction by the enlarged elderly lens, because at rest, a circumlenticular space is always present, even in elderly animals.[6] Ciliary body mobility is not totally lost and, in an occasional elderly animal, the circumlenticular space is noticeably narrowed or even obliterated during midbrain stimulation, indicating that factors other than ciliary body hypomobility or immobility (i.e., the lens itself) may be at least partly responsible for lenticular hypomobility or immobility (see the chapter, "Aging of the Human Crystalline Lens and Presbyopia"). Nonetheless, the histological and videographical data in the rhesus clearly raise the possibility that a loss of ciliary muscle excursion is involved in the pathophysiology of presbyopia.

Extralenticular Elastic Components

Loss of elasticity of Bruch's membrane could be responsible the loss of muscle movement and accommodative amplitude in rhesus monkeys. If this tissue became rigid, the ciliary muscle would not move anteroaxially when it contracted and would remain anchored posteriorly. The posterior elastic tendons of the ciliary muscle are thicker and have increased amounts of microfibrils and collagen fibrils in aged monkey eyes, consistent with decreased elasticity.[46] Further, in aged monkey eyes, when the muscle's posterior attachments were partially cut,[39] ciliary muscle mobility in response to choloinomimetic drugs was fully restored. Therefore, progressive age-related restriction of the ciliary muscle motility, due to an increasingly inelastic posterior attachment, may be a factor in the development of presbyopia. Clearly, presbyopia may be a condition caused by multiple factors,[33,47,48] and the lenticular and ciliary muscle immobility contributions to presbyopia are not mutually exclusive.[4,7,39]

Lens

Numerous age-related changes in lens properties and zonular properties are postulated to be involved in the development of presbyopia. (The optical and physical changes in the lens with age are addressed in a separate chapter by Glasser, p. 1.)

A change in the geometry of lens suspension due to lens growth has been theorized as a possible cause of presbyopia. In humans, the distance between the lens equator and the AZ insertion increases with age; the distance between the insertion ring and the ciliary body remains relatively constant.[49] This change in zonular insertion angle is thought to reduce the ability of the zonular fibers to release resting tension on the lens and to prevent the lens from accommodating, but no experimental evidence exists in support of this theory.

As the lens capsule is thought to mold the lens substance, age changes in capsular elasticity have been implicated in presbyopia. The capsule becomes thicker with age up to approximately 60[50] or 75 years[51] and thereafter thins again. The capsule becomes either less elastic[50] or less extensible and more brittle with age.[51] The contradictory results and the uncertainty of the precise role of the capsule in accommodation render capsular involvement in presbyopia unclear. Our data show that the capsule aids movement of the lens and ciliary processes during accommodation[36,37,52] and that its alteration with age might therefore play a role in the development of presbyopia.[36]

Vitreous

If the vitreous has a more significant role in accommodation than merely providing support and stabilization for the posterior surface of the lens (as discussed earlier),[18,19] one can speculate that age changes in the vitreous may play a pathophysiological role in presbyopia. With age, the vitreous becomes progressively more liquid, which could affect peripheral compression of the lens. Alternatively, growth of the lens itself may place the vitreous at a geometrical-mechanical disadvantage in subserving this accommodative function.[19]

■ Summary

Although our knowledge of the events accompanying aging of the accommodative mechanism has increased, we still do not completely understand the age-related changes in any of the components, nor how they interact to produce presbyopia. Lenticular growth and changes in external and internal lenticular geometry and optical properties, ciliary muscle mobility, extralenticular elastic tissue, and the vitreous all may conspire to produce age-related loss of accommodative amplitude.

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