Introduction and Overview on Myopia: A Clinical Perspective

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Key Points
- Myopia is a significant global public health and socioeconomic problem.
- Pathologic myopia has become a major cause of blindness or visual impairment in both Asian and Western populations.
- Myopia may be a highly heritable trait, with environmental influences such as outdoor activity playing important roles in its development and progression.
- Control of myopia in children is important, and various strategies including pharmacologic and lens-related interventions have proven efficacy.
- Imaging is important to detect complications of pathologic myopia, and both medical and surgical interventions may be useful for their management.
1.1 Global Epidemiology

Myopia has become a significant global public health and socioeconomic problem [1–4]. East Asia, and other parts of the world to a lesser extent, has been faced with an increasing prevalence of myopia [5, 6]. The prevalence of myopia and high myopia (HM) (the definition of myopia and HM is spherical equivalence (SE) of $-0.50$ diopters (D) or less and SE $-5.00$ D or $-6.00$ D, respectively) in young adults in urban areas of East Asian countries has risen to 80–90% and around 20%, respectively [7, 8]. According to a summary of 145 studies regarding the global prevalence of myopia and HM, there are approximately 1950 million with myopia (28.3% of the global population) and 277 million with HM (4.0% of the global population), and these numbers are predicted to increase to 4758 million (49.8% of the global population) for myopia, and 938 million (9.8% of the global population) for HM by 2050 [9].

The prevalence of childhood myopia is substantially higher in urban East Asian countries (49.7–62.0% among 12-year-old children) [7, 10] compared with other countries (6.0–20.0% among 12-year-old children) [9]. Similarly, in teenagers and young adults, the prevalence of myopia is higher in East Asian countries (65.5–96.5%) [8] compared with other countries (12.8–35.0%) [9]. However, the geographic difference of myopia prevalence in older populations is less than that in younger populations. The prevalence rates of myopia in adults in urban East Asian countries are only slightly higher than in Western countries.

The prevalence of myopia has remained consistently high among Chinese children in urban settings, but the evidence does not support the idea that it is caused by purely genetic difference [10]. The association of an urbanized setting with high myopia rates is likely to be influenced by possible modifiable risk factors such as near work and outdoor time.

Despite the relatively low prevalence in the general population, pathologic myopia (PM) is a major cause of blindness or visual impairment in both Asian and Western populations. One study has shown that the prevalence of PM was 28.7% among high myopes and 65% of those with HM and were over 70 years old had PM [11]. Based on the global prediction of HM on 2050, PM may increase to over 200 million in future [9]. Treatment strategies against PM have not been effective [12].

Generational differences in prevalence are seen with the highest rates in young adults (myopia 65.5–96.5% and HM 6.8–21.6%) and the lowest rates in older adults (myopia 25.0–40.0% and HM 2.4–8.2%). The disease progression pattern of HM and subsequent development of PM may be different between young adults and older adults due to generational differences, or changes in the lifestyle factors such as the education system, near work, and outdoor time exposure in rapidly developing urban Asian countries.

1.2 Pathogenesis of Myopia

Ocular Biometric Changes in Human Myopia The axial length of the eye or, more precisely, the vitreous chamber depth is the primary individual biometric contributor to refractive error in children, young adults, and the elderly [13–15], with
the vitreous chamber depth accounting for over 50% of the observed variation in spherical equivalent refractive error (SER), followed by the cornea (~15%) and crystalline lens (~1%) [15]. However, the dimensions, curvature, and refractive index of each individual ocular structure contribute to the final refractive state. The choroid is typically thinner in myopic compared to non-myopic eyes (most pronounced at the fovea [16, 17]) and thins with increasing myopia and axial length in both adults [18–25] and children [26–28]. Significant choroidal thinning is also observed in eyes with posterior staphyloma [29], and has been associated with the presence of lacquer cracks [30], choroidal neovascularization [31], and reduced visual acuity [32]. The choroid also appears to be a biomarker of ocular processes regulating eye growth given that the central macular choroid thins during the initial development and progression of myopia [33–35] and thickens in response to imposed peripheral myopic retinal image defocus [36, 37], topical anti-muscarinic agents [38, 39], and increased light exposure [40]; clinical interventions associated with a slowing of eye growth in children.

**Visual Environment, Emmetropization, and Myopia** Much of the knowledge on vision-dependent changes in ocular growth has emanated from animal experiments in which either the quality of image formed on the retina is degraded (known as form deprivation [FD]), or the focal point of the image is altered with respect to the retinal plane (known as lens defocus). Both FD and lens defocus result in abnormal eye growth and development of refractive errors.

**Monochromatic Higher-Order Aberrations as a Myopigenic Stimulus** Myopia may develop due to the eye’s emmetropization response to inherent ocular aberrations that degrade retinal image quality and trigger axial elongation [41]. Evidence concerning the relationship between higher order aberration (HOAs) during distance viewing and refractive error from cross-sectional studies is conflicting [41, 42]. However, during or following near-work tasks, adult myopic eyes tend to display a transient increase in corneal and total ocular HOAs, suggesting a potential role for near-work-induced retinal image degradation in myopia development [43, 44]. Longitudinal studies of myopic children also indicate that eyes with greater positive spherical aberration demonstrate slower eye growth [45, 46].

**Accommodation** Given the association between near work and the development and progression of childhood myopia [47], numerous studies have compared various characteristics of accommodation between refractive error groups. Typically, this involves the accuracy of the accommodation response, since lag of accommodation (hyperopic retinal defocus) may stimulate axial elongation as observed in some animal models. The slowing of myopia progression during childhood with progressive addition or bifocal lenses, designed to improve accommodation accuracy and minimize lag of accommodation, adds some weight to the role of accommodation in myopia development and progression [48, 49]. However, the exact underlying mechanism of myopia control with such lenses may be related to imposed peripheral retinal defocus or a reduction in the near vergence demand [50]. Certainly, elevations in measured lag observed in myopes arise after rather than before onset [51].
1.3 Key Environmental Factors on Myopia

**Near work and education:** Many studies have established a strong link between myopia and education [52–57]. Moreover, Mountjoy et al. have shown that exposure to longer duration of education was a causal risk factor for myopia [53]. The exact mechanism linking increased education with myopia is unclear. Although it is possible that optical [43, 58] or biomechanical [59, 60] ocular changes associated with near work could potentially promote myopic eye growth in those with higher levels of education (and hence near-work demands), population studies examining the link between near-work activities and myopia have been conflicting, with some studies suggesting an association between near work and myopia [47, 61], and others indicating no significant effects [62]. The relatively inconsistent findings linking near work with myopia development suggests a potential role for other factors in the association between education and myopia.

**Outdoor Activity** A number of recent studies report that the time children spend engaged in outdoor activities is negatively associated with their risk of myopia [62–68]. Both cross-sectional and longitudinal studies indicate that greater time spent outdoors is associated with a significantly lower myopia prevalence and reduced risk of myopia onset in childhood. Although some studies report significant associations between myopia progression and outdoor activity [66, 68], this is not a consistent finding across all longitudinal studies [69]. A recent meta-analysis of studies examining the relationship between outdoor time and myopia indicated that there was a 2% reduction in the odds of having myopia for each additional hour per week spent outdoors [70].

**Duration of Outdoor Activity and Myopia** In a large longitudinal study, Jones and colleagues [62] reported that children who engaged in outdoor activities for 14 h per week or more exhibited the lowest odds of developing myopia. A number of recent randomized controlled trials have reported that interventions that increase children’s outdoor time (by 40–80 min a day) significantly reduce the onset of myopia in childhood [71–73]. In the “Role of outdoor activity in myopia study” [74], children who were habitually exposed to low ambient light levels (on average less than 60 min exposure to outdoor light per day) had significantly faster axial eye growth compared to children habitually exposed to moderate and high light. These findings from human studies suggest that children who are exposed to less than 60 min a day of bright outdoor light are at an increased risk of more rapid eye growth and myopia development, and that approximately 2 h or more of outdoor exposure each day is required to provide protection against myopia development in the human eye.

1.4 Genetics of Myopia

Myopia is highly heritable; genes explain up to 80% of the variance in refractive error in twin studies. For the last decade, genome-wide association study (GWAS) approaches have revealed that myopia is a complex trait, with many genetic variants
of small effect influencing retinal signaling, eye growth, and the normal process of emmetropization. Particularly notable are genes encoding extracellular matrix-related proteins (COL1A1, COL2A1 [75, 76], and MMP1, MMP2, MMP3, MMP9, MMP10 [77, 78]). For candidates such as PAX6 and TGFBI, the results were replicated in multiple independent extreme/high myopia studies and validated in a large GWAS meta-analysis in 2018, respectively [79, 80]. However, the genetic architecture and its molecular mechanisms are still to be clarified, and while genetic risk score prediction models are improving, this knowledge must be expanded to have impact on clinical practice.

Gene–environment (GxE) interaction analysis has focused primarily on education. An early study in North American samples examined GxE for myopia and the matrix metalloproteinases genes (MMP1–MMP10): a subset of single nucleotide polymorphism (SNPs) was only associated with refraction in the lower education level [78, 81]. A subsequent study in five Singapore cohorts found variants in DNAH9, GJD2, and ZMAT4, which had a larger effect on myopia in a high education subset [82]. Subsequent efforts to examine GxE considered the aggregate effects of many SNPs together. A study in Europeans found that a genetic risk score comprising 26 genetic variants was most strongly associated with myopia in individuals with a university level education [83]. A study examining GxE in children considered near work and time outdoors in association with 39 SNPs and found weak evidence for an interaction with near work [83, 84]. Finally, a Consortium for Refractive Error and Myopia (CREAM) study was able to identify additional myopia risk loci by allowing for a GxE approach [85].

Mendelian randomization (MR) offers a better assessment of causality than that available from observational studies [86, 87]. Two MR studies found a causal effect of education on the development of myopia [53, 80]. Both found a larger effect through MR than that estimated from observational studies suggesting that confounding in observational studies may have been obscuring the true relationship [55, 79]. As expected, there was little evidence of myopia affecting education (−0.008 years/diopter, $P = 0.6$). Another study focused on the causality of low vitamin D on myopia found only a small estimated effect on refractive error [88] suggesting that previous observational findings were likely confounded by the effects of time spent outdoors.

Due to the high polygenicity of myopia and low explained phenotypic variance by genetic factors (7.8%), clinical applications derived from genetic analyses of myopia are currently limited. Risk predictions for myopia in children are based on family history, education level of the parents, the amount of outdoor exposure, and the easily measurable refractive error and axial length. Currently, we are able to make a distinction between high myopes and high hyperopes based on the polygenic risk scores derived from CREAM studies: persons in the highest decile for the polygenic risk score had a 40-fold greater risk of myopia relative to those in the lowest decile. A prediction model, including age, sex, and polygenic risk score, achieved an area under curve (AUC) of 0.77 (95% CI = 0.75–0.79) for myopia versus hyperopia in adults (Rotterdam Study I–III) [80]. To date, one study has assessed both environmental and genetic factors together and showed that modeling both genes and environment improved prediction accuracy [89].
1.5 Prevention of the Onset of Myopia

The vast majority of literature suggests that most cases of myopia develop during the school-going age in children. After the age of 6 years, the prevalence of myopia starts to rise [90–94]. The highest annual incidence of myopia is reported among school children from urban mainland China [92] and Taiwan [95], ranging from 20% to 30% through ages 7–14 years, with earlier onset of myopia also being identified [94]. A study in Japan showed that while the prevalence of myopia has been increasing from 1984 to 1996, the prevalence among children aged 6 or younger has remained unchanged. This suggests that the majority of increased myopia onset is secondary to increased educational intensity [94].

Rates of progression increase dramatically with the year of onset and this has been suggested by spherical equivalent refraction and axial length [96]. Myopic refractions tend to stabilize in late adolescent but can remain progressive until adulthood. The mean age at myopia stabilization is 15.6 years but this can vary among children of different ethnicities [97].

Several factors have been found to be associated with the development of incident myopia in school. Asian ethnicity [93, 98], parental history of myopia [62, 99], reduced time outdoors [62], and level of near-work activity [47, 100] are risk factors for incident myopia, although the evidence can be seen as controversial in some instances.

Evidence of time spent outdoors as a risk factor for myopia progression was first presented in a 3-year follow-up study of myopia in school children, showing that those who spent more time outdoors were less likely to progress [64]. Consistent results were reported in various studies, such as the Sydney Myopia Study, Orinda Study, as well as the Singapore Cohort Study of Risk Factors for Myopia [63, 65, 101]. This led to the commencement of several clinical trials which confirmed the protective effect and indicated a dose-dependent effect, among them, the randomized clinical trial in Guangzhou which reported that an additional 40 min of outdoor activity can reduce the incidence of myopia by 23% [63]. Additionally, the trial in Taiwan suggested that an extra 80 min may further reduce incidence by 50% [72, 73].

Near-work activity as a risk factor for myopia has not been entirely consistent. A meta-analysis reported a modest, but statistically significant, association between time spent performing near work and myopia (odds ratio, 1.14) [47]. Core techniques to implementing interventions of near-work activities include effective measures of near-work-related parameters, real-time data analyses, and alert systems. Wearable devices that possess these techniques have emerged in the last decade.

It has been estimated that without any effective controls or interventions the proportion of myopes in the population will reach up to 50% and 10% for high myopes by 2050 [9]. Approaches that have produced a reduction of at least 50% in incidence, such as time outdoors, lead to delayed onset and have the potential to make a significant difference on the impending myopia epidemic.

Another critical issue is the need to balance educational achievement and interventions to prevent myopia progression in East Asia. This balance can be seen in Australia [102], with not only some of the highest educational ranks in the world but
also high levels of outdoor activity and light intensity. Preventing the onset of myopia is certainly challenging in the East Asian population and requires a collaborative effort among clinics, schools, parents, and the entire society.

### 1.6 Understanding Pathologic Myopia

Pathologic myopia (PM) is a major cause of blindness in the world, especially in East Asian countries [103–107]. The cause of blindness in patients with PM includes myopic maculopathy with or without posterior staphyloma, myopic macular retinoschisis, and glaucoma or glaucoma-like optic neuropathy. The term “pathologic myopia” describes the situation of pathologic consequences of a myopic axial elongation. According to a recent consensus article by Ohno-Matsui et al. [108], pathologic myopia was defined by a myopic chorioretinal atrophy equal to or more serious than diffuse atrophy (by Meta-analysis for pathologic myopia (META-PM) study group classification [109]) and/or the presence of posterior staphylomas.

A posterior staphyloma is an outpouching of a circumscribed area of the posterior fundus, where the radius of curvature is less than the curvature radius of the surrounding eye wall [110], and can be associated with, or lead to, vision-threatening complications such as myopic maculopathy [109, 111–114] and myopic optic neuropathy/glaucma [115, 116]. Based upon and modifying Curtin’s [117] classical categorization of posterior staphylomas, with types I–V as primary staphylomas and types VI–X as compound staphylomas, Ohno-Matsui [118] used 3D-magnetic resonance imaging (3D-MRI) and wide-field fundus imaging to re-classify staphylomas into six types: wide macular, narrow macular, peripapillary, nasal, inferior, and others.

In the META-PM classification [109], myopic maculopathy lesions have been categorized into five categories from “no myopic retinal lesions” (category 0), “tessellated fundus only” (category 1), “diffuse chorioretinal atrophy” (category 2), “patchy chorioretinal atrophy” (category 3), to “macular atrophy” (category 4). These categories were defined based on long-term clinical observations that showed the progression patterns and associated factors of the development of myopic choroidal neovascularization (CNV) for each stage. Three additional features were added to these categories and were included as “plus signs”: (1) lacquer cracks, (2) fuch spot and (3) myopic CNV.

Myopic CNV is a major sight-threatening complication of pathologic myopia. It is the most common cause of CNV in individuals younger than 50 years, and it is the second most common cause of CNV overall [119, 120]. Anti-vascular endothelial growth factor (anti-VEGF) therapy is the first-line treatment for myopic CNV, as shown by the RADIANCE study [121] and the MYRROR study [122].

Panozzo and Mercanti proposed the term “myopic traction maculopathy (MTM)” to encompass various findings characterized by a traction as visualized by optical coherence tomography (OCT) in highly myopic eyes [123]. A dome-shaped macula (DSM) is an inward protrusion of the macula as visualized by OCT [124–126]. Imamura, Spaide, and coworkers reported that a DSM was associated with, and
caused by, a local thickening of the subfoveal sclera [127]. It was postulated that the local thickening of the subfoveal sclera was an adaptive or compensatory response to the defocus of the image on the fovea in highly myopic eyes.

1.7 Imaging in Myopia

Imaging the myopic eye can be challenging due to various structural changes (abnormal eye elongation, scleral and corneal curvature irregularities, cataracts leading to poor clarity; or retinal thinning causing abnormal projections of the final image [128, 129]).

Optic disc imaging can also be used to predict the development of glaucoma, where visualization of myopic tilting of the optic disc with peripapillary atrophy (PPA) and pitting of the optic disc [130] is a possible predisposing factor [131, 132]. Serial imaging investigative measures can therefore be utilized for monitoring the development of open-angle, normal-tension glaucoma [133]. Features such as optic disc tilt, PPA, and abnormally large or small optic discs are the earliest known structural alterations that potentially predict the development of pathological myopia and can be observed even in young highly myopic adults. Unfortunately, these features (some also with associations to glaucoma) also interfere with the visualization of optic disc margins [134, 135] and are also not easy to discern in highly myopic eyes [136]. There is also added difficulty in eyes with myopic maculopathy, where visual field defects result in further interference [137]. As such, the answer to these challenges may lie in imaging deep optic nerve head structures (such as parapapillary sclera, scleral wall, and lamina cribosa) [138] in highly myopic eyes for more precise diagnoses of glaucoma.

The ability to view distinct retinal layers with OCT has enhanced visualization of myopic traction maculopathy (MTM). Examples of features that can be seen include inner or outer retinal schisis, foveal detachment, lamellar or full-thickness macular hole, and/or macular detachment [139, 140]. Non-stereoscopic fundus photographs are inadequate for detailed studies of posterior staphylomas as the change in contour at the staphyloma edge is not always discernible. The OCT overcomes this limitation because of its excellent depth resolution [141, 142].

The OCT itself has its shortcomings; the sclera cannot be visualized using the OCT. These limitations also extend to the use of OCT angiography (OCTA). There is currently no standard protocol for segmentation; the outcome parameters for OCTA have not been clearly defined either. Although some authors have tried to use analysis of flow voids or signal voids in the choriocapillaris to quantify the area taken up by the microvasculature [143, 144], the data pertaining to myopic patients are but insufficient [145]. Looking into the future, there is, however, incipient research suggesting that the comprehension of blood supply and changes in vasculature from the anterior to the posterior segment of the myopic eye is crucial to the understanding of the disease [146–149].

Photoacoustic imaging has shown promise recently to fill the gaps between OCT and ultrasound in terms of penetration depth [150]. This modality has been used
before to image the posterior pole of the eye in vitro and in animal models in vivo. This can also be used in concurrence with angiography, measuring oxygen saturation and pigment imaging [151]. However, there are some limitations pertaining to this modality notwithstanding moderate depth resolution, pure optical absorption sensing, need for contact detection with ultrasound sensor, and a relatively long acquisition time. In view of these limitations, we are yet to receive tangible results from photoacoustic imaging for posterior pole imaging in humans.

### 1.8 Glaucoma in Myopia

Axial myopization leads to marked changes of the optic nerve head: (1) an enlargement of all three layers of the optic disc (i.e., optic disc Bruch’s membrane opening, optic disc choroidal opening, optic disc scleral opening) with the development of a secondary macrodisc, (2) an enlargement and shallowing of the cup, (3) an elongation and thinning of the lamina cribrosa with a secondary reduction in the distance between the intraocular space with the intraocular pressure (IOP) and the retro-lamina compartment with the orbital cerebrospinal fluid pressure, (4) a direct exposure of the peripheral posterior lamina cribrosa surface to the orbital cerebrospinal fluid space, (5) an elongation and thinning of the peripapillary scleral flange with development and enlargement of the parapapillary gamma zone and delta zone, (6) an elongation and thinning of the peripapillary border tissue of the choroid, and (7) a rotation of the optic disc around the vertical axis, and less often and to a minor degree around the horizontal axis and the sagittal axis. These changes make it more difficult to differentiate between myopic changes and (additional) glaucoma-associated changes such as a loss of neuroretinal rim and thinning of the retinal nerve fiber layer, and these changes may make the optic nerve head more vulnerable, potentially explaining the increased prevalence of glaucomatous optic neuropathy in highly myopic eyes.

Population-based investigations and hospital-based studies have shown that the prevalence of glaucomatous optic neuropathy (GON) was higher in highly myopic eyes than in emmetropic eyes [152–166]. A previous study revealed that at a given IOP in patients with chronic open-angle glaucoma, the amount of optic nerve damage was more marked in highly myopic eyes with large optic discs than in non-highly myopic eyes [165].

Highly myopic glaucomatous eyes as compared with non-highly myopic glaucomatous eyes may have a markedly lower IOP threshold to develop optic nerve damage. It could indicate that an IOP of perhaps lower than 10 mmHg might be necessary to prevent the development of GON in these highly myopic eyes, and that in highly myopic eyes with axial elongation-associated enlargement and stretching of the optic disc and parapapillary region as the main risk factors for GON in high myopia a normal IOP may be sufficient to lead to GON [136].

Although it has not yet been firmly proven that GON in high myopia is dependent on IOP, most researchers recommend lowering IOP in highly myopic patients with glaucoma. Based on the morphological findings described above, the target
pressure in highly myopic glaucoma may be lower than in non-highly myopic glaucoma. Due to the peculiar anatomy of the optic nerve head in highly myopic eyes, most diagnostic procedures fail in precisely assessing the status of the optic nerve in highly myopic eyes with glaucoma. It includes factors such as a decreased spatial and color contrast between the neuroretinal rim and the optic cup making a delineation of both structures more difficult; a peripapillary retinoschisis leading to an incorrect segmentation of the retinal nerve fiber layer upon optical coherence tomography; a large gamma zone (and delta zone) which makes using the end of Bruch’s membrane as reference point for the measurement of the neuroretinal rim useless; and macular Bruch’s membrane defects and other reasons for non-glaucomatous visual field defects which reduces the diagnostic precision of perimetry for the detection of presence and progression of GON.

1.9 Management of Myopic Choroidal Neovascularization

Myopic choroidal neovascularization (myopic CNV) is the second most common cause of CNV after age-related macular degeneration (AMD) [167, 168]. It is one of the most sight-threatening complications of pathological myopia [119, 169] and is the most common cause of CNV in those 50 years or younger [167], with significant social and economic burden. The prevalence of myopic CNV is between 5.2% and 11.3% in individuals with pathological myopia [12], with female preponderance seen in most studies [167–170]. The long-term outcome of CNV is poor if left untreated. In a 10-year follow-up study of 25 patients with myopic CNV, visual acuity deteriorated to 20/200 or worse in 89% and 96% of eyes in 5 years and 10 years, respectively [168].

On slit-lamp biomicroscopy, myopic CNV manifests as a small, flat, grayish subretinal lesion adjacent to or beneath the fovea [109, 168, 169, 171]. On SD-OCT, myopic CNV presents as a hyper-reflective material above the retinal pigment epithelium band (type 2 CNV), with variable amount of subretinal fluid. Clinical diagnosis is confirmed by fundus fluorescein angiography (FFA). Most myopic CNVs are type 2 neovascularization and present with a “classic” pattern on FA. OCT angiography (OCTA) was able to detect flow within myopic CNV vascular complexes and hence delineate vascular networks in these myopic neovascular membranes that lie above the retinal pigment epithelium (RPE) where flow signals are spared from attenuation [172].

Prior to the advent of anti-VEGF therapy, the main treatment options for myopic CNV were limited to thermal laser photocoagulation [173], photodynamic therapy with verteporfin (vPDT) [174, 175]. These treatments had limited efficacy in improving vision significantly and have now largely been relegated to the annals of history by anti-vascular endothelial growth factor (anti-VEGF) therapy [176]. Once active myopic CNV is diagnosed, prompt treatment with intravitreal anti-VEGF therapy should be administered as soon as possible [121, 177]. Current evidence suggests a pro-re-nata (PRN) regimen without a loading phase can be considered in most patients. Patients should be monitored monthly with OCT and treatment administered until cessation of disease activity on OCT or visual stabilization.
1.10 Management of Myopia-Related Retinal Complications

Myopic traction maculopathy (MTM) [123] is estimated to occur in approximately 8–34% in individuals with high myopia [178–180] and encompasses retinal thickening, macular retinoschisis, foveal detachment, lamellar macular hole with or without epiretinal membrane and/or vitreomacular traction [123], and/or full-thickness macular hole (HM) with or without retinal detachment. Central to the pathogenesis of MTM is traction, which was postulated to arise from one or more of the following mechanisms [181]: vitreomacular traction associated with perifoveal posterior vitreous detachment (PVD) [182–184]; relative incompliance of the internal limiting membrane (ILM) [185–189], epiretinal membrane (ERM) [180, 182, 190–192], and cortical vitreous remnant after PVD [193] to the outer retina which conforms to the shape of the posterior staphyloma; and traction exerted by retinal arterioles [188, 194, 195]. Not all patients with MTM require interventions [184, 196, 197]. There are numerous reported interventions for MTM. The principles of the treatment are: (1) to relieve traction, mainly achieved through pars plana vitrectomy (PPV) with or without ILM peeling; (2) to minimize surgical damage to the weakened macula through technique modifications in order to prevent the formation of postoperative MH; and (3) in the presence of full-thickness MH, to maximize the chance of hole closure through the use of various surgical adjuncts.

1.10.1 Proposed Adjuncts to Improve Outcome of Macular Hole Surgery

**Inverted Internal Limiting Membrane Flap**  This technique involves leaving a hinge of ILM flap at the edge of MH during ILM peeling. This ILM flap is then inverted upside-down to cover or fill the MH [198].

**Autologous Internal Limiting Membrane Transplantation**  In eyes where ILM around the macula hole has already been removed, an appropriately sized ILM can be peeled off from a distant site and placed as a free flap onto the persistent MH [199, 200].

**Autologous Blood**  In order to prevent subretinal migration of dye and the resultant retinal toxicity associated with vital stains, it was proposed to use autologous blood to cover the MH before injection of brilliant blue dye. It has been demonstrated that compared to conventional method, the use of pre-staining autologous blood led to better visual acuity outcomes and continuity of ellipsoid zone at all post-operative time points [201].

**Lens Capsular Flap Transplantation**  Chen et al. demonstrated a 100% MH closure rate with anterior capsular transplantation among patients with refractory MH,
whereas the complete closure rate of MH after posterior capsular transplantation was only 50% and with another 30% enjoyed partial MH closure [202].

**Macular Buckle** Macular buckles have been used to shorten the axial length of myopic eyeballs in conditions such as macular hole retinal detachment (MHRD), myopic foveoschisis with or without foveal detachment, and MH with foveoschisis. There are many types of macular buckle, including scleral sponge, T-shaped or L-shaped buckle, Ando Plombe, wire-strengthened sponge exoplant, and even donor sclera and suprachoroidal injectable long-acting hyaluronic acid [203].

**Autologous Neurosensory Retinal Transplantation** The technique involves bimanually harvesting a free flap of neurosensory retina superior to the superotemporal arcade, with the harvest site first secured by endolaser barricade and endodiathermy. The free flap was translocated in its correct orientation over the macular hole and perfluoro-\(n\)-octane heavy liquid (PFC) was instilled over it, followed by direct PFC–silicone oil exchange [204].

Figure 1.1 presents an overview of the management of myopia-related complications in adults.

1.11 Management and Control of Myopia in Children

Currently, there are many types of interventions to slow myopia progression in children, including spectacle lenses, contact lenses, pharmaceuticals, and environmental or behavioral modification. However, none of these myopia control methods have been proven to stop the development or progression of myopia completely and each method has their own limitations.
Spectacle Lenses  Under-correction of myopia in clinical trials has shown conflicting results and small, clinically insignificant effect on slowing myopia progression [205–207]. In view of these conflicting results, there is no convincing evidence to indicate that under-correction should be used to slow myopia progression.

Bifocal or Multifocal Spectacles  Most studies showed that progressive addition lenses (PALs) have an insignificant effect on slowing myopia progression rate (less than 0.2 D per year) overall [48, 208–214]. In contrast, a randomized, controlled trial showed that executive bifocal lenses slowed myopia progression in Chinese-Canadian children aged 8–13 years by 39% and up to 51% with base-in prisms incorporated over 3 years [215]. More recently, the Defocus Incorporated Multiple Segments (DIMS) spectacle lens enabled clear vision and myopic defocus simultaneously for the wearer [216]. Hong Kong Chinese children aged 8–13 years wearing DIMS lenses had approximately 60% less myopia progression and axial elongation when compared with children wearing single vision spectacle lenses over 2 years. Moreover, about 20% of the DIMS lens wearers had no myopia progression during the study period.

Peripheral Myopic Defocus Glasses  In 2010, Sankaridurg et al. published their results of three novel peripheral defocus spectacle lens. Unfortunately, there was no significant effect on myopic progression with all three designs [217]. In a recent randomized controlled trial (RCT) conducted in Japanese children with peripheral defocus lenses, no difference in myopia reduction was found [218].

Rigid Gas Permeable Contact Lenses  Two randomized clinical trials [219, 220] showed that rigid gas permeable (RGP) contact lenses did not retard axial eye growth. However, Walline et al. [219] reported significant slower myopia progression in the group of RGP lenses compared with soft contact lenses, despite that no differences were found in axial elongation between the groups. The proposed reason for a treatment effect on refraction may be due to the changes in corneal curvature.

Orthokeratology  Orthokeratology (Ortho-K) lenses are specially designed RGP contact lenses that are worn overnight to reshape the cornea and thereby temporarily correct low-to-moderate myopia. Various clinical studies have demonstrated the effectiveness of inhibiting myopic progression with Ortho-K. Individual studies and meta-analyses have shown a 32–63% reduction in the rate of axial elongation in East Asian children initially aged from 7 to 16 years and followed for up to 5 years [221–227]. Efficacy may decrease over time [224, 228], with a potential “rebound” after discontinuation, especially in children under 14 years [229]. There is also a potential non-response rate of 7–12% [223]. Interestingly, a recent study in Japan [230] showed that the combination of Ortho-K and low-concentration atropine (0.01%) eyedrops was more effective in slowing axial elongation over 12 months than Ortho-K treatment alone in myopic children. The risk of infective keratitis remains [231].
Soft Bifocal and Multifocal Contact Lenses  These lenses are worn during the
daytime. Compared to spectacles, contact lenses are more cosmetically acceptable,
more easily handled, and are more convenient for daily activities of some children, especially during sports [232, 233]. For most of eye-care practitioners, the fitting procedures of soft bifocal contact lenses are relatively simpler than Ortho-K. Overall, soft bifocal and multifocal contact lenses slow the progression of myopia in children by an amount comparable to that of Ortho-K lenses. Studies exploring the effect of these bifocal soft contact lenses indicate slowing of myopia progression by 25–50% and axial length by 27–32% in children aged 8–16 of various ethnicities over a period of 24 months [234, 235].

Atropine  The initial high doses of atropine (i.e., 0.5% or 1.0%) slowed myopia pro-
gression by more than 70% in Asian children aged 6–13 years over 1–2 years [229,
236–238]. However, lower doses (0.1% or less) can also slow refractive progression by
30–60% with less side effects (pupil dilation, glare, or blur) [238]. The Atropine Treatment of Myopia (ATOM) studies showed that there was a myopic rebound if atropine was stopped suddenly, especially at higher doses and in younger children [239, 240].

Time Spent Outdoors  In the Sydney Myopia Study, exposure to more than 2 h of
outdoor activity per day decreased the odds of myopia and countered the effects of
near work [65]. Interventions involving increasing time outdoors appeared to reduce
the onset of myopia and also its progression in myopic children [71]. A meta-
analysis has suggested a 2% reduced odds of myopia per additional hour of time
spent outdoors per week [70].

Environmental Interventions  Based on new evidence, the advice has shifted
from spending at least 2 h per day outdoors in addition to avoiding excessive near
work. This has changed health and school messaging in many East Asian coun-
tries [71].

Higher Light Intensities and Dopamine  Potential reasons why time outdoors
may be protective include higher light intensities [241], differences in chromatic
composition [242], the reduction in dioptic accommodative focus and psychomet-
ric influences encountered outdoors [243]. The role of chromaticity (red and blue)
and ultraviolet (UV) light is still uncertain [244], while that of higher vitamin D
levels has been debunked [88].

Figure 1.2 presents an overview of the management and prevention of myopia in children.
Fig. 1.2  Summary of the clinical management of myopia in children

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