

# ASSOCIATION OF GLAUCOMA WITH HIGH MYOPIA OR BEARING SUFFER THROUGH DESERT

Assoc. Prof. Vasile Potop

# High myopia and glaucoma

- Many clinical and fundamental studies have shown that high myopia (HM) and glaucoma are closely associated.
- The occurrence and progression of primary open-angle glaucoma interact with the progression of HM.



# Epidemic glaucoma ?

- The issue of myopia as a risk factor for glaucoma is important because there is an explosion in the prevalence of myopia in certain ethnic groups
- Dr. Lin, professor of ophthalmology and co-director, glaucoma service at the University of California San Francisco School of Medicine, outlined his points in a presentation entitled, "Myopia: The Next Glaucoma Epidemic?"



# Fatal attraction ?

- Perkins and Phelps found that compared with the normal population, myopic patients were more prone to POAG, ocular hypertension and low-tension glaucoma<sup>1</sup>.

<sup>1</sup> Perkins ES, Phelps CD. Open angle glaucoma, Ocular Hypertention, Low-tension glaucoma and Refraction. *Arch Ophthalmol* 1982; **100**: 1464–1467.



# Pathogenic mechanisms

Myopic patient may experience a higher IOP than a normal individual.

- IOP elevation may cause further elongation of the ocular axis.
- HM and glaucoma may interact to aggravate the condition.
- Two theories have been proposed:

***The hypertension gene theory***

***Collagen-related gene theory.***

Many studies, however, have suggested that the combination of the two theories may better explain the association between HG and glaucoma ( POAG).



# The hypertension gene theory

- Tang *et al.* tested the association between *MYOC* gene polymorphisms and HM in Hong Kong Chinese with a family-based association study.<sup>1</sup>
- ***They discovered that the MYOC gene polymorphism was highly associated with both myopia and glaucoma, suggesting that this gene may be a key molecular mechanism implicated in HM and glaucoma (especially POAG). Their finding also suggested that this gene may be a contributor to the hypersensitive response of HM patients to glucocorticoids.***

1. Tang WC, Yip SP, Lo KK *et al.* Linkage and association of myocilin (MYOC) polymorphisms with high myopia in a Chinese population. *Mol Vis* 2007; **13**: 534–544.



# Patients with HM respond more sensitively to glucocorticoids

- ❖ **Patients with HM or glaucoma respond more sensitively to glucocorticoid hormones compared with normal individuals.**

Armaly and Becker<sup>1</sup> found that only 4–5% of normal individuals responded hypersensitively to corticosteroids compared with 90% of POAG patients.<sup>1</sup>

Gentle et al. observed that 88% of HM patients with normal IOP responded to cortisone (i.e. IOP elevation), including 29% of patients with IOP >31 mmHg. They also found that approximately 27.8% of the HM patients had inherent IOP elevation, which was believed to be a pathological factor underlying HM.<sup>2</sup>

Other studies have shown that glucocorticoids disrupt the expression of 2–5% of the proteins in trabecular meshwork cells.<sup>2</sup> This disruptive effect has been suggested to be a major mechanism underlying the affects of glucocorticoids on trabecular meshwork cells as well as a major mechanism of glucocorticoid-induced ocular hypertension.<sup>2</sup>

1. Becker B, Hahn KA. Topical corticosteroids and heredity in primary open-angle glaucoma. *Am J Ophthalmol* 1964; **57**: 543–551.

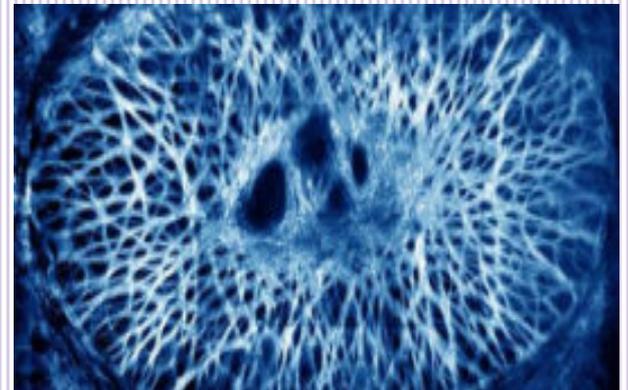
2. Gentle A, Liu Y, Martin JE, Conti GL, McBrien NA. Collagen gene expression and the altered accumulation of scleral collagen during the development of high myopia. *J Biol Chem* 2003; **278**: 16587–16594.



# Collagen-related gene theory

- Curtin and Karlin studied the posterior sclera of HM patients with electron microscopy and noticed a series of changes<sup>1</sup>
- ***Presumably, these changes increased the plasticity of collagen fibres and reduced their cross-link stability and increase its deformation under pressure.***
- Under a normal IOP, these changes reduce the separation, buffering and protection of the optic nerve fibres by collagen tissues and potential injuries to the fibres, which may be one mechanism responsible for the glaucoma-related optic disc changes. These results suggest that from the perspective of pathology, glaucoma and HM may both be caused by pathological collagen changes.

1. Curtin BJ, Karlin DB. Axial length measurements and fundus changes of the myopic eye. I. The posterior fundus. *Trans Am Ophthalmol Soc* 1970; **68**: 312–334



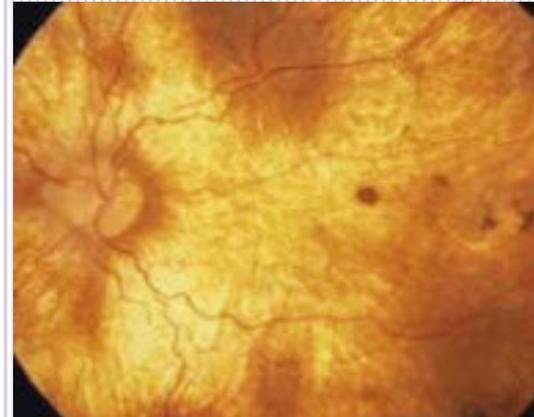
# High myopia

- Myopia affects 1.6 billion people worldwide, with increasing prevalence in many countries and regions.<sup>1-3</sup>
- High myopia (HM) is an extreme form of myopia accounting for 27–33% of all myopic patients
- HM is characterized by severe refractive and is accompanied by progressive degenerative changes of the fundus, such as ocular axial elongation, optic disc deformation, retinal thinning and choroidal atrophy
- HM has been recognized as a major cause of low vision and legal blindness

1. Kempen JH, Mitchell P, Lee KE *et al.* The prevalence of refractive errors among adults in the United States, Western Europe, and Australia. *Arch Ophthalmol* 2004; **122**: 495–505.

2. Robaei D, Huynh SC, Kifley A, Mitchell P. Correctable and non-correctable visual impairment in a population-based sample of 12-year-old Australian children. *Am J Ophthalmol* 2006; **142**: 112–118.

3. Vitale S, Ellwein L, Cotch MF, Ferris FL 3rd, Sperduto R. Prevalence of refractive error in the United States, 1999–2004. *Arch Ophthalmol* 2008; **126**: 1111–1119.



# High Myopia a genetic disorder

- Currently, High Myopia is widely regarded as a genetic disorder with monogenic inheritance including:
  - autosomal recessive inheritance
  - autosomal dominant inheritance
  - X-linked inheritance.



# The desert of High Myopia

- The optic disc appears pale, and the optic cup is relatively shallow.
- The temporal side of the cup wall is oblique, deformed with an obscure cup margin.
- The optic disc may be surrounded by an arc-shaped degenerative region with choroidal atrophy.
- The retina is thinned and likely has a tigroid fundus; the posterior pole is atrophic or depigmented, and the retinal nerve fibre layer (RNFL) may be thinned without the normal arched path of the retinal nerve fibre bundles (i.e. forming ‘pseudo-RNFL defects’)<sup>1,2</sup>



1. Jonas JB, Gusek GC, Naumann GO. Optic disk morphometry in high myopia. *Graefes Arch Clin Exp Ophthalmol* 1988; 226: 587–590.

2. Curtin

BJ, Karlin DB. Axial length measurements and fundus changes of the myopic eye. I. The posterior fundus. *Trans Am Ophthalmol Soc* 1970; 68: 312–334

# Peripapillary region

- Elongated and markedly thinned parapapillary scleral flange associated with an extended retrobulbar cerebrospinal fluid space and an absence of choroid, Bruch membrane, and retina, with the exception of the retinal nerve fiber layer.
- The thickness of the parapapillary sclera influences the biomechanics of the lamina cribrosa, - may partially explain the increased glaucoma susceptibility in highly myopic eyes.
- Bruch membrane acts as a stable element of the retina-choroid complex, the implications of its absence in the highly myopic parapapillary region for the biomechanics in that area have to be elucidated.
- The feeding vessels for the parapapillary choroid are of importance for the nutrition of the lamina cribrosa, the increased distance between the parapapillary choroid and the disc border may influence the vascular support of the highly myopic optic nerve head.<sup>1</sup>



1. Jost B, Jonas, Shefali B, Jonas, Rahul A, Leonard Holbach, Songhomita Panda-  
Jonas Histology of the Parapapillary Region in High Myopia. Am Journal of  
Ophthalmol vol 152./6 1201-1029 Dec. 2011

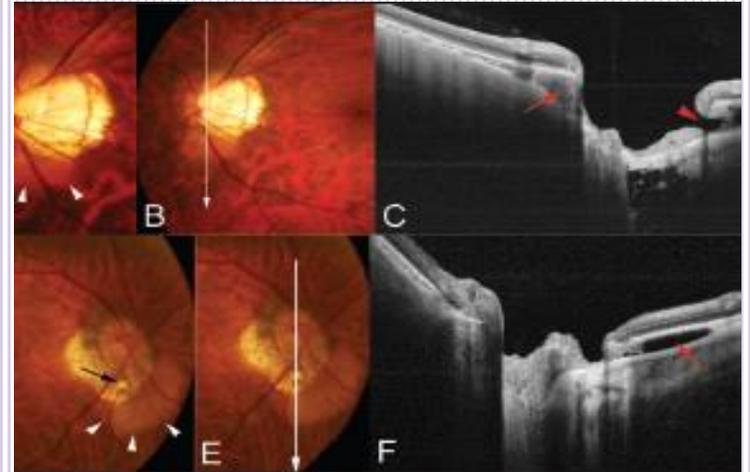
# Swept-source OCT in High Myopia

- ❑ Peripapillary intrachoroidal cavitation ICCs were observed in 5% (32/631) of eyes with pathologic myopia, and 71% the eyes with peripapillary ICCs had glaucomatous VF defects<sup>1-2</sup>

1. Shimada N, Ohno-Matsui K, Yoshida T, et al. Characteristics of peripapillary detachment in pathologic myopia. *Arch Ophthalmol.* 2006;124:46-52.

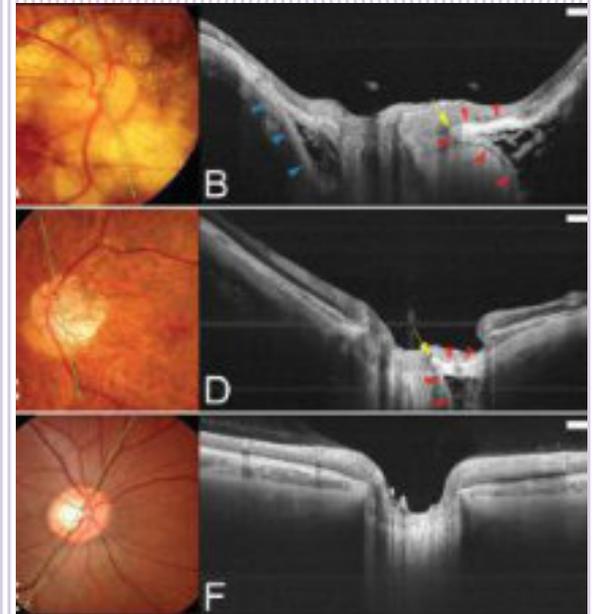
2. Shimada

N, Ohno-Matsui K, Nishimuta A, Tokoro T, Mochizuki M. Peripapillary changes detected by optical coherence tomography in eyes with high myopia. *Ophthalmology.* 2007;114:2070-2076..



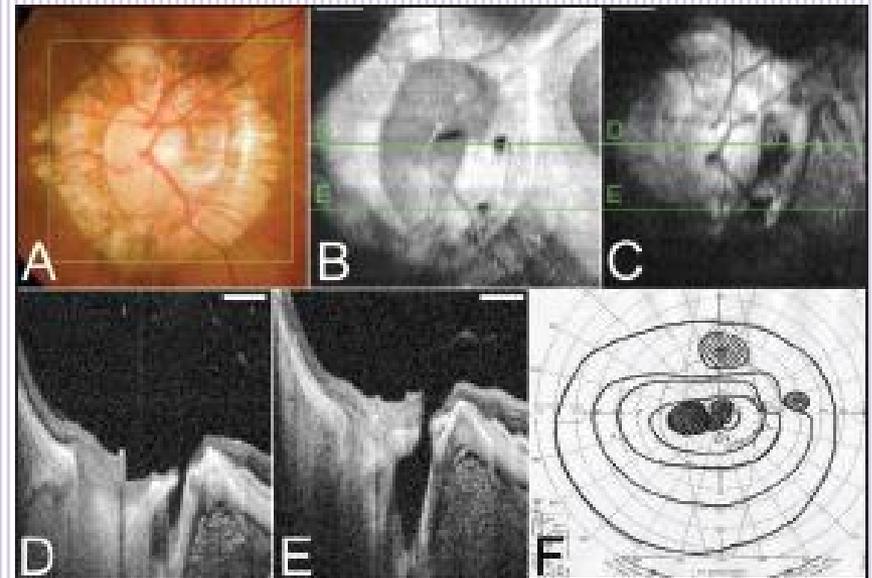
# Swept-source OCT ; the particular subarachnoid space

- Swept-source OCT ; the particular **subarachnoid space** SAS could be observed in 124 of 133 eyes (93%) with pathologic myopia (the average axial length was  $30.4 \pm 1.8$  mm).
- The optic SAS appeared to be dilated in highly myopic eyes.



# The enlargement of the perioptic SAS in a highly myopic eye

- *What kinds of effect would the enlargement of the perioptic SAS in a highly myopic eye have?*
- The expanded area of exposure to cerebrospinal pressure, along with thinning of the posterior eye wall, may increase the pressure load on the peripapillary sclera, as well as on the lamina cribrosa.
- This force has the potential to increase the glaucoma susceptibility in highly myopic eyes.<sup>1</sup>



<sup>1</sup>Kyoko Ohno-Matsui, MD, Peripapillary Changes In Pathologic Myopia .Swept-source OCT can help image changes in high myopiaD Retinal Phisician oct 2014

# HM/GPUD -similarities to the confusion

❑ Glaucoma (particularly POAG) has similar manifestations to High Myopia:

1. The disorder onset is insidious with a normal or slightly elevated IOP.
2. Anterior chamber is relatively deep with an open chamber-angle and normal chamber-angle structures.
- 3 The visual field may be normal shortly after onset with visual field defects (e.g. blind spots) appearing subsequently

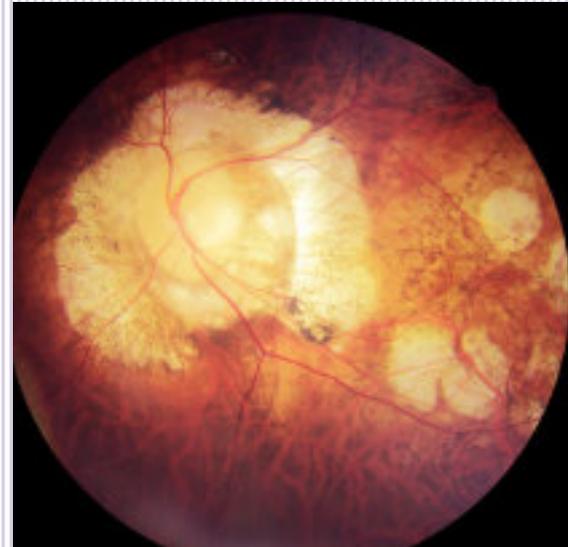


# Combined HM and glaucoma

1. The onset is insidious, in some cases without obvious symptoms.
2. The IOP may be normal or slightly elevated.
3. The visual field has irregular boundaries (or dark spots) and defects
4. The optic disc is surrounded by an arc-shaped degenerative region with choroidal atrophy.
5. The optic disc appears pale and is oval, oblique and deformed. The optic cup varies in morphology.
6. The disc excavation is eccentric and usually downward.
7. Diffused RNFL atrophy, which is closely related to visual field defects, occurs primarily in the inferior retina.<sup>1</sup>

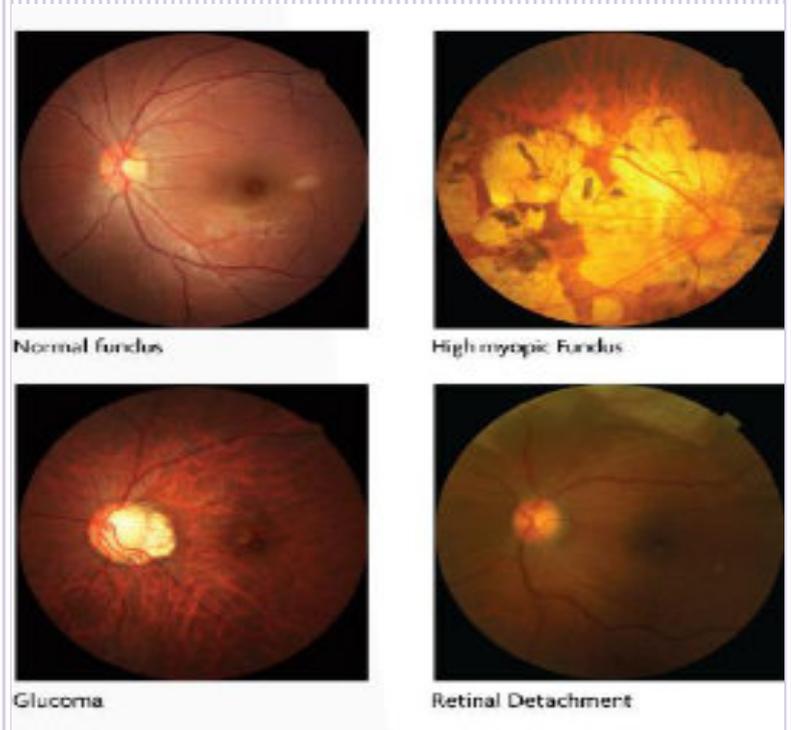
1. Chihara E, Liu X, Dong J *et al*. Severe myopia as a risk factor for progressive visual field loss in primary open-angle glaucoma.

*Ophthalmologica* 1997; **211**: 66–71.



# HM and GPUD has different evolutions

- Elongation of the eye in myopes places strain on susceptible axons within the prelaminar optic nerve head tissue, resulting in optic disc damage.
- However, once the myope reaches adulthood and the eye stops growing, the optic disc damage is fixed and any related visual field defect also stays static.



# Particular aspects of glaucoma associated with myopia

*HM is typically accompanied by a low baseline IOP*

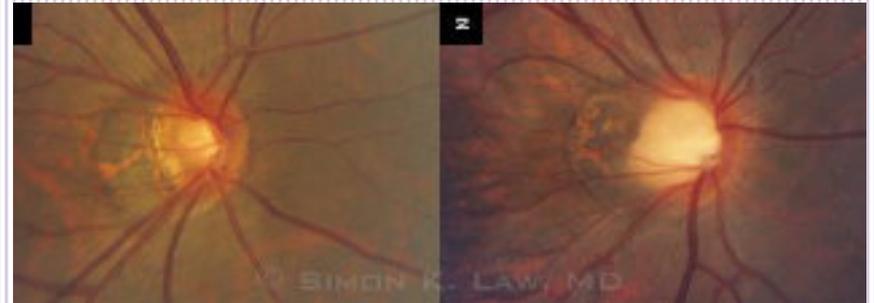
- The disc excavation is unclear, and the optic cup is large; therefore, difficult to accurately determine the cup:disc ratio.
- The myopic crescent enlargement, and the resulting retinochoroidal atrophy, makes the determination of a pale disc and disc atrophy difficult.
- The excessive traction of the scleral and choroidal tissues at the nasal side frequently straightens the retinal vessels on the temporal side, thereby preventing vessel bayoneting and translocation (i.e. indications of glaucoma).<sup>1</sup>

1. Chihara E, Sawada A. Atypical nerve-fiber layer defects in high myopes with hypertension glaucoma. *Arch Ophthalmol* 1990; 108: 228–232.



# Myopic patients who are suspected of having glaucoma.

- Follow the nerve; take pictures of the optic nerve to document its appearance over time.
- Visual field change isn't always the result of glaucoma but may represent other types of optic nerve damage. For example, nerves that tilt inferiorly may have visual field defects at the top hemifield.
- Other visual field defects may be caused by myopic retinal degeneration, not glaucoma.
- IOP Eyes with high myopia may be less able to tolerate IOP fluctuations than other eyes: - They have a longer globe, thinner lamina cribrosa, and thinner scleral wall with different elasticity.
- An IOP increase may be sufficient to cause damage in the posterior pole without causing abnormal corneal IOP readings.



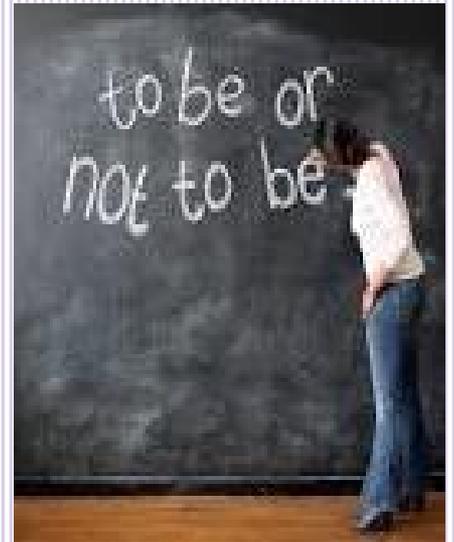
# Myopic glaucoma has an unclear profile

- Despite new discoveries in diagnostic tools, current techniques cannot accurately differentiate changes associated with HM and glaucoma.
- The examination should be performed with attention to several details :
- IOP should be calibrated or measured dynamically.
- The refractive error should be corrected during visual field measurement,
- The visual field progression should be monitored over a long time.
- Changes associated with the disc, peripapillary region and the retina should be carefully and dynamically monitored



# To or not to be glaucoma?

- High myopes may not have glaucoma, but the presentation looks like glaucoma.
- They may have glaucoma, and we are not sure



# Consider to initiate treatment.

- Treat each case differently, taking into account family history, degree of visual field defect
- A large proportion of high myopes truly have glaucoma.
- If you're not sure, you may want to treat it as if it's glaucoma if the visual field defect is severe or very close to fixation.
- Recognize when the visual field pattern does not follow the typical pattern of glaucoma.
- In myopic atrophy of the retina, the visual field usually doesn't respect the horizontal meridian. In contrast, in glaucoma, when there is focal damage to the optic disc, it usually does not cross the horizontal meridian



# HM/GPUD Treatment

- Glaucoma treatment is like GPUD with topical glaucoma medications, which are relatively safe
- Glaucoma surgery. People with high myopia have a greater chance of hypotony maculopathy after surgery, particularly young high myopes, who have a thinner, less rigid scleral wall. In such patients, the scleral wall tends to collapse easily when the pressure is lowered after glaucoma surgery.
- Surgery is most appropriate in patients in whom the location and rate of progression suggest a significant risk of the patient becoming symptomatic from the disease.
- Former high myopes, that is, patients whose myopia was reduced or eliminated by refractive surgery. That procedure thins the cornea, IOP measurements may be artifactually low.



# Glaucoma and Myopia a suffering in a desert

- The association of glaucoma with high myopia has all the data of suffering through a desert.
- In the desert, in addition to the implicit deprivations that threaten survival, there is also a high risk. It is the risk of getting lost, of the difficulty of orienting yourself
- The association of glaucoma with myopia involves the risk of a severity of glaucoma and the risk of "getting lost" in some structural (OCT) and functional landmarks of the disease
- The association of glaucoma with severe myopia exposes to a functional, structural and genetic interference of the two diseases. They potentiate each other and blur their characteristic aspects of each of them; glaucoma becomes myopic and myopia becomes glaucomatous

