Case 2 - Normal Tension Glaucoma

Learning outcomes

- To be aware of the signs and differential diagnoses for normal tension glaucoma
- To understand the systemic processes that can contribute to normal tension glaucoma, and to appreciate the importance of neurological imaging
- To discuss the potential role of neuroprotection in patients with normal tension glaucoma
- To be familiar with the management of patients with normal tension glaucoma

A 71-year-old Japanese lady presents to you for a routine examination.

Past ocular history: Right pterygium excision (2008), uncomplicated left cataract extraction with posterior chamber IOL (2009). Prior to cataract surgery she had low myopic refractive error. She has not had an eye exam since final cataract surgery follow-up ten years prior.

Past medical history: Occasional migraines without aura since her 20s, less frequent now.

Medications: None

Examination:

<table>
<thead>
<tr>
<th></th>
<th>Right eye</th>
<th>Left eye</th>
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<tbody>
<tr>
<td>BCVA</td>
<td>6/6</td>
<td>6/7.5–2</td>
</tr>
<tr>
<td>Pre-cataract surgery refraction</td>
<td>+0.50 DS</td>
<td>-0.75 /-0.25 x 180</td>
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<tr>
<td>Post-cataract surgery refraction</td>
<td>N/A</td>
<td>-0.50/-0.25 x 175</td>
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<td>Goldmann IOP at 3:00 pm</td>
<td>14 mmHg</td>
<td>15 mmHg</td>
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<td>Ishihara colour plates</td>
<td>14/14</td>
<td>14/14</td>
</tr>
<tr>
<td>Pupils</td>
<td>Small R RAPD</td>
<td></td>
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<tr>
<td>Slit lamp biomicroscopy</td>
<td>Anterior segment unremarkable aside from early nuclear sclerotic cataract. No evidence of pigment deposition or pseudoexfoliative material.</td>
<td>Anterior segment unremarkable, PCIOL observed. No evidence of pigment deposition or pseudoexfoliative material.</td>
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<tr>
<td><strong>Gonioscopy</strong></td>
<td>Open angle all quadrants, with lightly pigmented trabecular meshwork</td>
<td>Open angle all quadrants, with lightly pigmented trabecular meshwork</td>
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<tr>
<td>----------------</td>
<td>---------------------------------------------------------------</td>
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<tr>
<td><strong>Central corneal thickness (Pachmate)</strong></td>
<td>512 µm</td>
<td>519 µm</td>
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Figure 1a: Right eye – optic disc photo
Figure 1b: Left eye – optic disc photo
Figure 2: RNFL OCT Scan (OU)
Figure 3: Ganglion Cell Analysis (OU)
**Question 1:** Discuss the findings of the examination, features of the optic nerve appearance and OCT scan for this patient.

Our patient has good best corrected visual acuity, and low IOP. Her colour vision, and gonioscopy findings are unremarkable. Of note, she has a small R RAPD, and her central corneal thickness is thinner than average.

Figure 1a shows a disc photo of the right optic disc. The right optic disc is large in size and there is focal notching of the inferior neuro-retinal rim in the 7 o’clock position. The superior neuroretinal rim is also thin but there is no notch. There is a ring of pigmented peripapillary atrophy. There is a pathological deep cupping, with visibility of lamina cribrosa pores, particularly inferiorly, and the cup to disc ratio is approximately 0.9. There is no obvious disc pallor or drance haemorrhage noted.

Figure 1b shows a disc photo of the left optic disc. The left optic disc is also large and has a similar pattern of neuroretinal rim loss, with notching of the inferior rim at the 5-6 o’clock position and a thin superior rim with no notching. There is a temporal crescent of pigmented peripapillary atrophy. As in the right eye, there is a pathological deep cup, with visible lamina pores inferiorly. The cup to disc ratio is approximately 0.9. There is no obvious disc pallor or drance haemorrhage noted.

The pathological changes in optic nerve appearance prompt you to conduct further investigation with optical coherence tomography (OCT).

Figure 2 is an ONH and RNFL analysis of both eyes.

The RNFL OCT of the right eye is of good signal strength (8/10) and the reference circle is well positioned. The RNFL thickness map and neuro-retinal rim thickness plot show significant thinning of the inferior tissue at the 1% level. There is also some superior thinning at the 5% level.

The RNFL OCT of the left eye is also of good signal strength (8/10) and the reference circle is again well positioned. The RNFL thickness map and neuro-retinal rim thickness plot show extensive thinning of the inferior neuro-retinal rim as well as the inferior RNFL layer to the 1% level. Again, there is also superior thinning at the 5% level. There is high inter-eye symmetry. The OCT RNFL findings are in keeping with the disc appearance in both eyes.

Figure 3 is the macular ganglion cell complex (GCC) analysis of both eyes.

Macular GCC OCT of the right eye shows good signal strength (8/10) and retinal layer segmentation appears to be accurate. The GCC thickness values are thinned at the 1% level globally aside from sparing of the superonasal sector.

Macular OCT of the ganglion cell complex (GCC) of the left eye also shows good signal strength (9/10) and accurate retinal layer segmentation. Again there is thinning at the 1% level in all regions except the inferonasal region which has thinning to the 5% level, and the
superonasal region which is within normal limits. There is correlation between the structural findings on OCT and those observed on clinical examination of the optic disc.

**Question 2: Please discuss what further information, examination or investigations you would like to obtain in this case.**

Further history should be obtained from the patient to elicit further clues in the assessment of glaucomatous and non-glaucomatous optic neuropathy. This is particularly important as the patient has low IOPs.

- Neurological symptoms including headache, diplopia, sudden vision loss (may be monocular)
- Family history of glaucoma
- Previous history of ocular inflammation (eg. iritis) or trauma
- Previous episode of haemodynamic crisis (hypovolaemia / systemic hypoperfusion)
- Systemic (postural) hypotension
- History of Raynaud’s phenomenon
- History of sleep apnoea
- Past history of corticosteroid eye drops

Close examination of the retina should be performed to check for evidence of old retinal vascular occlusion.

Due to the examination and OCT findings, a threshold visual field assessment should be conducted.

The patient did not have any neurological symptoms or history of sudden vision loss. She had no known family history of glaucoma but did note that both of her parents died in their sixties (from heart disease and cancer). Aside from post-cataract and pterygium surgery, she had no history of eye drop use. She reported her blood pressure was ‘normal or slightly on the low side’ at her most recent GP visit (approximately 6 months prior). She did not have symptoms consistent with Raynaud’s phenomenon or sleep apnoea. She had never had major surgery or episodes of significant blood loss. Fundus examination did not reveal any evidence of previous vascular occlusive events.
Figure 4a: Right eye - visual field
OS Single Field Analysis

Central 24-2 Threshold Test

Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 1/15
False POS Errors: 10%
False NEG Errors: 12%
Test Duration: 07:00
Fovea: 36 dB

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Figure 4b: Left eye - visual field
Question 3: Describe the findings of the patient's visual fields and discuss the most likely diagnosis based on the available information.

Visual field testing (Humphrey SITA standard 24-2) is reliable in both eyes.

In the right eye, there is a dense superior altitudinal defect, with most points in this region reduced to <0 dB. The mean deviation (MD) in the right eye is -12.70 dB and the pattern standard deviation (PSD) is 15.94 dB. The glaucoma hemifield test is outside normal limits.

In the left eye, there is a superior arcuate relative scotoma, with test points ranging between the <5% and <0.5% level. There is a point of paracentral loss superior-nasally. The MD is -4.62 dB and the PSD is 7.95 dB. The glaucoma hemifield test is outside normal limits.

In both eyes, the visual field defects clearly respect the horizontal midline. Foveal sensitivity is normal in both eyes.

In this case, significant visual field defects are apparent on visual field testing of both eyes, with the right eye showing more severe visual field loss. These defects correspond with the loss of RNFL thickness seen on OCT, and the optic disc appearance on clinical examination and in the photographs.

Based on the above findings, the most likely diagnosis for this patient is normal tension glaucoma. Both optic discs show evidence of characteristic optic neuropathy. There is advanced glaucomatous visual field loss in the right eye and mild to moderate visual field loss in the left eye.

Although the IOP is low, significant optic nerve damage has occurred at this level and it is important to initiate anti-glaucoma therapy as soon as possible to reduce the risk of further progression of the existing visual field defects.

Normal tension glaucoma may be considered to be part of a spectrum of open angle glaucoma. In different parts of the world, a greater number of patients with open angle glaucoma have IOP <21 mmHg. For example, in a study of 3021 patients with open angle glaucoma in Japan, 92% of patients had IOP <21 mmHg (2). Although elevated IOP is still considered the primary risk factor in the development of glaucoma, it is possible to develop glaucomatous changes at any IOP level. Some studies have found certain phenotypic features more frequently in normal tension glaucoma, including higher prevalence of optic disc haemorrhages and paracentral visual field defects (closer to fixation). However, there is significant overlap and there are no features unique to normal tension glaucoma.

It is suggested that incorporating central 10-2 visual field assessments in the diagnosis and monitoring or normal tension glaucoma may be beneficial (3). To try explain these defects closer to fixation, it has been argued that certain regions of ganglion cells and axons react more sensitively to pressure than others – however these regions also appear to vary between patients. Also, if IOP was the only cause for glaucomatous damage in normal
tension glaucoma, then we would expect progression of damage to stop when lowering IOP, but this is not always the case (4).

**Question 4: Describe the role of IOP fluctuations in glaucoma.**

There is evidence that large diurnal, nocturnal and postural fluctuations of IOP increase the risk for progression of visual field defects in patients with glaucoma. Patients with normal tension glaucoma may have prolonged nocturnal IOP peaks (in the supine position) and have a greater variation of diurnal IOP than healthy subjects (5). Snapshot measurements of IOP in the daytime clinic setting may well miss peaks of elevated pressures in a number of patients with normal tension glaucoma. IOP fluctuations may be influenced by a wide variety of physiological factors including blood pressure, heart rate, respiration, eyelid blinking, pupillary size, eye movement, Valsalva manoeuvre (and effect of central venous pressure), ingestion of fluid, sleep, postural changes, physical activity and hormonal factors.

To give a better idea of diurnal IOP variation, multiple measurements of a patient’s IOP over the course of one day may be useful, however postural or nocturnal measurements are not assessed. Admission for 24-hour IOP monitoring is unrealistic for most cases but could be considered in progressive normal tension glaucoma cases with apparent well-controlled IOPs based on clinic measurements. Future techniques to provide information regarding IOP over a 24-hour period including implantable and contact lens systems are not in widespread clinical use (5).

**Question 5: Discuss the differential diagnoses of this condition.**

Differential diagnoses are discussed below (6) (2):

- High tension glaucoma
  - Pachymetry should always be used in conjunction with IOP measurements. Our patient has no history of LASIK or other corneal refractive surgery, and no evidence of keratoconus or other conditions that could lead to erroneous Goldmann IOP readings.
  - Variable IOP; as discussed above, diurnal, postural and nocturnal fluctuations may be missed with measurement of IOP in the clinic setting. This patient had not had serial IOP assessments. It is possible that IOP peaks could have been missed.
  - Past elevation of IOP; previous iritis, chronic use of corticosteroids, chronic intermittent angle closure, previous pigmentary glaucoma are examples of possible processes which may have caused damage to the optic nerve. However, there was no evidence of anterior segment abnormalities consistent with these conditions in our patient. The patient would have had a short course of topical corticosteroids following ocular surgeries but had not received any previous treatment for elevated IOP at that time.

- Pseudo-glaucoma
A congenital disc anomaly; for example, optic disc pit or optic nerve coloboma may reveal a notch in the rim tissue with absence of RPE and nerve fibres in that region and a corresponding visual field defect. If the patient’s optic disc appearances were congenital, this would have been noted at previous eye examinations and prior to intraocular surgery.

Moderate – high myopia; myopic tilted discs and peripapillary atrophy may manifest with arcuate-like visual field defects (wedge-shaped above the physiological blind spot) however these are non-progressive. Myopia is also a risk factor for open angle glaucoma secondary to optic disc anomalies and/or increased strain across the lamina cribrosa with increased axial length. The patient did not have a history of significant myopic refractive error.

Anterior ischaemic optic neuropathy; arteritic form may create a localized thinning or notch, and evaluation for giant cell arteritis would be warranted to prevent recurrence or involvement of the fellow eye. The patient did not have a history of sudden vision loss or systemic symptoms of giant cell arteritis, so no further investigations were undertaken for this patient.

Branch retinal vessel occlusion; may result in an arcuate region of nerve fibre loss and corresponding visual field defect, and history surrounding previous acute events or risk factors should be elicited. There was no evidence of previous retinal vascular occlusions in either eye on fundus examination.

Optic nerve drusen; multiple drusen are often obvious, otherwise careful inspection may reveal a congested-looking disc with indistinct margins and a lumpy appearance. Fundus autofluorescence reveals superficial optic disc drusen and evaluation with B-scan ultrasonography may reveal deeper disc drusen that relate to location of visual field defect. The patient’s optic disc appearance was not consistent with optic disc drusen.

Orbital or intracranial tumour (compressive optic neuropathy); localized thinning and related pallor of neuro-retinal rim may be appreciated in these cases. Further distinguishing features in history and examination can raise suspicion in these cases and this will be discussed in the next question of this case. The patient had no neurological symptoms. There was no evidence of disc pallor, or colour vision loss which may be present in compressive optic neuropathy.

Question 6: Discuss the role of further diagnostic imaging in normal tension glaucoma.

In the presence of elevated IOP, visual field defects which correspond with optic disc appearance and absence of other neurological signs or symptoms further neuro-imaging (eg. brain MRI) is not required.

In patients who have optic nerve features of glaucomatous optic neuropathy without elevated IOP, a careful examination of the afferent visual pathway for signs of dysfunction is essential. Features that arouse suspicion include the presence of optic disc pallor, a colour vision defect, lack of agreement between structural and functional changes, and reduced visual acuity.
Additionally, the patient should be questioned regarding neurological symptoms consistent with other causes of RNFL and visual loss. Multiple sclerosis, Alzheimer’s disease, Friedreich’s ataxia, and Charcot Marie Tooth type 2A may have associated optic disc changes, RNFL defects, and visual field defects.

In this case, further imaging was not undertaken despite normal IOP as there are characteristic features of glaucomatous optic neuropathy with no features suggestive of neurological pathology.

**Question 7: Discuss the associated systemic disease processes that may play a role in the pathogenesis of normal tension glaucoma.**

- Low ocular perfusion pressure has been found to be a risk factor for developing glaucoma. Ocular perfusion pressure is the calculated difference between mean arterial pressure and IOP, and this determines the perfusion of the optic nerve head. Ocular perfusion pressure can be roughly calculated with the following equation:

\[
OPP = \frac{2}{3}[DBP + \frac{1}{3}(SBP-DBP)] - IOP
\]

\[
OPP = \text{Ocular perfusion pressure}
\]

\[
DPB = \text{Diastolic blood pressure}
\]

\[
SBP = \text{Systolic blood pressure}
\]

Reduced OPP may render the glial and/or neural elements of the optic nerve more susceptible to pressure-induced damage or directly cause axonal loss and damage to the lamina cribrosa. One recent cohort study reported that nocturnal dips in diastolic blood pressure increased the risk of visual field progression in normal tension glaucoma (4)(7).

- Sleep apnoea syndrome; repetitive closure of the upper airway results in hypoxia and hypercapnia (elevated carbon dioxide levels), and it is postulated that abnormal autoregulation of optic nerve perfusion may occur as a result of these blood gas abnormalities. Obtaining a sleep study in patients with normal tension glaucoma and history suggestive of sleep apnoea can allow appropriate identification and treatment of sleep apnoea (2). As a sleep study is a significant undertaking, a sleep questionnaire, such as the Epworth Sleepiness Scale, may be used for screening purposes.

- Migraine and vasospasm (Raynaud’s phenomenon); the association of migraine and Raynaud’s phenomenon with normal tension glaucoma may be related to vasospasm or abnormal vascular autoregulation. Endothelin-1 is a vasoconstricting peptide which is thought to increase in response to cold in some vasospastic disorders, which may result in decline in ocular blood flow and visual function. Plasma endothelin-1 levels are shown to be higher in patients with normal tension glaucoma compared to the normal population (2). The Collaborative Normal-Tension Glaucoma Study group found that 3.75% of patients reported a history of Raynaud’s phenomenon. A history
of migraine was also reported as a risk factor for progression of normal tension glaucoma (8).

Question 8: Discuss the initial management options for this patient.

The mainstay of treatment in normal tension glaucoma is reduction of IOP from baseline. This can be achieved through medical, laser or surgical treatment.

The Collaborative Normal Tension Glaucoma Study demonstrated that a 30% reduction from baseline IOP resulted in a reduced rate of visual field loss. In this study of patients with no recorded IOP above 24 mmHg, criteria for treatment initiation included progression of visual field defects or optic nerve head cupping, visual field loss that threatened point of fixation or optic disc haemorrhage. An IOP reduction of 30% with IOP lowering treatment reduced the likelihood of progression to 12%, compared with a 27% risk of progression in untreated eyes over a five year period (8). In this patient, given the degree of visual field loss, particularly in the right eye, monitoring with no treatment would not be considered to be an option. The patient should receive prompt treatment in order to have the greatest chance of preserving remaining visual function.

Prostaglandin analogues are the first-line in medical therapy as they increase uveoscleral outflow without decreasing ocular blood flow, and they also help to reduce nocturnal IOP spikes. Beta-blockers should be used with caution as they may contribute to nocturnal systemic hypotension and optic nerve hypoperfusion. It may be helpful to refer the patient to their GP for a blood pressure assessment. Aqueous production naturally decreases during sleep and so aqueous suppressants may have little effect in lowering on nocturnal IOP (5). Brimonidine, an alpha-2 agonist is used in the treatment of normal tension glaucoma, both for its IOP-lowering ability, and for its potential neuroprotective effect (see question 9).

Generally, once treatment is initiated, an initial target of 30% reduction from baseline IOP is set. Patients should be reviewed in 6-8 weeks to assess adequate IOP reduction and associated side effects. Once satisfactory IOP control has been achieved, patients may be monitored every 3-4 months to assess maintenance of IOP and disease progression. If determined to be stable, patients may undergo optic disc assessment and visual field testing every 6-12 months. Target pressure may change over time, as it is dependent on a number of factors including glaucoma stage, the age and life expectancy of the patient and the presence of other risk factors. Factors that were identified to put patients at higher risk of progression in the Collaborative Normal Tension Glaucoma Study included presence of disc haemorrhage, female sex, history of migraine and family history of glaucoma (8).

A patient with more advanced visual field loss at presentation (as is the case for this patient) will require more aggressive treatment. Occasionally despite IOP reduction with eye drops or laser treatment, visual field loss can continue to progress, and these patients may require surgical intervention to lower their IOP to single-digit IOP targets which can reduce visual field progression.

In this case, our patient was commenced on travoprost 0.004% once daily as well as brimonidine 0.2% twice daily to facilitate a reduction in IOP. At follow up, IOP was reduced
to 10 mmHg in both eyes (approximately 30% reduction in the right eye and 33% in the left eye). IOP, clinical optic disc appearance and visual fields will need to be closely monitored and the patient may require escalation of treatment in the future.

Question 9: Discuss the potential role of neuroprotection in glaucoma.

The concept that glaucomatous damage to retinal ganglion cells may be prevented by intervening in neuronal death pathways gives rise to the potential for neuroprotective therapies. Studies investigating the role or neuroprotection in animal models have been challenging to extrapolate to human trials.

Brimonidine, an alpha-agonist has been shown to display neuroprotective properties in several animal models. Although the mechanism is not fully understood, one possible explanation involves modulation of retinal vascular tone through nitrous oxide signalling (5). A randomized control trial that suggested brimonidine 0.2% may prevent visual field progression compared with timolol 0.5%, however the high level of missing data made the results difficult to reliably interpret (10) (11). There have been no large scale RCTs with adequate follow-up in human subjects.

Betaxolol 0.5% is another commercially available glaucoma treatment that has been studied for its potential neuroprotective effects. In a double-masked study of patients with OAG, patients treated with timolol 0.5% b.d group had slightly lower IOPs at 18 months, but the patients in the betaxolol 0.5% b.d group had reduced visual field progression. However, another study, comparing betaxolol 0.5% with timolol 0.25%, showed no statistically significant difference at two years (12).

Glutamate antagonists may be effective in high levels of extracellular glutamate, as thought to occur in glaucoma. Memantine is a NMDA antagonist that was initially shown to protect retinal ganglion cells in several animal studies however failed to show superiority to IOP reduction alone in two large randomised controlled clinical trials (2).

Ginkgo Biloba extract is an anti-oxidant which has been shown to potentially improve visual field defects in a small group of normal tension glaucoma patients (13). It has been used as an adjuvant therapy alongside IOP reducing agents by some ophthalmologists. However, the follow-up period of the study was very short. A 2017 Cochrane review concluded that in order for a randomised controlled trial of neuroprotection in glaucoma to detect clinically meaningful results, a follow-up period of at least five years would be needed (11).

Resveratrol may prevent retinal ganglion cell death through inhibition of Bax-caspase-3 dependent apoptotic pathway, as well as other mechanisms involved with neuroprotection. One animal study reported reduced retinal damage and ganglion cell loss in retinal degeneration following ischaemia-reperfusion injury (14).

Other potential neuroprotective therapies are also being investigated, including neurotrophins, calcium channel blockers and stem cell treatments.
Further collaborative efforts in experimental and clinical studies regarding neuroprotection in glaucoma are required to develop clinically effective treatments (15) (16).

Recommended reading:


References:

Case 2 – Questions

1) Which of the following is not a risk factor for progression of normal tension glaucoma as identified by the Collaborative Normal Tension Glaucoma study? (Anderson, 2003)
   a. Male gender
   b. Family history of glaucoma
   c. Disc haemorrhage at presentation
   d. History of migraine
   e. Previous episode of major blood loss

2) Which of the following is most suggestive of a compressive optic neuropathy?
   a. Normal colour vision
   b. Visual acuity better than 6/12
   c. Visual field defect respecting vertical midline
   d. Monocular nasal step
   e. Peripapillary atrophy

3) Which of the following may not be useful in determining the presence or absence of a relative afferent pupillary defect? (Danesh-Meyer et al., 2007)
   a. Brightness perception
   b. Red saturation
   c. Swinging flashlight assessment
   d. Intercalpebral aperture
   e. Ishihara pseudoisochromatic colour plates

4) Which of the following is not a strong indicator for glaucoma?
   a. Focal thinning of the inferior neuro-retinal rim
   b. Nerve fibre layer haemorrhage inferiorly
   c. Small optic nerves with a cup to disc ratio of 0.6 in the right and 0.3 in the left
   d. Non-pigmented peripapillary atrophy in a region of neuro-retinal rim loss
   e. Large optic nerve with a cup to disc ratio of 0.8 in each eye with no neuro-retinal rim thinning

5) Disc haemorrhage is more common in high tension glaucoma compared to normal tension glaucoma. True or false?

6) What is the common etiology that is thought to link Raynaud’s phenomenon and normal tension glaucoma?
   a. Vasospasm
   b. Peripheral inflammation
   c. Neurodegeneration
   d. Sympathetic overstimulation
   e. Systemic vasodilation
7) Which of the following clues in the history would not implicate high IOP as cause of glaucomatous optic nerve damage?
   a. Previous episodes of inflammation (iritis)
   b. Previous steroid usage
   c. Previous episode of major blood loss
   d. History of ocular trauma
   e. Presence of pigment deposition at the trabecular meshwork

8) Intraocular pressure may have diurnal variations. At what time of day would you expect the highest value?
   a. 0100 hours
   b. 0800 hours
   c. 1200 hours
   d. 1800 hours
   e. 2100 hours

9) Which of the following findings is not suggestive of normal tension glaucoma?
   a. Para-central visual field defect
   b. Highest recorded IOP 19mmHg
   c. Narrow anterior chamber angles
   d. Presence of Drance haemorrhage
   e. Neuro-retinal rim thinning inferiorly

10) All patients with normal tension glaucoma require an MRI of the brain to rule out a compressive lesion. True or false?

11) Defects in which ocular structure are thought to contribute to glaucomatous nerve damage in high myopia?
   a. Circle of Zinn
   b. Bruch’s membrane
   c. Optic nerve sheath
   d. Lamina cribrosa
   e. Internal limiting membrane

12) Which of the following optic disc features is not common to both glaucoma and myopia?
   a. Enlarged CDR
   b. Peripapillary atrophy
   c. Neuro-retinal rim notching
   d. Large optic disc
   e. None of the above

13) What is pallor of the neuro-retinal rim most suggestive of?
   a. Compressive optic neuropathy
   b. Normal tension glaucoma
   c. Congenital disc abnormality
   d. Primary (high tension) open angle glaucoma
14) Which of the following is the least likely to cause a visual field defect that respects the vertical midline?
   a. Pituitary macroadenoma
   b. Occipital lobe infarct
   c. Glioblastoma involving the optic radiation
   d. Non-arteritic ischaemic optic neuropathy
   e. Parietal lobe stroke

15) Large diurnal fluctuations in IOP are associated with glaucoma progression. True or false?

16) Superior arcuate visual field defects may indicate:
   a. Normal tension glaucoma
   b. Myopia with tilted discs and peripapillary atrophy
   c. Optic disc drusen
   d. High tension glaucoma
   e. All of the above

17) Which of the following is not a possible indication for brain imaging in a patient suspected of having normal tension glaucoma?
   a. Marked asymmetry of the optic nerves
   b. Absence of neurological signs
   c. Colour vision deficit
   d. Visual field defects not corresponding to optic nerve damage
   e. Optic nerve pallor in excess of cupping

18) Which of the following is not a requirement for a diagnosis of normal tension glaucoma?
   a. Pre-treatment IOP never exceeding 21mmHg
   b. Open angles observed on gonioscopy
   c. Glaucomatous optic disc changes
   d. Decreased colour vision
   e. Visual field defect corresponding to disc changes

19) The aim of treatment in normal tension glaucoma is:
   a. To lower the IOP to a level that prevents or slows further damage to the optic nerve
   b. To achieve an IOP of 20% below baseline
   c. To reduce the IOP to less than 10 mmHg
   d. To lower the IOP as much as possible
   e. To use the greatest number of topical medications with the lowest side-effect profile

20) New onset of breathlessness after commencing beta-blocker therapy for glaucoma would be an indication to stop treatment and seek assistance. True or false?
21) Which of the following measurements is not required for calculation of ocular perfusion pressure?
   a. Intraocular pressure
   b. Pulse rate
   c. Systolic blood pressure
   d. Diastolic blood pressure
   e. None of the above

22) You have just diagnosed a patient with normal tension glaucoma and commenced a topical IOP lowering medication. Which of the following would be most appropriate for this patient’s next follow up?
   a. 6 months with IOP check, HVF 24-2 and optic disc exam to assess for progression
   b. 3 months with IOP check, HVF 24-2, and optic disc exam to assess for progression
   c. 1 week for IOP check
   d. 6 weeks for IOP check
   e. None of the above

23) Which of the following changes suggests glaucomatous progression between reviews?
   a. Presence of new afferent pupillary defect
   b. Increased size of visual field defect
   c. Increased cup to disc ratio
   d. Reduced of retinal nerve fibre layer thickness
   e. All of the above

24) Which of the following IOP lowering treatments is most likely to result in cataract formation?
   a. Selective laser trabeculoplasty
   b. Topical prostaglandin analogue
   c. Trabeculectomy
   d. Topical carbonic anhydrase inhibitor
   e. Topical beta-blocker

25) Lowering blood pressure is an effective tool for treating normal tension glaucoma. True or false?