Case 2 - Primary Open Angle Glaucoma

This case will outline the presentation of a patient with primary open angle glaucoma. It will also cover aspects of medical and non-medical glaucoma treatment, imaging with optical coherence tomography, and systemic associations with glaucoma.

A 57 year old woman was referred by her optometrist for further glaucoma assessment. The optometrist noted raised intraocular pressure in both eyes, optic nerve head asymmetry (with thinning of the inferior neuroretinal rim in the left eye) and a superior arcuate visual field defect in the right eye.

The patient had no family history of glaucoma. She had type II diabetes (diagnosed four years prior), well controlled with oral medication, and was also taking aspirin, medication for hypertension and hypercholesterolaemia.

Initial examination findings are given in the table below:

<table>
<thead>
<tr>
<th></th>
<th>Right Eye</th>
<th>Left Eye</th>
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<tbody>
<tr>
<td>Visual Acuity</td>
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<tr>
<td>Refraction</td>
<td>-2.75/-1.00 x 085</td>
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<tr>
<td>Ishihara Colour Plates</td>
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<tr>
<td>Pupils</td>
<td>Right RAPD</td>
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<tr>
<td>Slit-lamp biomicroscopy</td>
<td>Early nuclear sclerosis</td>
<td>Early nuclear sclerosis</td>
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<tr>
<td>IOP (at 3.45 pm)</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Gonioscopy</td>
<td>Open</td>
<td>Open</td>
</tr>
<tr>
<td>Central corneal thickness</td>
<td>531 µm</td>
<td>535 µm</td>
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Figure 1: Optic disc photographs of the right and left eyes

Question 1: Describe the appearance of the optic disc in each eye.
The cup to disc ratio in the right eye is approximately 0.9. There is thinning of the neuroretinal rim superiorly, and inferiorly, with more advanced rim loss inferiorly. There are no disc haemorrhages associated with the neuroretinal rim thinning. There is a temporal zone of pigmented peripapillary atrophy.

In the left eye, there is generalised cupping, with a cup to disc ratio of approximately 0.7. There is no focal loss of the neuroretinal rim. There is no evidence of a retinal nerve fibre haemorrhage. There is a temporal zone of pigmented peripapillary atrophy. Both optic nerves are moderately large in size.
Figure 2: Right eye visual field

Single Field Analysis

Name: DDB: 10-05-1958
ID:

Central 24-2 Threshold Test

Fixation Monitor Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 5/15 xx
False POS Errors: 8%
False NEG Errors: 0%
Test Duration: 06:27

Fovea: 30 dB

Stimulus: III. White
Background: 31.5 ASB
Strategy: SITA-Standard
Pupil Diameter: RX
Visual Acuity: DC X
Date: 17-02-2016
Time: 4:52 PM
Age: 57

*** Low Test Reliability ***
GHT
Outside Normal Limits

VFI 67%
MD -10.87 dB P < 0.5%
PSD 14.95 dB P < 0.5%

Total Deviation

Pattern Deviation

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**Figure 3: Left eye visual field**

**Single Field Analysis**

**Eyes**: Left

**Name:**

**ID:**

**Central 24-2 Threshold Test**

- **Fixation Monitor**: Gaze/Blind Spot
- **Stimulus**: III, White
- **Background**: 31.5 ASB
- **Pupil Diameter**: Date: 17-02-2016
- **Fixation Target**: Central
- **Strategy**: SITA-Standard
- **Visual Acuity**: Time: 5:03 PM
- **Fixation Losses**: 1/14
- **False POS Errors**: 6%
- **False NEG Errors**: 0%
- **Test Duration**: 04:49

**Fovea**: 20 dB

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**C/L**

**EYE INSTITUTE**

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HFA II 745-0084-5.0/5.0
Figure 4: Retinal nerve fibre layer analysis both eyes

### ONH and RNFL OU Analysis: Optic Disc Cube 200x200

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<thead>
<tr>
<th>Parameter</th>
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<th>OS</th>
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<tr>
<td>Average RNFL Thickness</td>
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<td>79 μm</td>
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<tr>
<td>RNFL Symmetry</td>
<td>25%</td>
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<tr>
<td>Rim Area</td>
<td>0.71 mm²</td>
<td>1.18 mm²</td>
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<tr>
<td>Disc Area</td>
<td>2.38 mm²</td>
<td>2.13 mm²</td>
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<tr>
<td>Average GD Ratio</td>
<td>0.83</td>
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<tr>
<td>Vertical GD Ratio</td>
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<tr>
<td>Cup Volume</td>
<td>0.379 mm³</td>
<td>0.200 mm³</td>
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### Comments

### Doctor's Signature

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SV 20130.0.281
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Figure 5: Ganglion cell complex analysis both eyes

**Ganglion Cell OU Analysis: Macular Cube 512x128**

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<th>OS</th>
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<td>17/02/2016</td>
</tr>
<tr>
<td>DOB:</td>
<td>10/05/1958</td>
<td>16:45</td>
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<tr>
<td>Gender:</td>
<td>Female</td>
<td>5090-5626</td>
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<td>Technician:</td>
<td>Operator, Cirrus</td>
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**OD Thickness Map** | **OS Thickness Map**

Fovea: 258, 67 | Fovea: 258, 70

**OD Deviation Map** | **OS Deviation Map**

**OD Horizontal B-Scan** | **OS Horizontal B-Scan**

BScan: 67 | BScan: 70

**Comments** | **Doctor’s Signature**

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SW Ver: 9.0.0.291
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Question 2: Describe the visual field testing results

The right eye’s visual field is moderately unreliable (fixation losses of 33%, but acceptable false positives and false negatives). Foveal sensitivity is normal. There is a dense superior arcuate scotoma encroaching on fixation. The glaucoma hemifield test is outside normal limits due to the difference between the superior and inferior visual fields. The mean deviation is -10.87 dB and the pattern standard deviation is 14.96 dB (both with a probability of <0.5%).

Reliability indices for the left visual field are all within accepted limits. The left visual field is normal, with a mean deviation close to zero and no significant pattern standard deviation. The glaucoma hemifield test is within normal limits. The left visual field took significantly less time to complete (under five minutes in the left eye compared with eight and a half minutes in the right eye).

Question 3: Comment on the optical coherence tomography (OCT) findings.

The RNFL thickness map shows a reduction of RNFL thickness (compared with an age-matched normative database) in the superior and inferior quadrants of the right eye. There is also loss of the neuroretinal rim in these regions. The inferior quadrant is most-affected, with a thickness of just 47 µm.

In the left eye, there is mild thinning of the inferior RNFL (at six o’clock) compared with the age-matched normative database. The thickness of the neuroretinal rim is within normal limits. There is significant asymmetry between the two eyes.

The GCC scan measures the thickness of the ganglion cell layer and the inner plexiform layer at the macula. The right macular scan shows there is a generalised reduction in GCC thickness, affecting both the superior and inferior regions. The left scan shows there is thinning of the ganglion cell complex in the inferior macular region. The superior region is within normal limits compared with an age-normal database. The inferior thinning in the left eye is less extensive than the inferior thinning in the right eye.

Both the GCC and RNFL scans are of good quality (with a signal strength of ≥6, the recommended cut-off signal strength value for the Zeiss Cirrus OCT).

Question 4: What are the factors that can affect OCT measurements?

A number of factors can influence the quality and accuracy of OCT scan measurements.

- Image quality is affected by eye movement, with larger eye movements leading to greater image degradation. Newer OCT technology attempts to counter eye movement with the use of eye tracking.
- Scans should be well centred. Macular scans should be centred at the fovea. RNFL scans should be centred precisely at the optic nerve head.
• The signal strength of the scan needs to be adequate. The manufacturer recommended signal strength varies between models.
• It is important to check for software segmentation defects. Even scans with adequate signal strength may show segmentation failure (where the automatic segmentation of the layers is incorrect). These scans should be re-taken.
• Although scans can be successfully acquired over a range of pupil sizes, scan quality may be affected if the pupil size is less than 3 mm.
• Lens opacities can give rise to lower thickness values (affecting results by up to 12%), with more advanced lens opacities leading to a greater decrease in thickness. Image repeatability improves following cataract extraction.
• OCT measurements are affected by axial length. Longer, more myopic eyes tend to have thinner RNFL thickness values.
• RNFL thickness decreases slowly with age, by approximately 2 µm per decade.

Question 5: What is the role of macular OCT assessment in glaucoma?
The use of OCT in glaucoma has previously been primarily focused on the assessment of peripapillary RNFL thickness. In recent years, the macular region has emerged as an area of interest; macular damage can occur early in the glaucomatous disease process. Although the macular region represents less than 2% of the retinal area, it contains 30% of the retinal ganglion cells. One of the main advantages of macular assessment in glaucoma is that a significant portion of the retinal thickness at the macula is composed of the RNFL, ganglion cell layer and the inner plexiform layer. Spectral-domain OCT retinal layer segmentation algorithms have allowed for the quantification of individual retinal layers in the macular region, and the measurement of GCC thickness (the combined thickness of the ganglion cell layer and the inner plexiform layer, although macular analysis in some models also includes the thickness of the RNFL). The GCC thins as the glaucoma damage progresses, and reduced thickness values are associated with poorer mean deviation scores on visual field testing. GCC thickness in glaucoma can correlate well with RNFL thinning and visual field loss. Repeatability of GCC measurements may be reduced in more advanced glaucoma. Additionally, GCC measurements will be reduced in patients with high myopic refractive error, or macular pathology, so it is important to take this into consideration when interpreting the results.

Question 6: What is the most likely diagnosis for this patient? Justify your answer.
The most likely diagnosis is primary open angle glaucoma, more advanced in the right eye. This diagnosis was made based on structural and function changes.
There was raised IOP in both eyes. There was a right afferent pupillary defect. The anterior chamber angle was open in both eyes and no angle abnormalities
were noted on gonioscopy. The right optic nerve had characteristic glaucomatous changes, with loss of neuroretinal rim tissue, particularly inferiorly. The optic nerve assessment correlated with the visual field finding; there was extensive inferior rim thinning and a dense superior arcuate scotoma. In addition, the RNFL and OCT scans correlated well with the optic nerve and visual field changes.

In the left eye, despite an identical IOP measurement, there was no functional vision loss, and the glaucoma was classified as pre-perimetric in this eye. There were early changes on OCT examination.

It is important to undertake a complete ophthalmic assessment to determine whether there is any alternative cause of these structural and functional changes. In this case, there was no evidence of any other ocular pathology. There were no signs of secondary glaucoma (eg. Pigment dispersion or pseudoexfoliation).

The patient was commenced on topical ocular antihypertensive therapy, with the first-line treatment being hysite (latanoprost 50mcg/ml) eye drops at night in both eyes.

The patient was reviewed six weeks after commencing hysite eye drops; IOP was 13 mmHg in each eye at 4.00 pm. The patient had an excellent response to hysite. A review examination was scheduled for six months later.

Question 7: Justify the first-line therapeutic agent used to treat this patient.

Latanoprost, a prostaglandin analogue, is commonly used as a first-line ocular antihypertensive in the treatment of ocular hypertension and glaucoma. Latanoprost has a good safety profile and there are few associated systemic side effects. In many patients, latanoprost may sufficiently lower IOP and may reduce the need for multiple IOP-lowering medications. The once a day dosing is preferable as this can help to ensure patient compliance.

Question 8: If, at the six month review appointment, IOP is no longer adequately controlled with latanoprost, what are your treatment options for this patient?

In some patients, latanoprost may not adequately control IOP in order to prevent glaucomatous progression. In these patients, there are several other treatment options.

1) Change from latanoprost to another prostaglandin analogue (eg. travoprost or bimatoprost). There is some evidence that shows a greater IOP lowering effect with these agents compared with latanoprost. Bimatoprost may be more effective than travoprost, however, other authors have found no significant difference between the prostaglandin
analogues. If a patient has already been on latanoprost therapy, they are less likely to experience hyperaemia when switching to travoprost or bimatoprost, than if they started on one of these agents straight away.

2) Consider the addition of a second ocular antihypertensive. In this case, timolol should not be used as a second-line treatment because the patient is on medication for systemic hypertension. An appropriate second-line agent for this patient may be the alpha-agonist, brimonidine 0.2%. There is, however, a high rate of allergy in patients taking this eye drop, and the patient should be made aware of this. In addition, the patient should be informed that brimonidine may cause daytime sleepiness.

3) Selective laser trabeculoplasty (SLT) may be a suitable, non-medical, treatment for this patient, particularly if they are experiencing eye drop-related side effects.

Question 9: In this patient, what other factors need to be taken into account when considering selective laser trabeculoplasty?

SLT is a safe method for lowering IOP. However, the IOP lowering effect of SLT is approximately 20% from baseline, and in this patient a 20% reduction (a 5 mmHg reduction from 25 mmHg) may not be sufficient alone to control IOP (particularly in the right eye), and it is likely that the patient would need to continue medical therapy in order to prevent glaucomatous progression. SLT can also help to reduce diurnal IOP fluctuations.

The cost of SLT needs to be taken into account. The Glaucoma Initial Treatment Study is currently undertaking a trial that is investigating the cost of SLT compared with topical anti-glaucoma medications.

One study has found that pre-treatment with prostaglandin analogues (eg. latanoprost) may reduce the IOP lowering effect of SLT. However, greater presenting IOP is associated with a greater absolute reduction in IOP following SLT.

Question 10: This patient has type II diabetes mellitus. What is the relationship between type II diabetes and glaucoma?

The relationship between type II diabetes and glaucoma is not completely understood. A number of studies have found a higher prevalence of glaucoma (40% higher in the Blue Mountains Eye Study) in patients with type II diabetes, however, some large studies have found no association between the two conditions (the Baltimore Eye Survey).

The Blue Mountains Eye Study found that IOP was statistically significantly higher in the diabetic group, however, the difference between diabetics and healthy subjects was clinically negligible at 0.64 mmHg.

It is thought that the positive association between type II diabetes and glaucoma may be due to detection bias, as patients with diabetes are more likely
to be under ophthalmological observation. It is therefore difficult to design the ideal study to investigate this relationship.

References and Recommended reading


Case 2 - Test

Question 1:
Which of the following features is not necessarily suggestive of glaucoma?

A) Focal thinning of the neuroretinal rim inferiorly  
B) A large optic nerve with a cup to disc ratio of 0.8 and no focal neuroretinal rim thinning  
C) A nerve fibre layer haemorrhage superiorly  
D) Non-pigmented peripapillary atrophy in the region of neuroretinal rim loss  
E) Small optic nerves with a cup to disc ratio of 0.5 in the right eye and 0.3 in the left

Question 2:
When examining the optic nerve head, what should you assess?

A) The size of the optic nerve head  
B) The presence of any beta peripapillary atrophy  
C) The symmetry of the optic nerve appearance between the eyes  
D) Evidence of any focal loss of the neuroretinal rim, particularly in the superior and inferior regions  
E) All of the above

Question 3:
The glaucoma hemifield test...

A) Can be used to diagnose a patient with glaucoma  
B) Was developed for the Medmont perimeter  
C) Analyses the results of five corresponding pairs of points based on the anatomy of the retinal nerve fibre layer  
D) Assesses the asymmetry between the nasal and temporal visual fields  
E) May be abnormal in some patients with no evidence of glaucomatous optic neuropathy

Question 4:
With regard to OCT scans, which of the following is false?

A) RNFL thickness decreases exponentially with age  
B) A patient with a dense cataract may have a falsely low measure of RNFL thickness  
C) It is not possible to directly compare retinal thickness values between different OCT models
D) Eye tracking software incorporated into some OCT models can be used to counter saccadic eye movement and blinking during scanning
E) The resolution of time domain OCT models is poorer than spectral domain

Question 5:
Eyes with greater axial length tend to have thicker RNFL values
TRUE or FALSE?

Question 6:
OCT examination....
A) Can be used in place of a clinical examination of the optic nerve head when monitoring patients with glaucoma
B) Utilises low-coherence interferometry to produce cross-sectional images of the retina
C) Is able to quantify visual function by measuring the thickness of the individual retinal layers
D) B and C
E) A, B and C

Question 7:
Macular ganglion cell analysis...
A) Is not useful in glaucoma as the macular region is not affected until late in the disease process
B) Repeatability is improved in patients with advanced disease due to a floor effect
C) Thickness tends to correlate well with visual field mean deviation in patients with glaucoma
D) May be particularly useful in glaucoma patients with other macular pathology
E) Is not affected by axial length and is therefore more useful than peripapillary RNFL measurements in glaucoma

Question 8:
Which of the following does not affect retinal nerve fibre layer OCT scan quality?
A) Media opacities
B) Saccadic eye movements
C) Axial length
D) Eye colour
E) Scan de-centration
Question 9:
Is the finding of a right relative afferent pupillary defect expected in this patient based on their presentation?

A) No, this is unexpected because the ganglion cell thickness is reduced in both eyes
B) Yes, this is an expected finding due to the asymmetric nature of this patient’s glaucoma, with more advanced structural and functional changes in the right eye
C) Yes, this is an expected finding because all patients with glaucoma will have an afferent pupillary defect
D) No, this is an unusual finding because an afferent pupillary defect indicates asymmetric retro-chiasmal visual field loss
E) Yes, this finding is expected because an arcuate visual field defect is always associated with an afferent pupillary defect.

Question 10:
When assessing glaucoma progression with OCT scans, it is important to discriminate disease-related change from age-related change and measurement fluctuation

TRUE or FALSE?

Question 11:
Prostaglandin analogues....

A) Are the most commonly used first-line treatment in POAG
B) Generally have an average IOP-lowering effect of 50% from baseline
C) Are all equally efficacious in all patients on glaucoma therapy
D) Are available in a combination eye drop (with a carbonic anhydrase inhibitor) in New Zealand
E) Are recommended in the initial management of patients with uveitic glaucoma

Question 12:
If your first-line treatment (in this case, latanoprost) does not cause a reduction in IOP to the target pressure, what is the most logical second-line option for this patient?

A) Take a ‘drug holiday’ for one month and re-start latanoprost to re-evaluate efficacy
B) Stop latanoprost and start monotherapy with a carbonic anhydrase inhibitor and re-evaluate IOP in 4-6 weeks
C) Perform left SLT as it is mainly important to preserve the vision in the least-affected eye
D) Continue latanoprost and add travoprost in the morning then re-evaluate IOP in 4-6 weeks
E) Stop latanoprost and try either travoprost or bimatoprost at night, then re-evaluate IOP in 4-6 weeks

Question 13:
With regard to topical glaucoma management, which of the following is false?

A) An adjunctive medication should provide at least an additional 15% reduction in IOP
B) Conjunctival hyperaemia is the most-commonly reported adverse effect in patients taking prostaglandin analogues
C) Latanoprost tends to give the greatest reduction in IOP when compared with travoprost or bimatoprost
D) The combination drop of timolol and travoprost is no longer subsidised in New Zealand
E) When patients are changed from latanoprost to bimatoprost, a small percentage of these patients will experience increased conjunctival hyperaemia

Question 14:
Before performing SLT, it is important to...

A) Perform gonioscopy to assess the angle structures
B) Discuss the possible risks of the procedure with the patient
C) Stop all IOP-lowering medications for one week prior to treatment
D) A and B
E) A, B and C

Question 15:
Before acquiring OCT scans of the RNFL and/or macula, it is essential to instil mydriatic eye drops

TRUE or FALSE?

Question 16:
If you had a patient with the same presentation as the patient outlined in this case, but they did not have diabetes, how would your initial management differ?
A) It would not differ
B) The target IOP would be higher in the non-diabetic patient
C) The non-diabetic patient would be followed up less frequently
D) Selective laser trabeculoplasty would have been a more appropriate first line treatment
E) You would refer them to their general practitioner for a glucose tolerance test

Question 17:
According to the results of the Blue Mountains Eye Study into account, which of the following is false?

A. Glaucoma prevalence was increased in patients with diabetes (5.5%) compared to those without (2.8%)
B. Diabetes was present in 25% of patients with a diagnosis of glaucoma
C. In 2/3 of cases, the patient was diagnosed with glaucoma before they were diagnosed with diabetes
D. For participants not receiving treatment for glaucoma, IOP was slightly higher in those with diabetes compared with those without diabetes
E. Ocular hypertension was found to be more common in diabetic patients compared with those without diabetes

Question 18:
Which of the following is not an adverse effect associated with selective laser trabeculoplasty?

A) Transient IOP spike
B) Anterior chamber inflammation
C) Swelling of the optic nerve head
D) Cystoid macular oedema
E) Ocular discomfort

Question 19:
If your patient had significant cataract and went on to have cataract surgery, what would you expect to happen to their OCT measurements?

A. Post-operative RNFL measurements would be likely to be higher compared with pre-operative measurements
B. There would be no change in OCT measurements
C. Signal strength would be reduced post-operatively due to increased reflectance from the intraocular lens
D. Any change in OCT measurement values would be due to increasing age
E. Macular thickness values would be reduced post-operatively, but there would be no change in RNFL thickness compared to pre-operative values
Question 20:
Selective laser trabeculoplasty should never be used as a first-line IOP lowering treatment in patients with POAG?
TRUE or FALSE?

Question 21:
Regarding the relationship between glaucoma and diabetes, based on the results of the Blue Mountains Eye Study, which of the following is true?

A) The relationship between glaucoma and diabetes was significantly different between genders
B) The relationship between glaucoma and diabetes was stronger in the older age groups due to smaller numbers
C) Genetic factors are definitely not involved in the relationship between diabetes and glaucoma
D) There was no relationship between diabetes and glaucoma after adjusting for family history, age and gender
E) The relationship between glaucoma and diabetes is difficult to assess as diabetic patients are more likely to receive regular eye examinations

Question 22:
Selective laser trabeculoplasty...

A) Is performed with a 750 nm Nd:YAG laser
B) Targets the non-pigmented cells of the trabecular meshwork
C) Usually leads to a reduction in IOP of at least 40% from baseline
D) Can be effective as both a first line treatment and as an adjunct to medical therapy
E) Is performed following pharmacological dilation of the pupil

Question 23:
Which of the following is true, taking into account this patient’s history and initial examination findings?

A) Brinzolamide 1% eye drops would have been an appropriate alternative first-line treatment for this patient
B) Cataract extraction alone may have produced a sufficient in reduction in IOP
C) The more advanced nature of the patient’s glaucoma in the right eye needs to be taken into account when considering a target IOP
D) The patient’s IOP was possibly overestimated due to the corneal thickness values
E) It would have been appropriate to monitor this patient without treatment for the first six months

Question 24:
Which of the following is not a possible adverse effect of timolol 0.5% eye drops?

A. Decreased libido
B. Depression
C. Hair loss
D. Bronchospasm
E. Daytime somnolence

Question 25:
A patient with type II diabetes is three times more likely to be diagnosed with POAG than an age-matched control

TRUE or FALSE?