

# **Glaucoma and ocular hypertension - assessment of the disc and RNFL**

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## **What's important for Norwegian optometrists**

- Primary Open Angle Glaucoma
- Primary Closed Angled Glaucoma
- Pseudoexfoliation
- Ocular hypertension (OHT)

This lecture will concentrate on these conditions .

## **What are the glaucomas?**

Glaucoma is the name applied to a group of potentially blinding diseases that share the common feature of a characteristic optic neuropathy and corresponding loss of visual function including progressive visual field loss (Salmon & Kanski, 2004)

There are a number of disease processes that lead to the many, varied sub-types of glaucoma, which explains the variety of clinical features that exist between the sub-groups such as differences in symptoms and signs.

## **Epidemiology**

A leading cause of blindness throughout the world. Prevalence of glaucoma throughout the world was 66.8 million cases in the year 2000. About 6.7 million bilaterally blind as a result of the disease. Chronic open angle glaucoma is the 3<sup>rd</sup> leading cause of blindness in the developed world Has recently found to be the second most common single-disease cause of UK blindness and partial sight registrations, accounting for 8% of all certifications.

## **Diagnosis of glaucoma and OHT**

There is no one test.

- Anterior segment assessment
- Optic nerve head and retinal nerve fibre layer assessment
- Visual fields
- Corneal thickness
- Intraocular pressure (up to 50% of POAG patients have “normal” IOP)

Although assessment of the optic nerve is important, it is imperative to understand that glaucoma and glaucoma risk can only be properly evaluated by carrying out a number of procedures

## Anterior segment assessment

### Corneal endothelium

Examine for

- deposited pigment (**PDS**)
- pseudoexfoliative (**PXF**) material
- and keratic precipitates (**KPs**)

Aqueous convection currents, driven by the temperature differential between the iris and cornea, typically cause pigment granules to be deposited in a spindle pattern (Krukenberg's spindle), orientated with its long-axis vertical.

KP are accumulations of inflammatory cells that settle on the corneal endothelium during episodes of uveitis. Ocular inflammation is generally associated with a decrease in IOP, because ciliary body involvement reduces aqueous humour production. However, it can elevate pressure, directly by involving the trabecular-meshwork (trabeculitis), obstructing trabecular outflow with leaked viscous protein and leukocytes, and encouraging the formation of peripheral anterior synechiae (PAS); and indirectly, by its management with corticosteroids.

Glaucoma is more commonly associated with uveitis when the inflammation is recurrent or chronic, and in the special case of Fuch's heterochromic iridocyclitis

### Crystalline lens

Pigment granules, liberated by pigment dispersion syndrome (PDS) or **pseudoexfoliation syndrome (PXF)**, or other causes may settle on any structure in the anterior chamber, including anterior lens capsule. In PXF syndrome, epithelium of lens, pigmented epithelium of iris, non-pigmented epithelium of ciliary body, and possibly zonules of lens, produce PXF material.

PSX is important for Norwegian optometrists as there is evidence that 50% of open angle glaucoma in Scandanavian countries is caused by PSX.

Histologically, PXF material consists of fibrillar proteoglycosaminoglycans that tend to aggregate linearly. They appear as white-translucent granular material.

Deposited PXF material on anterior lens surface classically has bull's eye configuration, because the mid-peripheral region is rubbed clear by the movement of the touching inner border of the iris.

Bright slit-lamp → pupil constriction = < visibility of scalloped edge of these zones. Therefore, often requires mydriasis.

PXF syndrome is an ocular manifestation of a systemic disorder. In affected individuals, PXF material can be detected in visceral organs and the skin, but it is only in the eye that it is known to be of consequence.

## Optic nerve head and retinal nerve fibre layer assessment

### Introduction

*Open angle glaucoma is defined as a slowly progressive optic atrophy, characterized by midperipheral visual field loss and excavated appearance of the optic disc.” (HA Quigley 1996).*

Clinical ability to identify individuals with optic nerve head (ONH) and retinal features consistent with **glaucomatous optic neuropathy (GON)** by ophthalmoscopic examination remains a fundamental skill and cornerstone of clinical practice

### Qualitative Evaluation of the Fundus and Optic Nerve Head in Glaucoma

#### *Retinal Nerve Fibre Layer (RNFL)*

RNFL best viewed with bright, red-free light (green filter), although may also be reasonably visualised with bright achromatic illumination. Best viewed through a dilated pupil, easier to see in eyes with heavily pigmented retinal pigment epithelium (RPE) and choroid and may be indistinguishable in eyes with blonde fundi.

The RNFL appearance consists of bright ‘silver’ striations emanating from the ONH towards the retinal periphery

Rather than being actual retinal nerve fibres, the striations consist of groups of nerve-fibres bundles (grouped ganglion cell axons) held within supportive Müller cell processes. Physiologically, RNFL is most easily seen within 2 disc diameters (DD) of the ONH and is brightest infero- and supero-temporally, where the fibre bundles are most dense, being least visible superior, inferior, temporal and nasal meridians. Visibility decreases with both age and presence of media opacities

In **Glaucomatous Optic Neuropathy (GON)**, RNFL defects can be focal localized or diffuse. Their identification is of considerable value because they have been

shown to precede development of glaucomatous ONH signs and achromatic visual field defects

In primary open angle glaucoma (POAG), the loss of ganglion cell axons follows a characteristic pattern. Initially, there is loss of fibres, most frequently at the inferior and superior poles of the ONH. This results in the development of wedge-like defects in the RNFL. Localized RNFL defects consist of slit, or wedge shaped defects (not spindle-shaped) wider than retinal vessels that are darker than the adjacent areas, within 2DD of the disc margin

The visibility of retinal arterioles provides a clue to the depth of an RNFL defect. In healthy eyes, the vessel walls appear blurred. In contrast, in eyes with RNFL defects the vessel wall appears to stand out in relief due to lack of overlying nerve fibres.

The amount of fundus pigmentation affects the visibility of the RNFL. A dark pigment epithelium enhances nerve fibre layer visibility. The visibility of the RNFL is less good in lightly pigmented eyes, eyes of older subjects and in those with a tessellated fundus.

Loss of striations results in a matt appearance and retinal vasculature within areas of RNFL loss appear more sharply demarcated. Defects smaller than retinal vessels within 2DD of the disc margin, or broader than vessels but >2DD from the disc margin are usually physiological

Diffuse thinning of the RNFL, unless segmentally affecting a single horizontal hemi-retina is difficult to identify.

Because RNFL is not always visible and the difficulties associated with determining the presence of diffuse loss, RNFL defects have been shown to occur in only around 20% of eyes with GON and so have limited sensitivity.

It is also very important to remember that they are not pathognomonic of GON and are markers of optic nerve atrophy of any cause

### ***Parapapillary Atrophy (PPA)***

PPA consists of irregularities of the retinal tissues surrounding some or all of the disc margin. PPA represents disruptions of the retina, with the underlying choroid remaining intact. It differs histologically from myopic scleral crescents and scleral crescents found in tilted discs in which both retina and choroid are affected. It has been divided into two distinct sub-types;

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**Beta zone ( $\beta$  PPA).** This is a pale zone bordering the peripapillary scleral ring and is characterized by visible sclera and large choroidal blood vessels

**Alpha zone ( $\alpha$  PPA).** This is characterized by variable irregular pigmentation of the RPE. On its outer edge it is adjacent to normal retinal tissue, with the inner edge either next to beta PPA, or the peripapillary scleral ring if no  $\beta$  PPA is present

Degrees of  $\alpha$  PPA are present in almost all normal eyes, with  $\beta$  PPA being found in about 15-20% of normal individuals. When present in normal eyes, both zones tend to occur in the temporal horizontal, supero- and infero-temporal regions of the disc margin.

PPA is a valuable sign in identification of glaucomatous structural damage. GON has been shown to be associated with larger size of both PPA zones, and frequency of  $\beta$  PPA occurrence. PPA location has also been shown to be spatially correlated to angular region of greatest glaucomatous disc damage. Change in PPA does not appear to occur in non-glaucomatous optic neuropathies.

### ***Neuroretinal Rim***

When studying ONH features, the first step in any decision-making process should be identification of the relevant landmark structures of the disc margin, (peripapillary ring) and the edge of the optic cup.

### **NRR configuration**

The normal NRR has a characteristic configuration whereby it is usually widest inferiorly, followed by superiorly, nasally and thinnest temporally (>80% of normal individuals). This has been termed the ISNT rule.

This configuration is produced by a number of predisposing anatomical factors including thicker disc arteriole vessels inferiorly, position of the fovea below above the disc centre and least lamina tissue (and greater numbers of nerve fibres) at the disc poles.

The ISNT rule is valuable in detection of glaucomatous changes in the NRR, however it important to remember that: not all normal discs obey the ISNT rule.

Sometimes the differences in NRR width between vertical and horizontal meridians is so slight as to be hard to be sure about whether the ISNT rule is obeyed and in some eyes with glaucoma diffuse NRR loss may be not disturb the ISNT configuration.

As ganglion cell axons are damaged in the course of GON, a progressive reduction in NRR area occurs. NRR configuration will then change and may depart from the physiological ISNT rule.

Glaucomatous NRR loss can take a variety of courses although it is earliest changes occur in the supero- or infero- temporal areas.

### **NRR pallor**

The healthy NRR has an orange or pink colour provided by its internal capillary plexus. The NRR typically takes on a white or even greyish hue with GON which may occur throughout the rim in localised areas. In GON, areas of affected NRR are often associated with pallor within the base of the adjacent cup

Glaucomatous rim pallor is hard to identify in early disease, and so is often one of the later signs to be identified. As with RNFL defects, it should be remembered that pallor is associated with all causes of optic neuropathy and is not pathognomonic of GON.

If the NRR is initially pale, and other features of glaucoma are not present or mild, care should be taken to exclude other optic neuropathies as the cause

### ***Cup Shape***

The optic cup is the 3-dimensional depression in the ONH centre devoid of neural tissue. Cups are present in most ONHs, although size is dependent upon disc size, whereby larger discs are physiologically associated with larger cups.

Physiological cups are usually horizontally oval with depth dependent upon size, larger cups being deeper. Normal cups can appear can be 'dimple' shaped punched out or have a sloping temporal wall

When looking at the cup, care should be taken to distinguish the true cup edge, as identified by a contour change on the disc surface ('contour cupping') from the deepest part of the cup.

True cup edge is best evaluated from looking at small blood vessels as they bend away from the plane of the retina into the cup. It is easy to mistake the pale cup centre closest to the pale underlying lamina cribrosa for the entire cup.

Use of this pale area, which represents the deepest part of the cup ('pallor cupping'), will result in underestimation of cup size – a problem with direct ophthalmoscopy.

As NRR is progressively lost in GON, cup shapes will alter regardless of their initial appearance. Erosion of NRR is such that the cup shape will become increasingly distorted, eventually undercutting the disc margin with most pronounced changes usually occurring at the superior and inferior poles of the disc.

### ***Lamina Cribrosa***

The lamina cribrosa underlies the NRR. It is a connective tissue structure composed of a series of aligned sieve-like plates through which nerve fibre bundles pass on exiting the eye. Although the lamina may not be seen directly, it is often faintly visible through neural tissue at the base of deep optic cups. Visualisation of the lamina ('lamina sign') is therefore useful in discrimination of deep from shallower cups. Physiologically, the lamina is usually relatively flat and normal lamina pores tend to be round.

In GON, the lamina has been shown to be progressively pushed backwards away from the scleral plane and the array of plates compacted, disrupting their alignment.

These changes tend to be most pronounced where least lamina connective tissue is present at the disc poles, and occur least along the better supported horizontal plane. These glaucomatous pathological changes result in elongation of the lamina pores, making them oval or slit-like in appearance when viewed ophthalmoscopically.

### ***Haemorrhages***

Splinter haemorrhages at or directly adjacent to the ONH the disc occur rarely in normal eyes and in between 4-7% of eyes with chronic open angle glaucoma. They occur more frequently in cases of normal pressure type primary open angle glaucoma (POAG).

Observation of such haemorrhages in both normal and high pressure types of POAG suggests that they are caused by a common pathological mechanism.

Although they are therefore a highly specific sign (~99%) and their presence implies that the eye is unlikely to be normal, their low prevalence in glaucoma means they are an insensitive sign for glaucoma detection, although studies are clearly limited by the minimum clinically observable haemorrhage size and review frequency. Furthermore, nerve head haemorrhages are not pathognomonic of glaucoma: they can occur in diabetes, retinal vein occlusion and papilloedema.

**Splinter** haemorrhages are so-called because of their shape, created by the blood following the architecture of the retinal nerve fibre layer. If large, they can adopt a **flame-shape**. Less commonly, deeper haemorrhages of glaucomatous origin can create juxtapapillary **blot** haemorrhages. The time course of splinter haemorrhages is thought to be relatively short, in the order of weeks, although recurrences are common. Photography is useful as evidence of their presence especially when referral may take time.

Areas affected frequently go on to develop focal NRR or RNFL loss. It has been postulated that their frequency increases from early to moderate disease, and decreases with advanced damage.

### ***Vessel Calibre Changes***

Reduction in the diameter of retinal arterioles occurs physiologically with age, but greater amounts of diameter reduction has been shown to associated with optic neuropathies. These changes are thought to be stenotic rather than vaso-spastic in origin. Narrowing can be diffuse or focal in nature.

Without a repeatable measurement technique and baseline measurement, diffuse narrowing can be hard to identify clinically although intra- or juxtapapillary focal narrowing easier. Some studies have shown focal diameter reductions of up to 50%. Because of its age-related physiological occurrence and association with other neuropathies, observation of focal vessel calibre reductions alone is not a good discriminatory variable for GON

### ***Vessel Position***

Blood vessel position does not vary due to direct glaucomatous insult, although is indirectly related due to support by adjacent neural tissue. The position of blood vessels within the ONH can therefore provide clues about areas of NRR loss

### ***Baring of circumlinear vessels***

These vessels are small arteriole or venules that sit upon neural tissue and have a route temporally across the disc towards the macula region. With NRR loss, these vessels are left without adjacent supportive tissue and are said to be 'bared'. They are sometimes referred to as, "flyover vessels". Alternatively, unsupported circumlinear vessels may move towards the cup floor, looking out-of-place due to their angular, superficial appearance.

### ***Bayonet sign***

Vessels that move nasally across the cup base can indicate degrees of glaucomatous NRR loss that has resulted in the remaining NRR being undercut by the pathological excavation. Because these blood vessels travel up the temporal cup face, they will disappear from view when the NRR becomes severely undermined, producing a mismatch between their position at the cup base and on the remaining NRR. Termed "bayonet sign" due to characteristic misaligned appearance, analogous to a bayonet fixing upon a rifle.

### ***Nasalisation of blood vessels***

Physiologically the central retinal artery and vein move through the lamina cribrosa at a locus close the disc centre, the central retinal artery usually being more nasal than the vein. Both make a primary bifurcation into superior and inferior branch

vessels soon after the point at which they are first visible. In the majority of normal eyes, these branch vessels move up the superior and inferior aspects of the nasal cup face towards the retinal plane. More nasal location of the larger branch vessels can be seen as the cup expands pathologically in GON as supportive nasal NRR becomes reduced in breadth.

## Quantitative Evaluations of the Optic Nerve Head

### Optic Disc Size

Like many biological variables, a near Gaussian distribution of optic nerve head sizes exists in the population. Average disc area is around  $2.7\text{mm}^2$  with a range of  $0.8$  to  $6.0\text{mm}^2$ . Discs with areas that exceed 2 standard deviations from the mean have been termed macro- or microdiscs if large or small, respectively.

Although disc size itself should not be used in determining risk of glaucoma development it is important due to well-known physiological relationship between cup size and disc size. Measurement of the vertical disc diameter ('height') and knowledge of normal spread is therefore a fundamental element in routine glaucoma assessment.

A recent large population study found an average disc height of  $\approx 1.5\text{mm}$ , with 98.8% of normal eyes being between  $1.2$  and  $1.9\text{mm}$

Disc height can be estimated using the slit lamp and a condensing (e.g., Volk) lens

Using a narrow slit beam positioned co-axially with observation axis the beam height can be adjusted to match disc height, using the peripapillary scleral ring ('Elshnig's rim') as an external landmark - This landmark should not be included in the measurement as it is not part of the disc

The measured height should be adjusted according to a multiplicative correction based on the magnification factor of the lens used and optical dimensions of the eye to obtain height in millimeters

60D	x0.9
66D	x1.0
78D	x 1.1
90D	x1.3
Superfield	x1.5

### ***Cup to Disc Ratio***

Cup-to-disc ratio (CDR) is the decimal ratio of the size of the cup, as defined by contour, to the disc diameter. Small CDR values therefore indicate that the cup occupies a small proportion of the disc diameter and vice-versa.

Intuitively, because NRR loss due to GON causes a change in CDR, use of this variable would seem appropriate in glaucoma. Given that NRR loss usually occurs at the vertical poles, vertical CDR generally has higher performance than horizontal CDR for discrimination between normal and glaucomatous ONHs and is the measure of choice. However, vertical CDR does not completely separate these two populations.

As mentioned above, this is partly because physiological cup size is positively correlated with disc size and also due to physiological variability in CDR

Although correlated, there is not a direct linear relationship between cup and disc size: large normal discs can have large physiological cups, but cups are often absent in most normal small discs.

For these reasons, clinical use of CDR should always be accompanied by a measurement or statement about disc size.

In order to use CDR to assist differentiation between normal individuals and those with GON, a general rule is that larger CDRs are less likely to be physiological **Inter-eye CDR asymmetries** are suspicious unless there is an inter-eye morphological or disc size asymmetry.

Glaucomatous discs do not have to a large CDR. If an eye with a physiologically small CDR develops glaucoma, the degree of NRR loss may not cause CDR to move into the extreme of the physiological distribution until the disease is advanced.

Taking into account disc size, use of vertical CDR for initial identification of glaucoma can therefore be specific, but has limited sensitivity.

### **Discriminating Between Physiological and Pathological Discs**

It is important to recognise that no single variable allows complete discrimination between physiological and pathological ONHs, because normal individuals sometimes exhibit features associated with glaucoma and individuals with glaucoma sometimes may not exhibit a number of expected disc signs.

In order to be entirely sure that an ONH with features suspicious of GON, corroboration should be obtained from corresponding loss of visual field

In the absence of visual field loss, the most important disc signs suggestive of GON are NRR shape, CDR (accounting for disc size), RNFL defects and presence of disc haemorrhages.

For early detection of GON prior to the development of visual field loss, discs that exhibit a suspicious appearance should be monitored for change over time to increase certainty.

## **Summary points**

- PSX common in Norway. Use slit lamp on all adults and also check van Herick routinely
- Think 50% of POAG have normal IOP
- Careful, skilled ophthalmoscopy important and longitudinal monitoring of discs very helpful
- Without visual checks optometrists' sensitivity and specificity for detecting glaucoma will not be optimum

## Example referral letter

Dear Dr

Re: Mrs

I saw Mrs for a routine eye examination today. She is asymptomatic and had lost her reading glasses. She is in good health, is not taking any medicines and there is no family history of ocular disease.

Unaided vision is R. 6/5 L. 6/5. Refraction gave R. +0.25DS = 6/5 L. 0.00DS = 6/5 Add +2.00DS for reading = N4 at 40 cm.

External eyes, pupillary reflexes, ocular motility and ocular motor balance are normal. Slit lamp microscopy shows open angles but I did observe some pseudoexfoliative deposits on the anterior lens capsule right eye. The ocular media were otherwise clear and the ocular fundi appeared normal with CD ratios of 0.3 on 1.8 mm diameter discs. Intraocular pressures were R. 18 L. 18 mmHg.

In view of the pseudoexfoliation findings I would be pleased if you would keep her under ophthalmological review.

Yours sincerely

## **Acknowledgments**

I wish to fully acknowledge the adaption of this lecture from the Institute of Optometry Prescriber course module on glaucoma.

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