CLINICAL EVALUATION OF PRIMARY OPEN ANGLE GLAUCOMA

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INTRODUCTION

An in-depth clinical evaluation is important for the correct diagnosis of primary open-angle glaucoma (POAG).

A full assessment involves the following:

- Preliminary tests
- Anterior segment slit-lamp examination
- Posterior segment examination
    - Optic nerve head
    - Retinal nerve fiber layer
- Psychophysical assessment and Imaging

PRELIMINARY TESTS

A large number of clinical tests may be performed in order to decide if a person has POAG. These tests are also beneficial to monitor any progression of the disease process.

PATIENT CASE HISTORY

Taking a patient's history is used to aid in the diagnosis of POAG and to identify risk factors for development and progression of glaucoma.

It is important to uncover risk factors for primary open angle glaucoma that include the following:

- Age
- Race
- Family history
- Systemic hypotension, migraines, Raynaud's syndrome
- Sleep apnea, Graves Disease/Thyroid disease
- Diabetes, systemic hypertension
- Past use of topical or oral corticosteroids
- History of trauma
- History of inflammatory conditions (uveitis)
- Determine the use of any medications and ascertain the presence of any allergies.
- Determine the use of any systemic Beta-blockers or other IOP lowering systemic medications.

VISUAL ACUITY MEASUREMENT

- Visual acuity is not affected in early to moderate glaucoma
- It is affected in the later stages of disease
- Cloudy vision and reduced visual acuity occurs with angle closure glaucoma

Measurement of Refractive Error

- Important for accurate perimetry
- Hyperopia – increased risk of angle closure
- Myopia
  - association with increased risk of open angle glaucoma
  - associated with pigmentary glaucoma

PUPIL REACTIONS

- Not affected until later stages of the glaucoma disease process
- Relative afferent pupillary defect (RAPD) can occur in advanced asymmetric POAG

CONFRONTATION VISUAL FIELD ASSESSMENT

- Not affected until later in disease
- Constriction of four quadrants or hemifield may be noted in advanced glaucoma
- Necessary to monitor the progression of any glaucoma diagnosis

EXTERNAL EXAMINATION

- Not affected in POAG but may be abnormal in secondary glaucoma
- Ptosis, facial scars may help differentiate traumatic glaucoma
- Port wine stain – Sturge-Weber syndrome
- Thyroid orbitopathy – proptosis, lid swelling, etc

ANTERIOR SEGMENT SLIT-LAMP EXAMINATION

Careful examination with the slit-lamp of the anterior segment can assist in the differentiation of primary open angle glaucoma from other types of glaucomas (Table 1).

Structure	POAG	Other Glaucoma
Conjunctiva, episclera, sclera	Unaffected (if untreated)	Injection: Elevated episcleral venous pressure
Cornea	Unaffected (Punctate epithelial defects seen with treatment)	Opacities – trauma, developmental anomalies Krukenberg Spindle – Pigmentary Dispersion Syndrome (PDS) Grey fibrilo-granular material - Exfoliation Syndrome Keratic precipitates – past or current uveitis
Iris	Unaffected	Transillumination and/or atrophy – PDS, Exfoliation syndrome, ICE, pigment or exfoliative material Synechiae – past or active uveitis Heterochromia – Fuchs' iridocyclitis, pigmentary glaucoma, chronic uveitis
van Herrick Angle and Anterior Chamber	Open	Narrow
Lens	Unaffected Early cataracts with treatment	Pigment – PDS, uveitis glaucoma Exfoliative material – Exfoliation syndrome Early PSC – long term steroid use Asymmetric cataract – trauma

Table 11.1: Anterior segment signs associated with glaucoma

This topic is covered in greater detail in Chapter 13, *Differentiating primary open angle glaucoma.*

GONIOSCOPY

- This procedure provides a view of the anatomical angle and its supporting structures.
- Importance of gonioscopy:
  - Aids in identifying the type of glaucoma present and subsequent management
  - Aids in risk assessment related to angle closure upon dilation
  - Can identify developmental abnormalities in the anterior chamber (see Chapter 6)
  - Can assist in therapeutic management as well i.e. laser trabeculoplasty, breaking of synechiae
- Can be performed by using either a 3 or 4 mirror gonioscopy lens
  - A 3-mirror lens requires coupling solution and rotation of the lens to obtain a view of each quadrant
  - A 4-mirror lens does not require coupling solution. The light source is moved into each mirror

- Performing the procedure
  - Examine the anterior segment, paying close attention to the cornea for smoothness
  - Instill a drop of topical anesthetic for comfort
  - Apply the gonioscopy lens safely and efficiently
  - Rotate the lens to view all four quadrants (inferior, superior, nasal, and temporal)
- Recording results
  - Identify the most posterior structure visible (ciliary body, scleral spur, posterior trabecular meshwork (Schlemm's Canal), anterior trabecular meshwork, Schwalbe's Line
    - Begin the procedure by viewing the inferior angle – as it is the widest with easily identifiable structures
  - Notation of amount of pigment present, PXE debris, neovascular vessels, synechiae
  - Notation of the iris approach
    - For example: in PDS the approach will be concave
- Gonioscopy is contraindicated in cases of a hyphema, open globe injury, or active corneal keratitis

POSTERIOR SEGMENT ASSESSMENT

Structural assessment of the optic nerve and retinal nerve fiber layer is important for the diagnosis of glaucoma and monitoring of its progression.

Some of the instrumentation available to the clinician is as follows:

- Ophthalmoscopy
- Slit-lamp assessment with appropriate lenses
- Stereoscopic photography
- Scanning laser tomography
  - Heidelberg Retinal Tomographer
- Optical Coherence Tomography (OCT)
- Scanning Laser Polarimetry
  - GDx

OPTIC NERVE HEAD EVALUATION

The optic nerve should be evaluated stereoscopically through a dilated pupil. This provides a better view of the neuro-retinal rim tissue. Lenses that are ideal for the stereoscopic evaluation of the optic nerve often include a 90 D, 78 D or 60 D lens used in conjunction with a slit-lamp. A Hruby lens used with the slit lamp is also an excellent lens to evaluate the optic nerve. It is important to remember that the observed image is reversed and inverted. Stereo photos are an excellent way to record the appearance of the optic nerve.

There are five major aspects of an optic nerve head evaluation listed below.

1. Scleral ring – Physiological nerve size
2. Neuro-retinal rim tissue
3. Retinal nerve fiber layer
4. Region of peri-papillary atrophy
5. Retinal nerve haemorrhages

1. SCLERAL RING

The optic nerve shape typically takes a vertical oval form. An abnormal optic disc shape is significantly correlated with corneal astigmatism and amblyopia but does not correspond to an increase in glaucoma susceptibility.

PHYSIOLOGICAL OPTIC NERVE SIZE

There are normal physiological variations in the size of the optic disc and the cup to disc ratio. Generally speaking, large physiological discs will have large physiological cups (and higher cup to disc ratios). A small disc with a moderate cup (example of cup to disc ratio of 0.5) could be indicative of a glaucomatous optic nerve.

- Clinical optic nerve size estimation
  - Should be done on every patient
  - Population variation:
    - African Americans have larger optic discs and larger optic cups than Caucasians
  - Gender variation:
    - Optic disc is 2-3% larger in men than women
- Symmetry of optic nerve size
  - Helpful in differentiating asymmetric cupping from asymmetric optic nerve size (ie. if one optic nerve is larger than the other, the cup to disc ratios will also be asymmetric)

MEASURING OPTIC NERVE SIZE

- Different options for measurement of optic nerve
  - Measure with instrumentation (e.g. HRT)
  - Estimate the number of arterial blood vessel widths (should be 10-12)
  - Estimate with VOLK (60 D, 66 D, 78 D) lenses at slit lamp
    - Thin vertical beam of light focused on retina
    - Adjust beam length to coincide with superior and inferior edge of optic disc
    - Read measurement from slit lamp scale in mm
    - Adjust for magnification
      - Volk 60 D x 1.0
      - Volk 78 D x 1.1 (Figure 11.1)
      - Volk 90 D (or SuperField) x 1.3

It is always important to keep in mind the size of the optic nerve. If the patient has asymmetrical optic nerve size, then the cup may be asymmetrical as well without having glaucoma.

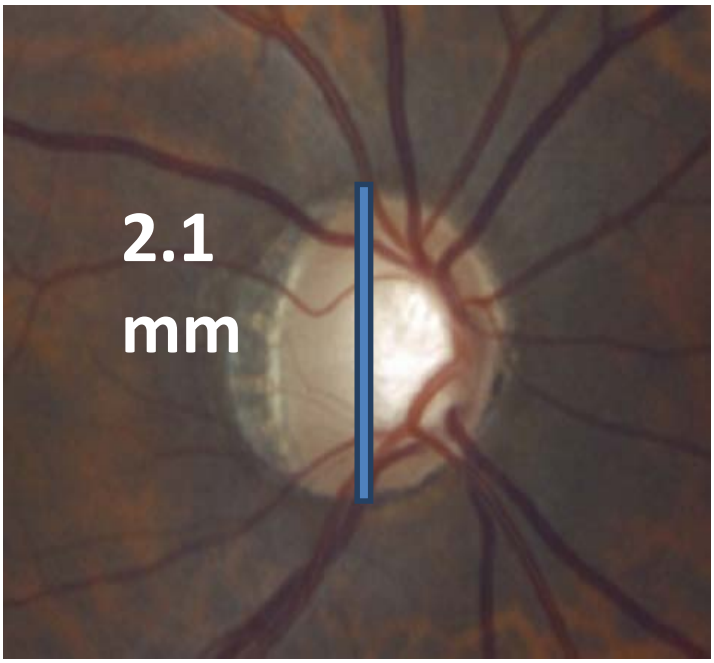
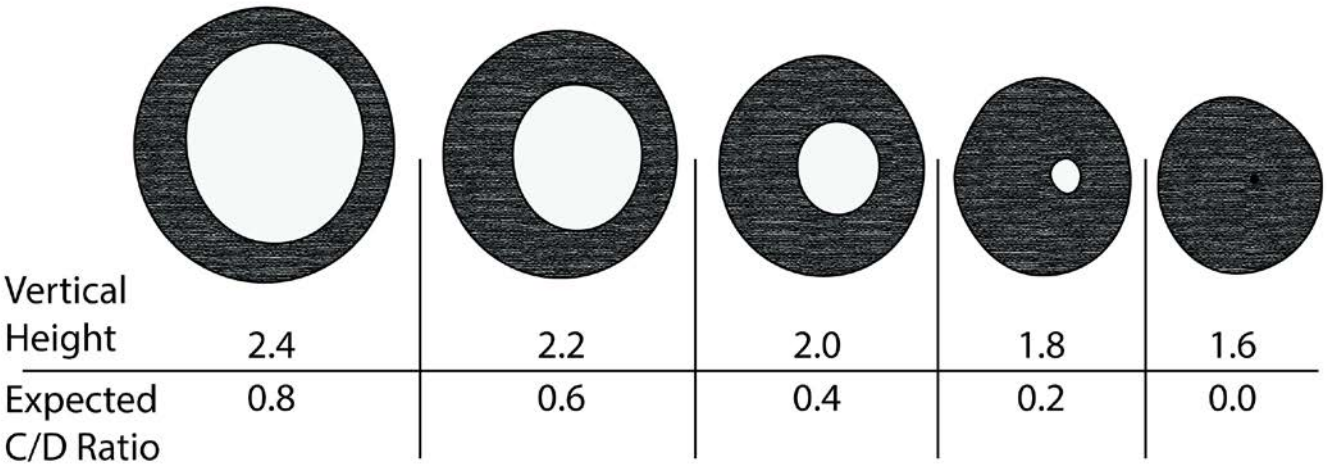


Figure 11.1: *Measurement of the optic nerve size using a 78 D lens*

2.1 x 1.1 = 2.31 mm - this is a greater than average nerve size



Adapted from Litwak A, Glaucoma Handbook

Figure 11.2: *Optic nerve size and estimated C/D ratio. This is an estimation of what you would expect a normal cup to disc ratio to be in different size nerves.*

2. NEURO-RETINAL RIM TISSUE

Assessment of the neuro-retinal rim tissue is a key factor in glaucoma diagnosis.

RIM SHAPE

- Need to assess the health of the rim tissue
  - Colour – rule out pallor
  - 'ISNT' Rule – most neuroretinal rims follow this pattern
    - Inferior rim thickest
    - Superior rim
    - Nasal rim
    - Temporal rim thinnest
  - Greater risk of damage vertically
    - Vertical poles 1.5-2.0 x thicker
    - Superior and inferior rim should be thicker than the nasal and temporal rim

ASYMMETRY

- Asymmetry in vertical meridian could indicate glaucoma
- Asymmetry between the two eyes can be used to diagnose glaucoma damage
  - Be careful there is no asymmetry between the optic nerve size
  - $\geq$ 0.2 asymmetry is abnormal – in symmetric sized nerves

PATTERN OF NEURO-RETINAL RIM LOSS

- Most common pattern of rim tissue loss:
  - Infero-temporal > Supero-temporal > Temporal horizontal > Nasal inferior > Nasal superior
- This sequence of loss correlates with the progression of visual field defects
- Glaucomatous loss of neuro-retinal rim can be more diffuse and can occur in all sectors of the optic nerve which is harder to determine on clinical exam

FACTORS ASSOCIATED WITH PATTERN OF RIM LOSS

- Physiological configuration of the rim is broader at the inferior and superior disc poles than at nasal and temporal poles
- The inner surface of the lamina cribrosa shows larger pores and a higher ratio of pore to inter-pore connective tissue area in the inferior and superior regions
- Backward bowing of the lamina cribrosa to the outside is mainly in the inferior and superior disc regions
- The lamina cribrosa is thicker in the disc periphery where the nerve fiber bundles have a more bent course through the lamina

JUDGING CUP TO DISC RATIO

This measurement is recorded as a ratio of the size of the cup relative to the size of the disc. To be most accurate this measurement is recorded as a vertical cup to disc ratio and a horizontal cup to disc ratio (Figure 11.5).

The ratio is written as a percentage in the vertical/horizontal meridians – e.g. if the cup consumes 35% of the disc vertically and 25% horizontally, the ratio would be .35/.25

In glaucoma, the cup to disc ratio value is less important than the assessment of the rim tissue of the optic nerve

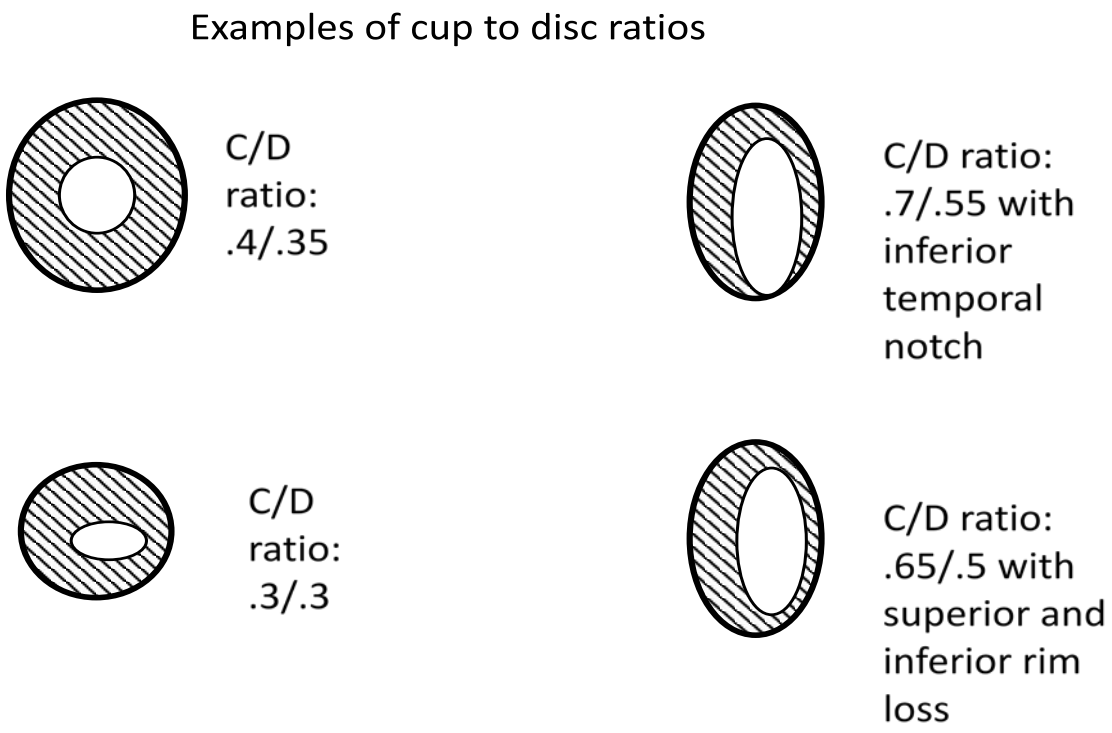


Figure 11.5: *Examples of the cup/disc ratio*

NORMAL DISC APPEARANCE

There are normal physiological variations in the size of the optic disc and the cup to disc ratio. As discussed earlier in this chapter, large physiological discs will have large physiological cups.
A small disc with a moderate cup could be a glaucomatous optic nerve.

TIPS ON USING THE CUP/DISC RATIO

- There is a significant degree of inter-observer variability when judging the cup/disc ratio
- A stereoscopic view is needed to make the best assessment
- Judge the deflection points of the disc vessels to get borders of optic cup
- Don't rely on colour changes only
    - Border of the cup is determined by the contour, not the pallor
    - Saucerization of the cup occurs causing a larger cup when viewed stereoscopically
- Stereo optic nerve photographs are the key to monitoring successfully any glaucoma progression

3. EXAMINATION OF THE RETINAL NERVE FIBER LAYER (RNFL)

In addition to assessing the optic nerve and neuroretinal rim, a glaucoma assessment should include evaluation of the retinal nerve fiber layer (NFL). Defects of the NFL may precede structural changes to the optic nerve.

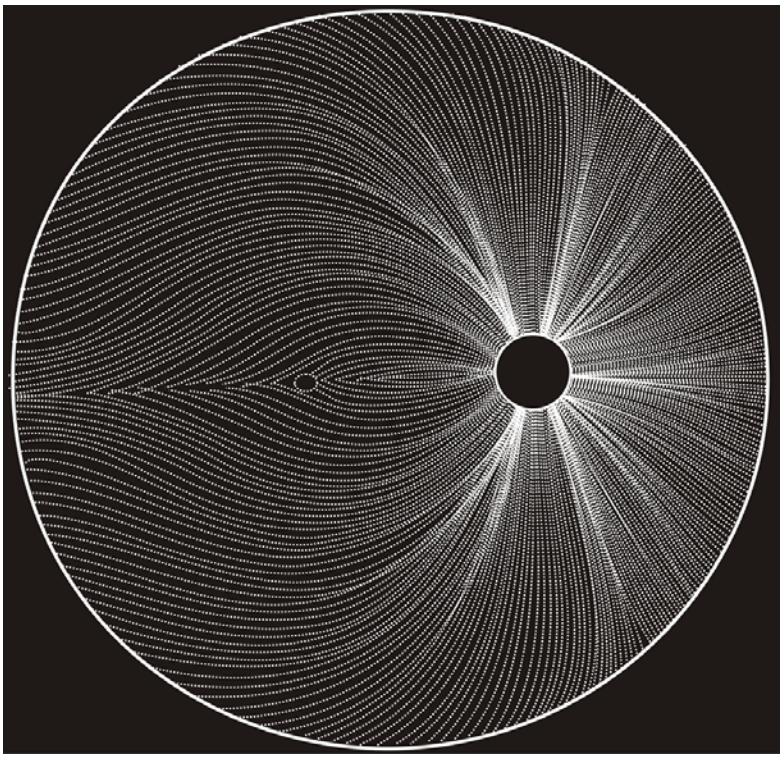


Figure 11.6: *Anatomy of the retinal nerve fiber layer*

- Axons from the temporal retina arc above and below the fovea form the arcuate bundles
- These axons become the superior and inferior neuro-retinal rim tissue of the optic nerve – these regions of the rim are typically affected first in glaucoma
- Nerve fiber layer is thicker and clinically appears brighter in the arcuate bundles than in the papillo-macular and nasal bundles
- Characteristic bright-dimmer-bright pattern, RNFL casts a white haze over the underlying retinal structures and obscures the smaller tertiary retinal blood vessels
- Nerve fibers within the neuro-retinal rim are retino-topically arranged
- Axons from ganglion cells close to the disc lie more centrally and axons from cells peripherally lie at the optic nerve head margins – this corresponds to the distribution in the RNFL
- Damage is at level of the lamina cribrosa → retrograde atrophy back to ganglion cell body in retina
    - Ganglion cell axons die → corresponding loss of neuro-retinal rim tissue → visual field defect occurs

- Selective damage to superior and inferior arcuate bundles with relative sparing of papillo-macular and nasal bundles
- Defects appear as darker zones in areas of expected brightness
- 20-50% of ganglion cell axons die before a visual field defect occurs
    - RNFL damage can precede white-on-white field defects by 6 years
- Therefore RNFL analysis is **important for early diagnosis**!

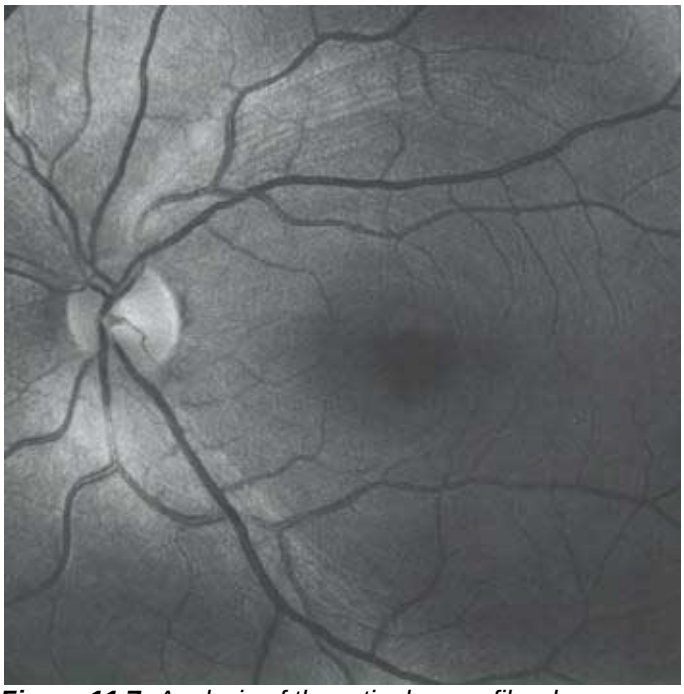


Figure 11.7: *Analysis of the retinal nerve fibre layer*

CLINICAL RNFL EXAMINATION

Using a red-free (green) filter on the slit lamp and a bright light source, dark slit-like defects within the RNFL may be noticed in patients with glaucoma. The wedge-like defects or diffuse defects in the RNFL are perhaps the earliest of all objective signs, but they are only detectable with experience and optimal viewing conditions.

Some of the main features for viewing RNFL defects are as follows:

- Examination can be done at slit lamp with stereoscopic view (using 60 D, 78 D lens)
- Bright light source and red-free (green) filter are required
- Green light produced by red-free (green) filter is absorbed by the pigment in the retinal pigment epithelium and choroid
    - Creates a dark background to highlight the RNFL defect
- RNFL defect will reflect light and be contrasted against the dark background
- Best done after the optic nerve evaluation
- This technique can be performed with black and white or red-free (green) filter photography.
- Brightness depends on:
    - Integrity of the RNFL bundles
    - Amount of pigmentation in the retinal pigment epithelium and the choroid
    - Proximity to optic nerve
        - Ideally should examine within 1-2 disc diameters (DD) from the ONH
    - Age
        - Humans naturally lose 2500 ganglion cells axons per year
- Brightness pattern should be symmetric between superior and inferior arcades, and between the two eyes

Advanced software on newer Spectral-Domain OCT's also allows for analysis of the ganglion cell layer, as well as glaucoma progression analysis. For more information on OCT analysis in glaucoma, see *Chapter 9: Imaging in Glaucoma.*

FOCAL DEFECTS: SLIT VERSUS WEDGE

Slit Defect

- Normal variation
- Usually less than the width of an arteriole
- Does not expand into periphery
- Does not go all the way back to nerve

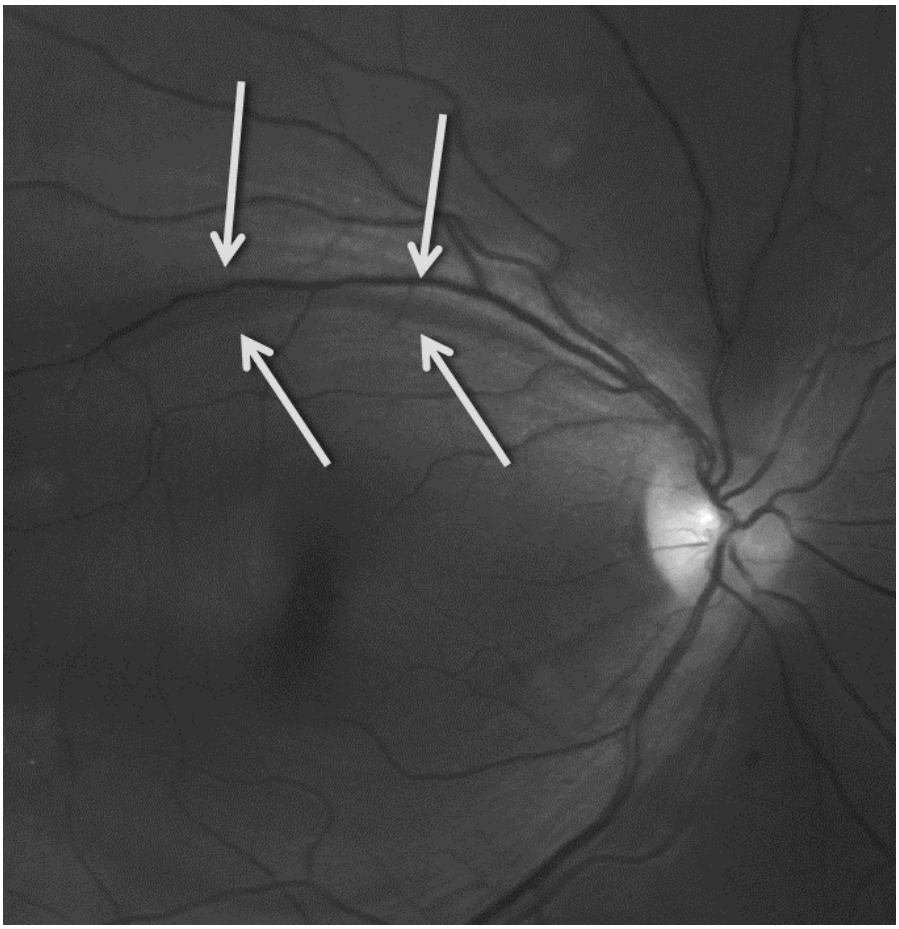


Figure 11.8: *Slit defect*

Wedge Defect

- Pathological
- Larger than slit defects, greater than the width of an arteriole
- Expands into periphery
- Narrows close to the optic nerve
- Extends back to the optic nerve
- Usually associated with a notch at the disc
- Will generally have a corresponding visual field defect

Figure 11.9: *Wedge defect*

Diffuse Loss

- Most common pattern of RNFL loss in POAG
- NFL slit or wedge defects may progress to diffuse NFL defects typically in the superior and inferior arcuate zones. This corresponds to loss of rim tissue in the affected area on the optic disc.
- NFL starts to look thinned or raked
- Look at:
    - Brightness comparison between upper and lower
    - Visibility of tertiary blood vessels
        - Normal will be blurred
        - RNFL defects vessels will be visible
        - May see whitening around vessel wall

4. REGION OF PERIPAPILLARY ATROPHY

Peripapillary atrophy is characterized by irregular pigmentation around the nerve head. This is a non-specific finding because it does occur in normal eyes. PPA has been thought to occur more frequently in normal tension glaucoma than POAG.

- Divided into alpha and beta zones
    - Beta = beside the nerve
    - Alpha = away from the nerve
- Is associated with acquired damage to optic nerves from glaucoma when located adjacent to a pathologically thin neuro-retinal rim

- Alpha and Beta zones
    - Beta Zone:
        - Area adjacent to the optic nerve
        - Width of beta zone inversely correlates with rim width
        - Larger beta zone → thinner rim
        - Progression is associated with progressive glaucoma
        - More extensive in glaucomatous eyes
    - Alpha Zone:
        - Adjacent to the outer surface of zone beta – areas of atrophy are hyper or hypo-pigmented with thinning of the chorio-capillaris
        - Non-specific finding

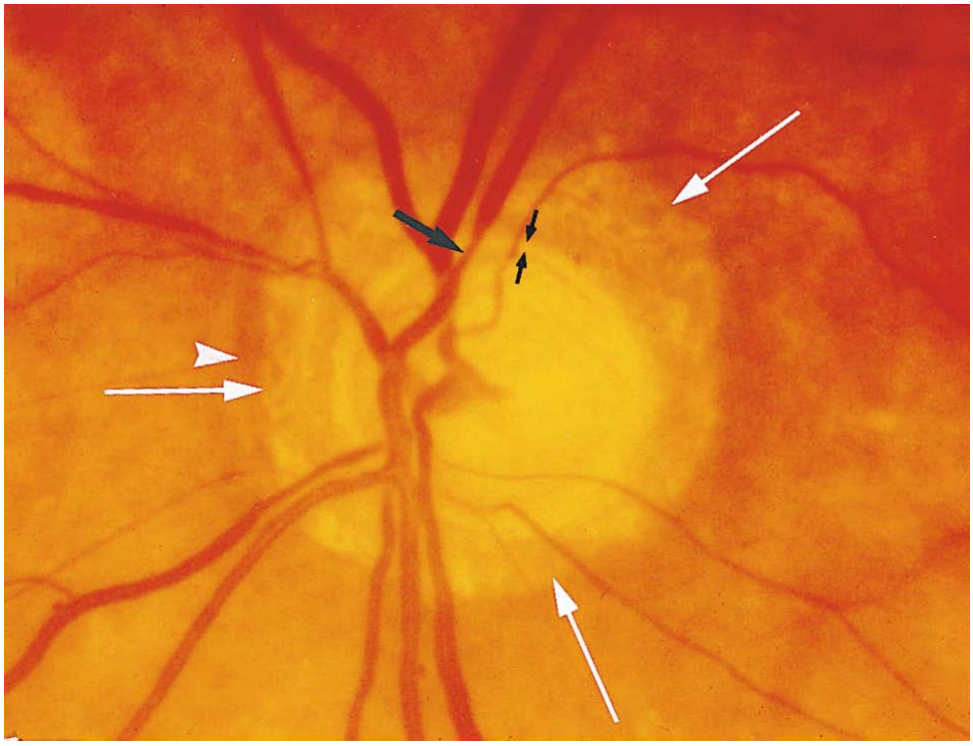


Figure 11.10: *Zones of peri-papillary atrophy*
Large arrows = beta zone
Arrow heads = alpha zone

5. RETINAL OPTIC NERVE HEMORRHAGES: DRANCE HAEMORRHAGE

The appearance of disc haemorrhages may precede RNFL loss, notching and visual field defects. Disc haemorrhages are associated with progressive visual field defects in glaucoma.

- The haemorrhages are often very subtle in appearance
- Appear on or near the disc surface
- Occurs on neuro-retinal rim (often inferior) or in the peripapillary area

- Occur in up to 30% of glaucoma patients
- More likely in Normal Tension Glaucoma
- More commonly occur in the inferior pole
- **Drance hemorrhage by definition is** a hemorrhage located within 1 DD of the optic nerve that is caused from glaucoma
    - Flame shaped = RNFL
    - Dot shaped = Optic disc
- Haemorrhages may also be seen in other eye diseases such as (if present from other disease would not be called 'Drance' hemorrhage):
    - Posterior vitreous detachments
    - Diabetes Mellitus
    - Branch retinal vein occlusions
    - Anticoagulation therapy

HOW TO EXAMINE AN OPTIC NERVE: SUMMARY

1. Scleral Ring – Physiological Nerve Size and Shape
    - Optic nerve head size
    - Optic nerve head shape
2. Neuro-retinal Rim – Rim Size and Shape
    - ISNT Rule i.e. the inferior rim is the thickest and the temporal rim is the thinnest
    - Position of central retinal vein (CRV) trunk exit
    - Rim asymmetry
    - Focal damage – rim, vessels
    - Colour – is there any pallor?
    - Depth of cup
3. Retinal Nerve Fiber Layer
    - Focal or diffuse loss
4. Region of Peripapillary Atrophy
    - Alpha or Beta Zone
5. Retinal Nerve Haemorrhages
    - Presence or absence

DIFFERENT GLAUCOMATOUS CUP/DISC CLASSIFICATIONS

The differences in classification of the cup/disc appearance in glaucoma are based on the cup depth and the rim shape.

FOCAL

Discs of this type are characterized by localized neuro-retinal rim tissue loss which occurs within the cup at the inferior and superior pole – further progression results in thinning and eventually the complete loss of rim tissue in the area of the original notch – eventually a focal area of rim sharpening develops that may be associated with a bayonetting of disc vessels lying in the region of the notch.

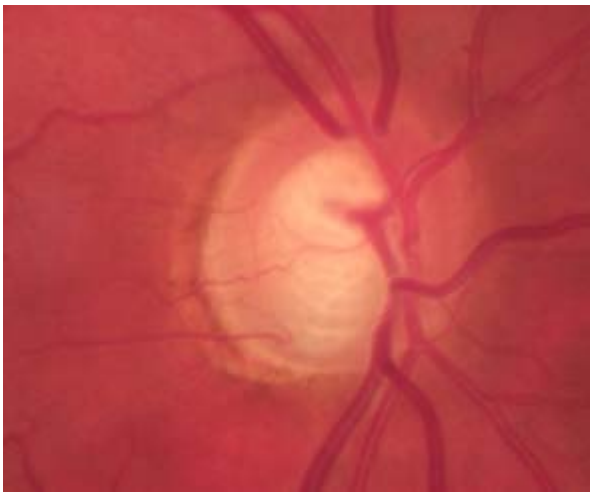


Figure 11.11: *Inferior focal notching*

MYOPIC

Myopic Disc (Type 2) – myopic patients with tilted discs may develop glaucoma with a characteristic, myopic glaucomatous optic disc appearance. Discs of this type are tilted (obliquely inserted) with a shallow appearance and may have a myopic temporal crescent. Such a disc will usually develop thinning of the superior and/or inferior neuro-retinal rim.

Figure 11.12: *Myopic tilted disc with temporal crescent*

SENILE SCLEROTIC

Senile sclerotic (atrophic glaucoma) – diffuse neuro-retinal rim tissue loss may result in tissue thinning within the rim, the absence of rim area or a volume loss. The tissue can be likened to having the consistency of a sponge rather than a solid.

CONCENTRIC

Concentric Cupping – generalized enlargement of the optic cup with no localized areas of defect and no moth eaten appearance of the rim tissue. This appearance is often associated with generalized nerve fiber layer loss.

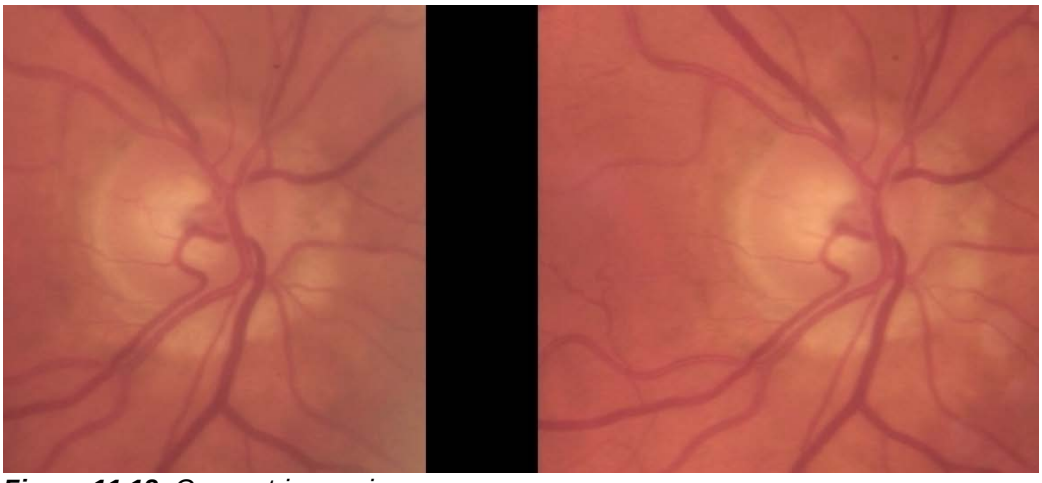


Figure 11.13: *Concentric cupping*

SAUCERIZATION

As reduction in neuro-retinal tissue occurs, the loss pattern produces a disc with shallow cupping and gently sloping cup margins surrounding a central pale cup. The cupping is greater than pallor alone.

ADVANCED

In advanced glaucoma, the rim remnants are located mainly in the nasal disc sector.

SUMMARY OF CLINICAL FEATURES OF GLAUCOMATOUS OPTIC NEUROPATHY

Clinical Feature	High-Tension POAG	Low-Tension POAG
IOP	> 21 mmHg	< 22 mm HG
Optic Cup Appearance	Round and concentric, steep-walled, often deep	Sloping, eccentric, often shallow
Neuro-retinal Rim Tissue Appearance	Even, symmetrical, no notches	Greater loss at superior and inferior poles
Disc Haemorrhages	Less frequent	More frequent
Peripapillary Atrophy	Less Common	More common
RNFL defects	Diffuse atrophy	Localized atrophy

NORMAL TENSION GLAUCOMA (NTG)

Some important characteristics of NTG are:

- It is no longer considered a separate entity
- It is on the other end of the continuum of open-angle glaucoma
    - Mechanism shifts from elevated IOP to factors independent of IOP
        - Vascular?
        - Intracranial pressure?
- It is a bilateral, slowly progressive condition

  - Evidence that it may progress at a slower rate than high IOP POAG
- Distinguishing clinical features that differentiate it from high IOP-induced glaucomatous optic neuropathy
  - Paracentral visual field defects, greater peripapillary atrophy, more focal rim thinning

REFERENCES

Gonioscopy: A Text And Atlas (With Goniovideos) By Tanuj Dada, Reetika Sharma, Amit Sobti Jaypee Brothers Medical Publishers New Dehli 2013