The Retina
An anatomical journey from the foveola to the periphery

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MOptom programme
Retina Course
Hadassah College 2011

I am indebted to my friend, Professor Jan Bergmanson, University of Houston for much pure anatomy parts of this lecture which I have adapted for this lecture

Lecture Outline

• Retinal development
• Retinal anatomy
• Clinical landmarks
• Vitreous

Development

• Optic vesicle develops before 4th week of pregnancy
• Invaginates during 4th week to form optic cup
• 2 layers of neuroectodermal cells are joined at apices
• External one becomes RPE and remains a monolayer

• Internal one differentiates to become neural portion of retina
• Final organisation of neural retina not completed until after birth

• Initially, the retina obtains blood supply from the hyaloid circulation
• Retinal artery and vein appear in the fourth month to replace hyaloid vessels
• Takeover by retinal artery and vein completed by 5th month
• But final adult vasculature pattern not achieved until after birth – note retrolental fibroplasia/retinopathy of prematurity

Glial remnants
• Posterior portion of hyaloid artery may persist extending into the vitreous from the disc surrounded by glial tissue (Bergmeister's papilla)
• Persistent hyperplastic primary vitreous

• Optic nerve becomes progressively myelinated in a proximal to distal direction and at birth this process has reached lamina cribrosa
• Myelination normal stops at this point but in some individuals the process continues beyond the time of birth

• Normal retina transparent except for pigment in blood
• Sensory retina thin and weak
• Susceptible to full thickness breaks
Retina composed of inner neural or sensory layers and outer pigment epithelium

1. Pigment epithelium layer
   - RPE made up of cuboidal cells which contain the two pigments:
     - Melanin
     - Lipofuscin
   - In retinal separation these cells tend to remain attached to the choroid and separate from the rest of the retina

• The function of the pigment epithelium is to:
  - Remove water and maintain ionic micro-environment
  - Nourish the outer parts of the retina
  - Phagocytose detached discs from the rod and cone outer segments

• Shed discs from the outer rod segment are enclosed by delicate cytoplasmic extensions of the pigment epithelium (PE)
• Are drawn into the cytoplasm of the PE and broken down

Retinal layers (outermost to innermost)
1. Pigment epithelium (RPE)
2. Photoreceptor Outer and Inner Segment Layers (OS & IS)
3. External Limiting Membrane (ELM)
4. Outer Nuclear Layer (ONL)
5. Outer Plexiform Layer (EPL)
6. Inner Nuclear Layer (INL)
7. Inner Plexiform Layer (IPL)
8. Ganglion Cell Layer (GCL)
9. Nerve Fibre Layer (NFL)
10. Internal Limiting Membrane (ILM)
2. Photoreceptor outer and inner segment layers

- Made up of outer and inner segments of the rods and cones
- **Cones** are receptors for high acuity and colour under light adapted conditions and are found in greatest concentrations at fovea
- **Rods** are used in dim light and dominate periphery of visual field
- Rod density highest approximately 20° outside fovea

- Inner and outer segment of rods and cones connected by a ciliary stalk which functions as a supply channel
- Proteins and lipids will pass from the inner to the outer segment through the cilium

- Outer segments are composed of approximately 2000 discs stacked upon each other
- They contain visual pigment proteins called **opsins**
- Rods contain **rhodopsin**; cones contain **opsins** tuned to long, medium and short wavelengths

- In monkey, 80-90 new discs are formed each day and the entire stack of membranes is replaced every 9-12 days, throughout life
- To compensate, there is regular shedding of discs from scleral end of outer segment
- A similar process occurs in cones
There is an age-related receptor cell loss in retina and in diseases such as Age Related Macular Degeneration this loss becomes accelerated.

3. External Limiting Membrane
- Due to the perforations by receptor cells, this membrane appears as a netting
- Not a true membrane but is made up of desmosomal contacts between Müller fibres and receptor cells arranged in a line
- The Müller cells have their nucleus in the inner nuclear layer
- They are large complex neuroglial cells stretching from ILM to just beyond ELM

Müller cells important in:
- Breakdown of glutamate
- Homeostasis of the ionic micro-environment
- Neuronal survival

4. Outer nuclear layer
- 22-50μ – composed of the cell bodies of the rods and the cones with their nuclei and cytoplasm
- Rod nuclei are round/oval (5.5 μ)
- Cone nuclei are oval (5-7 μ)

5. Outer plexiform layer
- (2μ) Outer plexiform layer is made of axons of the rods and cones
- They contact processes from the bipolar and horizontal cells that are also found in this layer

The synaptic endings of the rods and cones are known as spherules and pedicles respectively.
• There are two main types of cone to bipolar cell contact
  – Synaptic Ribbon Synapses
  – Basal (or Flat) Junctions
• Horizontal cells have much wider spread of processes and contact more photoreceptors than bipolar cells and it has been suggested that the horizontal cells mediate lateral interactions
• Bipolar cells convey visual signals vertically from outer to inner plexiform layer

6. Inner Nuclear Layer
• Horizontal cells, Müller cells, Bipolar cells, interplexiform cells and amacrine cells all have their nuclei in this layer
• 8 nuclei deep in the fovea
• 5 deep at the ora serrata

7. Inner Plexiform Layer
• Thicker than outer plexiform layer (18-36μ)
• Layer where second and third order neurons of the retina meet
• In this layer, bipolar, amacrine, interplexiform and ganglion cells form synapses
• Bipolar cells release neurotransmitter glutamate and synapse with amacrine cell processes and ganglion cell dendrites

• Amacrine cells inter-relate adjacent areas of retina and that conduction can be both ways – suggests a local feedback system exists

8. Ganglion cell layer
• 1-2 cells thick (10-20 μ) except at macular region where it thickens to 80 μ or more
• 3 major types of ganglion cell
  – Midget – Narrow dendrite tree - 70% of all ganglion cells in central retina
  – Parasol – Vary in size and shape – more common in peripheral retina – about 10% of all ganglion cells
  – Small bistratified – receive input from blue cone bipolar cells – about 10%

9. Nerve Fibre Layer
• 20-30 μ at the optic disc
• Consists of the axons of ganglion cells
• Radiate towards optic nerve in characteristic manner
At this point they will form the optic nerve and become myelinated at lamina cribosa.

- Fibres arising from more peripheral retina are located more externally in the globe (near the pigment epithelium) and optic nerve.
- Fibres arising near the optic nerve are located closer to the vitreous in the globe and deep in the optic nerve.

The origin of a nerve fibre and its location within the nerve fibre layer explain the pattern of visual field loss associated with particular diseases such as POAG.

RNFL analysis

Zeiss Cirrus normal v glaucoma
10. Inner Limiting Membrane

- 1-2 μ
- Basement membrane, so different from External Limiting Membrane
- Absent at the optic disc

- Sometimes sheets of persistent glial tissue are seen covering the optic disc in part or as a whole and producing a slightly grey filmy (gossamer) appearance

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Modifications of the Retina

1. Fovea

- At the fovea, the layers of the retina are excavated
- As a result there is a modification of the layers
- The foveola is the most central part of the fovea and is completely rod and blue cone free

- Approximately 10,000 are found at the foveola
- The foveal pit acts as a mirror and one can see the reflex from it when using an ophthalmoscope
- Neither the choriocapillaris nor the RPE are modified at the fovea
- The cones at the foveola are much longer and thinner than elsewhere
- The smaller diameter of foveal cones allows more of them per unit area give better resolution

- A yellow pigment, xanthophil is thought to be in the fovea
- As a yellow filter, it absorbs blue light
- This area is “blue blind”, foveal tritanopia partially because of xanthophil but mainly because it lacks blue cones

- Zeiss cirrus – normal macula
2. Optic Disc

- Only nerve fibres and astrocytes are present here
- The “Blind” spot

The nerve

- tract consisting mainly of axons of the retinal
- axons converge on the (1.5mm diameter)...
- ...pierce the sclera at the lamina cribosa (sieve-like structure)...
- ...form bundles of myelinated fibres separated by connective tissue septa

- myelin sheaths & septa behind lamina cribosa give the optic nerve a greater diameter at the point at which it leaves the globe than at it’s head (the optic disc)
- Each optic nerve is encased in sheaths continuous with and similar to the meninges of the cranium (pia, arachnoid, and the dura).
The optic nerve may be considered as consisting of four parts...

- **head & ocular portion** traverses the sclera
- **orbital portion** - 3cm in length - S-shaped course so that globe is able to move freely
- **portion in the optic canal** 5-7mm long
- **intracranial portion** extends from the optic canal to the anterior part of the optic chiasm

**Blood supply**

- arterial supply to ON anterior to the lamina cribosa is derived from the short ciliary arteries.

- immediately behind the lamina cribosa vessels derived from the Circle of Zinn (which is itself supplied by the short ciliary arteries) enter the optic nerve
- the orbital portion of the optic nerve derives its blood supply from the pial circulation (and also to some extent from the ophthalmic artery & branches including the central retinal artery)
- That portion of the optic nerve lying in the optic canal derives its arterial blood supply from the ophthalmic artery
- the intra-cranial part of the optic nerve is supplied centripetally through the pial vessels
- venous drainage from the ocular and orbital portions of the optic nerve is chiefly into the central retinal vein

**Developmental anomalies**

- Rather common
- Need to be differentiated from old or active pathology
Aplasia and hypoplasia

- Aplasia (rare) & hypoplasia is a failure of the optic nerve to develop

- Hypoplasia is bilateral in about 60% of cases.
- May be a sporadic developmental anomaly or hereditary
- Small disc often surrounded by halo of hypopigmentation due to choroidal & RPE abnormality (“double ring”)
- reduced VA & visual field defects

3-month old - born 2 months premature

Coloboma

- Incomplete closure of foetal cleft
- May be associated with choroidal/iris coloboma
- Corresponding field
- VA may be affected
**Optic nerve pit**
- Not related to coloboma
- Rare (1 per 11,000)
- Bilateral in 15% of cases
- Occasionally more than one hole
- Usually inferotemporal quadrant of papilla
- 0.1 to 0.7 disc diameter (average 0.3)
- Depth varies from 0.5D to 20D
- Usually grey
- Visual field defects
- Cause not certain.
- Central serous retinal detachment

**Myelinated nerve fibres**
- bright white flame-shaped streaks
- *usually* contiguous with the margin of the optic disc

**Crowded nerve head**
- Physiological variation from the norm
- High axial hypermetropia.
- Margins of disc appear blurred and disc tissue somewhat elevated, sometimes one quadrant only
• Major points in favour of diagnosis of crowded disc as opposed to pathological "choked-disc" are
  – the type of eye
  – absence of exudates or haemorrhages
  – normal visual field + small-sized physiological blind spot
  – normal fluorescein angiogram
  – OCT

Myopic or temporal crescent

• Appearance margin of the optic disc determined by the distances from disc margin at which the RPE, Bruch's membrane and the choroid terminate
• In axial myopes these tissues are often absent over a crescent-shaped area on the temporal side of the disc (myopic crescent)

• Chorioretinal atrophy and/or traction of retina & choroid on the nasal side due to elongation of the globe at the posterior pole

Tilted disc

• Occasionally the optic nerve leaves the sclera more obliquely than usual giving rise to an inferior or superior conus
• Visual field anomalies may be present
3. Peripheral retina

- Near the ora serrata, the retina is less well developed than more central regions
- General thinning and the presence of vacuoles makes tearing of the retina more likely

- A gradual thinning is observed towards the ora serrata
- Sometimes the delineation can be more precise (Thin Anterior Retina or TAR)
- This explains why nearly all retinal detachments begin in this region

Retinal Circulation

- Outer retina is dependent on choroidal vascular supply
- Internal retina is provided for by retinal circulation
- *Ophthalmic artery gives off branch Central Retinal Artery (CRA)*
- CRA enters the central aspect of the optic nerve in its intraorbital course

- At this point the artery has a well developed *tunica media* consisting of 6 layers of smooth muscle cells
- The CRA receives both parasympathetic and sympathetic autonomic innervation (CNVII) (Ruskell, 1972)
• As the artery branches and emerges from optic disc it’s muscular sheath is replaced by incomplete layer of pericytes making the branches arterioles and not arteries
• The four branches: superior temporal; superior nasal; inferior temporal; inferior nasal; give rise to non-fenestrated capillaries which will not move further externally than inner nuclear layer

• Retina external to this is supplied by the choriocapillaris which are fenestrated and have a much greater permeability than the retinal ones

• The venous circulation, draining in to the ophthalmic venous system, accompany their arterial counterparts closely in the retina
• It follows that the venous vessels as seen with the ophthalmoscope are venules
• Only one way out

The fovea is avascular and totally dependent on choroidal circulation
• A failure of interaction between choroid and retina is an important factor in the development of AMD

Clinical landmarks—peripheral retina
• Equator
• Ciliary nerves
• Vortex veins
• Ora serrata
Equator

- Equator of fundus = approx 14 mm from limbus
- Located by finding vortex veins

Ora serrata

- Anterior limit of neural retina
- Scalloped appearance; approx 1.5 mm wide; 7 mm from the limbus
- Rounded extensions of pars plana into ora are called ora bays
Vitreous

- Fills 2/3rds of the globe
- Structural and metabolic support for retina
- Collagen type II
- Cloquet’s canal traverses anterior/posterior
- Vitreous base is a 3-4 mm zone straddling pars plana

Vitreoretinal adhesions

Normal eye
- Cortical vitreous loosely attached to ILM of sensory retina
- Strongly attached to vitreous base
- Fairly strongly to optic disc margin
- Weakly around fovea
- Weakly along peripheral blood vessels

That completes normal anatomy and some of its variations

I hope this has “refreshed” your memory

Thanks for listening!