What is Optic Nerve Hypoplasia (ONH)?
Optic nerve hypoplasia (ONH) refers to an abnormally small, underdeveloped optic nerve (ON). It is a congenital abnormality, thought to occur in the mid trimester of pregnancy in which a reduced number of axons form the optic nerve. The earlier in pregnancy it occurs, the more severe the hypoplasia. It usually affects both nerves (75% of cases) but may be asymmetrical.

What is the significance of ONH?
ONH is probably the single most common ON anomaly, thought to occur in around 7/100,000 live births. It is estimated to account for 12% of childhood blindness in the UK and may be associated with neurological or endocrine abnormalities, particularly septo-optic dysplasia. In bilateral cases, 46% have absence of the corpus callosum or septum pellucidum and 12% have panhypopituitarism. 27% of all children with ONH have endocrine abnormalities, the commonest of which is growth hormone (GH) deficiency. Some studies suggest up to 75% have associated CNS abnormality.

Risk factors and associations
Studies of children with ONH have suggested associations with young maternal age, first child, maternal diabetes, prematurity, periventricular leukomalacia and exposure to various toxins during pregnancy (alcohol, anticonvulsants, smoking, SSRIs, and cocaine) but no firm cause has been established.
It does occur in aniridia, anterior visual system tumours, with some brain malformations (holoprosencephaly, schizencephaly, porencephaly), in septo-optic dysplasia in combination with agenesis of the corpus callosum and/or pituitary insufficiency) and can also be inherited.

How does ONH present?
Optic nerve hypoplasia may present to the ophthalmologist with primary visual problems, or it may be suspected during endocrine or neurological assessment for associated conditions (eg neonatal hypoglycaemia, developmental impairment). Visual presentation depends on severity.

- **Bilateral/severe ONH**
  - Roving eye movements, blindness, sluggish pupil responses
  - May have see-saw nystagmus in septo-optic dysplasia
  - Delayed visual maturation

- **Mild ONH**
  - May be asymptomatic. Nystagmus and/or strabismus may be evident.

- **Unilateral/asymmetric bilateral**
  - Strabismus, unsteady fixation, relative afferent pupillary defect (RAPD)

What are the clinical features that define ONH?
The classic ophthalmological feature of ONH is the ‘double-ring’ sign where the true nerve size is represented by the inner ring.
The size of the disc can be estimated by calculating the disc-to-macula (DM) to disc diameter (DD) ratio. If DM/DD is over 3, this is suspicious of ONH, and if it is greater than 4, then ONH is very likely. Abnormal disc configurations with reduced nerve fibres can occur with sectoral ONH.
The ‘figure 8’ disc is a variant of temporal hypoplasia, it occurs in conjunction with developmental suprasellar tumours. Hypoplasia of the upper part of the optic nerves is seen in children born to mothers with diabetes mellitus.
Ex-premature babies with periventricular leucomalacia (PVL) may show abnormal ON cupping as a variant of optic nerve hypoplasia in normal sized optic discs with reduced axonal numbers. In this case the mechanism is retrograde transynaptic degeneration occurring after 28 weeks.

MRI features
Children with ophthalmoscopic appearances of ONH have reduced cross-sectional intracranial ON diameters. A cross-sectional area of <2.9mm² in a child over 12 months of age (by which time the ON has achieved most of its adult size) suggests ONH.

Visual evoked potentials (VEP)
The VEP can be reduced in severe ONH with reduced acuity. Reduced VEP can be predictive of a poor visual prognosis. The flash ERG is usually normal.
VINCYP/ SPEG Optic Nerve Hypoplasia Diagnostic and Investigative Pathway

Ophthalmology
History examination

Clinically obvious ONH

Diagnosis uncertain

Chiasmal signs
• See-saw nystagmus
• 'figure-8' disc
• Temporal hypoplasia

Consider
Electrophysiology / VEP
MRI brain, ON and chiasm if > 12mths

Rule out: Ophthalmic associations eg aniridia

Investigate chiasm (Brain MRI)
• Suspect anterior visual system tumour

If Concerns re development
Refer to neurodevelopmental service

Diagnosis made - Commence treatment
Refractive correction, patching etc

If VI confirmed: Refer via VI central Referral System

DIAGNOSIS OF ONH CONFIRMED
Refer Endocrinology

Abnormal Pituitary on MRI

No MRI yet performed
Or
Normal pituitary on MRI

Symptoms or signs suggestive of pituitary insufficiency?

Provocation Tests of Pituitary Function
Plus MRI if not already done

Abnormal pituitary function
Normal pituitary function

Treat deficiency
Indefinite endocrinology follow up

Abnormal
Normal

Baseline tests of pituitary function
(blood glucose, cortisol, TSH, freeT4, IGF-1, PRL & electrolytes)

4-6 monthly follow up for 12 months minimum dependent on age
• Normal growth & asymptomatic: Discharge
• Abnormal growth/ symptoms: continue follow up and consider MRI & provocation tests if not done

If VI confirmed
Refer via VI central Referral System
References

2. Garcia ML, Ty EB et al. Systemic and ocular findings in 100 patients with optic nerve hypoplasia. Journal of Childhood Neurology 2006;21(11)949-956