Nystagmus is defined as rhythmic to-and-fro oscillation of one or both eyes. The incidence of nystagmus has been reported as 2.4 per 1000. If it occurs within the first few months of life it is termed infantile nystagmus (INS). INS can be further subdivided based on etiology into the following groups:

1. Idiopathic infantile nystagmus (IIN).
2. Albinism.
3. Nystagmus associated with ocular disease. This includes aniridia (PAX6 mutations), congenital cataracts, optic nerve hypoplasia and retinal dystrophies such as achromatopsia and congenital stationary night blindness (CSNB).
4. Latent or manifest latent nystagmus (MLN).
5. Spasmus nutans.

If nystagmus occurs later in life it is termed acquired nystagmus. This can result from a variety of neurological diseases including multiple sclerosis (MS), diseases of the vestibular system, cerebrovascular accident, trauma, tumors and drug toxicity.

In addition to impaired vision, congenital and acquired nystagmus impact on many aspects of daily life such as cosmesis, difficulties with relationships and social interaction.

Clinical Assessment
The assessment of a patient with nystagmus involves recording a detailed history including family history, time of onset, symptoms such as blurred vision, oscillopsia and any associated neurological symptoms. Visual acuity (VA) is recorded monocularly and binocularly, both for distance and near, with and without spectacle correction. It is important to note any associated head postures during each test, particularly when the patient is exerting their maximal visual effort. When VA is tested without spectacles the abnormal head turn is often even larger as gaze is not limited by frames. An up-to-date refraction is carried out. An orthoptic assessment is performed detailing the presence of any squints and nystagmus form (amplitude, frequency, direction, conjugacy).

Slit lamp examination helps to determine the presence of iris transillumination defects (TID) (which can suggest a diagnosis of albinism), aniridia and cataract. Examination of family members for iris TID can also provide a diagnostic clue as this is a typical carrier feature in albinism. Dilated retinal examination is performed to document if there are any optic nerve or retina abnormalities such as optic nerve and foveal hypoplasia or abnormalities of pigmentation such as hypopigmentation in albinism.

Investigations
This initial assessment is the most important stage in diagnosing the etiology of the nystagmus and in directing any further investigations. This is summarised in Figure 1. If there is a clear history of onset in early infancy and no oscillopsia or other neurological symptoms are present then the etiology is most likely congenital infantile nystagmus. If however it is later onset or associated with oscillopsia or other neurological symptoms then it is most likely an acquired form of nystagmus. Eye movement recordings (EMR) can be used to distinguish between the different subtypes of nystagmus based on characteristic waveforms. Magnetic resonance imaging of the brain is essential if the nystagmus appears to be acquired in origin; if there are any associated neurological signs/symptoms or if the nystagmus appears atypical for congenital infantile nystagmus, for example disconjugate or vertical nystagmus.

The presence of iris TID on examination in conjunction with ocular and/or cutaneous hypo-pigmentation hints at a diagnosis of albinism. Optical coherence tomography (OCT) examination in albinism normally demonstrates typical foveal hypoplasia. In a normal OCT, the inner retinal layers which includes the ganglion cell layer, inner plexiform layer, inner nuclear layer and outer plexiform layer are absent from the central fovea. In typical foveal hypoplasia these inner retinal layers are present at the fovea. Visual evoked potentials (VEPs) can help to diagnose albinism based on the presence of crossed asymmetry. Normally, the right and left eyes have similar deflections at the same time point on VEP (i.e. they are symmetrical). In albinism the deflections may occur in opposite directions in each eye (i.e. they are asymmetrical).
A close scrutiny of the motility examination can provide a diagnosis of IIN or MLN. IIN presents with typical horizontal conjugate nystagmus which does not change upon covering one eye. Normally no other abnormality other than nystagmus and squint are found. Binocular vision is often present. Testing for FRMD7 gene mutation which is known to cause IIN, should be considered as it can confirm X-linked IIN. In contrast to this, MLN is typically associated with a congenital squint syndrome, typical nystagmus which increases upon covering one eye and beats in the direction of the open or fixing eye. Binocular vision is absent. In both cases, slit lamp, fundus, OCT and electrophysiology examinations are all normal, although mild foveal hypoplasia can be present on OCT in cases of FRMD7 IIN. IIN and MLN can occur concurrently in the same patient. This can easily be seen on eye movement recordings.

Diagnosis of nystagmus associated with ocular disease is dependent on a thorough history and ocular examination. Some conditions associated with nystagmus such as congenital cataract and optic nerve hypoplasia may be immediately apparent on clinical examination. If a diagnosis of optic nerve hypoplasia is made, MRI screening for septo-optic dysplasia should be considered as this is known to be associated with this condition. PAX6 mutations are autosomal dominant and are often associated with a family history of the condition. Vertical nystagmus is a feature of PAX6 mutation. All parts of the eye may be affected and findings may include aniridia, cataract, optic nerve and foveal hypoplasia. OCT demonstrates typical foveal hypoplasia. VEP is normal.

Retinal conditions that are associated with nystagmus include retinal dystrophies such as achromatopsia and congenital stationary night blindness (CSNB). These conditions may present with horizontal or vertical conjugate or dysconjugate nystagmus, light sensitivity and problems with night vision or color vision. In achromatopsia, nystagmus is usually low amplitude and rapid and there is severe photophobia. The retinal examination can appear normal in the early stages of the diseases. In these cases the electroretinogram (ERG) is very useful in distinguishing between these conditions. In achromatopsia, the cone function is abnormal and this results in a flat response on photopic testing. In CSNB, the rod function is abnormal and this results in a negative deflection on scotopic testing. OCT studies in achromatopsia have demonstrated atypical foveal hypoplasia (where in addition to the abnormal continuation of the inner retinal layers, there are also abnormalities of the photoreceptor layer) which is almost always pathognomonic of achromatopsia.

Spasmus nutans consists of the triad of rapid pendular nystagmus, head nodding and abnormal head position. Clinically it resolves spontaneously within a few months to a year after onset. However, it is important to rule out optic nerve and chiasmal gliomas before labeling it as benign, as these tumors have been found to be associated with spasmus nutans syndrome.

Treatment
Treatment for nystagmus includes optical, pharmacological and surgical options. Vision should be optimized with up-to-date spectacle corrections or contact lenses. Tinted glasses can be beneficial in photophobic patients. Contact lenses may be of benefit in those patients with high astigmatic refractive errors associated with head turns who cannot achieve their full visual potential with normal spectacles as their head postures do not allow them to look through the center of their lenses. Hard contact lenses as opposed to soft contact lenses should be used as these are more stable on the moving eye of a nystagmus patient. Prisms can be used to treat abnormal head turns, decrease squints or dampen nystagmus by increasing convergence.

There are a small number of randomized control trials relating to the pharmacological treatment of nystagmus. These include Memantine, Gabapentin and 3,4 Diaminopyridine (DAP). Gabapentin and Memantine can improve both infantile and acquired nystagmus in terms of EMR, VA and visual function scores. Memantine is efficacious in treating acquired nystagmus secondary to MS. DAP has been shown to be of benefit in both idiopathic and acquired down-beat nystagmus. There are also case reports that suggest other medications including: Baclofen, Clonazepam, topical Brinzolamide and Acetazolamide may also be effective.

Surgical treatment options include corrections for head turns (Kestenbaum-Anderson procedure) which involve large recessions and resections of the extra ocular muscles in order to shift the null point to the primary position. They can be done for horizontal, vertical and torsional head positions. This is beneficial in several ways. Firstly, in patients with astigmatic corrections it allows them to gain the full benefit of their spectacle correction in the primary position. Secondly, this treats the associated muscular neck pain that these patients often have as a result of their head posture. Finally, cosmesis is significantly improved in the primary position. Before considering surgery for abnormal head position, it is important to rule out periodic alternating nystagmus (PAN) preferably using EMR as this procedure may not be appropriate in PAN. Tenotomy of all four horizontal muscles has also been advocated to reduce nystagmus intensity.

Summary
A detailed history and examination can often direct the diagnosis of any associated conditions in nystagmus and focuses subsequent investigations. Additional investigations with OCT, eye movement recordings and electrodiagnostics are often needed for diagnosis. There are several management options available; including optical/refractive, pharmacological and surgical treatments.

References

Further reference: a Diagnostic Algorithm for Nystagmus will be published on www.rcophth.ac.uk alongside this Focus feature.