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## **Clinical assessment of nystagmus**

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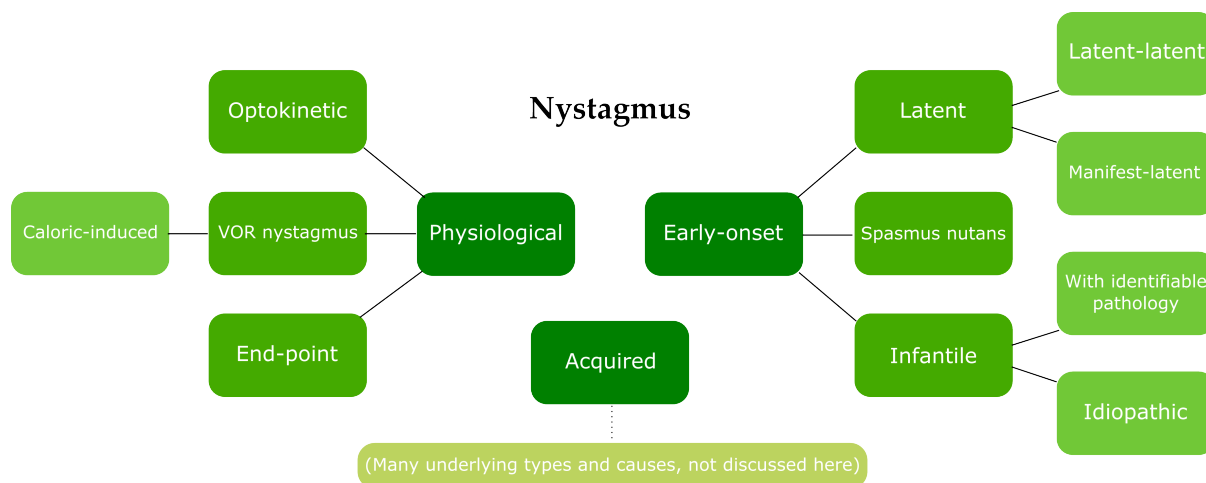
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## Introduction

Nystagmus describes a constant, involuntary, oscillation of the eyes. This can occur for a multitude of reasons, both pathological and physiological. The prevalence of pathological nystagmus is estimated to be between 0.24 and 0.35% in the general population<sup>1,2</sup>.

As many as 45 types of nystagmus have been reported in the literature<sup>3</sup>. Understandably, the condition is often considered both complicated and mysterious. Whilst it is true that nystagmus is relatively poorly understood, many of these 45 'types' represent non-nystagmoid *saccadic oscillations*, synonyms or speculative forms that may never have existed at all<sup>4</sup>. True nystagmus can, more simply, be divided into three categories: *physiological*, *early-onset* and *acquired* (see Figure 1). This article focuses on the pathological forms that are likely to be encountered in primary practice; particularly the *early-onset* forms of nystagmus. Acquired nystagmus invariably requires onward referral; the clinical signs to look out for are discussed later.



**Figure 1: Simple classification system for nystagmus. While not exhaustive, this list covers the most relevant types for optometrists in primary care.**

## Physiological nystagmus

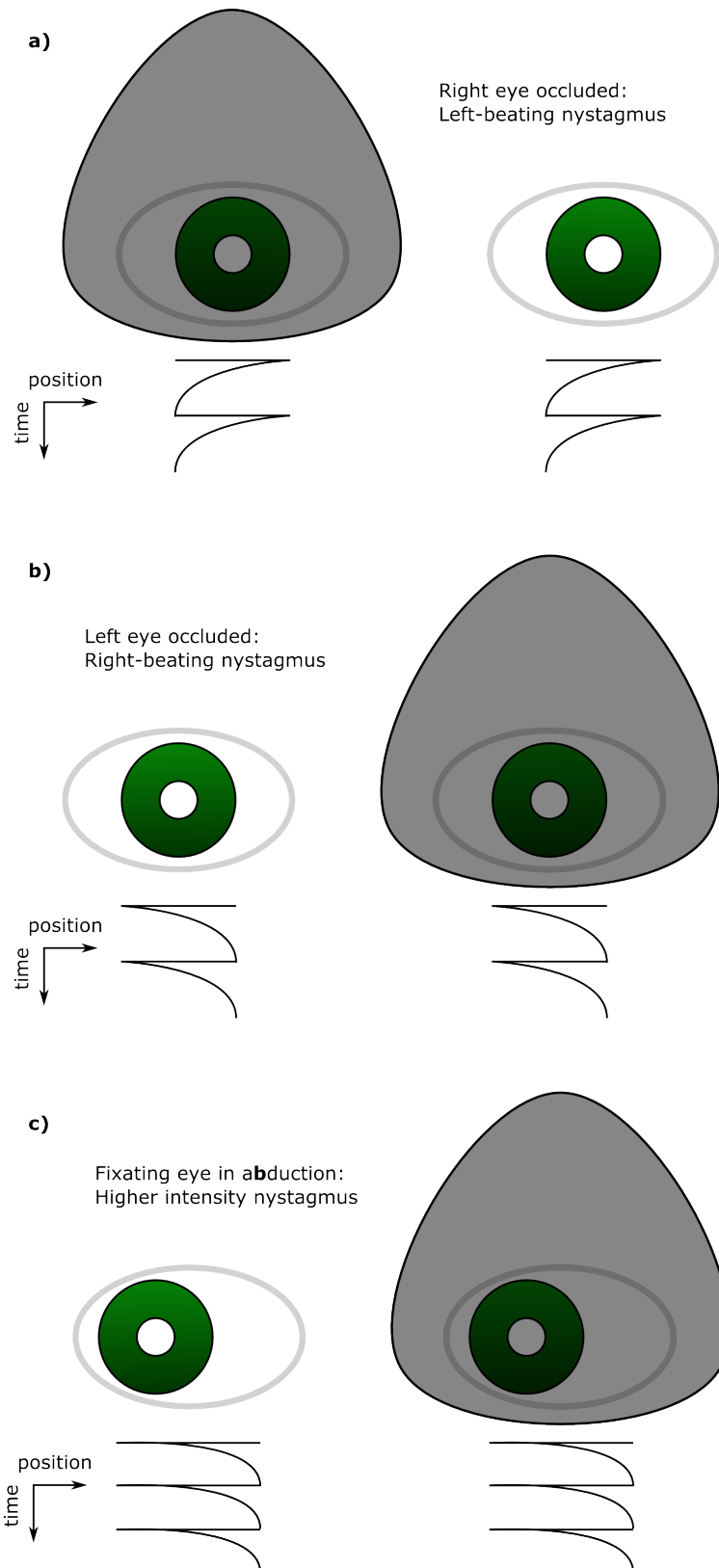
Under some circumstances, nystagmus may be induced in normal, healthy individuals. For example, *optokinetic nystagmus* is an oculomotor response to minimise retinal slip provoked by large moving visual stimuli or the entire visual field. *Vestibulo-ocular reflex (VOR) nystagmus* occurs during and following rotation of the body, and describes the response to movement of fluid in the inner ear and related saccadic refixations. A similar nystagmus may also be induced using *caloric irrigation*: by irrigating the ear canal with warm or cold water, convection currents are set up, driving the same mechanism as the *vestibulo-ocular reflex*<sup>5</sup>. Finally, one form of nystagmus commonly encountered in practice during motility testing is *end-point nystagmus*. This is seen when looking to extreme positions of gaze, and is due to a 'leaky' neural integrator<sup>6,7</sup>. Although this form of nystagmus is an unremarkable clinical finding, end-point nystagmus that is sustained after returning to the primary position is known as *gaze evoked nystagmus*, and is indicative of neuropathology<sup>8</sup>, warranting onward referral.

## Early-onset nystagmus

Early-onset nystagmus describes any form of nystagmus that presents within the first few months of life, unless precipitated by a condition causing acquired nystagmus within that time. The three most common forms are *latent nystagmus*, *infantile nystagmus* and *spasmus nutans*. Each of these are described below.

## Latent Nystagmus

Also known as *fusion maldevelopment nystagmus syndrome*<sup>9</sup>, latent nystagmus describes a form of nystagmus that either only appears when one eye is occluded (*latent-latent nystagmus*) or worsens upon occlusion of one eye (*manifest-latent nystagmus*). Latent nystagmus has a *jerk* waveform, and the beat direction is always towards the fixating eye. This means that covering the right eye will lead to jerk nystagmus, with both eyes jerking to the left (Figure 2a). Switching occlusion to the left eye will reverse the beat direction, so that the eyes now jerk to the right (Figure 2b). Another diagnostic feature of latent nystagmus is that the eye movements follow *Alexander's law*; i.e. when looking in the direction of the quick phase, nystagmus intensity increases (Figure 2c).



**Figure 2: Demonstration of the effects of occlusion on latent nystagmus. In (a), the right eye is occluded. Latent nystagmus beats towards the fixating eye; in this case, left-beating nystagmus. Lines beneath the eyes show the nystagmus waveform (stereotyped and not to scale). (b) shows the effect of occluding the left eye: right-beating nystagmus. In (c), the patient moves their eyes to the right (i.e. in the direction of the quick phase). According to *Alexander's law*, this results in increased nystagmus intensity.**

## Spasmus Nutans

Spasmus nutans syndrome is a rare disorder, causing (in combination): a high frequency, low amplitude nystagmus of a disconjugate nature; irregular head nodding; and an abnormal head posture. Its onset is usually within the first year of life and the condition ceases spontaneously, usually within two years of onset, although it has been known to persist for over eight years. However, a low-amplitude nystagmus (not detectable clinically) may persist until at least five to twelve years of age, when it spontaneously resolves<sup>10</sup>. The pathogenesis of spasmus nutans syndrome is unknown<sup>8</sup>.

## Infantile nystagmus

Infantile nystagmus (IN) is a constant nystagmus, usually predominantly in the horizontal axis, of similar amplitude in each eye, and at an average frequency of 2-3 Hz<sup>11</sup>. Vertical and/or torsional movement may also be exhibited, either as a major or secondary component<sup>11</sup>. In the past, IN has been referred to under a number of (now erroneous) names, which undoubtedly has contributed to confusion surrounding the condition. Older terms such as *congenital nystagmus*, *sensory nystagmus* and *motor nystagmus* have now fallen out of favour, with '*infantile nystagmus*' taking their place. Since IN is not usually present *at birth*, the term '*infantile*' is now preferred over '*congenital*'<sup>9</sup>, but note that *infantile nystagmus* does not refer to all forms of nystagmus occurring in infancy (i.e. both *latent nystagmus* and *spasmus nutans* begin in infancy but are distinct from *IN*). The condition develops within six months of birth, and persists throughout life<sup>12</sup>; i.e. the phrase '*infantile*' is used regardless of the patient's age. The prevalence of IN is estimated at 0.14%<sup>1</sup>.

In most cases of IN, a thorough workup will reveal comorbid afferent visual system pathology<sup>8</sup>. Whether or not this can be said to 'cause' nystagmus is still a point of disagreement within the literature. In any event, the unusually high prevalence of coincident pathology demands that a comprehensive ophthalmic examination be performed in every case. Such an examination should include optical coherence tomography and electrophysiology (electroretinography and visual evoked potentials), so referral to a hospital eye service is warranted in every child first presenting with nystagmus. Nonetheless, in many patients, no additional pathology can be found – these cases are labelled as '*idiopathic*'.

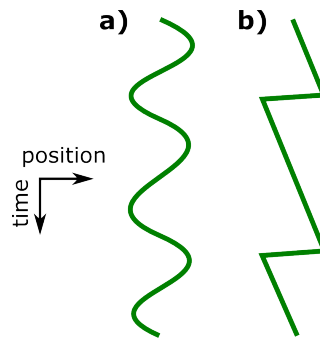
There are mixed reports as to whether early intervention can prevent IN developing. For example, one longitudinal study found that the timing of surgery to remove congenital cataracts had no significant impact on whether or not nystagmus later developed<sup>13</sup>.

Individuals with IN almost always have reduced visual acuity (VA); in idiopathic cases, VA is typically around 6/13, although in some (rare) cases, patients may see 6/5 or better. For those with comorbid pathology, VA is related to the underlying condition (approximately 6/28 in albinism and 6/21 in other pathologies)<sup>11</sup>.

## Waveforms and the null zone

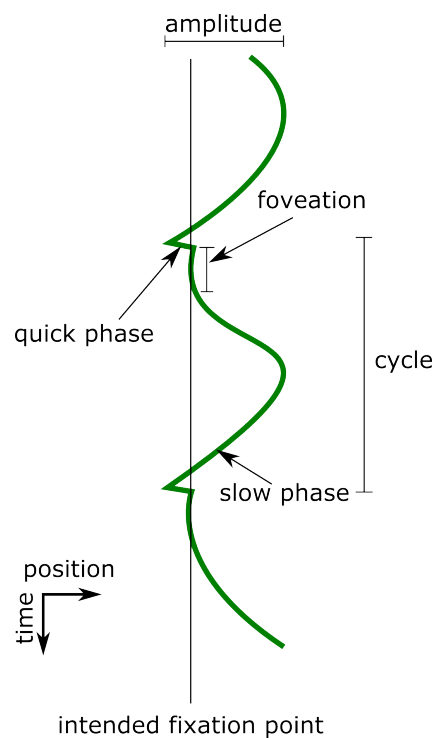
The pattern of eye movements seen in IN (i.e. how eye position changes from beat-to-beat) varies between individuals, and often, within the same individual at different times or gaze angles<sup>14,15</sup>. This pattern of movement is known as the '*waveform*', and 12 such waveforms have been described<sup>15</sup>. Broadly, however, most waveforms fall into the categories of being either '*jerk*' or '*pendular*' (see Figure 3). The exact waveform a

patient with IN uses has little bearing on their diagnosis. However, there are some trends which may inform visual prognosis. For example, a child that changes from a 'pendular' to 'jerk' waveform early in infancy is likely to develop better visual function than a child who progresses later<sup>16</sup>.



**Figure 3: Eye movement traces showing the basic waveforms of (a) pendular nystagmus, and (b) jerk nystagmus**

Figure 4 shows the hallmark features of a typical nystagmus waveform. Note the presence of both quick and slow phases. Notice also the acceleration of the slow phase following the foveation period – this acceleration is usually present in IN waveforms, and is useful in arriving at a diagnosis.



**Figure 4: The components of a nystagmus waveform (specific type 'PFS'<sup>15</sup>). Note that, in this example, the quick phases are very brief. Frequency is inferred from cycles per second.**

Eye movement traces such as the one in Figure 4 are only available through the use of high-speed eye tracking, which, at present, is not available to most clinicians. However, it is usually possible to ascertain at least whether the patient has 'pendular' or 'jerk' nystagmus, and in the case of jerk nystagmus, to determine the beat direction. Usually, if

the patient turns their head in the direction of the jerk, the nystagmus will dampen. Most patients will have a particular gaze angle at which the nystagmus is minimised, which is termed the 'null zone'<sup>17</sup>.

Approximately 73% of patients with IN have a null zone within 10° of the primary gaze position, and most will use a precise head posture to facilitate this, particularly if the null zone is more than 20° from the primary position<sup>11</sup>. In around 44% of individuals with IN, convergence also reduces nystagmus intensity<sup>11,18,19</sup>. Although the exact mechanism remains a mystery, this dampening has been shown to be solely due to a reduction in the angle between the eyes (as opposed to accommodation)<sup>18</sup>.

### *Oscillopsia*

Despite the constant retinal image motion, most individuals with IN will not report oscillopsia<sup>20</sup> (perception of the world moving back and forth<sup>21</sup>) except under rare circumstances, such as when tired or ill. Patients with acquired nystagmus are more likely to experience oscillopsia, but the presence or absence of this symptom should not be considered diagnostic.

### *Psychological factors*

Nystagmus intensity in IN is related to the patient's state of attention and fatigue<sup>22-26</sup>. It is important to bear this in mind when examining patients, as the stress involved with attending for a sight test may increase nystagmus intensity, resulting in worsened visual function.

### *Head shaking*

Around 27% of patients with IN also exhibit regular head oscillations. These may not occur all the time, are known to increase in intensity with 'effort to see', and can usually be voluntarily suppressed by the patient<sup>27</sup>. The direction and speed of head shaking does not appear to counteract the oscillations of the eyes, and therefore is unlikely to be a compensatory mechanism<sup>28</sup>.

### *Refractive error*

High refractive error is common in IN, perhaps due to poor emmetropisation. A broad range of refractive errors may be found, although there is a tendency towards myopia<sup>29</sup>.

The incidence of corneal with-the-rule astigmatism (i.e. negative axis ~180) is unusually high in IN<sup>30,31</sup>, with 57% of individuals exceeding 2.00 DC<sup>11</sup> (1.85 DC is the average<sup>29</sup>). Astigmatism tends to increase with age<sup>31</sup>, and is believed to be due to interaction between the cornea and eyelids. Even when corrected, horizontally-oriented stimuli are more easily seen than vertical<sup>32-36</sup>, possibly due to meridional amblyopia<sup>35,37</sup>.

### *Idiopathic infantile nystagmus*

The 'idiopathic' label is a diagnosis by exclusion, i.e. all other possible causes and associated conditions must first be ruled out. Detailed electrophysiological testing is essential to rule out many of the conditions known to be associated with IN<sup>38</sup>. Thirty per cent of people with IN are considered to be idiopathic<sup>39</sup>, although it is possible that some (currently) undetectable pathology of the visual pathway remains undiagnosed in these individuals. Note that high ametropia and/or strabismus associated with nystagmus in the absence of other ocular pathology is still classified as 'idiopathic'.



## Acquired nystagmus

Pathological nystagmus may develop at any point in life as a result of disease or injury, often to the vestibular or central nervous systems. The most common causes are multiple sclerosis and stroke<sup>40</sup>. As an optometrist in primary practice, any suspicion of acquired nystagmus should result in a prompt onward referral. The many forms and causes of acquired nystagmus are beyond the scope of this article, but interested readers are directed to Leigh and Zee's textbook<sup>8</sup> for further information. Importantly, every patient with any form of pathological nystagmus should have (or have had) a thorough neuro-ophthalmological workup. Any patient presenting for the first time with nystagmus requires urgent referral to rule out life-threatening causes. To illustrate the importance of eye movements recordings, consider the case of an 18-month old presenting with apparently symmetrical nystagmus. Following high-speed eye movement recordings, it was noted that the left eye exhibited much larger nystagmus than the right. This patient was sent for an MRI, which revealed a large anterior visual pathway glioma (Jay Self, personal communication 2016).

Features that should raise the suspicion of acquired pathology are:

- Asymmetry, i.e. disconjugacy of the nystagmus eye movements
- A significant vertical component to the nystagmus
- Reports of oscillopsia
- Saccadic oscillations without any apparent slow phase (note that saccadic oscillations are not technically nystagmus, but are often confused as such)

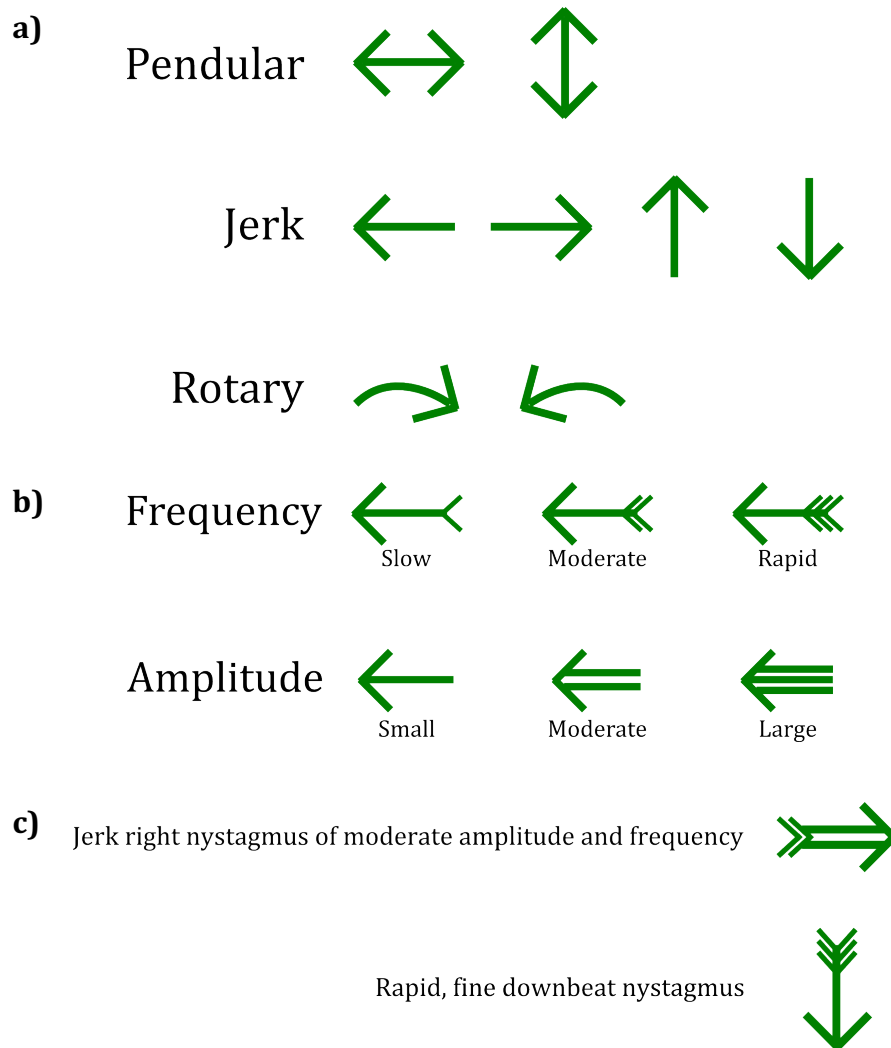
There are of course exceptions, and the above features do not indicate sinister pathology in every case. Bear in mind that it is possible for a patient with IN to suffer unrelated brain damage leading to concurrent acquired nystagmus. IN is non-progressive following visual development; i.e. changes in nystagmus are **not** expected in adulthood. Therefore, any change in nystagmus should always be referred.

## Recording nystagmus in practice

Clinicians in routine practice will not have access to high speed eye movement recording, yet it is important to document the nystagmus as best as possible using the tools available. The following aspects should be recorded:

- History and symptoms:
  - How long has nystagmus been present?
  - Is oscillopsia perceived?
  - Is there a history of strabismus?
  - Is there a family history of nystagmus?
- Does nystagmus intensity increase with occlusion?
- Is the movement symmetrical?
- Does beat direction depend on which eye is covered?

- Is head shaking present?
- Does convergence cause dampening of nystagmus?
- Is there a null zone? (Is a head posture used?)
  - Nystagmus features should be noted in primary and secondary gaze positions. Figure 5 demonstrates a graphical notation system. Note that, in jerk nystagmus, the 'direction' refers to the *quick phase* direction.



**Figure 5: Graphical notation system for clinical recording of nystagmus. Nystagmus should be noted in at least five positions of gaze. (a) Pendular, jerk and rotary nystagmus notation. (b) Methods for notating frequency and amplitude. (c) Example notation, combining the above symbols.**

### Routine clinical tests

The presence of nystagmus can make many of the routine aspects of sight testing more challenging. For example, non-contact tonometry can be difficult to perform, and great care should be taken to avoid corneal abrasion if performing contact tonometry, taking advantage of the patient's null zone to dampen nystagmus as much as possible.

Obtaining an accurate refraction in nystagmus *is* possible with some modifications. Phoropters should be avoided in favour of a trial frame, to allow patients to turn their head and view using the null zone. Wide-aperture trial lenses are preferable for the same reason, although even this may not be sufficient for some patients to obtain the same quality of vision as with glazed spectacles or contact lenses. There is evidence that IN causes a 'slowness to see'<sup>41,42</sup>, so it is wise to give patients plenty of time to respond to letters when reading the chart. In addition, the use of a +10.00 DS lens for occlusion can help prevent increasing nystagmus intensity when measuring monocular VA in individuals with a latent nystagmus component.

Perimetry may be performed in patients with nystagmus (using their null zone if available), but due to the constant eye movements, the results should be considered less sensitive to small field defects.

Strabismus is present in 64% of individuals with early-onset nystagmus, with 98% of these cases being horizontal (esotropia or exotropia)<sup>11</sup>. This is particularly the case in *latent* nystagmus, which is almost always accompanied by a history of squint. Observation of cover test can be more difficult, but a reasonable level of precision is usually obtainable.

## Conclusion

The various forms of nystagmus can be broadly grouped into physiological types occurring in the normal population, those occurring in infancy, and acquired forms which may present at any time in life (including infancy). Any patient presenting for the first time with pathological nystagmus of any form requires referral to rule out life-threatening causes. Latent nystagmus and IN, the forms of nystagmus most commonly encountered in clinical practice, are non-progressive, and once formally diagnosed, modifications to the standard routine allow for accurate refraction and monitoring within primary care.

Next month's article will cover the management options available for patients with nystagmus.

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