its thickness that removing small amounts showed no change. Given the limited resolution of the current study, it suggests that the major barrier to resistance must reside within the inner collagenous layer.

To date, there is no morphologic evidence that the inner collagenous layer undergoes major changes throughout the first four decades of life, nor is there any physiological evidence of significant changes in Young’s10 modulus of elasticity of Bruch’s membrane in the young. In the older concept of subretinal neovascularization, the loss of elasticity of Bruch’s membrane through calcification was postulated as a mechanism for inducing breaks in the system, and such breaks were suggested as the causal agent for penetration by choroidal vessels. Although no empirical evidence exists for the loss of elasticity with increasing age, the breaks in Bruch’s membrane seen in the current study between intercapillary columns and across vascular components suggest that even under the low hydrostatic pressure used, the elastic constants were exceeded. To support this concept, it should be noted that the occurrence is seen more commonly in older eyes.

The uneven nature of ablation in some specimens and the breaks in others did not confound the overall finding that the high-resistance barrier resides within the inner collagenous layer of Bruch’s membrane.

**Key Words**
ageing, age-related macular degeneration, Bruch’s membrane, excimer laser, hydraulic conductivity

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**References**

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**Infantile Nystagmus**

**Development Documented by Eye Movement Recordings**

*Irene Gottlob*

**Purpose.** To report on the development of infantile nystagmus in a patient’s first year of life.

**Methods.** A case study using consecutive photo-oculographic and electro-oculographic eye movement recordings in the subject ranging between 1 and 12 months of age.

**Results.** Although no nystagmus was present at 5 weeks of age, square-wave jerks were recorded at 7 weeks, and a small pendular nystagmus was recorded at 8 weeks. At 10 weeks of age, evaluation revealed predominantly larger jerk-type nystagmus with increasing and decreasing exponential velocities of the slow phase. After 14 weeks of age, the nystagmus became smaller and was predominantly pendular. Between 7 and 12 months of age, binocular electro-oculography recordings showed conjugate pendular nystagmus typical of infantile nystagmus.

**Conclusion.** This is the first report documenting that, at least in some forms of infantile nystagmus, eye movement abnormalities are not present at birth. Before the...
Infantile nystagmus (congenital idiopathic nystagmus) is characterized by conjugate eye movements with pendular or jerk waveforms. In the literature, there are only few reports of the exact time of onset of nystagmus. Although congenital nystagmus typically has been defined as nystagmus with age of onset at birth, Reinecke et al found in a study of case histories that nystagmus developed in the first 2 weeks of life in only 3 of 35 patients. Therefore, the term “infantile” nystagmus was introduced instead of congenital nystagmus. We confirmed these results in a previous study and found a mean time of nystagmus onset determined by history at 1.9 months of age. However, in these patients, neither eye movement recordings nor ophthalmologic examination results were obtained before the clinical manifestation of nystagmus. Therefore, earlier subclinical nystagmus or small amplitude nystagmus unobserved by parents or pediatricians cannot be excluded. Reinecke et al reported that infantile nystagmus often starts with large triangular waveforms evolving into pendular and, subsequently, jerk waveform nystagmus. Hertle et al, however, observed saccadic oscillations preceding the development of infantile nystagmus in a 4 1/2-month old infant.

In this report, we describe a patient who was included as a presumed normal subject in an ongoing infant vision development study. Eye movement recordings were obtained before the onset of nystagmus, and the evolution of the type of nystagmus was documented.

MATERIALS AND METHODS. A full-term, healthy baby girl was examined at 5, 7, 8, 10, 11, and 14 weeks and at 6 1/2 and 7 1/2 months of age by photo-oculography (POG) and at 7 1/2, 9 1/2 and 12 months of age by electro-oculography (EOG).

An ophthalmologic examination was performed at 5, 8, 10, 11, and 14 weeks and at 6 1/2, 7 1/2, 9 1/2, and 12 months. Preferential looking was recorded with the Teller Acuity Card test at a distance of 38 cm from the patient at ages 11 and 14 weeks and at 5 1/2, 7 1/2, 9 1/2, and 12 months. The research followed the tenets of the Declaration of Helsinki. Informed consent was obtained from the parents after the nature and possible consequences of the study were explained.

Photo-oculography was recorded from the right eye with a photo-oculographic technique developed for the examination of infants. It is based on the measurement of the relative position of the reflected image of an infrared source on the cornea and the pupil center. The subject was seated in an infant car seat 30 cm from a cathode ray tube, where stimuli for pursuit were generated. Infrared light (880 nm) was directed to the subject’s right eye, and the image of the eye was recorded by an infrared camera. Both the infrared source and the camera were placed over the infant’s head. The infrared light was reflected by a hot mirror (dichroic filter separating visible light and infrared light) positioned in the center of the cathode ray tube. The reflected image of the eye movements was analyzed automatically and stored on a computer with a 30/second sampling frequency. For the stimulation of visual pursuit, a square of 9.4° of visual angle with white and black vertical gratings (contrast 95%, luminance 5 cd/m², spatial frequency 0.1, 0.2, or 0.4 cpd) moved at a constant velocity of 7°/second on the screen of the cathode ray tube with identical luminance. Calibration is defined by the geometry of the anterior chamber. It was estimated from biometry data of eyes from subjects the same age as those used in our study. Sensitivity was 10 minutes of arc.

Using a Vision Monitor System (Metrovision, Villeneuve d’Ascq, France), EOG was recorded binocularly. Stat-Trace II (Niko Med USA, New Brunswick, NJ) electrocardiographic electrodes were placed nasally to the medial canthi and temporally to the lateral canthi. The indifferent electrode was positioned centrally above the glabella. Signals were DC-amplified (X6000) and filtered (DC bandpass, 76 Hz). Eye position was recorded on a digital computer with a sampling rate of 230 Hz. Data were converted from analog to digital with 12 bits.

RESULTS. Clinical Examinations. This infant, who was included as a presumed normal subject in an ongoing infant vision development study at Kantonspital St. Gallen, initially was examined at 5 weeks of age. Until that time, no abnormal eye movements nor any vision problems had been observed by the parents or the pediatrician. Orthoptic examination results were within normal limits for the patient’s age. Motility of both eyes was normal, and no nystagmus or other pathologic eye movements were observed. At the next clinical examination, at age 8 weeks, fine, intermittent nystagmus was observed on orthoptic examination. The patient did not fix objects or light. However, no visual abnormalities were observed by the mother. At 11 weeks of age, the mother reported that the baby did not react any more to her smile and did not fix objects. On orthoptic examination, the patient did not fix or follow objects or light. A conjugated jerk nystagmus to the right was observed clinically. Fundus
examination results were normal, and retinoscopy revealed hyperopia of 1.25 D in each eye. The preferential looking test disclosed a grating acuity in the normal range in each eye (OD, 2.4 cpd; OS, 1.3 cpd). Neuropediatric and ultrasound examination results of the patient’s head were normal. At 14 weeks of age, conjugated pendular nystagmus was observed. Binocular preferential looking test was again in the lower range of normal (1.6 cpd). At 5 1/2 months of age, the nystagmus amplitude appeared smaller. The mother reported that the infant’s vision had improved. Grating acuity measured with preferential looking was in the lower normal range on monocular testing (OD and OS, 2.4 cpd) and binocular testing (4.8 cpd). At 7 1/2 months of age, a fine, predominantly pendular nystagmus was observed. No change in nystagmus was observed when either eye was covered. The preferential looking test was within normal limits (OD, 4.8 cpd; OS, 6.5 cpd). Examinations at 9 1/2 and 12 months of age revealed no changes in nystagmus. Preferential looking developed within normal limits. On all examinations, pupillary reactions were normal, and the patient appeared orthotropic by corneal light reflexes and cover test. At the age of 7 1/2 months, the child clearly pointed to the cat (1200 seconds of arc) and the car (550 seconds of arc) on the Lang I stereo acuity test, and at 12 months she pointed to the star (200 seconds of arc). No photophobia was noticed or reported by her parents.

Eye Movement Recordings. Figure 1A represents POG recordings of the right eye of the patient at 5 weeks of age. The target was followed predominantly using small saccades. No nystagmus was observed. At this age, several of the normal children in our ongoing infant vision development study showed predominantly saccadic pursuit (unpublished observations, 1996). Therefore, eye movement recordings were considered normal at 5 weeks of age in our subject (Fig. 1A). Examples of normal subjects are shown in Figure 2. The POG in Figure 2A shows that at 6 weeks of age, portions of smooth pursuit without saccades could be found in normal infants. Normal control infants with saccadic pursuit are shown at the age of six weeks (Fig. 2B) and 11 weeks (Fig. 2C). In our patient at 7 weeks of age (Fig. 1B), several portions of the eye movement recordings showed square-wave jerks and macro square-wave jerks (amplitude, 5° to 20°). Other parts of the eye movement recordings showed saccadic pursuit and occasionally small portions of pendular oscillations, with a maximum of three consecutive beats of small amplitude (approximately 5°). At 8 weeks of age (Fig. 1C), a pendular nystagmus (frequency, ~4 Hz; amplitude, 4° to 20°) was present on eye movement recordings (Fig. 1C). Almost no square-wave jerks were detectable. Figure 1D shows eye movement recordings at 10 weeks of age. Large right and left beating jerk nystagmus were recorded (frequency, 1 to 3 Hz; amplitude, ~20°). Slow phases had increasing as well as decreasing velocities. Parts of the eye movement recordings showed a pendular nystagmus similar to that recorded in Figure 1C. At 11 weeks of age, the nystagmus amplitude increased to approximately 30° (Fig. 1E). The nystagmus had waveforms similar to those at 10 weeks of age. At the age of 14 weeks (Fig. 1F), the nystagmus was smaller (amplitude, 10° to 20°) and predominantly pendular (frequency, 4 to 6 Hz. At this time, almost no smooth pursuit was recorded. The eyes fixated the target with large saccades. At 6 1/2 months (Fig. 1G) and 7 1/2 months (Fig. 1H), predominantly pendular nystagmus at a frequency of 4 to 6 Hz with smaller amplitude (4° to 10°) was observed. No square-wave jerks were observed.

At 7 1/2, 9 1/2, and 12 months (Fig. 3), EOG recordings showed conjugate pendular nystagmus at a frequency of ~3 Hz and an amplitude from 3° to 6°. If either eye was covered, no change in the nystagmus waveform or amplitude was observed.

DISCUSSION. In summary, we have described the development of infantile nystagmus in an otherwise healthy infant. Although we did not observe any eye movement abnormality at 5 weeks of age, square-wave jerks were recorded at 7 weeks of age, pendular nystagmus at 8 weeks of age, and jerk nystagmus with increasing and decreasing velocities at 10 and 11 weeks of age. After the 14th week of age, the nystagmus became pendular and was typical for infantile nystagmus. Nystagmus amplitude reached its maximum between the 11th and 14th weeks of life.

Until the age of 12 months, neurologic development and visual development (visual acuity measured by preferential looking) of the patient was normal. No photophobia or paradoxical pupillary reactions were observed. Ophthalmoscopic examination results were normal. Therefore, nystagmus caused by ocular disease, such as Leber’s congenital amaurosis or achromatopsia, are unlikely in this patient. Nystagmus criteria typical for spasmus nutans—such as intermittent, asymmetric, dysconjugate, oblique nystagmus—were not present in our patient. The normal development and the nystagmus characteristics of our patient were, therefore, typical of infantile nystagmus.

Clinical examination and quantitative eye movement recordings did not reveal any nystagmus or eye movement abnormality at the age of 5 weeks. Therefore, we demonstrated that, at least in some forms of infantile nystagmus, the eye movement abnormalities are not present at birth. The fine, intermittent, pendular nystagmus we recorded at 8 weeks of age was recorded before the parents or
FIGURE 1. Horizontal photo-oculography (POG) of the patient's right eye between 5 weeks and 7½ months of age, recorded during presentation of a horizontal smooth pursuit stimulus.
the pediatrician were aware of the nystagmus. This may, therefore, represent an early stage of transition from preclinical to clinical nystagmus.

It is interesting that before the nystagmus was apparent, the patient had predominantly saccadic pursuit. This may be observed in normal subjects, as shown in Figure 2. However, most of the patients included in our ongoing infant vision study showed, at the same age, pursuit with higher gain and smaller saccades or smooth pursuit without saccades. Therefore, the predominantly saccadic pursuit at this age could represent a first sign of abnormality of slow eye movements.

At age 7 weeks, an increased number of square-wave jerks and macro square-wave jerks were recorded. Changes such as these in the saccadic systems preceding the development of infantile nystagmus were recorded in one patient by Hertle et al.4 In their patient, square-wave jerks and square-wave oscillation without nystagmus were observed at 4\(\frac{1}{2}\) months of age, and pendular nystagmus and square-wave jerks were observed at 9\(\frac{1}{2}\) months of age. They concluded that it was probable that the two different oscillations seen in their patient were coincidental, that square-wave oscillations did not evolve in infantile nystagmus, and that square-wave oscillations delayed the development of infantile nystagmus. Because we demonstrated in a second patient that saccadic abnormalities can precede the development of infantile nystagmus, the relation between the saccadic abnormalities and infantile nystagmus may not be coincidental. In our patient, the nystagmus developed at 2 months of age, corresponding to earlier clinically observed data in most of the patients with infantile nystagmus.2,3 Saccadic abnormalities did not delay the onset of nystagmus. After the onset of nystagmus, square-wave jerks disappeared. Therefore, the saccadic abnormalities in our patient may have evolved into infantile nystagmus. This would be in contrast to current theories of the origin of infantile nystagmus representing a gain instability in the slow eye move-

FIGURE 2. Horizontal photo-oculography (POG) of three normal subjects' right eyes at ages 6 weeks (A,B) and 11 weeks (C), recorded during presentation of a horizontal smooth pursuit stimulus.

FIGURE 3. Horizontal electro-oculography (EOG) of the patient's right and left eyes at 9\(\frac{1}{2}\) and 12 months of age following a sinusoidal pursuit stimulus 20° to the right and to the left at a maximal velocity of 30°/second.
ment system.\textsuperscript{1} However, different eye movement subsystems may be altered simultaneously in infantile nystagmus. In addition, the simultaneous or consecutive presence of pendular and jerk-type nystagmus in most patients with infantile nystagmus suggest that different mechanisms are involved in the origin of infantile nystagmus. A relation between the saccadic system and infantile nystagmus was demonstrated in other studies. Shallo-Hoffmann et al\textsuperscript{2} showed fast-phase instabilities in normally sighted relatives of patients with congenital nystagmus. Similarly, an increased number of square-wave jerks were observed in obligate carriers of blue-cone monochromatism with nystagmus.\textsuperscript{3}

We confirm the findings of Reinecke et al\textsuperscript{2} that the waveform of nystagmus changes with the patient's age. They recorded predominantly triangular waveform nystagmus in patients 1 through 4 months of age, which evolved into smaller amplitude and higher frequency pendular waveforms, which subsequently gave way to jerk waveforms by 7 to 18 months of age. In our patient, however, the evolution of the nystagmus waveform followed a different course. We observed small, intermittent, pendular nystagmus at 8 weeks, large, jerk-type nystagmus at 10 and 11 weeks, and smaller, pendular nystagmus after 14 weeks of age. The pendular nystagmus was typical of infantile nystagmus: It was conjugate in both eyes, and there was no change when either eye was covered. The early observed jerk-type nystagmus had increasing as well as decreasing exponential velocities of slow phases. Decreasing velocities of the slow phases are typical of latent nystagmus. However, our patient did not demonstrate a change of nystagmus when either eye was covered, and there were no signs of infantile esotropia, both of which are associated with latent nystagmus.\textsuperscript{4} Contrarily, her eyes were aligned straightly, and they demonstrated depth perception on the Lang 1 stereoaucity test. Therefore, typical latent nystagmus was excluded in our patient. As do the square-wave jerks, the slow phases of decreasing exponential velocities shown in our patient between the ages of 10 and 14 weeks may represent a form of transient nystagmus before the typical pattern of infantile nystagmus waveform is established. They show again that different subsystems of eye movement control may be involved.

Most studies of childhood nystagmus have used the EOG for eye movement recordings. Because this technique is less sensitive than infrared oculography,\textsuperscript{5} subtle, slow-phase abnormalities could have been missed in previous studies.

The changes in nystagmus form, frequency, and amplitude documented within several weeks are interesting. They may correspond to adaptation mechanisms that occur in a short period of time in the brain of young infants. After the onset of nystagmus, adaptive mechanisms may develop to suppress oscillopsia and to increase visual acuity, such as the establishment of foveation strategies and the reduction of nystagmus amplitude. These adaptive mechanisms may be reflected by changes in nystagmus waveforms.

As observed by the infant's mother and revealed by orthoptic examination, the child had poor visual acuity between the eighth week and the first several months of life. At this time, she did not fix or follow objects. However, preferential looking showed values within the lower limits of normal, and the child followed the pursuit stimulus during POG. Therefore, without measurement, large nystagmus amplitudes may lead to underestimation of visual acuity on clinical examination. In patients with large nystagmus amplitudes without organic disease of the anterior visual pathway, the parents may be reassured of usually relatively good visual outcome.

In conclusion, this report represents, to our knowledge, the first documentation of the appearance and evolution of infantile nystagmus by quantitative eye movement recordings. We showed with quantitative eye movement recordings that infantile nystagmus may not be present at birth and that different subsystems that control eye movements may be involved in its origin.

Key Words
eye movement recordings, infantile nystagmus, nystagmus development, nystagmus waveform, square-wave jerks

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References
Effects of Eye and Head Position on Horizontal and Vertical Smooth Pursuit

Christopher A. Mann and Mark J. Morrow

Purpose. To identify and explain the effects of eye and head position on smooth pursuit eye movements in normal humans.

Methods. Horizontal and vertical smooth pursuit were measured in different eye-in-orbit positions in normal subjects, using a magnetic search coil technique with sinusoidal and step-ramp stimuli. Pursuit also was tested in different horizontal head-on-trunk positions.

Results. Pursuit gain to sinusoidal targets averaged approximately 15% less with the eyes centered compared to 30° horizontally or vertically from the primary position than with the eyes near the orbital midline. In contrast, pursuit responses to step-ramp stimuli were similar regardless of eye position. For sinusoidal and step-ramp responses in eccentric eye positions, no significant differences were found between pursuit movements directed toward the orbital midposition and pursuit movements directed away from it. Changes in head position had no effect on smooth pursuit.

Conclusions. Sinusoidal smooth pursuit function decreases modestly for horizontal and vertical motion in eccentric eye positions. This effect is not caused by reductions in gain for centrifugal movements compared to centripetal movements, implying that the pursuit nonlinearities expected to arise from orbital mechanics are largely eliminated by central processing. Eye position-related differences in retinal or eye motion feedback or in predictive input may explain the influence of eye position on smooth pursuit maintenance. Changes in target position with respect to a trunk-centered frame of reference did not produce the orbital eccentricity effects that were documented because sinusoidal pursuit gain did not vary with head rotation. Invest Ophthalmol Vis Sci. 1997;38:773–779.

Structural constraints limit the human ocular motor range to approximately ±55° horizontally and ±45° vertically in young normal subjects. Ocular motor function is not uniform throughout this range. Using DC-coupled electro-oculography (EOG), Yee and colleagues found that mean horizontal smooth pursuit gain was lower for sinusoidal targets aligned with eccentric horizontal eye positions than for the same targets when they were centered relative to the orbit. These authors noted that pursuit gain generally was higher with motion toward the orbital midline (centripetal movement) than with motion away (centrifugal movement) and suggested that the centripetally directed elastic forces generated chiefly by the extraocular muscles explain the effects of eccentric eye position on pursuit.

To extend the findings of Yee and colleagues, we measured the influences of horizontal and vertical eye position on smooth pursuit in normal subjects, using horizontal and vertical stimuli. Sinusoidal targets measured pursuit maintenance, whereas unpredictable step-ramp stimuli tested the initial acceleration generated by the pursuit system before it can use eye or retinal motion feedback. Horizontal pursuit was tested with the head in different orientations with respect to the trunk.

METHODS. Subjects. Nine normal subjects (mean age, 29.9 years; range, 20 to 37 years) participated in this study; all subjects did not take part in each experiment. No subject reported a history of neu-