Photopic abnormalities in congenital stationary nightblindness

Alex E. Krill and Deidre Martin

Fourteen patients with congenital nightblindness, representing all three hereditary types, were studied, and all were found to have some type of photopic abnormality. The photopic abnormalities consisted of abnormal visual acuity, slower-than-normal final cone thresholds, elevated cone thresholds, subnormal photopic responses, slower-than-normal photopic a- and b-wave implicit times, and low flicker fusion frequencies. One or more of these abnormalities were noted in all patients. Only visual acuity could be related to the specific type of inheritance involved. No other photopic or scotopic abnormality bore a constant relation to the hereditary pattern. Congenital nightblindness, regardless of the hereditary type, is characterized by both scotopic and photopic abnormalities.

Key words: congenital nightblindness, photopic abnormalities, scotopic abnormalities, visual acuity, cone threshold, flicker fusion frequency, a- and b-wave implicit times

Congenital stationary nightblindness is a well-defined condition with three types of inheritance. All hereditary types are characterized by normal eye grounds, normal daylight visual fields, the absence of secondary or rod dark adaptation, and lack of progression. The stationary nature of the condition has been established by long follow-up of affected members. The finding of similar visual function abnormalities in younger and older affected members in long pedigrees also supports this notion.

Long pedigrees of all hereditary types have been studied.1-9

Major scotopic abnormalities are well known in this condition and will not be emphasized in this paper. Rather, this report emphasizes the frequent occurrence of photopic abnormalities in congenital stationary nightblindness. Photopic abnormalities, cited in the past,10-20 usually have received insufficient attention. In fact, abnormalities of cone dark adaptation are not even mentioned in some reports, although they are evident in accompanying photographs.

Visual acuity is almost always abnormal in X-linked recessive nightblindness, which is invariably associated with myopia. In addition, some patients with autosomal re-
cessive nightblindness have abnormal vision. Those with abnormal vision are frequently myopic as well. In contrast, all patients with the autosomal dominant form of congenital nightblindness have normal vision.

Elevated cone thresholds on subjective dark adaptation have been noted in all hereditary types of congenital nightblindness. Some patients took an abnormally long time to reach a final cone threshold.

Subnormal single flash photopic responses in the electroretinogram (ERG) have been noted in all hereditary forms of nightblindness. In some patients the entire response was small, but in others only the b-wave was reduced. Photopic flicker fusion frequency in the ERG was reduced in some patients. Slow and subnormal visual evoked responses have recently been noted in a few patients.

This report demonstrates the high frequency of photopic abnormalities in congenital stationary nightblindness when such abnormalities are searched for. In fact, in 14 patients with this condition whom we studied, all had some type of photopic abnormality. These data are discussed in this report and a new abnormality, a slower-than-normal photopic a- or b-wave implicit time, is presented.

Methods

The age, visual acuity, hereditary pattern, and some of the functional findings of the 14 patients in our study are shown in Table I. We had one patient with autosomal dominant inheritance, six patients with X-linked inheritance, and seven with autosomal recessive inheritance. All patients had a history of severe congenital nightblindness; all had normal eye grounds. Dark adaptation tests were done on 12 patients and only monofunctional curves were noted. Visual fields with the Goldmann perimeter were obtained in eight patients; all were normal. In the two youngest patients (ages three and five), subjective dark adaptation could not be done; however, the diagnosis was made from the history of nightblindness in each patient, a family history of nightblindness in one (Case 1), and characteristic ERG findings in both.

An ERG was not obtained from Case 13, but the history of nightblindness in this patient, the characteristic monofunctional dark adaptation curve, and the presence of typical ERG findings in his brother (Case 5) and uncle (Case 10) made the diagnosis certain. Eleven patients were followed for two to twelve years with no evidence of progression of symptoms on any parameter evaluated.

The ERG was done with the subject supine. The active electrode was a Burian-Allen recording contact lens. Usually binocular recordings were obtained. An indifferent electrode was centered on the forehead above the nose. The light adaptation source used was a 61 degree field provided by a 60 watt, 130 volt tungsten filament, illuminating a plastic diffuser in front of the bulb. This source produced a “white” light of 590 footlamberts luminance. The test stimulus was a Grass model PS-2 photostimulator providing an estimated maximum illumination at the position of the subject’s eye of 450,000 footcandles with the lamp centered about 18 inches away from the subject’s eye. The brightest light stimulus was obtained by using a maximum intensity setting on the instrument, and eight dimmer light stimuli, each differing by one-half log step, were obtained by interposing a series of four-inch square neutral density filters in front of the lamp. Control of eye position was attempted by having the subject fix on a 1.5 mm. red fixation bulb placed below the center of the lamp.

The electrodes led to a specially constructed junction box from which all impulses were conducted into two parallel systems. One of the two systems was used for single flash evaluation. This system consisted of two RM 122 Textronix low-level preamplifiers connected to a dual-beam type 512 Textronix oscilloscope. The single-flash responses on the oscilloscope were photographed with a Textronix C-13 oscilloscope camera. Single flash photopic responses were obtained with the highest intensity light stimulus and the room lights on. Single flash scotopic responses were obtained in total darkness after five minutes of light adaptation to the light source described above. The methodology is described in detail elsewhere.

The second system to which impulses from the junction box led was used for recording flicker responses. A flicker ERG, as well as a single-flash photopic and scotopic ERG, was obtained from eight patients. In six patients this was done in the dark-adapted state with a high-intensity light. The system consisted of an Öffner transistorized unit with a type 483 preamplifier, type 482 power amplifier, and a type B Dynograph. The highest intensity setting with a one log unit neutral density filter was used as the light stimulus. Responses were obtained to at least 13 flicker frequencies ranging from one to 70 flashes per second. Further details are described elsewhere.
Congenital stationary nightblindness

Fig. 1. The dark adaptation data, divided into three sections, from the nine patients who were tested immediately after the completion of preadaption. An average normal curve is shown in each section. Eight patients showed a slower-than-normal time in reaching the cone final threshold. Five patients (Cases 3, 7, 9, 11, and 14) had elevated cone thresholds. Most of the patients also showed an initial delay in seeing the light.

For this study a control group of 20 subjects was used to calculate normal a- and b-wave implicit times. The normal data (mean plus or minus two standard deviations) are shown in Figs. 2 and 3, and the exact values are indicated in Table I. The mean b-wave amplitudes of the flicker responses from ten normal subjects calculated from the X-Y plotter, ranged between 80 to 95 microvolts for frequencies between one and 20 cycles per second and gradually decreased with each frequency after that, so that between 70 to 75 cycles per second no responses were obtained. These data are shown in Fig. 7.

Dark adaptation studies were performed after a careful period of instruction and an initial short trial run. The tested eye was dilated to about 7 to 8 mm. with tropicamide, 0.5 per cent. The patient was first placed in complete darkness for three minutes and then exposed to a preadapting illumination of 3.13 log millilamberts (2400 lux) luminance for seven minutes, after which threshold measurements were started immediately. The subject initially fixated on a 2 mm. red light that varied in brightness, located about 15 degrees above the center of a test light with a retinal subtense of one degree. The stimulus was pre-
Table I

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Type</th>
<th>Vision</th>
<th>Photopic ERG</th>
<th>Scotopic ERG</th>
<th>Dark adaptation</th>
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<td></td>
<td></td>
<td></td>
<td>a-IT</td>
<td>b-IT</td>
<td>b-AMP</td>
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<td>XL</td>
<td>Abnormal</td>
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<td>40</td>
<td>100</td>
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<td>5</td>
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<td>80</td>
</tr>
<tr>
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<td>34</td>
<td>XL</td>
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<td>8</td>
<td>26</td>
<td>40</td>
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<td>6</td>
<td>AR*</td>
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<td>110</td>
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<td>AR</td>
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<td>120</td>
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<td>R = 20/80</td>
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<td>50</td>
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</table>

Normal mean ± 2 S.D.

11 ± 4  29 ± 4  146 ± 47  13 ± 4  325 ± 125  48 ± 10  515 ± 165  4.8 ± 4  3.1 ± 2.0

a-IT = a-wave implicit time; b-IT = b-wave implicit time; ND = neutral density; CT = cone threshold; Time = time to reach cone threshold; a-AMP = a-wave amplitude; b-AMP = b-wave amplitude; XL = X-linked; AD = autosomal dominant; AR = autosomal recessive; S.D. = standard deviation; R = right eye; L = left eye.

*Autosomal recessive with worse than 20/30 vision.
Figs. 2 and 3. A plot of the photopic peak or implicit times for the a-wave (2) and b-wave (3) along with a normal control group (normal mean plus or minus two standard deviations). Ten patients had slower-than-normal a-wave implicit times (2), and seven had slower-than-normal b-wave implicit times (3).

Presented as light flashes of one second in duration separated by a dark interval of one second. The test light was calibrated at a maximum intensity of 9.4 log micromicrolamberts (20 lux) and at the onset was presented at an intensity of 8.4 log micromicrolamberts (2 lux) with the subsequent direction of change dependent on the response of the subject. At each test time, four "on" and "off" thresholds were noted, and the approximate true absolute threshold was calculated as an average of these values. Each subject was tested in this same retinal area for a total of 40 minutes, by which time a constant final threshold value was usually obtained in normal subjects. The responses were charted at 30 second or one- or two-minute intervals depending on the time of the test.

In 9 subjects complete dark adaptation functions were obtained. The other three subjects did not receive initial light adaptation but were placed in the dark for 30 minutes before testing. Further details of testing are described elsewhere. The data from cone thresholds from 25 normal subjects were used as a control group. The values (mean plus or minus two standard deviations) for the cone threshold and time to reach the cone threshold are indicated in the table and the average values are plotted in Fig. 1.

An electrooculogram (EOG) was done in four
patients; the Offner unit described above was used for recording. The technique of testing and normal data are described elsewhere. In evaluating the record, the average amplitude of each test period was measured and the ratio of the maximum light-adapted response was calculated and compared with similar ratios from a normal control group. Ratios less than 1.85 were considered definitely abnormal.

**Results**

**Visual acuity.** The patient with autosomal dominant inheritance (Case 11) had normal acuity. All six patients with X-linked recessive inheritance (Cases 1, 3, 5, 10, 12, and 13) were myopic and could not be corrected to normal acuity. Vision varied from 20/40 to 20/80 in five of these patients. The degree of myopia ranged from 6 to 17 diopters. The sixth patient (Case 1) was too young to test, so the diagnosis of abnormal vision was made by the performance of the child and also by the presence of nystagmus.

Of the seven patients with autosomal recessive inheritance, two had 20/20 vision, one had 20/30 vision, and four (two of whom were myopic) had vision between 20/60 and 20/100. The three patients with 20/30 or better vision and the four patients with worse than 20/40 vision were studied as two separate groups.

**Dark adaptation.** Only monofunctional dark adaptation curves were obtained in the 12 patients tested, regardless of how long they remained in the dark. Cone thresholds were elevated in five patients (Cases 3, 7, 9, 11, and 14). Three of the five patients with abnormal cone threshold had acuity worse than 20/30, whereas two had 20/20 vision. Eight of the nine patients in whom the initial portion of the dark adaptation curve was obtained (Cases 3, 5, 7, 8, 9, 11, 13, and 14) took longer than normal to reach a constant final cone threshold, and the ninth patient (Case 6) was at the upper limit of normal (Table I and Fig. 1). The dark adaptation abnormality could not be related to vision or hereditary pattern.

**ERG.** Four patients (Cases 2, 3, 4, and 10) had subnormal photopic responses (Table I). Photopic implicit or peak times were slower than normal in ten of the 13 patients tested (Figs. 2 and 3). In seven of the ten (Cases 1, 2, 9, 10, 11, 12, and 14) both a- and b-wave implicit times were slow. In the other three (Cases 4, 5, and 6), only a-wave implicit times were slow. Examples of two patients with slower-than-normal photopic a- and b-wave implicit times and normal amplitudes are shown in Fig. 4.

Scotopic b-wave amplitudes were subnormal at all intensities in all patients tested (Fig. 5). Scotopic a-wave amplitudes were normal in six patients (Cases 3, 7, 8, 11, 12, and 14) and subnormal in the seven others tested (Table I). Scotopic a-wave implicit times at the highest light intensity used were slower than normal in six patients (Table I and Fig. 6). This was not true at lower intensities. On the other hand, b-wave implicit times were faster than normal in nine patients (Cases 1, 2, 3, 6, 7, 8, 10, 11, and 12) at the highest light intensity used (Table I). In general, this was true at all intensities of light stimulation.

In three of the six patients in which dark-
Fig. 5. A plot of b-wave amplitudes from all patients tested compared with a normal control group (normal mean plus or minus two standard deviations). Note that the amplitudes are reduced at all intensities for all patients.

Fig. 6. A plot of scotopic a-wave implicit times at four intensities along with a normal control group (mean plus or minus two standard deviations). At the highest intensity six patients had slower-than-normal implicit times.

adapted flicker studies were done with a high-intensity stimulus, fusion frequencies were abnormal (Cases 2, 4, and 10). The data from Cases 2 and 4 are plotted in Fig. 7.) In the two patients (Cases 5 and 11) in which light-adapted flicker studies were done, fusion frequencies were also abnormal (Fig. 8).

EOG. The ratio of the maximum light-adapted to minimum dark-adapted response was abnormal in three of the four patients tested. The values were 2.80 for Case 7, 1.50 for both Cases 3 and 12, and 1.20 for Case 9. In all three patients with an abnormal ratio, the response increase with light was smaller than normal, whereas the response decrease in the dark-adapted eye was normal or close to normal (Fig. 9).
Discussion

Photopic abnormalities were found in all 14 patients in this study. These abnormalities included abnormal visual acuity, a delayed final cone threshold or plateau, an elevated cone threshold, subnormal single-flash photopic responses, slow photopic implicit times, and a low flicker fusion frequency. All abnormalities have been noted previously, except for the slow photopic implicit times.

The b-wave normally interferes with "full expression" of the a-wave because the falling phase of the a-wave is inter-
ruptured by the rising edge of the b-wave. This is best seen by studies which show the appearance of the a-wave before and after the development of the b-wave,31 or before and after the use of experimental methods which selectively eliminate the b-wave (for example, ligation of the central retinal artery32). Therefore the normal a-wave implicit time is "artificial" in the sense that it is directly dependent on the b-wave latency. An increase in b-wave latency can occur with either an increase in the b-wave implicit time or decrease in the b-wave amplitude. In only two of the ten patients with slower-than-normal photopic a-wave implicit times (Cases 5 and 6) were both b-wave amplitudes and b-wave implicit times normal (Table I and Fig. 10). It is therefore likely that the slower-than-normal a-wave implicit time is secondary to an increase in b-wave latency.

The occurrence of a slower-than-normal photopic b-wave implicit time in the presence of a normal b-wave amplitude in five of seven patients (Fig. 10) suggests an independent effect on the b-wave implicit time. A reduction in b-wave implicit time can be secondary to a reduction in b-wave amplitude, but this is unlikely to be the case here.

It may be that these data reflect a basic cone abnormality, but localization is impossible from the single-flash photopic ERG abnormalities cited. However, the lower-than-normal objective flicker fusion frequencies in several patients, the slower-than-normal cone threshold frequently noted in subjective dark adaptation, and the slower-than-normal visual evoked responses noted in another report13 are all additional data suggesting a possible basic cone abnormality in this condition.

The scotopic a-wave implicit time was slow in six patients only at the highest light intensity used. It is difficult to explain this abnormality as secondary to a slower-than-normal b-wave latency (which is secondary to a slower-than-normal b-wave implicit time or a decrease in b-wave amplitude). First of all, the scotopic b-wave implicit time was faster than normal in these patients, even in the presence of a subnormal b-wave amplitude. Secondly, the slower-than-normal a-wave implicit time was seen only at the highest light intensity used, even though the scotopic b-wave amplitude was
Fig. 10. A plot of implicit times in relation to b-wave amplitudes for all patients tested (case number is shown near plotted value) and 15 normal subjects. Upper half of photograph shows a-wave implicit time and lower half b-wave implicit time. All normal values fall in cross-hatched areas. Note that four patients show subnormal b-wave amplitudes, ten have slower-than-normal a-wave implicit times, and seven have slower-than-normal b-wave implicit times. All but two of the patients with slower-than-normal a-wave implicit times (Cases 5 and 6) have subnormal b-waves or slower-than-normal b-wave implicit times. The independence of b-wave implicit time and amplitude is obvious in the lower half of the photograph.

subnormal at all stimulus intensities. A possible explanation is that only the brightest light stimulus produced responses reflecting significant cone as well as rod activity. Thus, the high-intensity scotopic a-wave implicit time abnormality may be caused by the postulated cone defect in this condition.

Frequent scotopic abnormalities noted in this study were a marked reduction of the b-wave amplitude and a faster-than-normal implicit time of the remaining b-wave. This distinguishes congenital nightblindness from other conditions with subnormal b-waves, in which the b-wave implicit time is slow as well. In some patients both scotopic a- and b-waves were reduced in amplitude. These responses were often similar in appearance to the patients' photopic responses, conforming to the type of abnormality initially reported by Riggs in congenital nightblindness. In such patients the photopic response was often small as well. In another group of patients there was a reduction mainly in the scotopic b-wave, conforming more to the abnor-
mality initially reported by Bornschein and Schubert in congenital nightblindness.

Three of the four patients tested had an abnormal EOG. The interpretation of this abnormality, previously described in some patients with congenital nightblindness, is uncertain. The only parameter that can be correlated with inheritance is visual acuity. All patients with autosomal dominant nightblindness have normal vision, whereas all with the X-linked recessive type have abnormal vision. All other photopic and scotopic abnormalities, on the basis of data from our study and other reported studies, have been cited for each type of hereditary nightblindness. It is obvious from combining our data and those of previous reports that an abnormal EOG can occur in all three hereditary types. The explanation for both the photopic and scotopic abnormalities in congenital nightblindness is uncertain. The only pathologic study shows no structural abnormality on light microscopy and only a borderline histochemical abnormality. The pathogenesis of this intriguing condition remains a mystery.

REFERENCES