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Scotopic Vision Deficits in Young Monkeys Exposed to Lead

Abstract. *Rhesus monkeys were reared on diets designed to produce blood lead concentrations of 14 (untreated), 55, or 85 micrograms per 100 milliliters for the first year of life. Eighteen months later, blood lead levels were normal in all animals. At this time, however, visual discrimination performance in the 85-microgram group was impaired under dim light relative both to their own performance under bright light and to the performance of the other groups under all light levels used. We interpret these results to reflect a deleterious, enduring impairment of scotopic visual function (night blindness) as a result of early lead intoxication.*

The sequelae of acute lead poisoning in humans and animals include visual system damage (*1*) and blindness (*2*). These effects are usually described simply as "optic atrophy" or "blurred vision" and appear only with lead poisoning severe enough to induce encephalopathy (*3*). Although it can be dramatic, lead-induced blindness is nevertheless a rare and usually transient phenomenon (*4*). Recently, some effects of subclinical (*5*) lead exposure have been described (*6*), but we are aware of no data relating visual perceptual deficits to this form of lead intoxication. We report here that rhesus monkeys exposed during infancy to subclinical levels of lead acetate, and exhibiting no overt (*7*) signs of intoxication, nevertheless manifest a deficit in scotopic vision measured 1½ years after termination of exposure to lead.

Ten rhesus monkeys were separated from their mothers at birth and reared on Similac (Ross Laboratories) in individual cages (*8*). Lead acetate was added to the Similac given to six of the animals in a daily 7 a.m. feeding of 100 ml from day 5 to day 365 post partum. Doses were adjusted to maintain target lead concentrations in whole blood at 55 μg per 100 ml in three "low-lead" monkeys, and at 85 μg in three "high-lead" monkeys; the remaining four animals served as untreated controls. Weekly midafternoon blood samples were assayed for lead concentrations (*9*). Treatment parameters and physiological responses of the three groups are shown in Table 1.

Initial lead doses averaging 0.53 mg kg^{-1} day^{-1} elevated the blood lead levels of the low-lead group to 55 μg per 100 ml by 4 weeks, after which appropriate dose adjustments were made to maintain that level. In contrast, initial doses averaging 1.15 mg kg^{-1} day^{-1} raised the blood lead levels of the three high-lead subjects to 137, 152, and 300 μg per 100 ml by 6, 9, and 5 weeks of age, respectively (*10*). With subsequent modifications of dose, these peak levels declined to near the 85 μg per 100 ml chronic target level over the next 6 to 8 weeks (*11*) and remained at that level for the rest of the treatment year.

The present experiments began 18 months after termination of lead treatment. At this time mean blood lead concentrations (in micrograms per 100 ml) were essentially normal (*12*) for all groups, with means ± standard errors of 13.50 ± 1.45 (control), 19.75 ± 5.04 (low-lead), and 22.67 ± 4.02 (high-lead). Funduscopic examination revealed no indication of optic atrophy or other observable retinal damage in any animal.

A semiautomatic Wisconsin General Test Apparatus (*13*) was equipped with eight 100-watt incandescent lamps whose brightness was controlled by a voltage regulator. Prior experiments had adapted all animals to the apparatus and to the discrimination procedure employed here. On each trial, two planometric stimuli were presented, each covering a food well located 32.5 cm from a second identical well and 3.2 cm behind the raised front edge of a gray test tray. A trial began when an opaque screen was lowered, revealing to the monkey the test tray with the two stimulus plaques lying flat upon it. The animal responded by pushing aside just one of the plaques, uncovering either a food reward in the well under the correct stimulus or an empty food well under the incorrect one. The opaque screen was then interposed, the next trial set up, and the process repeated, 50 trials per session. Subjects were tested once per day and had been fasted for 17 to 24 hours at the time of testing. The stimuli consisted of a set of six tagboard cards, 7.62 cm square, upon which were mounted photographically reproduced, black-on-white Landolt rings, 3.81-cm outside diameter and 1.90-cm inside diameter, with gap widths of 7.5 (A), 3.75 (B), 1.0 (C), 0.4 (D), and 0.0 mm (Standard); a protective transparent polyester film was laminated over the stimuli for durability. The sixth stimulus was a duplicate Standard (St+) which was always associated with reinforcement. Several stimulus sets were

Table 1. Summary of treatment parameters and physiological responses of animals during the year of exposure to lead acetate. Values shown are group means and ranges of individual animal averages for the treatment year, with the exception of body weights, which were obtained at the end of the year. All values (except those of lead consumption and blood lead concentrations) fall within normal limits for infant monkeys.

Group	Lead consumption (mg kg^{-1} day^{-1})	Blood lead conc. (μg/100 ml)	Hemoglobin (g/100 ml)	Hematocrit (%)	Blood total protein (g/100 ml)	Albumin/ globulin ratio	Similac intake (ml kg^{-1} day^{-1})	Body weight (kg)
Control	No lead	14 (10 to 20)	13.1 (12.7 to 13.6)	40.2 (38 to 42)	6.7 (6.4 to 6.9)	1.35 (1.32 to 1.43)	309 (305 to 315)	1.92 (1.7 to 2.2)
Low-lead	0.326 (0.313 to 0.346)	55 (44 to 62)	12.6 (12.2 to 13.3)	38.3 (37 to 40)	5.77 (5.6 to 6.0)	1.75 (1.59 to 2.00)	312 (310 to 315)	2.00 (1.9 to 2.1)
High-lead	1.018 (0.989 to 1.040)	85 (73 to 95)	11.8 (11.6 to 13.0)	37.5 (36 to 41)	6.33 (6.0 to 6.8)	1.72 (1.61 to 1.81)	313 (310 to 315)	1.90 (1.7 to 2.1)

used and stimuli were replaced when they showed any signs of wear. The five comparison stimuli, illustrated schematically above the abscissas of Fig. 1, were always incorrect. Stimuli A, B, C, and D were always positioned on the test tray with the gap oriented toward the monkey.

Animals were trained to respond to St+ at a stimulus luminance level of +1.73 log millilamberts (mlam) (*14*) and were then adapted to progressively reduced light levels over the course of at least 15 test sessions. For experiment 1, all animals received at least one 50-trial session at each of four luminance levels (+1.73, −0.29, −0.81, and −1.55 log mlam) in order of decreasing intensity. Each session consisted of ten five-trial blocks; each block contained one pairing of St+ against each other stimulus. The order of such pairings within each block was randomized, and St+ appeared equally often on both sides of the test tray in a random left-right sequence. Animals were dark adapted for 10 minutes prior to testing at the two lowest light levels used.

The control and low-lead groups showed essentially no change in discrimination accuracy as light intensities were reduced, whereas the discrimination accuracy of all three monkeys of the high-lead group was severely impaired at −0.81 log mlam and was reduced virtually to chance at −1.55 log mlam (Fig. 1). This interaction of the effect of light intensity with lead treatment was statistically significant by analysis of variance (*15*), with $F = 3.88$; d.f. = 6,21; $P < .025$.

Since the discrimination deficit occurred in the high-lead group only at light levels below the photopic range, it could reflect either a loss of scotopic function or some response deficiency related to the increased difficulty of the task under dim light. The latter explanation may be ruled out, however, by the fact that absolutely no discrimination deficit relative to control and low-lead monkeys was seen in the high-lead monkeys when task difficulty was increased by reducing the stimulus gap width (Fig. 1). Discrimination accuracy in all monkeys declined with the decrease in gap width ($F = 72.63$; d.f. = 4,28; $P < .001$), and did not interact with lead treatment ($F = 1.65$; d.f. = 8,28; $P > .10$). Therefore, the high-lead monkeys were not generally sensitive to increased task difficulty, but rather showed a discrimination decrement specific to the reduction of light intensities below the photopic range.

In experiment 2, we determined the threshold light intensity below which each animal could not reliably discern a 1.0-mm gap from a closed ring. All procedures of experiment 1 were followed except that St+ and C were paired on every trial and light intensities were manipulated within each test session on a "titration" schedule designed to maintain 75 percent correct responding (*16*). Each animal began the first session at +0.82 log mlam; after three consecutive correct responses the luminance was reduced to +0.50 log mlam and so on through seven additional decrements of +0.04, −0.29, −0.81, −1.30, −1.55, −1.66, and −1.74 log mlam. After each error, the luminance was increased by one increment. Succeeding sessions were begun at the luminance value last used on the previous session; each subject received four such sessions.

Average threshold values were calculated for each animal as the mean luminance level used on its last 150 trials (three sessions). The control and low-lead groups achieved mean thresholds of −1.70 (S.E. = −2.64) and −1.73 (S.E. = −3.70) log mlam, which reflected accurate performance below the lower limit of photopic vision (*17*). The thresholds of the three high-lead subjects (−0.96, −0.69, and −1.00 log mlam) lay within the transition range of mixed photopic and scotopic function (−1 to +1 log mlam). To test whether the performance of the high-lead animals reflected retarded dark adaptation, each high-lead animal was given two further tests after a 1-hour dark adaptation period. No consistent improvement was observed: thresholds obtained were −0.81, −1.22, and −0.96 log mlam for the three animals. Comparison of the group's mean thresholds (−0.95 log mlam for 10 minutes of dark adaptation, and −0.97 log mlam for 60 minutes of dark adaptation) showed no significant change (matched $t = 0.100$, d.f. = 2, $P > .90$).

While retinopathies and structural abnormalities in the eye may occasionally result from lead intoxication, the most common visual disturbances from this agent are of central nervous system origin (*4*). Since rods are relatively poorly represented in visual cortex (*18*), and since lead appears to induce encephalopathy nonspecifically by means of vasogenic edema and demyelinization (*19*), one might expect visual system deficits to appear first in rod-mediated vision. Such a model has been proposed to account for similar deficits in monkeys chronically exposed to methylmercury (*20*).

The close psychophysical similarity of the macaque visual system to that of the human has been well documented (*21*). On the basis of the present data, therefore, one may suspect transient blood lead levels in the range of approximately 200 μg per 100 ml early in life and chronic exposure at 85 μg per 100 ml thereafter to induce similar impairments of scotopic vision in the human child, even if exposure has been terminated and lead levels have returned to normal (*12*). A recent Public Health Service survey (*22*)

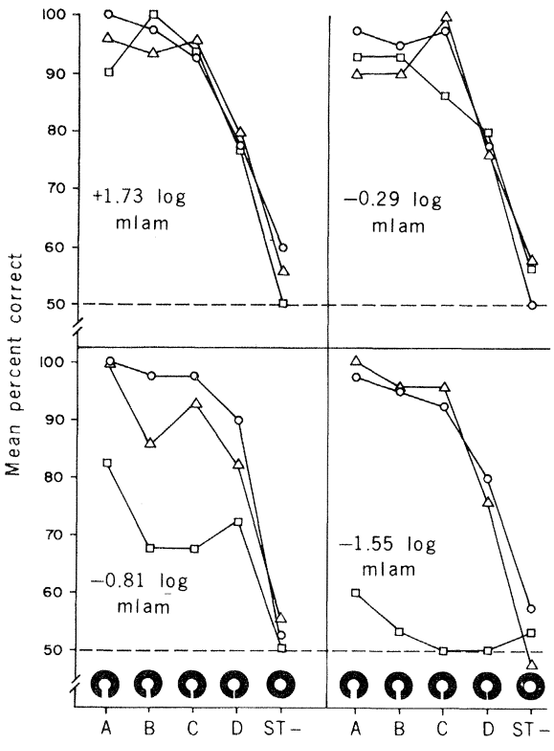

Fig. 1. Each panel summarizes the performance of the three lead treatment groups of monkeys at one of the four light intensities used in experiment 1. Comparison stimuli, with gap widths exaggerated for clarity, are shown on the abscissas. Controls are represented by circles, low-lead animals by triangles, and high-lead animals by squares. Chance performance (responding at or near 50 percent correct) represents failure to discriminate the St+ from the comparison stimulus; on trials pairing St+ with St−, it indicates the absence of extraneous cues governing the discrimination.

found 480 of 98,328 (0.49 percent) U.S. children living in high-risk areas to have blood lead concentrations in excess of 85 μg per 100 ml, indicating the possible magnitude of the present health hazard. This hazard may be complicated by a lack of overt symptoms of lead poisoning associated with these blood lead levels, rendering early diagnosis fortuitous in the absence of explicitly directed screening tests.

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10. Unavoidable delays between blood sampling and blood lead assays occurred for these monkeys. Thus, their blood lead concentration exceeded the target levels of 85 μg per 100 ml before the assays detected the overshoot.
11. Weekly blood lead concentrations (in micrograms per 100 ml) in the three high-lead animals for the first 15 weeks of life were: for subject No. 1: 10, 30, 42, 53, 70, *137*, 108, 120, 105, 123, 91, 114, 100, 65, and 83; for subject No. 2: 9, 23, 42, 59, 37, 69, 64, 42, *152*, 72, 95, 124, 78, 140, and 84; and for subject No. 3: -, -, 9, 52, *300*, 123, 136, 129, 142, 112, 85, 58, 60, 63, and 77. Peak values are italicized.
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The Capsian Escargotières: A Clarification

D. Grébénart of the Université de Provence, Aix-en-Provence, France, has asked us to point out that, in our article "The Capsian escargotières" (*1*), we neglected to properly cite his work. Grébénart's publications (*2*, *3*) on the region provided us with the map coordinates and brief descriptions of most of the Capsian sites shown in our figure 1 (*1*, p. 911). His suggestion that the deposits exposed in Wadi Hamaja represented two distinct periods of occupation originally triggered our interest in the Aïn Misteheyia escargotière.

To avoid confusion for those readers familiar with the literature, we also wish to point out that the Aïn Misteheyia is identified as Aïn Messaïa (site number 36) by Grébénart, who followed the nomenclature used on the French topographic maps for the region. After extensive discussion in both 1973 and 1976 with the local inhabitants, who all insisted that the correct name was Aïn Misteheyia, we elected not to use the apparently incorrect Aïn Messaïa.

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