CHILDHOOD BLINDNESS AND VISUAL LOSS: AN ASSESSMENT AT TWO INSTITUTIONS INCLUDING A "NEW" CAUSE

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"Deprivation of vision in the early years of life can have far-reaching psychosocial, educational and economic effects, not only for the affected child but also for the family and the community."

-World Health Organization, 1992[1]

ABSTRACT

Purpose: This study was initiated to investigate the causes of childhood blindness and visual impairment in the United States. We also sought a particular etiology—congenital lymphocytic choriomeningitis virus (LCMV)—which has been considered exceedingly rare, in a fixed target population of children, the severely mentally retarded.

Methods: We undertook a library-based study of the world literature to shed light on the causes of childhood blindness internationally and to put our data in context. We prospectively examined all consented children (159) at 2 institutions in the United States to determine their ocular status and the etiology of any visual loss present. One of the institutions is a school for the visually impaired (hereafter referred to as Location V), in which most of the students have normal mentation. The other is a home for severely mentally retarded, nonambulatory children (hereafter referred to as Location M). This institution was selected specifically to provide a sample of visual loss associated with severe retardation because the handful of cases of LCMV in the literature have been associated with severe central nervous system insults.

Histories were obtained from records on site, and all children received a complete cyclopleged ophthalmic examination at their institution performed by the author. Patients at Location M with chorioretinal scars consistent with intrauterine infection (a possible sign of LCMV) had separate consents for blood drawing. Sera was obtained and sent for standard TORCHS titers, toxoplasmosis titers (Jack S. Remington, MD, Palo Alto, Calif), and ELISA testing for LCMV (Centers for Disease Control and

Prevention, Atlanta, Ga).

Results: The diagnoses at Location V were varied and included retinopathy of prematurity (19.4%), optic atrophy (19.4%), retinitis pigmentosa (14.5%), optic nerve hypoplasia (12.9%), cataracts (8.1%), foveal hypoplasia (8.1%), persistent hyperplastic primary vitreous (4.8%), and microphthalmos (3.2%).

The most common diagnosis at Location M was bilateral optic atrophy, which was found in 65% of the patients examined who had visual loss. Of these, the insults were most often congenital (42.6%), with birth trauma, prematurity, and genetics each responsible for about 15% of the optic atrophy. The second most common diagnosis was cortical visual impairment (24%), followed by chorioretinal scars (5%), which are strongly suggestive of intrauterine infection. Of 95 patients examined at Location M, 4 had chorioretinal scars. Two of these had dramatically elevated titers for LCMV, as did one of their mothers. One of the other 2 children died before serum could be drawn, and the fourth had negative titers for both TORCHS and LCMV.

Conclusions: At both locations studied, visual loss was most often due to congenital insults, whether genetic or simply prenatal. The visual loss at Location V was twice as likely as that at Location M to be caused by a genetic disorder. The genetic disorders at Location V were more often isolated eye diseases, while those among the severely retarded at Location M were more generalized genetic disorders. Our study identified optic atrophy as a common diagnosis among the severely mentally retarded with vision loss, a finding that is supported by previous studies in other countries.

In our population of severely retarded children, the target etiology of lymphocytic choriomeningitis virus was responsible for half the visual loss secondary to chorioretinitis from intrauterine infection. This is more common than would be predicted by the few cases previously described in the literature, and strongly suggests that LCMV may be a more common cause of visual loss than previously appreciated. We believe that serology for LCMV should be part of the workup for congenital chorioretinitis, especially if the TORCHS titers are negative, and that perhaps the mnemonic should be revised to "TORCHS + L."

Childhood blindness and visual impairment are tragic and costly. Most of the visual loss in the children we studied—including those manifesting our sample etiology of LCMV—had its origins in congenital causes and, as such, is preventable through better prenatal care, prevention of childhood abuse, and advances in genetic research.

INTRODUCTION

PREVALENCE OF CHILDHOOD BLINDNESS

Blindness in childhood is a significant health problem. The World Health Organization (WHO), in a 1992 study,[1] reported an estimated 1.5 million cases of childhood blindness, 90% of them in underdeveloped countries. Even in developed countries such as the United States, the WHO estimates a prevalence of 0.3 per 1,000 children (Table I). This same report warns that "there are very few reliable data on the prevalence or incidence of childhood blindness, and estimates should be viewed with caution; but in general they tend to underestimate the size of the problem."

TABLE I: ESTIMATED NUMBER OF BLIND CHILDREN IN THE WORLD*

REGION	POPULATION IN MILLIONS, 1989	NO. PER 1,000	TOTAL BLIND CHILDREN
Africa	240	1.1	264,000
Latin America	130	0.6	78,000
North America, Europe, Japan, Oceania, former USSR	240	0.3	72,000
Asia	1,200	0.9	1,080,000
Total	1,810		1,494,000

Data from World Health Organization.[1]

A mission statement published in 1991 by the American Association of Pediatric Ophthalmology and Strabismus, entitled *Eye Care for the Children of America*, states, "Prevention and risk counseling aids in reducing the occurrence of eye diseases in children."[2] We felt it appropriate to gain a better understanding of the risks of blindness and how they might be prevented by studying fixed patient populations of children who are affected visually, specifically one residential home for visually impaired children and one residential home for severely retarded children.

There was an additional impetus for seeking children at a home for the severely retarded, since an explicit goal of our study was to investigate the lymphocytic choriomeningitis virus (LCMV) as a possible cause of visual loss in this population. Until the spring of 1996, there were 6 documented cases of congenital LCMV in the United States and none in the eye

literature.[3-5] We happened upon 2 cases within 2 months. It was our strong suspicion that this devastating congenital central nervous system disorder, which generally results in psychomotor retardation and visual loss, was more prevalent than was suggested by the few cases documented in the American literature.

DEFINITION OF TERMS

Blindness and Visual Impairment

The WHO defines blindness as corrected visual acuity in the better eye of less than 3/60 (count fingers at 3 meters) or a central field of less than 10 degrees. The WHO defines severe visual impairment as corrected vision in the better eye of 3/60 or better, but less than 6/60.[1] The National Society to Prevent Blindness defines blindness as best corrected visual acuity of 20/200 or worse in the better eye; and visual impairment as best corrected visual acuity of worse than 20/40, but better than 20/200 in the better eye.[6] The author's state of residence defines legal blindness as 20/70 or less in the better eye, or a bilateral visual field of less than 140°.

Cortical Visual Impairment

Cortical blindness, defined as a bilateral loss of vision with spared pupils and a normal eye examination, is attributed most commonly to perinatal or postnatal hypoxia-ischemia.[7,8] It is referred to by Good and associates[9] as cortical visual impairment, the term we will use in this paper. It may also be seen secondary to trauma such as "shaken baby" syndrome;[10] bacterial meningitis,[11,12] especially that due to Haemophilus influenzea;[13] hydrocephalus;[14] hypoglycemia;[15] poisons such as carbon monoxide;[16] and cardiac arrest, in which case it may be reversible.[17] The visual loss is due to damage to the geniculate or extrageniculate pathways or both, and the event that causes it often causes insult to other areas of the brain, chiasm, optic nerves, or retina. Therefore, these children most often have multiple handicaps. The visual picture includes variable visual performance; staring at bright lights, although some exhibit photophobia; a preference for brightly colored objects; and a characteristic head turn when observing an object, as if the child is using peripheral rather than central vision. It has been suggested that the concept and diagnosis of "delayed visual maturation" may represent the milder end of the spectrum of cortical visual impairment.[18]

Mental Retardation

Mental retardation is defined as severe when the developmental quotient is below 55 and mild when it is between 55 and 75.[19] The prevalence of severe mental retardation in North America and Europe has been

estimated at between 3 and 4 per 1,000 children.[20] Estimates of the prevalence of mild retardation range from 4 per 1,000 (Sweden, 1981)[21] to 6.1 per 1,000 children (Great Britain, 1983).[22] The relationship between mental retardation and blindness as documented in the world literature is explored in more detail below.

CONSEQUENCES OF CHILDHOOD BLINDNESS

Cost in Dollars

The monetary cost of childhood blindness in the United States can be calculated on the basis of federal spending in programs for all blind individuals in 1990. The cost for one individual over a lifetime is about $560,000, which, multiplied by the 1,500 projected cases of childhood blindness in that year, equals $840 million.[23] However, childhood blindness has other wide-ranging effects that cannot be quantified, as it clearly impedes normal development of the central nervous system and thought processing.

Impact on Normal Childhood Development

Compared to the congenitally blind, children who lose their sight at a later age and whose visual impairment is less severe excel in the areas of spatial development and socialization.[24] Fraiberg[25] studied 10 "congenitally" blind children who were otherwise considered normal. Three had retinopathy of prematurity (ROP) and 3 had optic nerve hypoplasia; both diseases are sometimes associated with other abnormalities. Nonetheless, Fraiberg's observations are useful in our understanding of the impact of vision on development. Sight is integral to emotional bonding and development of concepts (both secondary to the bonding and autonomously), and is required for learning fine motor skills. The absence of eye contact, mutual gaze, and smiling reinforced by smiling can affect the bonding process and effective interaction between parent and child, which build the foundation for further cognitive development.

Tactile and auditory sensory communication are essential compensations for the absence of vision. In a visual sensory void, the infant depends on its parents to provide opportunities to develop the concept of object permanence. This concept assures that an object is not out of mind when out of sight, and is necessary for the development of internal thought. A sighted infant practices the disappearance of objects and challenges gravity at the same time by pushing objects off the feeding tray and any other gravity-defying structure. A blind child can substitute sound for sight in this experiment with the world. Since he knows sounds come and go, if he can reach for a sound and find a sound-associated toy, he can learn that it exists even when he cannot perceive it.

Head raising, crawling, and walking are all visually motivated developments. The visually impaired infant is restricted by anxiety or the unknown space beyond and lacks the visual motivation to pursue a distant object. Again, sound can be substituted for sight, and tactile exploration can replace some of the information usually gathered visually. Visual concepts such as colors, darkness, and change from light to darkness present conceptual difficulties. Compensations certainly can be made, but childhood visual loss—and especially congenital blindness—is more than simply loss of sight. It affects our thought development; our perceptions of the world; our ability to perceive the world, both visually and conceptually; our socialization; our ability to support ourselves; and, especially in underdeveloped countries, our ability to survive.

CAUSES OF CHILDHOOD BLINDNESS

Worldwide Studies

The etiologies of childhood blindness and visual loss and their prevalence differ over time and from nation to nation (Table I).[1] Distinct etiologic patterns emerge through a study of the world literature, ranging from the least developed countries, where infection is key; to transitional countries, where improvements in medical care are beginning to have effects; to highly developed countries, where cases of blindness are fewer and more congenital in nature.

Developing countries with severe poverty and poor health care, such as those in Africa, Asia, and parts of Latin America, report corneal opacification or phthisis as the major cause of blindness.[1] There appears to be a predilection for corneal ulceration following measles infection, and the causes include herpes simplex infection, vitamin A deficiency, and use of traditional medicines.[26-41] In the transition countries, such as Saudi Arabia, there have been relatively rapid changes in medical care over recent years that have caused fluctuations in the incidence of diseases such as ROP and rubella.[42] As these countries become more developed, blindness secondary to corneal disease decreases owing to implementation of measles vaccination programs, improved nutrition, decreased use of traditional medicines, and prevention of ophthalmia neonatorum. The major cause of childhood blindness became genetic in Saudi Arabia, partly because of the tradition of consanguinity, with many of the diseases being autosomal recessive.

In other transitional countries—such as some parts of Latin America, eastern Europe, and the more economically sound parts of Africa and Asia—major causes of blindness include congenital cataract and glaucoma, frequently associated with congenital rubella.[1,43] In the most well-devel-

oped countries with advanced health care services, these sequelae of rubella have long since been alleviated through the wide availability of rubella vaccines. Retinopathy of prematurity as an etiology for childhood blindness rises and later falls as more attention is given to arterial oxygen concentrations. The prevalence of childhood blindness decreases, and the percentage due to congenital causes, either known genetic syndromes or other prenatal occurrences, increases. There appears to be a higher prevalence of visual disorders among the mentally retarded in highly developed countries, a finding that is supported by studies from the United States.

These differences are reflected in the types of studies that appear in the literature. There are many more reports on the epidemiology of childhood blindness from the developing countries (especially Africa) and Europe (especially Great Britain and the Scandinavian countries) than the Western countries, with few such reports from the United States. Reports on childhood blindness are from 3 sources, including schools for the blind, surveys, and state registries for blind individuals.[44] The first of these may overlook some children who are blind and mentally retarded who reside at institutions for the mentally retarded.

Studies in the United States

There are few published studies of childhood blindness in the United States. Hatfield's 1972 paper is a survey,[45] performed by the National Society for the Prevention of Blindness, of records from United States agencies providing services to blind infants and young children; it describes 3,115 blind children ranging from birth to age 7 years. The most common etiologies were hereditary (47.4%), other prenatal causes (13.4%), and infectious diseases (10.2%). The most common diagnoses were cataract (20.5%), optic atrophy (10.2%), and ROP (9.0%). As a consequence of the control measures instituted for administration of oxygen to premature babies, the study shows a decrease in the incidence of blindness due to ROP compared to a previous study by the same author.[46] However, there was an increase of blindness due to infection, attributable for the most part to rubella. Another significant finding in this report was an increase in the rate of blindness due to afflictions of the optic nerve and optic pathways; in two thirds of the cases, the specific diagnosis was cortical visual impairment due to unknown cause.

In 1987, Williamson and associates[47] published a study on visual impairment in infants, for which the investigators surveyed in the early 1980s the records in 22 Texas school districts that were providing services for the visually impaired. About half the 102 patients had visual problems caused during the prenatal period. Of these, 42 had a definitive syndrome, known genetic disorder, or structural abnormality of the orbit or central

nervous system, and another 10 had prenatal infections. One third had problems in the perinatal period. The most frequent diagnoses were abnormalities of the optic nerve, optic pathway, and visual centers of the brain. Severe developmental delay with IQ of less than 50 were found in three quarters of the subjects for whom developmental data were available. This study confirms that there are large numbers of mentally delayed children among the visually impaired in developed countries.

A prevalence report by Drews and associates[48] studied 10-year-old blind children in Atlanta from 1985 to 1987. The report addresses causes of blindness and associations with other developmental disabilities. The most common diagnosis was ROP (21.3%). Two thirds of the children were blind by age 1 month, suggesting congenital etiologies. Two thirds of the children had other disabilities, of which mental retardation, epilepsy, and cerebral palsy were the most common.

VISUAL LOSS ASSOCIATED WITH MENTAL RETARDATION

Studies in the United States, Great Britain, Canada, Denmark, Norway, and South Africa all conclude that there is a higher prevalence of visual disorders among the mentally retarded and recommend routine screening for visual impairment in this population.[20,49-58] Warburg's study (Denmark) showed that 5% of mentally retarded children have a best corrected vision of less than 6/60 (20/200), while only 0.02% of the child population with normal mentation has vision in that range.[59] Older studies have reported, depending on the degree of mental retardation, a range of 5% to 14% of retarded children who are also blind or visually impaired.[60-62] It appears that severe visual handicap is seen more in association with severe retardation.[63,64] A 1983 study (Finland) showed that 57% (89/149) of mentally retarded children examined by an ophthalmologist in one city had a significant vision problem; of these, eye abnormalities were found in 79% of the severely retarded, 75% of the moderately retarded, and 36% of the mildly retarded children.[65]

The reports from the United States are screening studies for vision and strabismus from the optometric literature.[49,50] There is one ophthalmologic report from 1972 describing the findings in 728 developmentally handicapped children.[66] Thirty-seven percent of the children were found to have severe to profound mental impairment, 16% were considered moderately impaired, 40% borderline to mild, and the rest normal. Visual problems included refractive errors (18%), strabismus (17%), retinal disease (3%), optic nerve disorders (2%), and cataracts (2%), and the frequency of the vision problems was highest in patients with the most severe

developmental handicaps. Similar findings were reported in a study of Israeli children.[67]

LCMV AND ASSOCIATED VISUAL LOSS

Lymphocytic choriomeningitis virus is an arenavirus that was discovered in 1933 but not classified until the late 1960s, when it was placed in the newly formed arenavirus family.[68,69] This group of viruses has a single-stranded RNA and tends to be harbored in rodents; in the case of LCMV, these are old world rodents (*Mus musculus*).[70] LCMV is the family prototype for the arenaviruses and was isolated during serial monkey passage of human material that was recovered from a fatality in the first epidemic of St Louis encephalitis.[68] It is believed that the monkey was contaminated by LCMV, which was inadvertently isolated and thus discovered.[71]

M musculus is both the natural host and reservoir for the virus, which is transferred vertically within the mouse population by intrauterine infection.[72] Evidence shows that there is less prolonged persistence in other species such as guinea pigs,[73] Syrian hamsters,[74,75] chicks,[71,76] rats, and rabbits.[71,77] Infections from wild mice are associated with substandard housing, such as trailer parks and inner city dwellings, rodent-infested barns, and the fall infestation of field mice.[70] Outbreaks have also been attributed to laboratory mice and hamsters, and laboratory workers, especially those handling mice or hamsters, have a higher risk of infection.[71,78-80] It is possible that the increased encroachment of humans into the environment and the now fashionable trend of restoring inner-city dwellings may have increased human contact with *M musculus* and increased the incidence of associated disease. There have also been several outbreaks associated with pet hamsters.[79,81,82]

Transmission is thought to be primarily air-borne or from contamination of food by infected mouse urine[71] or, possibly, from rodent bites.[70] The virus is present in congenitally infected asymptomatic mice and is excreted in their urine, feces, saliva, tears, semen, milk, and respiratory secretions. LCMV has been experimentally transmitted by bloodsucking insects, including Rocky Mountain wood ticks (*Dermacentor andersoni Stiles*),[83] mosquitoes (*Aedes aegypti*),[84] bedbugs (*Cimex lectularius*),[85] fleas,[86] and Trinchinella spiralis nematodes.[87] It can be regarded as an arthropod-borne virus, and blood-sucking insects may transmit it from rodent to rodent and possibly to humans.[71] The incubation period ranges from 5 to 10 days, and the period preceding central nervous system signs is 2 to 3 weeks.[70]

When acquired postnatally by older children and adults, symptoms of LCMV infection usually vary from none (about one third of cases) to an

acute febrile illness with or without meningeal signs.[4,82] Transient and permanent hydrocephalus has also been reported.[3] Rarely, other symptoms have been associated, including encephalitis,[88,89] myocarditis,[90] parotitis, orchitis,[91,92] and pneumonia.[93] Very rarely, infection has resulted in a fatal systemic disease.[94-97] Chronic sequelae have been reported, including fatigue, headache, memory impairment, depression, and personality changes.[98-102] More rarely still, sequelae of meningoencephalitis[100] and paralysis[103,104] have been documented. LCMV has been demonstrated as the causative agent in about 10% of cases of aseptic meningitis.[105-107] Human infections, whether from domestic or laboratory exposures, are very easily acquired.[68,71,78,97,108-112] Person-to-person transmission has not been demonstrated.

The first documented case of LCMV as a human fetal pathogen occurred in 1955 in Great Britain; a mother became ill 12 days before delivery, and her child subsequently became ill 7 days postnatally.[113] The child developed signs of meningoencephalitis and died on the 12th day of life. Maternal acute LCMV infection has been associated with spontaneous abortion,[81,114,115] and with congenital hydrocephaly, microcephaly, and chorioretinitis.[116-120] However, it has received little attention in the United States.[121]

The first case of congenital LCMV in the United States was reported in 1993.[3] The infant weighed 2,898 g and was born full-term to a 21-year-old primagravida. The mother lived in a well-maintained, older inner city apartment and experienced a febrile illness for 1 week during her fifth month of pregnancy. The child was born with hydrocephalus and microphthalmia of the right eye, with "pseudomembranous clouding of the anterior chamber which obscured the iris and pupil." Follow-up computed tomographic (CT) scan showed dense calcification of the lens and increased density of the microphthalmic globe. On examination, the left eye showed leukocoria, cloudy vitreous, and exudative retinitis.

The next 2 cases documented in the United States were a pair of twins reported in the same year.[4] The mother had lived in a trailer during the first 7 months of her pregnancy with 1 hamster, 2 gerbils, and 3 dogs. House mice and animal excreta were reported in the trailer. She experienced a febrile illness associated with nausea, vomiting, chills, sweats, and myalgia at 13 weeks' gestation. The twins were delivered at 37 weeks' gestation by cesarean section due to breech presentation and decreased fetal heart rate. APGAR scores were 8 at 1 minute for both, and 8 and 9 respectively for twins A and B at 5 minutes. Both twins were examined at 5 months by an ophthalmologist because of developmental delay. Twin A exhibited fine, roving nystagmus, and fundus examination revealed a

"large, atrophic lesion involving the retinal pigment epithelium and choriocapillaris of each macula, and encroaching upon the fovea in both eyes." Also described were bilateral mild optic atrophy and multiple peripheral punched-out lesions of the retinal pigment epithelium. Twin B demonstrated a large chorioretinal scar in the right macula and punched-out lesions in the periphery of both eyes. Cerebral CT scans revealed decreased brain substance and periventricular calcifications in both children, with twin A also showing some hydrocephalus. Personal communication with Dr Barton (July 1998) revealed that in follow-up, twin A continued in a state of blindness with quadriparesis and seizures, while twin B had a normal neurological examination (except for the eye exam) and appeared to have caught up on developmental milestones.

In 1995, 3 additional cases of congenital LCMV were reported in a dispatch in *Emerging Infectious Diseases*.[5] The eye and central nervous system manifestations are not described in this report. Personal communication with Dr Barton (July 1998) identified the following findings in the fourth child: Fundus examination revealed retinal pigment epithelial mottling in the right macula and peripapillary retinal pigment epithelium irregularity bilaterally. Again, personal communication with Dr Barton (July 1998) revealed that the fifth child "had very advanced chorioretinopathy and dramatic hydrocephalus," and the mother had experienced a long febrile illness during the fifth month of pregnancy.

The seventh case of LCMV was reported in 1997.[122] The patient presented at age 22 months as a consult from the pediatrics service. She was born at 37 weeks' gestation and weighed 2,567 g at birth. Ophthalmologic examination revealed no response to light and a searching pendular nystagmus. Fundus examination demonstrated moderate optic atrophy and diffuse chorioretinal scarring involving the macula and posterior pole in both eyes. Past medical history included hydrocephalus at birth and placement of a ventriculoperitoneal shunt at age 5 days.

A subsequent publication identified 23 cases of congenital LCMV in the world literature between 1955 and 1996 and added three new US cases, for a total of ten.[123] This report states that the most common neonatal findings are ocular abnormalities, macrocephaly, or microcephaly, and it notes abnormal eye findings in 2 of the 3 new US case reports. One had bilateral scarring with chorioretinal atrophy and "scalloping resembling the ocular features of Aicardi's syndrome." The second had "pale optic discs and bilateral retinal atrophic changes." The third had normal examination results. A review of the literature associated with this report found that 21 infants (88%) had "chorioretinopathy," which was bilateral in 16 of the cases. Other documented abnormalities included optic atrophy (11),

microphthalmia, vitreitis, leukocoria, and cataract.

FIELD STUDY: METHODS AND PATIENTS

SOURCES AND DOCUMENTATION OF DATA

Histories were obtained from records on site. In the cases with chorioretinal scarring, we obtained hospital records and/or spoke to parents or guardians on the telephone. All patients received a complete cyclopleged ophthalmoscopic examination on site by the author, including vision assessment, external evaluation including nystagmus and lid assessment, extraocular muscle evaluation, and pupillary examination prior to cycloplegia. Vision was assessed by the use of Allen cards, the Snellen chart, and, in cases of very poor acuity, a penlight. Subjects' pupils were dilated with a combination of cyclopentolate hydrochloride (0.5%, 1.0%, or 2.0%), phenylephrine hydrochloride (2.5%), and tropicamide (1.0%), depending on age and pigmentation. Following cycloplegia, all subjects were evaluated by slit-lamp examination, retinoscopy, and indirect ophthalmoscopy. Instrumentation for examination, all of which we brought to the site, included a hand-held slit lamp (Zeiss), an indirect ophthalmoscope (Heine), a retinoscope (Copeland), a hand-held fundus camera (Kowa), prisms (Luneau Fr.), lens bars +/– (Luneau), Finhoff penlight (Welch Allen), Snellen chart, Allen cards, OKN drum, eye drops (as above), eye patches (Opticlude), and paper clips.

A standardized data sheet was compiled for each subject at the time of examination, for both history and physical (Figs 1 and 2). A narrative evaluation was also prepared for each subject, copies of which were sent to the institution for their records. A computerized database was compiled using File Maker Pro 3.0 (Claris Corporation, Santa Clara, Calif) and Microsoft Excel 5.0 (Microsoft Corporation, Seattle, Wash).

On the basis of the ophthalmologic examination, all subjects were given an ophthalmologic diagnosis, recorded simply as "diagnosis" in the tables. For the purpose of further analyzing data, a primary "cause" was assigned to each subject using the following categories: congenital genetic, congenital prenatal, prematurity, birth trauma, accidental trauma, infection, drug abuse, child abuse, and unknown.

Cases were designated *congenital genetic* only if the patient carried a known genetic diagnosis or, for instance, in the case of congenital cataracts, only in the presence of a family history. The category *congenital prenatal* included all other congenital abnormalities unless there was another known cause, such as infection. (Many of the infections may have been undiagnosed because there were a number of cases of micro-

DATA SHEET

1. Name: Initials
2. Assigned Number
3. Birth Date
4. Systemic Diagnosis

5. Hydrocephalus — Head Circumference
6. Microcephaly
7. Seizures
8. Functional level
9. Previous surgeries

10. Previous eye history

11. Any neuroimaging: CT, MRI results, ? Intracranial Ca++

12. Possible hearing deficit
13. Maternal pregnancy history: animal exposure:
    - Mice in house
    - Lab mice
    - Hamsters
    - Any rodents
    - Febrile illness

    } Time frame w/in pregnancy

14. Birth history BW: Length: Head Circumference:
    Complications:

15. APGAR
16. Family history: MR, Seizures

17. Meds
18. Allergies
19. Height and weight

FIGURE 1

Data sheeet used to record history.

cephalus.) Please note that when a patient had more than one cause, such as infection (congenital cytomegalovirus) and prematurity, the primary cause assigned was "infection"; however, in order to analyze the cases of prematurity, all babies who were premature were listed with associated findings. Therefore, the total number in the prematurity table (Table XII) is 15, while the total number of babies with a primary cause of prematurity is 11 (Table X).

OPHTHALMOLOGY 31

NAME _____ DOB _____ Exam Date _____

Cooperation Examined by _____

Child Crying ____ Child Quiet ____

	Right Eye		Left Eye		Specify *
Mom's Fundus	O Normal	O Abnormal	O Normal	O Abnormal	
Vision Central	O Normal	O Abnormal	O Normal	O Abnormal	
V.A. changed	O Yes	O No	O Yes	O No	
Pupils Response	O Normal	O Abnormal	O Normal	O Abnormal	
Synechiae	O Absent	O Present	O Absent	O Present	
EOM Strabismus		O Absent	O Present		
Ext Nystagmus	O Absent	O Present	O Absent	O Present	
Microphthalmia	O Absent	O Present	O Absent	O Present	
Phthisis	O Absent	O Present	O Absent	O Present	
Ant Segment					
Conjunctivia					
Inflammation	O Absent	O Present	O Absent	O Present	
Cornea	O Normal	O Abnormal	O Normal	O Abnormal	
Microcornea	O Absent	O Present	O Absent	O Present	
Opacification	O Absent	O Present	O Absent	O Present	
Sclera					
Scleritis	O Absent	O Present	O Absent	O Present	
Iris					
Iritis	O Absent	O Present	O Absent	O Present	
Synechiae	O Absent	O Present	O Absent	O Present	
Persistent Pupillary Membrane	O Absent	O Present	O Absent	O Present	
Ant Chamber					
Depth	O Normal	O Abnormal	O Normal	O Abnormal	
Inflammation	O Absent	O Present	O Absent	O Present	
Lens Cataract	O Absent	O Present	O Absent	O Present	
Refraction	O Normal	O Abnormal	O Normal	O Abnormal	
Myopia	O Absent	O Present	O Absent	O Present	
Hyperopia	O Absent	O Present	O Absent	O Present	
Anisometropia		O Absent	O Present		

* note with * if not seen before

Severity score: 0=normal vision, no lesions; 1=normal vision, nonmacular lesions; 2=normal vision, macular lesions; 3=impaired vision, nonmacular lesions; 4=impaired vision, macular lesions; 4.5=impaired vision, inability to view posterior pole because of cataracts or another etiology; and 5=no observable light perception (detached retina, grossly abnormal electroretinogram).

FIGURE 2 FRONT

Data sheet used to record ophthalmologic examination results.

"Etiologies" are historical data or systemic diagnoses that explain the findings. For instance, patient MA at location M had a "diagnosis" of optic atrophy, a "cause" of birth trauma, and an "etiology" of perinatal hypoxia, placenta abruptio.

Location V

We prospectively examined 64 students at Location V during the period January 21 through 23, 1998. Location V is a state-supported school for the

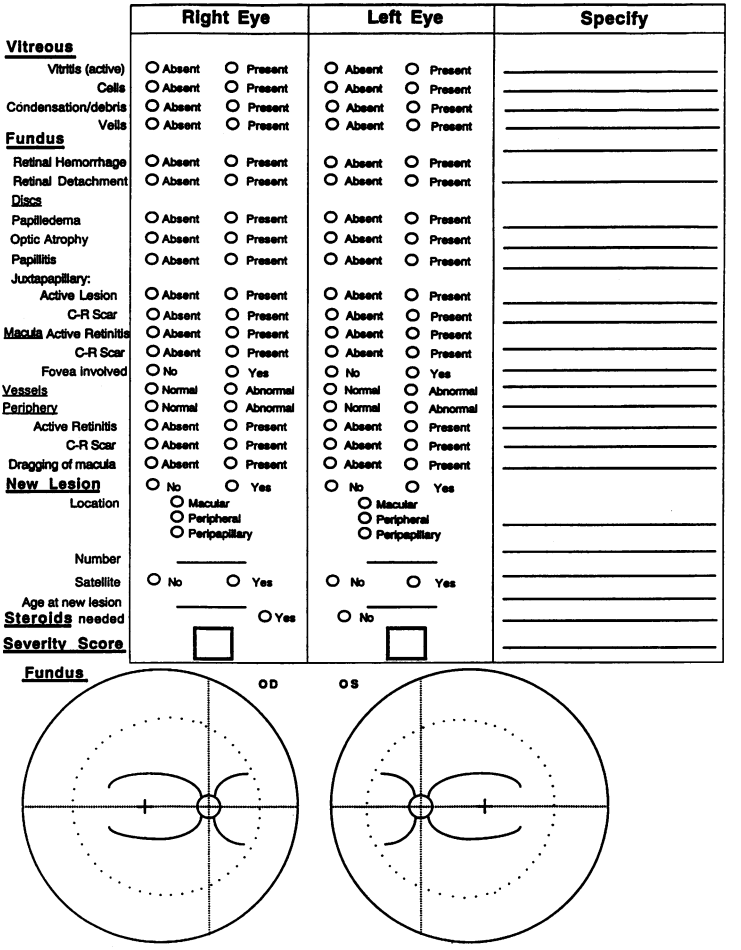

FIGURE 2 BACK
Data sheet used to record ophthalmologic examination results.

visually impaired that admits students having difficulty in school due to a visual disability. There were 80 residential students and 7 day students, for a total of 87 students enrolled at the time of our examination. We were able to obtain consents for 64; of these, 33 were considered normal and 31 mildly delayed in their mental development. Ages ranged from 3 to 22 years, with 35 male students and 29 females.

Location M

During 1997, we prospectively examined 95 patients at Location M, a res-

idential home for severely retarded children who must be nonambulatory. Consents for eye examinations were obtained by staff at the home for each child examined. There were 107 registered patients at the home at that time, and we were able to obtain consents for 95. Ages ranged from 2 to 32 years, with a mean age of 7.6 years. There were 58 males and 37 females. Consents, histories, examinations, and data were managed in the same manner as described for Location V with one exception. Owing to the severity of visual impairment in this population, vision assessment techniques were limited to having the subjects follow a finger puppet or face; data were recorded using the categories of central, steady, follows (CSF), or central, steady, maintained (CSM).

FIELD STUDY: RESULTS

LOCATION V

Table II lists the visual acuities of the 64 patients examined at the school for the visually impaired. Applying the criteria of the National Society to Prevent Blindness, 54 of the patients were classified as blind, 8 as visually impaired, and 2 as unimpaired visually, for a total of 62 students with blindness or visual impairment. Strabismus was present in 13 students, 2 of whom showed esotropia and 11 exotropia. Forty-eight manifested nystagmus. Of the 2 sighted children, 1 had William's syndrome and visual acuities of 20/30 in the right eye and 20/40 in the left. The other had congenital cataracts with subsequent retinal detachment and acuities of 20/20 in the right eye and light perception with projection in the left.

CAUSES OF VISUAL LOSS AT LOCATION V

Table III lists the diagnoses that caused the visual loss in the 62 visually impaired students, with ROP, optic nerve atrophy, retinitis pigmentosa, optic nerve hypoplasia, cataracts, and foveal hypoplasia topping the list. ROP and optic atrophy were each responsible in 12 cases. There were associated findings in 10 of the students with ROP (retinal detachment) and 4 of the students with optic atrophy (optic nerve hypoplasia, ROP, high myopia, and a retinal pigment epithelial disturbance secondary to extensive retinal hemorrhages due to child abuse). Of the 9 subjects with retinitis pigmentosa–type findings, 3 had Batten's disease, 2 had Leber's congenital amaurosis, 2 had Bardet-Biedl syndrome, and 2 had Usher's syndrome. Of the 8 students with optic nerve hypoplasia, 2 had septo-opto-pituitary dysplasia. One of the 5 patients with congenital cataracts had bilateral retinal

TABLE II. VISIONS AT LOCATION V

INITIALS	OD	OS	COMMENTS
JB	20/100	20/200	
BB	19/200	8/200	
BB	NLP	NLP	
JB	No visually directed behavior		Shaken baby
DC	20/150	6/150	
BC	No visually directed behavior		Cerebral palsy
EC	LP no projection	LP no projection	
GC	20/70	20/100	
BF	1/30 A.C.	1/30 A.C	Mod to severe mental handicap
CH	HM	NLP	
JG	20/200	20/200	
JG	20/70	20/100	
JJ	NLP	NLP	
LG	2"/200	10"/200	
SG	20/70	NLP	
AG	NLP	LP	
AH	NLP	NLP	
LH	NLP	NLP	Autism
BH	12/150	20/200	
CH	16/150	1/150	
JH	LP no projection	LP no projection	
MH	16/150	HM 1"	
GH	LP	LP	
CH	NLP	NLP	
AK	3"/30	LP	
GK	3"/150	NLP	
DK	1"/150	20/70	
JK	LP	1/200	
JL	3/150	2/150	
WL	20/50 +2	20/50 + 2	Nystagmus + foveal hypoplasia
AMAC	20/100	20/70	
DM	LP with projection	LP with projection	
JMC	NLP	NLP	
KMC	20/30	20/40	William's syndrome
JM	20/70	20/50 +2	Congenital cataracts
NM	20/20 -1	LP with projection	Aphakia OU,+ FH RD OS
TM	20/50	20/50	Congenital cataracts OU + FH
NM	18/200	Prosthesis	
AN	20/200	20/200	
BO	20/200	20/200	
JR	20/20	20/20	10% fields Ushers
RR	20/25	20/25	10% fields Ushers
JR	LP	LP	

TABLE II (CONTINUED): VISIONS AT LOCATION V

INITIALS	OD	OS	COMMENTS
KR	2/150	12/150	
AR	Unable to assess (LP)		Batten's
SR	LP no projection	LP no projection	Batten's
SR	NLP	NLP	Batten's
SR	NLP	18/150	
RS	20/100	20/40	
MS	20/200	20/200	
RS	20/100	20/100	
TS	NLP	HM	
SS	3"/150	1.5"/150	
LS	20/100	20/100	
HS	LP	LP	
JS	4/200	20/100	
KS	NLP	Prosthesis	
NT	LP	LP	
JV	20/70	20/70	
SV	No visually directed behavior		
CV	NLP	NLP	
BW	NLP	NLP	
AW	LP with projection	LP with projection	
JY	20/100	20/100	

TABLE III: DIAGNOSES FOR VISUAL LOSS AT LOCATION V

DIAGNOSIS	NO. (%)
Retinopathy of prematurity	12 (19.4)
Optic atrophy	12 (19.4)
Retinitis pigmentosa	9 (14.5)
Optic nerve hypoplasia	8 (12.9)
Cataracts	5 (8.1)
Foveal hypoplasia	5* (8.1)
Persistent hyperplastic primary vitreous	3 (4.8)
Microphthalmos	2 (3.2)
Morning glory	1 (1.6)
Congenital herpes	1 (1.6)
Peter's anomaly	1 (1.6)
Stargardt's syndrome	1 (1.6)
Congenital rubella	1 (1.6)
Ametropic amblyopia	1 (1.6)
Total	62 (100)

*Three with albinism.

detachments. Three of the 5 students with foveal hypoplasia had albinism. One student with ametropic amblyopia had a refractive error of +10.00 bilaterally and manifested nystagmus.

Frequency of Congenital Causes

Seventy-one percent of the visual loss can be attributed to congenital causes; 42% were prenatal, 29% genetic, and 20% due to prematurity (Table IV). Specific diagnoses in each of the first 2 categories are listed in Tables V and VI. Table V includes 2 individuals with congenital cataracts in whom there was no positive family history, while the 3 assigned to Table VI all had a positive family history. Table V includes the 2 students who had isolated foveal hypoplasia, while the 3 who also had albinism are included in

TABLE IV: CAUSES OF VISUAL LOSS AT LOCATION V

CAUSE	NO. (%)
Congenital prenatal	26 (42)
Congenital genetic	18 (29)
Prematurity	13 (20)
Child abuse	2 (3)
Accidental trauma	1 (2)
Birth trauma	1 (2)
Infection	1 (2)
Total	62 (100)

TABLE V. DIAGNOSES IN CONGENITAL PRENATAL CAUSES AT LOCATION V

DIAGNOSIS	NO.
Optic nerve hypoplasia	8
Optic atrophy	4
Persistent hyperplastic primary vitreous	3
Congenital cataracts (no family history)	2
Microphthlamia	2
Foveal hypoplasia	2
Morning glory syndrome	1
Nystagmus	1
Congenital rubella	1
Peter's anomaly	1
Unknown	1
Total	26

TABLE VI: DIAGNOSES IN CONGENITAL GENETIC CAUSES AT LOCATION V

DIAGNOSIS	NO.
Congenital cataracts (possible family history)	3
Batten's	3
Albinism	3
Bardet-Biedl syndrome	2
Leber's congenital amaurosis	2
Optic atrophy	2
Usher's syndrome	2
Stargardt's disease	1
Total	18

TABLE VII. REFRACTIONS AT LOCATION V

INITIALS	REFRACTIONS	
JB	-0.50 + 2.00 x 100	-0.50 + 1.50 x 80
BB	over refraction +0.50	plano
BB	-	-
JB	-0.50 + 1.50 x 180	-0.50 + 1.75 x 180
DC	over refraction -1.50	plano
BC	-	-
EC	+1.50	+1.50
GC	over +0.75 sph	+0.50
LC	-	-
BF	+2.50	+2.00 + 0.50 x 90
JG	+1.00	+1.00
SG	+0.50	+1.00
JG	plano	+0.50 + 0.50 x 90
AG	-	-
AH	-	-
LH	-	-
BH	over refraction plano	+0.50
JH	+8.50	+8.50
MH	over refraction plano	+0.50 + 1.50 x 180
JH	-0.50	-0.50
CH	-0.50	-0.50 + 1.00 x 75
CH	-	-
JJ	-	-
SJ	cataract	plano
AK	-	-
GK	+2.00	-
DK	+0.50	plano
JK	no reflex	reflex _ no end point
JL	-1.00 + 2.00 x 90	-1.00 + 2.00 x 90
WL	-1.75 + 2.00 x 90	-7.75 + 2.00 x 90

TABLE VII (CONTINUED): REFRACTIONS AT LOCATION V

INITIALS	REFRACTIONS	
AM	over refraction +0.50	plano
DM	-	-
KMc	plano	+1.00
JMc	opacified cornea	white dense cataract
JM	-1.00	-1.00
NM	+1.00	poor reflex
TM	+0.5	pupil too small
NM	over refraction -1.00	-
CN	poor reflex	poor reflex
AN	-1.50	-1.50
BO	-1.50 + 1.00 x 90	-1.50 + 1.00 x 90
JR	+0.50	plano
RR	-	-
JR	-	-
KR	plano +1.50 x 80	plano + 0.50 x 180
AR	+1.00	+1.50
SR	+1.00	+0.75
SR	+1.00	+1.50
SR	-	-
RS	-1.50 + 0.50 x 80	+0.75
MS	+0.50	+0.25
RS	-	-
TS	poor reflex	+1.00
SS	-	-
LS	plano	plano
HS	+1.00	+1.00
KS	-	-
NT	ë plano difficult	ë plano
JV	plano	plano
SV	-	-
CV	-	-
AW	-	-
JY	plano	plano
BW	-3.50	-3.50

Table VI under albinism. One of the students with optic atrophy in Table VI had a positive family history, and the other had optic atrophy from optic nerve gliomas secondary to neurofibromatosis type I. All subjects for whom prematurity is listed as the cause of blindness had an ocular diagnosis of ROP. All cycloplegic refractions obtained are listed in Table VII.

LOCATION M

The categories of blindness and visual impairment used at Location V

could not be applied to the patients at Location M because their severe mental retardation precluded quantitative visual acuities. Therefore, we included patients who appeared to have visual loss, either by their inability to follow a face or puppet at near, or by the presence of bilateral optic atrophy (white discs) or macular chorioretinal scars on fundus examination. (We realize that unilateral macular scars may not result in "visual impairment." However, we considered those patients to have visual loss in this severely impaired population, where quantitative visions could not be assessed, in order to consider all infectious etiologies.) All tables for this population are based on the 83 patients out of the 95 examined who were considered to have abnormal vision according to the above criteria. Of the 95 examined, 46 were strabismic (11 esotropic and 35 exotropic). Of these, 3 showed a fixation preference; however, since amblyopia is a diagnosis of exclusion, and all these patients also had organic lesions, no visual loss could be attributed to amblyopia in this population. Thirty-three children manifested nystagmus.

TABLE VIII: DIAGNOSES FOR VISUAL LOSS AT LOCATION M

DIAGNOSIS	NO.	(%)
Optic atrophy	54	(65)
Cortical visual impairment	20	(24)
Chorioretinal scars	4	(5)
Optic nerve hypoplasia	2	(2.4)
Retinitis pigmentosa	1	(1.2)
Cataract	1	(1.2)
Phthisis (ROP)	1	(1.2)
Total	83	

TABLE IX: CAUSES OF OPTIC ATROPHY AT LOCATION M

CAUSE	NO.	(%)
Congenital prenatal	15	(27.8)
Birth trauma	8	(4.8)
Congenital genetic	8	(14.8)
Infection	7	(13.0)
Accidental trauma	4	(7.4)
Child abuse	2	(3.7)
Unknown	2	(3.7)
Total	54	(100)

Causes of Visual Loss at Location M

Table VIII lists the diagnoses in the 83 patients examined with vision loss at Location M. The most common diagnosis, found in 54 patients (65%), was bilateral optic atrophy, the causes of which are listed in Table IX. Of those patients with optic atrophy, the most common cause was congenital prenatal, present in 15 patients (27.8%). This was followed by genetic causes, birth trauma, and prematurity, each of which were reported in 8 patients (14.8%), and infection, which was reported in 7 (13%).

All of the patients examined had suffered profound central nervous system insults resulting in their severe mental retardation. Cortical visual impairment, the second most common diagnosis, was responsible for visual loss in 20 patients (24%) (Table VIII). Four had chorioretinal scars, 2 had optic nerve hypoplasia (one of whom had septo-opto-pituitary dysplasia), 1 had retinitis pigmentosa as part of the Bardet-Biedl syndrome, 1 had phthisis from end-stage ROP, and 1 had cataracts and a seizure disorder.

Frequency of Congenital Causes

The primary causes for the visual loss at Location M are tabulated in Table X. Most of the insults were congenital; 22 were prenatal (26%), and 12 were genetic (15%), for a total of 34 (41%). Prematurity was the primary cause in 11 (13%). Those with congenital prenatal causes included 1 patient whose mother had a cholecystectomy with general anesthesia at 22 weeks' gestation and another whose mother during pregnancy was a starvation victim and treated with an unknown "worm medicine." Specific genetic causes are itemized in Table XI.

Associated findings in babies who were born prematurely are listed in Table XII. (Note that the total number of premature babies in Table XII is

TABLE X: CAUSES OF VISUAL LOSS AT LOCATION M

CAUSE	NO.	(%)
Congenital prenatal	22	(26)
Congenital genetic	12	(15)
Infection	13	(16)
Birth trauma	12	(14)
Prematurity	11	(13)
Accidental trauma	4	(5)
Child abuse	4	(5)
Unknown	4	(5)
Drug abuse	1	(1)
Total	83	(100)

TABLE XI: DIAGNOSES IN CONGENITAL GENETIC CAUSES AT LOCATION M

Chromosomal abnormalities
Chromosomal 1 abnormality
Chromosomal 4 deletion short arm
Chromosomal 7 abnormality
Chromosomal 18 trisomy

Single gene abnormalities
Bardet-Biedl
Canavan's disease
Cornelia Delange
Down's syndrome (stroke in infancy)
Icthyosis
Neurocutaneous syndrome

Multiple congenital anomalies
(Two siblings possible autosomal recessive syndrome)

TABLE XII: CAUSES OF VISUAL LOSS IN ALL PREMATURE CHILDREN AT LOCATION M

CAUSE	NO.
Intraventricular hemorrhage	4
Isolated	4
Infection°	3
Congenital cytomegalovirus	3
Birth trauma	1
Total	15

° Herpes simplex, pneumomeningitis, *Haemophilus influenzae* meningitis.

15 instead of 11 as listed in Table X, where prematurity is the primary diagnosis.) Table XII includes three babies whose primary diagnosis was infection (congenital cytomegalovirus) and one whose primary diagnosis was birth trauma (birth weight, 5 lb). Six of the premature babies had associated infections, including the 3 cases of congenital CMV and 1 each of herpes simplex, pneumococcal meningitis, and *H influenzea meningitis*. One of the 6 was also affected by maternal drug abuse in utero. Four premature children had a history of intraventricular hemorrhage.

Frequency of Traumatic and Infectious Causes
Twenty of the 83 children had experienced trauma (24%) (Table X). Of

these, 12 suffered birth trauma, 1 of which was associated with drug abuse. The other 11 were simply recorded as perinatal asphyxia. The 4 with accidental trauma included aborted sudden infant death syndrome at age 7 mo, anoxic encephalopathy caused by a toy box lid falling at age 13 mo, an anesthetic accident at age 9 mo, and an automobile accident with head injury. Four children were victims of child abuse. All 20 of the children suffering trauma had diagnoses of optic atrophy or cortical visual impairment.

Sixteen children had documented infections, of which 1 was associat-

TABLE XIII: CAUSES OF INFECTION IN ALL CHILDREN AT LOCATION M

CAUSE	NO.
Meningitis*	5
Congenital cytomegalovirus	4
Lymphocytic choriomenigitis virus†	2
Infection unknown†	2
Congenital syphilis	1
Herpes simplex	1
H influenzae pneumonitis—respiratory arrest	1
Total	16

*Two Haemophilus influenzae, one pneumococcal, two unknown.
† Chorioretinal scar.

ed with maternal drug abuse and another was associated with child abuse (Table XIII). Note that Table X lists 13 children with a primary diagnosis of infection; an additional 3 patients are included in Table XIII who had primary diagnoses of prematurity but who also had infections. Five of the 16 infections were secondary to meningitis, 2 from *H influenzae*, one to pneumococcus, and 2 to unknown agents. One other was due to a respiratory arrest from severe influenza pneumonitis, and 4 had chorioretinal scars (2 from LCMV and 2 from an unknown infection).

TABLE XIV. REFRACTIONS AT LOCATION M

PATIENT INITIALS	REFRACTION	
MA	-3.00 + 3.50 x 90	-3.00 + 3.50 x 90
AA	+2.00	+2.00
LA	+2.50	+2.50
KA	Plano + 1.00 x 90	Plano + 1.00 x 90

TABLE XIV (CONTINUED): REFRACTIONS AT LOCATION M

PATIENT INITIALS	REFRACTION	
EB	Plano	Plano
SB	Plano + 1.00 x 90	Plano + 1.00 x 90
TB	-16.00	-16.00
RB	-1.00 + 3.00 x 90	-1.00 + 3.00 x 90
KB	-9.00 + 3.00 x 90	-9.00 + 3.00 x 90
NB	-5.00 + 4.00 x 90	-5.00 + 4.00 x 90
AB	+2.50 + 2.00 x 90	+2.50 + 2.00 x 90
EB	-2.00 + 2.00 x 90	-8.50 sph
DB	+1.50	+1.50
MB	-0.50 + 1.00 x 90	+0.50 + 1.00 x 90
CB	-	-
BB	-3.00	-13.00
JC	+1.50	+1.50
CC	-1.00 + 3.00 x 90	-8.00 + 5.00 x 90
RC	+0.75 + 1.00 x 90	+0.75 + 1.00 x 90
CC	-1.00 +0.50 x 90	-1.00 + 0.50 x 90
JC	-1.00 + 1.00 x 90	-1.00 + 1.00 x 90
JC	-1.25 + 2.00 x 90	+1.25 + 2.00 x 90
NC	+16.00	+14.00 + 2.00 x 90
DC	-5.00 + 2.00 x 90	-5.00 + 2.00 xt 90
OC	-1.50 + 1.00 x 90	-1.50 + 1.00 x 90
TC	+2.00 + 1.00 x 90	+2.00 + 1.00 x 90
ND	-1.00 + 1.00 x 90	plano + 1.00 x 90
DD	-2.00 + 2.00 x 90	-2.00 +2.00 x 90
ME	+2.25	+2.25 sph
SG	-2.00 + 1.00 x 90	-1.00 + 1.00 x 90
HG	-1.50 + 2.50 x 90	-1.50 + 2.50 x 90
JG	-0.50 + 2.00 x 90	-0.50 + 2.00 x 90
GG	-4.00 + 2.50 x 90	-4.00 + 2.50 x 90
AG	-2.00 + 0.75 x 90	-2.00 + 0.75 x 90
KG	+1.50 + 4.50 x 90	+1.50 + 4.50 x 90
GG	-4.50	-4.50
MH	-1.50 sph	-2.00 + 1.00 x 90
HH	plano + 1.00 x 90	plano + 1.00 x 90
AH	-5.50 + 3.50 x 90	-5.50 + 3.50 x 90
BH	+2.00	+1.00 + 2.00 x 130
MH	+2.00 + 0.50 x 80	-
KH	-2.00 + 2.25 x 90	-2.00 + 2.50 x 90
LH	Plano	Plano
CH	-3.00 + 1.00 x 90	-3.00 + 1.00 x 90
TJ	+1.50	+1.50
JJ	+1.00 + 1.50 x 90	+1.00 + 1.50 x 90
LK	Plano + 2.50 x 60	Plano +2.50 x 120
SL	Plano + 4.00 x 90	+1.00 + 3.00 x 75
SL	Plano + 3.00 x 90	Plano + 3.00 x 105

TABLE XIV (CONTINUED): REFRACTIONS AT LOCATION M

PATIENT INITIALS	REFRACTION	
FL	Plano	Plano
SL	+0.75 + 2.00 x 90	+1.50 + 2.00 at 90
RL	+1.25 + 3.50 x 90	-1.00 + 4.00 x 90
TL	+3.00 + 1.00 x 90	+3.00 + 1.50 x 90
JM	Plano	Plano
MM	-2.00 + 1.00 x 90	No view
DM	-1.00 + 1.00 x 90	-1.00 + 1.00 x 90
AM	-3.00 + 2.00 x 90	-3.00 + 2.00 x 90
DM	-3.00 + 3.00 x 90	-
Jmc	+2.00	+2.00
RMc	-0.25 + 2.00 x 90	-0.25 + 2.00 x 90
JMc	-8.50 + 4.00 x 90	-3.50 + 2.00 x 90
KN	-1.00	-1.00
MO	Plano	Plano
BO	-7.50 + 4.00 x 115	-8.50 + 5.00 x 75
KO	-1.50 + 6.00 x 80	-1.50 + 1.00 x 90
AO	-2.50	-2.50
M P	-2.00 + 3.00 x 90	-2.00 + 3.00 x 90
M P	-7.00	-6.00 + 2.00 x 90
M P	-4.00 + 2.00 x 90	-4.00 + 2.00 x 90
JP	Plano +2.00 x 90	Plano + 2.00 x 90
EP	-1.00 + 1.00 x 90	-1.00 + 1.00 x 90
JP	Plano	Plano
TP	-2.50 + 1.00 x 90	-2.00 + 1.00 x 90
MP	+1.00 + 1.00 x 90	+1.00 + 1.00 x 90
DP	-3.00 + 2.00 x 90	-3.00 + 2.00 x 90
KR	-1.00	-5.00
MR	+2.00 + 2.00 x 90	+2.00 + 1.00 x 95
KS	-1.00 + 1.50 x 90	Plano + 1.50 x 90
NS	+0.50	+0.50
JS	-8.00	-2.00
MS	-12.00	-12.00
RT	Plano	Plano
TT	-	-2.00 + 1.00 x 90
TT	-	-
DT	-20.00 + 5.00 x 90	-
RV	-2.00 + 0.50 x 90	-2.00 + 0.50 90
BW	-1.50	-1.50
MW	-9.00 + 6.00 x 90	-11.00 + 8.00 x 90
DW	-2.00 + 1.25 x 90	+8.50 + 3.00 x 90
TW	-0.50	-0.50
AY	-9.00 + 1.00 x 90	-9.00 + 1.00 x 90
DY	-1.00 sph	-1.00 sph
KZ	+1.25	+1.25
MZ	-4.00	-4.00

Cyclopleged refractions were performed (Table XIV). Refractive errors ranged from –20.00 to +20.00 (aphakic patient).

LCMV as a Cause of Visual Loss at Location M

Of the 95 patients examined at Location M, four had chorioretinal scars. Of these, case 1 had an unknown etiology; case 2, which had been attributed to toxoplasmosis, was found on further search of the records to have no record of positive titers. Cases 3 and 4 also had no known etiology. Sera were obtained and sent for TORCHS (toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and syphilis) titers, and sera of the first 3 cases were also sent for LCMV titers. The case 4 child died before sera were drawn.

The sera for toxoplasmosis were sent to Jack Remington's laboratory at Stanford University. The sera for LCMV were sent to the Special Pathogens Branch at the Centers for Disease Control and Prevention in Atlanta, Ga. TORCHS titers were negative for cases 1, 2, and 3, and LCMV titers were positive for cases 1 and 2, and negative for case 3. The LCMV titers for cases 1 and 2 were, respectively, IgG 1/6,400 and IgG 1/400. The mother in case 2 was also positive for LCMV (with a titer of IgG 1/400), confirming that her child's infection was congenital in origin. The case 1 mother has declined to have sera drawn for testing.

Case 1 was examined at Location M at age 11 years. He is a black male born at 3 lb 14 oz (1,770 g) and a gestational age of 32 weeks. He was delivered by cesarean section secondary to an abruptio placenta and had APGARS of 8 and 9. His mother's pregnancy history was notable for hyperthyroidism complicated by "chemical hepatitis." The mother was living in a major urban area adjacent to an excavation that resulted in rats entering her house. During the child's perinatal period, he manifested bronchopulmonary dysplasia and was diagnosed with osteomyelitis of his right distal femur.

At 4 months, the mother noted decreased attentiveness in the child, and his neurologist diagnosed microcephaly. A CT scan revealed periventricular calcifications and cerebral atrophy secondary to mild lateral ventricle dilation. An eye consultation was obtained for a chorioretinal scar. There was no visually directed behavior observed, and the pupils and anterior segment examinations were normal. He demonstrated an exotropia of 50 diopters and cyclopleged retinoscopy was +0.50 OU. Dilated fundus examination revealed normal disc and vessels OU with a normal macula on the right and a chorioretinal scar filling the macula on the left. (The author was surprised to find, on review of the records, that this consultation was performed by the author 11 years before at another institution.)

The current examination at age 11 years showed a vision of fixing and

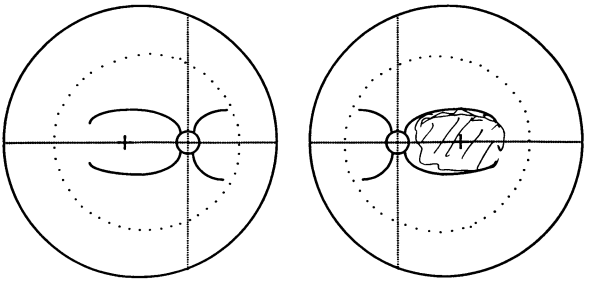

FIGURE 3
Case 1. Retinal drawing based on fundus examination of lymphocytic choriomeningitis virus documents a macular scar in left eye.

following OU. The pupillary and slit-lamp examinations were within normal limits, and cyclopleged retinoscopy revealed a –1.00 + 3.00 x 90 OD and a –8.00 + 6.00 x 90 OS. The fundus examination was normal on the right, and on the left, the posterior pole was filled with an irregular chorioretinal scar to the arcades (Fig 3).

Case 2 was examined at Location M at age 7 years. She is a black female with a medical history including a birth weight of 5 lb 8 1/2 oz at 32 weeks gestation. Her mother's pregnancy history was positive for back pain and headaches, as well as for sickle cell trait. She lived on Chicago's south side in the inner city and denies any exposure to mice or other rodents. She states that her child was "normal" until age 7 months, when there was an onset of seizures. At that time, CT examination revealed hydrocephalus and schizencephaly. She was given a presumptive diagnosis of congenital toxoplasmosis.

The current examination at age 7 years demonstrated visions of CSF (central, steady ,and follows) OU. She did not show good, smooth pursuit, however. The pupils were slightly sluggish and the slit-lamp examination was within normal limits. The extraocular muscle examination was normal, and cyclopleged retinoscopy revealed –2.00 + 3.00 x 90 OU. The fundus examination of the right eye showed a chorioretinal scar 1 disc diameter (DD) wide, located about 1 DD nasal to the disc. The fundus of the left eye contained 3 chorioretinal scars, one superior to the disc and 2 in the macula, 1 above and 1 below the fovea (Fig 4).

DISCUSSION

OUR RESULTS COMPARED TO OTHER STUDIES

There are very few studies from the United States on childhood visual loss.

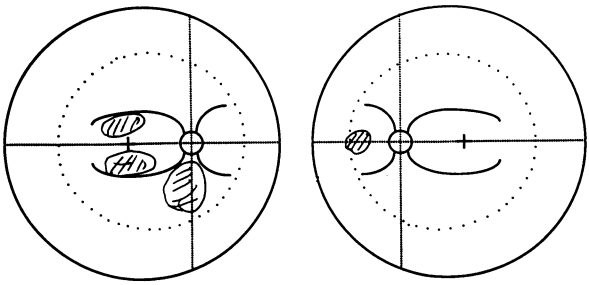

FIGURE 4
Case 2. Retinal drawing based on fundus examination of lymphocytic choriomeningitis virus documents chorioretinal scars bilaterally.

TABLE XV: COMPARISON OF OUR FINDINGS TO TWO OTHER US STUDIES

CAUSE	HATFIELD '72	WILLIAMSON '87	OUR STUDY '98	
			V	M
Infection	10%	18%	2%	16%
Prematurity	4%	21%	20%	13%
Injury	2%	18%	7%	25%
Congenital:				
Genetic	48%	12%	29%	15%
Prenatal	13%	28%	42%	26%
Other	23%	3%	0%	5%
Total	100%	100%	100%	100%

Table XV compares our study to the two most informative US studies, that by Hatfield[45] and that by Williamson and associates.[47] This table addresses the causes of visual loss and uses categories that are applicable to the design of the 3 studies. These previous 2 are both survey studies. The former reviewed data from agencies providing services to blind infants and children, and the latter surveyed 22 Texas school districts that provided services for visually impaired children. In the latter study, 75% of the children had associated mental retardation. Our Location M results are similar to the Williamson study for causes due to infection. The 2 studies with fewer mentally impaired children, that by Hatfield and our Location V, have fewer infectious causes. In addition, the Hatfield study states that rubella was responsible for the majority of infections, and the lower percentage in our Location V probably reflects the decreased incidence of

rubella over time.

Note that prematurity accounted for 4% of the decreased vision in the 1972 study, 21% in the 1987 study, and 20% and 13% in our study (1998). This is probably explained by the fact that a greater number of sicker and younger babies can be sustained as medical technology progresses, as reflected in the 2 more recent studies. Injury was highest in our Location M population of severely retarded children. Congenital causes form the majority in all 3 studies, while frequency in the subsets of "hereditary" and "other" vary among the 3 studies. Congenital causes also predominate in other modern studies in developed countries, including Scandinavia, Great Britain, Australia, and Ireland.[55,124-133] However, it is interesting that the numbers among the 3 studies, carried out at different times and using different methods, are comparable with few exceptions.

Table XVI summarizes the diagnoses and causes of childhood visual loss at the 2 locations we investigated. The diagnoses found at Location V were much more varied, while the causes were less generalized than those found at Location M, with 71% of causes classified as congenital. At Location M, optic atrophy was the diagnosis in 65% of the patients, all of whom, as mentioned above, were severely retarded. At Location V, however, optic atrophy was present in only 19.4%, and these were normal developmentally except for a few mildly delayed students. The other common diagnosis at Location V was ROP, which was also found in 19.4% of the students.

The diagnoses at Location V are compared to a large 1980 Japanese study of schools for the blind[134] and a 1987 study from the Royal School for the Blind in Scotland[135] in Table XVII. Optic atrophy was the second most common known diagnosis in both the Japanese and the Scottish studies, and, along with ROP, was our most common diagnosis. Cataracts, microphthalmia, and myopia were the first, third, and fourth most common diagnoses in Japan. It may be that the improved treatment of cataracts over the last 18 years explains the difference from our study. The 1987 Scottish study reported cataracts as the third most common cause of blindness. Combining the number of patients with a diagnosis of PHPV, which is associated with microphthalmos, and microphthalmia from the Location V study yields a total of 8%, which is closer to the 11.2% in the Japanese study. The Scottish study showed a comparable 6% due to microphthalmos. The most common diagnosis in the Scottish study was retinitis pigmentosa (RP and Leber's), which was our third most common diagnosis (Batten's, Leber's, Bardet-Biedl, and Usher's). Blindness secondary to myopia, found in 11.2% of the students in the Japanese study, may represent a genetic difference in populations, since it was not seen at all in our study or the Scottish study.

TABLE XVI. SUMMARY OF DIAGNOSES AND CAUSES OF VISUAL LOSS

DIAGNOSES

LOCATION V	NO.	%	LOCATION M	NO	%
Retinopathy of prematurity	12	(19.4)	Optic atrophy	54	(65)
Optic atrophy	12	(19.4)	Cortical visual impairment	20	(24)
Retintis pigmentosa	9	(14.5)	Chorioretinal scar	4	(5)
Optic nerve hypoplasia	8	(12.9)	Optic nerve hypoplasia	2	(2.4)
Cataracts	5	(8.1)	Retinitis pigmentosa	1	(1.2)
Foveal hypoplasia	5	(8.1)	Cataract (aicardi)	1	(1.2)
Persistent hypoplasia of the primary vitreous	3	(4.8)	Phthisis	1	(1.2)
Microphthalmos	2	(3.2)		83	100
Morning glory	1	(1.6)			
Congenital herpes	1	(1.6)			
Peter's anomaly	1	(1.6)			
Stargardt's disease	1	(1.6)			
Congenital rubella	1	(1.6)			
Ametropic amblyopia	1	(1.0)			
Total	62	100			

CAUSES

LOCATION V	NO.	%	LOCATION M	NO.	%
Cognenital prenatal	26	(42)	Congenital prenatal	22	(26)
Congenital genetic	18	(29)	Congenital genetic	12	(15)
Prematurity	13	(20)	Prematurity	11	(13)
Child abuse	2	(3)	Child abuse	4	(5)
Infection	1	(2)	Infection	13	(16)
Accidental trauma	1	(2)	Accidental trauma	4	(5)
Birth trauma	1	(2)	Birth trauma	12	(14)
			Unknown	4	(5)
			Drug abuse	1	(1)
Total	62	100		83	100

TABLE XVII. DIAGNOSES AT SCHOOLS FOR THE BLIND

	V SCHOOL '98 (N = 62) PERCENTAGES	JAPAN '80 (N = 8248) PERCENTAGES	SCOTLAND '87 (N = 99) PERCENTAGES
Retinopathy of Prematurity	19.4	0	11
Optic Atrophy	19.4	11.4	15
Retinitis Pigmentosa	14.5	9.8	16
Optic Nerve Hypoplasia	12.9	0	2
Cataracts	8.1	15.0	14
Foveal Hypoplasia	8.1 (Albinism 4.8)	1.8	2
Persistent Hyperplastic Primary Vitreous	4.8	0	0
Microphthalmos	3.2	11.2	6
Morning Glory	1.6	0	0
Congenital Herpes	1.6	0	0
Peter's syndrome	1.6	0	0
Stargardt's Disease	1.6	0	0
Congenital Rubella	1.6	0	0
Ametropic Amblyopia	1.6	11.1 (Myopia)	0
	100	6.8 (Buphthalmos)	2
		3.6 (Cornea)	0
		1.7 (Disorganized eye)	0
		27.6 (Other)	25 (Other)
		100	7 (Aniridia)
			100

In many of the cases at Location M, the inciting event resulted in an anoxia that caused severe insult to the central nervous system, which is often associated with bilateral optic atrophy. The optic nerve is relatively resistant to hypoxic damage, and one does not see isolated optic atrophy secondary to hypoxia; rather, associated severe central nervous system damage accompanies optic atrophy caused by hypoxia, as was seen in this group of patients.[136]

This observation of a preponderance of optic atrophy among the mentally retarded has been seen in other studies as well. Table XVIII compares our populations to a large, composite Scandinavian study previously mentioned, in which mentally retarded and non–mentally retarded populations were compared in the Netherlands, Belgium, Denmark, and Sweden.[124] Optic atrophy was found to be more common among the mentally retarded populations in all 4 countries as well as in our study, which had the highest percentage. This is most likely due to the very severe degree of retardation in this population.

Genetic disorders were the second most common cause at both institutions (Table XVI); however, those seen at Location V were primarily

TABLE XVIII: COMPARISON OF DIAGNOSIS OF OPTIC ATROPHY

NETHERLANDS		BELGIUM		DENMARK		SWEDEN		OUR STUDY	
MR	Not	MR	Not	MR	Not	MR	Not	MR	Not
25%	11%	35%	20%	50%	16%	23%	12%	58%	19%

MR, mentally retarded; Not, not mentally retarded.

isolated hereditary eye disorders, while those at Location M were severe disorders, including chromosomal anomalies, which are associated with profound mental retardation. It should be noted that in our study, only known genetic disorders were included in this category, and any disorder that appeared ambiguous was classified as congenital prenatal. Therefore, our genetic category is most likely an underestimate.

LCMV AS A NEW CAUSE OF VISUAL LOSS

Four of the patients of the 95 examined at Location M had chorioretinal scars suggesting intrauterine infection. One was negative for all screening, 1 died before we were able to obtain serum, and 2 had positive serum titers for LCMV. One of their mothers also had positive titers, and this is very strong evidence for intrauterine LCMV infection. There are 10 documented cases of congenital LCMV in the United States and 26 cases in the world literature; yet, in our study, of the 4 cases showing chorioretinal scars, the ocular sign of intrauterine infection, half were positive for LCMV. This suggests that congenital LCMV is more common than is suggested by the 10 reported cases in the United States. A study in urban Baltimore in 1992 shows that the prevalence of positive serum antibody testing by ELISA in house mice (*M musculus*) is 9%, with a range of 3.9% to 13.4%, and that the positivity tends to cluster. This supports the theory of vertical (ie, intrauterine) transmission among the mouse population.[72] Prevalence studies, again for positive serum antibodies, have been carried out in Birmingham, Ala, in 1992 among healthy black women, showing a rate of 5.1%;[137] in Argentina in 1994 among males 15 to 65 years of age, with a rate of 2.38%;[138] and again in Birmingham in 1997, with an overall rate of 3.5%, a rate in individuals less than 30 years of age of 0.3%, and a rate in those 30 years and older of 5.4%.[139] This relatively low prevalence lends more credence to positive serologic testing than for either toxoplasmosis or cytomegalovirus, which are considerably more common. In one of our 2 patients, the positive titer demonstrated in the mother further confirms the diagnosis.

One of our patients with LCMV had been carrying a diagnosis of congenital toxoplasmosis. Review of the chart revealed no positive laboratory

confirmation, and toxo titers performed by Dr Remington's laboratory were negative. However, this finding suggests that there may be other patients with presumptive diagnoses of toxoplasmosis who actually have LCMV. The eye findings are similar, and there certainly is an overlap of the systemic findings, although the patients with toxoplasmosis more often have obstructive hydrocephalus.

Other infections in the differential diagnosis include the rest of the TORCHS cluster: rubella, CMV, herpes simplex, and syphilis. The eye findings are quite different in all of these except for possibly CMV, which may have a macular chorioretinal scar, although CMV more often manifests as a developmental disturbance such as optic nerve hypoplasia. There may also be some overlap of herpes simplex retinitis, but acute retinal necrosis has a distinctive appearance, as does the scarring seen following infection. The generalized salt-and-pepper retinopathy of rubella and syphilis is usually not confused with the findings of LCMV or toxo. The diagnosis cannot be definitively made without serology, and presumptive diagnoses should be avoided.

It has been suggested by Wright and colleagues[123] that the eye findings in Aicardi's syndrome are similar. The chorioretinal lacunae seen in Aicardi's syndrome are quite different,[140] and the characteristic absence of the corpus callosum is not part of the findings seen in congenital LCMV. Again, we urge that serology be performed in all cases.

The eye findings of LCMV are similar to those found in congenital toxoplasmosis (Fig 5), and we feel there may be cases that have been misdiagnosed as congenital toxoplasmosis, as was our case 2. However, there

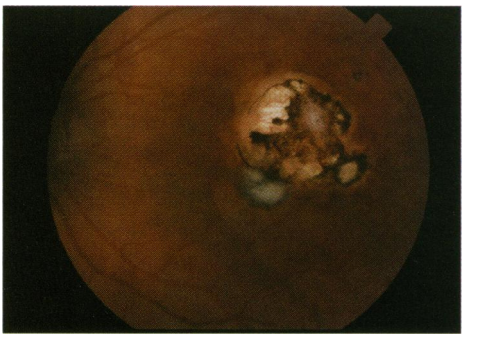

FIGURE 5

Fundus photo of left eye in patient with congenital toxoplasmosis showing characteristic macular scar. About disc diameter from scar, at 1-o'clock position, is a satellite lesion. There is also evidence of satellite lesions inferiorly at 5-o'clock and 7-o'clock positions, adjacent to larger scar. Satellite at 7-o'clock position has been shown by fluorescein angiography to be a choroidal neovascular membrane.

may be differences in appearance, as demonstrated by our case 1. This patient had a large macular scar with irregular, scalloped borders, while the typical toxo macular scar is usually smaller and has smoother borders, although subsequent satellite lesions (Fig 5) can mimic the irregular border. The multiple scars in case 2 (Fig 4) are very similar to congenital toxo scars. Figure 6 shows a large macular chorioretinal scar in a patient with

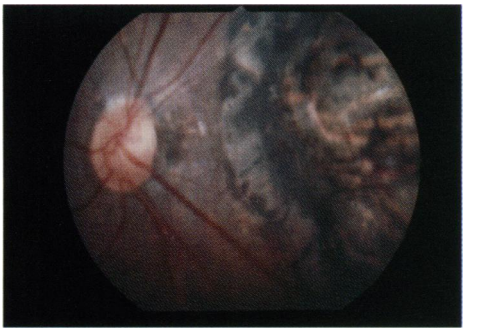

FIGURE 6

Left eye of patient with congenital lymphocytic choriomeningitis virus showing large macular chorioretinal scar with straightening of major arcades. There is also peripapillary irregularity of retinal pigment epithelium just temporal to disc, and peripapillary tuft of what appears to be glial tissue at about the 11-o'clock position.

confirmed congenital LCMV. As before, however, serology is required for definitive diagnosis, and we feel that serology for LCMV should be a part of the standard workup for congenital chorioretinitis, especially if the TORCHS titers are negative. Perhaps it would be appropriate to revise the mnemonic to "TORCHS + L."

The pathogenesis of the retinitis is not well understood; however, some work by del Cerro and associates[141,142] is intriguingly suggestive of an autoimmune phenomenon. Rats were inoculated intracranially as neonates with LCMV. This resulted in an acute, cell-mediated, necrotizing retinitis followed by a chronic inflammatory process that destroyed the remaining retinal tissue. These rats were then allowed to bear offspring, whose retinas showed a range of morphologic variation from normalcy to complete disruption, although no virus was found in the offspring. The authors hypothesized that this was a model of a vertically transmitted autoimmune disease and suggest that most of the retinal damage was due to autoimmune phenomena rather than direct toxicity of the virus.

Although this is an interesting hypothesis, it does not rule out direct toxic damage to the retina and choroid in the human population.

PREVENTION

A primary impetus for a study such as this one is to assess what happened in the past, evaluate it, and attempt some approach toward prevention in the future. Table IV summarizes causes of visual loss at Location V, and Table X does so for Location M. The populations are clearly different, but there is some overlap. Better prenatal care would most likely have reduced the frequency of the first and third most common causes at Location V (congenital prenatal problems and prematurity) and 3 of the 4 most common causes at Location M (congenital prenatal problems, birth trauma [which was often associated with abruptio placenta], and infection, which may in some cases be preventable). For instance, avoiding contact with rodents—especially mice—during pregnancy should be encouraged. There were 30 cases at both institutions with genetic causes (29% at Location V and 15% at Location M). Advances in understanding and treating genetic disease may reduce this number in the future. Child abuse was a cause at both institutions, for a total of 6 children. There were 7 children whose mothers abused drugs during pregnancy (found as the primary cause in only one case), and one who was also abused (from Location M), for a total of 14 children (9.7%) documented as victims of abuse at the two institutions. Abuse is a potentially preventable cause of tragedy but one that is not easily approached.

CONCLUSION

Childhood blindness, visual impairment, and visual loss in general are more common in underdeveloped and developing countries but are tragic and costly wherever they occur, even more so when they are associated with mental retardation. We examined children at 2 institutions, one for the visually impaired and the other for severely mentally retarded and quadriplegic patients. At both locations, decreased vision was most often due to congenital problems, either genetic or simply prenatal. This was also the finding in the 2 previous major US studies. The most common diagnosis among the severely retarded was optic atrophy, and the previous literature supports this observation. The genetic abnormalities among the mentally retarded tended to be more generalized, while those observed at the school for the visually impaired were more often isolated eye disorders.

Four patients at Location M had chorioretinal scars, suggesting intrauterine infection. Of these, 2 had sera positive for lymphocytic chori-

omeningitis virus (LCMV), an organism believed to be extremely rare, reported in the congenital form only 10 times in the United States and 26 times in the world literature. Our finding suggests that this congenital infection may be more common than previously appreciated. We believe it should be part of the standard workup for congenital chorioretinitis and advocate updating the mnemonic for testing from TORCHS to "TORCHS + L." Additional attention and resources should be directed to investigating the contribution of congenital LCMV to childhood visual loss and retardation in the United States.

Prevention, if possible, is of utmost importance. A reduction in the number of affected children in the future may be accomplished through improved prenatal care, an approach to the social problem of abuse, and advances in genetics research. Further studies should be initiated in the United States to expand our knowledge of the causes of childhood blindness. Better state and national registries should be established for documentation. Only when we have a better understanding of the problem will we be able to best address it.

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REFERENCES

1. World Health Organization. *Prevention of Childhood Blindness*. Geneva: World Health Organization; 1992;1-50.
2. American Association for Pediatric Ophthalmology and Strabismus. Eye care for the children of America. *J Pediatr Ophthalmol Strabismus* 1991;28:64-67.
3. Larsen P, Chartrand S, Tomashek, et al. Hydrocephalus complicating lymphocytic choriomeningitis virus infection. *Pediatr Infect Dis J* 1993;12:528-531.
4. Barton L, Budd S, Morfitt W, et al. Congenital lymphocytic choriomeningitis virus infection in twins. *Pediatr Infect Dis J* 1993;12:942-946.
5. Barton L, Peters C, Ksiazek T. Lymphocytic choriomeningitis virus: An unrecognized teratogenic pathogen. *Emerg Infect Dis* 1995;1:152-153.
6. America PB. Vision Problems in the U.S. Schaumburg, Ill: National Society to Prevent Blindness; 1994;1-20.

7. Lambert S, Hoyt C, Jan J. Visual recovery from hypoxic cortical blindness during childhood. *Arch Ophthalmol* 1987;105:1371-1377.
8. Whiting S, Jan J, Wong P, et al. Permanent cortical visual impairment in children. *Dev Med Child Neurol* 1985;27:730-739.
9. Good W, Jan J, DeSA L, et al. Cortical visual impairment in children. *Surv Ophthalmol* 1994;38:351-364.
10. Han D, Wilkinson W. Late ophthalmic manifestations of the shaken baby syndrome. *J Pediatr Ophthalmol Strabismus* 1990;27:299-303.
11. Acers T, Cooper W. Cortical blindness secondary to bacterial meningitis. *Am J Ophthalmol* 1965;59:226-229.
12. Ackroyd R. Cortical blindness following bacterial meningitis. *Dev Med Child Neurol* 1984;26:227-230.
13. Newton N, Reynolds J, Woody R. Cortical blindness following Hemophilus influenzae meningitis. *Ann Ophthalmol* 1985;17:193-194.
14. Arroyo H, Jan J, Mc Cormick A. Permanent visual loss after shunt malfunction. *Neurology* 1985;35:25-29.
15. Mukamel M, Weitz R, Nissenkorn I. Acute cortical blindness associated with hypoglycemia. *J Pediatr* 1981;98:583-584.
16. Katafuchi Y, Nishimi T, Yamaguchi Y, et al. Cortical blindness in acute carbon monoxide poisoning. *Brain Dev* 1985;7:516-519.
17. Weinberger H, van der Woude R, Maier H. Prognosis of cortical blindness following cardiac arrest in children. *JAMA* 1962;179:134-137.
18. Roland E, Jan J, Hill A, et al. Cortical visual impairment following birth asphyxia. *Pediatr Neurol* 1986;2:133-137.
19. Young J. Definitions and size of the problem. In: Capute A, Accardo P, eds. *Developmental Disabilities in Infancy and Childhood*. 2nd ed. Baltimore: Paul H. Brookes Pub Co; 1996:211-212.
20. Young J. Definition and size of the problem. Bailliere's Clin Obstet Gynaecol 1988;2:1-7.
21. Hagberg B, Hagberg G, Lewerth A, et al. Mild mental retardation in Swedish schoolchildren. I. prevalence. *Acta Paediatr Scand* 1981;70:441-444.
22. Drillen C, Drummond M. Developmental screening and the child with special needs: A population study of 500 children. *Clin Dev Med* 1983;86:114.
23. Chiang Y, Bassi L, Javitt J. Federal budgetary costs of blindness. *Milbank Qtly* 1992;70:319-340.
24. Schneider A, Moomaw M. Care of the visually handicapped child. *Pediatr Rev* 1982;4:73-81.
25. Fraiberg S. *Insights From the Blind*. New York: Basic Books Inc; 1977;113-283.
26. Olurin O. Etiology of blindness in Nigerian children. *Am J Ophthalmol* 1970;70:533-540.
27. Quere M. Ocular complications of measles as a major cause of blindness in children in tropical countries. *Ophthalmologica* 1964;148:107-120.
28. Quere M, Satoga P, Graveline J, et al. Infantile keratopathies of kwashiorkor and the severe nutritional deficiencies in tropical Africa. *Bull Mem Soc Fr Ophthalmol* 1967;80:68.
29. Merin S. Malnutrition as a cause of blindness in children. *Malawi Med Bull* 1967;2:6-10.
30. Foster A, Gilbert C. Epidemiology of childhood blindness. *Eye* 1992;6:173-176.
31. Blumenthal C. Malnutritional keratoconjunctivitis; a disease of the South African Bantu. *South Afr Med J* 1950;24:191-198.
32. Kagame K, Schwab L. Childhood blindness: Dateline Africa. *Ophthalmic Surg* 1989;20:128-131.

33. Awdry P, Cobb B, Adams P. Blindness in Luapula valley. *Cent Afr J Med* 1967;13:197-201.
34. Chirambo M, Ben-Ezra D. Causes of blindness among students in blind school institutions an a developing country. *Br J Ophthalmol* 1976;60:665-668.
35. Sandford-Smith J, Whittle H. Corneal ulceration following measles in Nigerian children. *Br J Ophthalmol* 1979;63:720-724.
36. Sauter J. Causes of blindness detected in nineteen schools for the blind in Tanzania. In: Salaam DE, ed. *A Final Report for the Ministry of Health* 1978;1-14.
37. Faal H, Minassian D, Sowa S. National survey of blindness and low vision in the Gambia: Results. *Br J Ophthalmol* 1989;73:82-87.
38. Gilbert G, Wood M, Waddel K, et al. Causes of childhood blindness in East Africa: Results in 495 pupils attending 17 schools for the blind in Malawi, Kenya and Uganda. *Ophthalmic Epidemiol* 1995;2:77-84.
39. Foster A, Sommer A. Corneal ulceration, measles, and childhood blindness in Tanzania. *Br J Ophthalmol* 1987;71:331-343.
40. Sommer A, Quesada J, Doty M, et al. Xerophthalmia and anterior-segment blindness among preschool-age children in El Salvador. *Am J Ophthalmol* 1975;80:1066-1072.
41. Rojas J, Lavado L, Echegara L. Childhood blindness in Peru. *Ann Ophthalmol* 1990;22:423-425.
42. Tabbara K, Badr K. Changing pattern of childhood blindness in Saudi Arabia. *Br J Ophthalmol* 1985;69:312-315.
43. Foster A, Johnson G. Magnitude and causes of blindness in the developing world. *Int Ophthalmol* 1990;14:135-140.
44. Kahn H, Moorhead H. *Statistics on Blindness in the Model Reporting Area.* Washington, DC: US Government Printing Office; 1970;1-143.
45. Hatfield F. Blindness in infants and young children. *Sight Sav Rev* 1972;42:69-89.
46. Hatfield E. Causes of blindness in school children. *Sight Sav Rev* 1963;33:218-233.
47. Williamson W, Desmond M, Andrew L, et al. Visually impaired infants in the 1980's. *Clin Pediatr* 1987;26:241-244.
48. Drews C, Yeargin-Allsopp M, Murphy C, et al. Legal blindness among 10-year-old children in metropolitan Atlanta: Prevalence, 1985 to 1987. *Am J Pub Health* 1992;82:1377-1379.
49. Evans J, Wachs H, Borger J. A survey of visual skills of institutionalized retarded patients. *Am J Ment Defic* 1972;76:555-560.
50. Maino D, Maino J, Maino S. Mental retardation syndromes with associated ocular defects. *J Am Optom Assoc* 1990;61:707-716.
51. US HEW. Vision and hearing screening in selected classes for the mentally retarded Detroit, Michigan. *Eye Ear Nose Throat Monthly* 1969;48:97-103.
52. Gardiner P. Visual defects in cases of Down's syndrome and in other mentally handicapped children. *Br J Ophthalmol* 1967;51:469-474.
53. Bankes J. Eye defects of mentally handicapped children. *BMJ* 1974;8:533-535.
54. Woodruff M. Prevalence of visual and ocular anomalies in 168 non-institutionalized mentally retarded children. *Can J Public Health* 1977;68:225-232.
55. Warburg M. Causes of severe visual impairment in children and their prevention. *Doc Ophthalmol* 1975;39:285-286.
56. Prokesova V, Kriz S, Berg L, Halvorsen I. Ophthalmologic examination of the mentally retarded at a central institution. *Tidsskr Nor Legeforen* 1990;110:1659-1662.
57. Bader D. The visual appraisal of the mentally retarded. *South Afr Med J* 1974;48:2077-2080.
58. Blackhurst R, Radke E. Testing retarded children for defects in vision. *Dig Ment Retard*

1967;4:63-64.
59. Warburg M. Why are the blind and severely visually impaired children with mental retardation much more retarded than the sighted children? *Acta Ophthalmol* 1982;157(suppl):72-81.
60. Berg J, Kirman B. Some aetiological problems in mental deficiency. *BMJ* 1959;2:848-852.
61. Kato K, Konyama K, Nakagawa O, et al. Ocular manifestations in mental deficiency. *Acta Soc Ophthalmol Jap* 1970;74:1215-1224.
62. Iivanainen M. A study on the origins of mental retardation. An academic dissertation. London: Heinemann Medical Books Ltd; 1974;37-38.
63. Rogow S. Considerations in the assessment of blind children who function as severely or profoundly retarded. *Child Care Health Dev* 1978;4:327-335.
64. Ellis D. Visual handicaps of mentally handicapped people. *Am J Ment Defic* 1979;83:497-511.
65. Tuppurainen K. Ocular findings among mentally retarded children in Finland. *Acta Ophthalmol* 1983;61:634-644.
66. Edwards W, Price W, Weisskoph B. Ocular findings in developmentally handicapped children. *J Pediatr Ophthalmol Strabismus* 1972;9:162-167.
67. Landau L, Berson D. Cerebral palsy and mental retardation: Ocular findings. *J Pediatr Ophthalmol Strabismus* 1971;8:245-248.
68. Armstrong C, Lillie R. Experimental lymphocytic choriomeningitis of monkeys and mice produced by a virus encountered in studies of the 1933 St Louis encephalitis epidemic. *Pub Health Rep* (Wash) 1934;49:1019-1027.
69. Rowe W, Murphy P, Bergold G, et al. Arena viruses: Proposed name for a newly defined virus group. *J Virol* 1970;5:651-652.
70. Peters C, Johnson K. Lymphocytic choriomeningitis virus, Lassa virus, and other arenaviruses. In: Mandell G, Bennet J, Dolin R, eds. *Infectious Diseases and Their Etiologic Agents*. 4th ed. New York: Churchill Livingstone; 1995:1572-1579.
71. Hotchin J. The contamination of laboratory animals with lymphocytic choriomeningitis virus. *Am J Pathol* 1971;64:747-769.
72. Childs J, Glass G, Korch G, et al. Lymphocytic choriomeningitis virus infection and house mouse (MUS musculus) distribution in urban Baltimore. *Am J Trop Med Hyg* 1992;47:27-34.
73. Traube E. Persistence of lymphocytic choriomeningitis virus in immune animals and its relation to immunity. *J Exp Med* 1936;63:847-861.
74. Smadel J, Wall M. Lymphocytic choriomeningitis in the Syrian hamster. *J Exp Med* 1942;75:581-591.
75. Volkert M, Larsen J. Studies on immunlolgical tolerance to LCM virus.5. The induction of tolerance to the virus. *Acta Pathol Microbiol Scand* 1965;63:161-171.
76. Tobin JH. The growth of lymphocytic choriomeningitis virus in the developing chick embryo. *Br J Exp Pathol* 1954;35:358-364.
77. Blanc G, Bruneau J. Comportment du virus de la choriomeningite chez la lapine engestation. *C R Acad Sci* 1951;233:1704-1705.
78. Baum S, Lewis A, Rowe W, et al. Epidemic non-meningitic lymphocytic-choriomeningitis infection: An outbreak in a population of laboratory personnel. *N Engl J Med* 1966;274:934-936.
79. Hirsch M, Moellering R, Pope H, et al. Lymphocytic-choriomeningitis-virus infection traced to a pet hamster. *N Engl J Med* 1974;291:610-612.
80. Dykewicz C, Dato V, Fisher-Hoch S, et al. Lymphocytic choriomeningitis outbreak associated with nude mice in a research institute. *JAMA* 1992;267:1349-1353.

81. Biggar R, Woodall J, Walter P, et al. Lymphocytic choriomeningitis outbreak associated with pet hamsters: Fifty-seven cases from New York state. *JAMA* 1975;232:494.
82. Deibel R, Woodall J, Decher W, et al. Lymphocytic choriomeningitis virus in man: Serologic evidence of association with pet hamsters. *JAMA* 1975;232:501-504.
83. Shaughnessy H, Milzer A. Experimental infection of Dermacentor andersoni Stiles with the virus of lymphocytic choriomeningitis. *Am J Pub Health* 1939;29:1103-1108.
84. Coggeshall L. The transmission of lymphocytic choriomeningitis by mosquitoes. *Science* 1939;89:515-516.
85. Milzer A. Studies on the transmission of lymphocytic choriomeningitis by arthropods. *J Infect Dis* 1942;70:152-172.
86. Fedorov I, Igolkin N, Tyushnyakova M. Some data on fleas, virus carriers in foci of tick-borne encephalitis and lymphocytic choriomeningitis. *Med Parazitol* (Mosk) 1959;28:149-152.
87. Syverton J, McCoy O, Koomen J. The transmission of the virus of lymphocytic choriomeningitis by Trichinella spiralis. *J Exp Med* 1947;85:759-769.
88. Treusch J, Milser A, Levinson S. Recurrent lymphocytic choriomeningitis: Report of a case in which treatment was with pooled normal adult serum. *Arch Intern Med* 1943;72:709-714.
89. Shvarev A, Remezov P. A clinical and virological study of lymphocytic choriomeningitis. *Probl Virol* 1959;4:67-69.
90. Thiede W. Cardiac involvement in lymphocytic choriomeningitis. *Arch Intern Med* 1962;109:50-54.
91. Lewis J, Utz J. Orchitis, parotitis, and meningoencephalitis due to lymphocytic choriomeningitis virus. *New Engl J Med* 1961;265:776-780.
92. Blattner R. Parotitis, orchitis, and meningoencephalitis due to lymphocytic choriomeningitis virus. *J Pediatr* 1962;110:633-635.
93. Colmore J. Severe infections with the virus of lymphocytic choriomeningitis. *JAMA* 1952;148:1199-1201.
94. Silicott W, Neuberger K. Acute lymphocytic meningitis: Report of three cases with histopathologic findings. *Am J Med Sci* 1940;200:253-259.
95. Armstrong C. Some recent research in the field of neurotrophic viruses with especial reference to lymphocytic choriomeningitis and herpes simplex. *Mil Surg* 1942;91:129-146.
96. Smadel J, Green R, Paltauf R, Gonzales T. Lymphocytic choriomeningitis: Two human fatalities following an unusual febrile illness. *Proc Soc Exp Biol Med* 1942;49:683-686.
97. Scheid W, Jochheim K, Mohr W. Laboratoriumsinfektionen mit dem Virus der lymphozytaren Choriomeningitis. *Deutsch Arch Klin Med* 1956;203:88-109.
98. Gunther A. Uber akute "aseptische" Meningitis. *Jahrb Kinderh* 1930;128:127-154.
99. Viets H, Watts J. Acute aseptic meningitis. *J Nerv Ment Dis* 1934;80:253-273.
100. Skogland J, Baker A. An unusual form of lymphocytic choriomeningitis. *Arch Neurol* 1939;42:507-512.
101. Baker A. Chronic lymphocytic choriomeningitis. *J Neuropath Exp Neurol* 1947;6:253-264.
102. Chang H, Ch'iu F, Wang H. Lymphocytic choriomeningitis: Report of a chronic case. *Chin Med J* 1954;72:113-117.
103. Findlay G, Alcock N, Stern R. The virus etiology of one form of lymphocytic meningitis. *Lancet* 1936;1:650-654.
104. MacCallum F, Findlay G. Lymphocytic choriomeningitis: Isolation of the virus from the nasopharynx. *Lancet* 1939;1:1370-1373.
105. Jahrling P, Peters C. Lymphocytic choriomeningitis virus. A neglected pathogen of man. *Arch Pathol Lab Med* 1992;116:486-488.

106. Lehmann-Grube F. Diseases of the nervous system caused by lymphocytic choriomeningitis virus and other arena viruses. In: Vinken P, Bruyn G, Mc Kendall R, eds. *Handbook of Clinical Neurology*. Amsterdam: Elsevier Science Publishers; 1989;355-381.
107. Roebroek R, Postma B, Dijkstra U. Aseptic meningitis caused by the lymphocytic choriomeningitis virus. *Clin Neurol Neurosurg* 1994;96:178-180.
108. Lepine P, Sautter V. Contamination de laboratoire avec les virus de la choriomeningite lymphocytaire. *Ann Inst Pasteur* 1938;61:519-526.
109. Milzer A, Levinson S. Laboratory infection with the virus of lymphocytic choriomeningitis. *JAMA* 1942;120:27-30.
110. Hayes G, Hartman G. Lymphocytic choriomeningitis: report of laboratory infection. *Bull Johns Hopkins Hosp* 1943;73:275-286.
111. Lehmann-Grube F, Ackermann R, Jocheim K, et al. Uber de technik der neutralization des virus der lymphozytaren choriomeningitis in der maus. *Arch Ges Virusforsch* 1959;9:64-72.
112. Armstrong D, Fortner J, Rowe W, et al. Meningitis due to lymphocytic choriomeningitis virus endemic in a hamster colony. *JAMA* 1969;209:265-267.
113. Komrower G, Williams B, Stones P. Lymphocytic choriomeningitis in the newborn. Probable transplacental infection. *Lancet* 1955;1:697-698.
114. Ackermann R, Stammler A, Armbruster B. Isolierung von Virus der lymphozytaren Chorioimeningitis aus Abrasionmaterial nach Kontakt der Schwangeren mit einem Syrischen Goldhamster. *Infection* 1975;3:47-49.
115. Ferencz A, Binder L, Telegdy L, et al. Occurrence of lymphocytic choriomeningitis infections among adult patients between 1971 and 1976. *Orv Hetil* 1979;120:1563-1567.
116. Ackermann R, Korver G, Turss R, et al. Prenatal infection with the lymphocytic choriomeningitis virus. *Dtsch Med Wochenschr* 1974;13:629-632.
117. Chastel C, Bosshard S, Le Goff F, et al. Infection transplacentaire par le virus de la choriomeningite lymphocytaire. *Nouv Presse Med* 1978;7:1089-1092.
118. Sheinbergas M, Tulevichiene J, Kleiziene C, et al. Antibody to lymphocytic choriomeningitis virus in children with congenital hydrocephalus and in their mothers. In: *Proceedings of the All Union Conference on Pediatrics, Moscow*. 1974;270-272.
119. Sheinbergas M. Antibody to lymphocytic choriomeningitis virus in children with congenital hydrocephalus. *Acta Virol* 1975;19:165-166.
120. Sheinbergas M. The role of lymphocytic choriomeningitis virus in the etiology of congenital hydrocephalus. *Vop Virusol* 1976;1:94-99.
121. Barton L, Peters C, Seaver L, et al. Congenital lymphocytic choriomeningitis virus infection. *Arch Pediatr Adolesc Med* 1996;150:440.
122. Bechtel R, Haught K, Mets M. Lymphocytic choriomeningitis virus: A new addition to the TORCH evaluation. *Arch Ophthalmol* 1997;115:680-681.
123. Wright R, Johnson D, Neumann M, et al. Congenital lymphocytic choriomeningitis virus syndrome: A disease that mimics congenital toxoplasmosis of cytomegalovirus infection. *Pediatrics* 1997;126-127.
124. Schappert-Kimmijser J. Causes of severe visual impairment in the children and their prevention. *Doc Ophthalmol* 1975;39:213-241.
125. Haustrate-Gosset M. Causes of severe visual impairment in children and their prevention. *Doc Ophthalmol* 1975;39:249-270.
126. Hansen F. Causes of severe visual impairment in children and their prevention. *Doc Ophthalmol* 1975;39:263-270.
127. Skydsgaard H. Causes of severe visual impairment in children and their prevention. *Doc Ophthalmol* 1975;39:271-284.
128. Lindstedt E. Causes of severe visual impairment in children and their prevention. *Doc*

Ophthalmol 1975;39:287-313.
129. Flage H, Rosenberg T, Rudanko S-L, et al. Visual impairment in Nordic children. *Ophthalmologica* 1992;70:597-604.
130. Rosenberg T, Flage T, Hansen E, et al. Incidence of registered visual impairment in the Nordic child population. *Br J Ophthalmol* 1995;80:49-53.
131. Fraser G, Friedmann A. *The Causes of Blindness in Childhood*. Baltimore: The Johns Hopkins Press; 1967;1-245.
132. Fraser G. The causes of severe visual handicap among schoolchildren in South Australia. *Med J Aust* 1968;1:615-620.
133. Goggin M, O'Keefe M. Childhood blindness in the Republic of Ireland: A national survey. *Br J Ophthalmol* 1991;75:425-429.
134. Nakajima A, Fujiki K, Yasuda N, et al. Population genetics of eye diseases among the Japanese. In: Eriksson A, Forsius H, Nevanlinna H, et al, eds. *Population Structure and Genetic Disorders*. New York: Academic Press; 1980;409-430.
135. Phillips C, Lev A, Newton M, et al. Blindness in school children: Importance of heredity, congenital cataract, and prematurity. *Br J Ophthalmol* 1987;71:578-584.
136. Good W, Hoyt C, Lambert S. Optic nerve atrophy in children with hypoxia. *Invest Ophthalmol Vis Sci* 1987;309.
137. Stephensen C, Blount S, Lanford R, et al. Prevalence of serum antibodies against lymphocytic choriomeningitis virus in selected populations form two U.S. cities. *J Med Virol* 1992;38:27-31.
138. Ambrosio A, Feuillade M, Gamboa G, et al. Prevalence of lymphocytic choriomeningitis virus infection in a human population of Argentina. *Am J Trop Med Hyg* 1994;50:381-386.
139. Park J, Peters C, Rollin P, et al. Age distribution of lymphocytic choriomeningitis virus serum antibody in Birmingham, Alabama: evidence of a decreased risk of infection. *Am J Trop Med Hyg* 1997;57:37-41.
140. DelPero R, Mets M, Tripathi R, et al. Anomalies of retinal architecture in Aicardi's syndrome. *Arch Ophthalmol* 1986;104:1659-1664.
141. del Cerro M, Grover D, Monjan A, et al. Chronic retinitis in rats infected as neonates with lymphocytic choriomeningitis virus: a clinical, histopathologic, and electroretinographic study. *Invest Ophthalmol Vis Sci* 1982;23:697-714.
142. del Cerro M, Grover D, Monjan A, et al. Congenital retinitis in the rat following maternal exposure to lymphocytic choriomeningitis virus. *Exp Eye Res* 1984;38:313-324.