Dallas, and the Department of Ophthalmology, The Hallamshire Hospital, Sheffield, England. Submitted for publication March 23, 1974. Reprint requests: Dr. J. D. Brodrick, University of Texas Southwestern Medical School, 3323 Harry Hines Blvd., Dallas, Texas 75235.

Key words: conjunctival cytology, megaloblastic, smear, nuclear size, chromatin pattern.

REFERENCES

Genesis of light-induced avian glaucoma.

Adrienne Kinear, Jean K. Lauber, and T. A. S. Boyd.

Light-induced avian glaucoma is characterized by eye enlargement, high intraocular pressure (IOP), low outflow facility (C), and reduced aqueous space volume. In this study we have identified several lesions occurring in the early pathologic process, from five to 28 days of age. At seven days, corneal lactic dehydrogenase (LDH) is low and aqueous LDH is high. By 28 days, aqueous LDH is 3.5 times normal levels and corneal LDH is reduced by 10 per cent. By nine days, aqueous space volume is reduced, and eye enlargement is evident by three weeks. IOP and C remain normal during this period, although C is later impaired (at six weeks) and homeostatic control of IOP breaks down at approximately 16 weeks. Though the primary cause(s) for the dimensional changes in cornea and vitreous body have not been identified, the difference in the time of their appearance indicates that these two lesions may be independent of one another. The corneal LDH change suggests early alteration in endothelial permeability, allowing excessive enzyme loss to the aqueous humor.

Domestic chicks reared under continuous light (24L/0D) develop severe morphologic and physiologic ocular lesions which culminate in glaucoma and blindness. We have called the condition light-induced avian glaucoma. Although human open-angle glaucoma is a serious clinical problem, few experimental animals develop such a disease and in no others, to our knowledge, can the condition be precipitated at the will of the investigator. Light-induced avian glaucoma is associated with increased eye weight and diameter, reduced corneal curvature, impaired outflow facility, and elevated intraocular (IOP) pressure.1,2 Eye enlargement and refractive error are detectable several weeks before outflow facility is impaired, and IOP is elevated still later in the disease process.3 Although the iridocorneal angle is narrow, iridectomy of chicks, subsequently reared under 24L/0D, failed to alter the course of the developing glaucoma, as might be expected if pupillary block had contributed to iris bombé.4 A systemic rather than a local etiology was suggested by the finding that eyes of 24L/0D birds, when covered by an opaque vision occluder, showed no less enlargement than those not so covered.5

However, these positive findings have provided few clues about the etiology of light-induced avian glaucoma. Improvements in our techniques have now made it possible to monitor aqueous fluid dynamics in chicks as young as seven days after hatching; we here detail these early pre-glaucomatous changes. We have also measured lactic dehydrogenase levels during the same period. This enzyme is thought to be essential for normal corneal metabolism6 and its relative activity in cornea and aqueous has been used as an indication of the viability of the corneal endothelium.7

Materials and methods. White Rock (broiler type) chicks were reared from hatching in either continuous incandescent light (24L/0D) or a diurnal photoperiod of 14 hours of light per day (14L/10D). Birds were maintained in temperature-controlled environment chambers and were supplied with food (commercial chick starter crumbs) and water ad libitum. Brooder heat without light was supplied by heating the inflow air of the positive-pressure ventilation system.

Eye weight, corneal height, corneal diameter, and aqueous space volume were determined as previously described.2,8 To separate the effect of body growth from eye enlargement, a number of chick pairs were selected, one bird from each lighting treatment, but having equivalent body weights. Eye weights of these birds were compared by paired t-test. In evaluation of all other data, Student’s t-test was applied. Under Combuthal anesthesia,5 IOP was monitored by closed manometry and aqueous outflow facility (C) was estimated after constant-rate perfusion, as previously described.3

Downloaded From: http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/932881/ on 04/11/2017
In an attempt to assess aqueous flow, the rate of accumulation of fluorescein in the anterior chamber was monitored for 10 minutes immediately following intravenous injection of the dye, according to a previously described technique. The amount of dye in the aqueous was monitored via a plastic fiber optic probe and directed to a highly sensitive spectroradiometer, set to read at 535 nm, the fluorescence emission wavelength of fluorescein.

Lactic dehydrogenase was measured in aqueous and homogenized cornea by the Boeringer-Mannheim method, as employed by Kim, Campbell, and Hassard. The concentration of enzyme is expressed in International Units per unit volume (U./ml.) or per unit weight (mU./Gm.) of sample. One International Unit represents the amount of enzyme which catalyzes the conversion of one micromole of substrate per minute under standard conditions (25° C. and pH 7.5).

Results. Eye weight. Eye enlargement under-24L/0D is evident early in the preglaucomatous period. Eye weight was significantly greater at three weeks (p < 0.05), with slight but non-significant increases at nine and 11 days (Fig. 1). When the influence of body growth was eliminated by pairing birds of equal body weight, eye enlargement (p < 0.05) was first significant at three weeks (Table 1).

Aqueous space volume. Up to eight days, aqueous space volume was similar in chicks of the two lighting treatments. At nine days, 24L/0D birds had significantly smaller corneal height (p < 0.001). This was reflected in reduced aqueous space volume from nine days onward (Fig. 2). Corneal diameter of 24L/0D, as compared with 14L/10D, birds was significantly smaller from 14 days (p < 0.01). Despite the reduction in aqueous space volume of 24L/0D birds, the rate of fluorescein accumulation in the aqueous was similar to that in 14L/10D birds, from seven to 28 days of age.

Lactic dehydrogenase. Enzyme activity was lower in the cornea, and higher in aqueous humor of 24L/0D chicks from one week of age onward (Fig. 3). The corneal difference was statistically significant by four weeks (p < 0.05), and the aqueous disparity was significant at two weeks (p < 0.05).

Intraocular pressure and outflow facility. Although our previous work had shown that light-induced avian glaucoma is characterized, in the adult, by elevated IOP and impaired C, neither of these changes occurred early in the disease.
Fig. 2. Aqueous space volumes of normal (14L/10D) and preglaucomatous (24L/0D) chicks; mean ± S.E.M.

Fig. 3. Lactic dehydrogenase levels in cornea and aqueous humor of normal (14L/10D) and preglaucomatous (24L/0D) chicks; bars represent the means, the vertical lines indicating one S.E.

Discussion. During the first 20 weeks of life, eye weight of the normal chick increases tenfold. It has previously been shown that the eye weight of 24L/0D chicks is further increased from four weeks onward. The present study, concentrating on very young chicks, shows that eye enlargement is clearly discernible at three weeks of age. The small increase seen at two weeks both in this and in a previous study was not seen when chicks of equal body weight were compared.

One of the earliest lesions in light-induced avian glaucoma is a failure of the corneal curvature to increase normally as the eye grows. Previously, retinoscopy had revealed refractive error, probably arising from dimensional changes, in three-week old chicks reared under 24L/0D. The present study shows that this apparent retardation in corneal growth begins as early as nine days of age, and is both rapid and conspicuous in its onset. As a result, aqueous space volume of 24L/0D birds falls to increase at a normal rate. By four weeks of age, the aqueous space is only 75 per cent of normal volume, and by 20 weeks, it is reduced to one-third of normal volume. In spite of this reduction in the anterior segment, the globe of the eye becomes progressively larger. However, the onset of vitreous body enlargement does not coincide with the first appearance of corneal lesions, which suggests that the two dimensional changes may be independent phenomena.

Previous studies utilizing a fluorescein dye technique to estimate aqueous flow indicated that the rate of aqueous flow in 24L/0D birds is reduced by 10 weeks of age. Although this flow method was designed for the adult chicken eye, and is not easily applied to the smaller eye of the young chick, we did attempt here to monitor the rate of accumulation of fluorescein in the aqueous humor after intravenous administration of the dye, but we could detect no difference between 24L/0D and 14L/10D birds up to four weeks of age. However, we have recently undertaken a detailed mathematical analysis of the
dye accumulation curve. Measurements based on this critical evaluation of fluorescein appearance in the aqueous show that the rate of aqueous flow is reduced in 24L/0D birds at two to four weeks of age (Kinnear, Lauber, and Boyd, unpublished results). These data, and an analysis of the improved flow method, will be published fully elsewhere.

The earliest preglaucomatous lesion detected in this study was a reduction in corneal LDH in 24L/0D eyes, and a simultaneous increase in aqueous LDH. This shift in enzyme distribution precedes the first dimensional changes by at least two days. Similar alterations in LDH occur during refrigerated storage of mammalian eyes. It has been suggested that, as viability of the endothelium declines after enucleation, the resultant increase in permeability allows excessive loss of enzyme to the aqueous humor. The data from our preglaucomatous birds similarly suggest "leakage" of LDH from the cornea. However, in light-induced avian glaucoma, corneal transparency is maintained until late in the disease process, which might not be expected if the endothelium were severely damaged. Additional biochemical studies on the aqueous and vitreous are underway, which may shed further light on preglaucomatous lesions.

Despite these major biochemical and dimensional changes occurring very early in the preglaucoma period, and the subsequent reduction in outflow facility at six weeks, IOP homeostasis is maintained in 24L/0D birds until at least 15 weeks of age. Smith, Becker, and Podos found that IOP was increased at four weeks in chickens reared in continuous light. However, both the genetic strain of chicken (New Hampshire) and the method for measuring IOP (applanation tonometry) differed from those of our study.

By focusing on the earliest detectable lesions during genesis of glaucoma, we have further elucidated the pathologic progress of this disease, though the primary pathologic event(s) is still obscure. Nevertheless, this light-induced glaucoma in an experimental animal presents a unique opportunity for the study of the etiology and genesis of a disease of clinical importance.

From the Departments of Zoology and Ophthalmology, University of Alberta, Edmonton, Alberta, Canada. Supported by a grant (MT-2154) from the Medical Research Council of Canada. Submitted for publication June 24, 1974. Reprint requests: Dr. Jean K. Lauber, Department of Zoology, University of Alberta, Edmonton, T6G 2E1, Alberta, Canada.

Key words: light-induced avian glaucoma, chickens, continuous light, diurnal photoperiod, early lesions, eye enlargement, corneal dimensions, aqueous space volume, lactic dehydrogenase.

REFERENCES


Fibrinolytic activity of the vitreous body.

J. V. FORRESTER, C. R. M. PRENTICE, J. WILLIAMSON, AND C. D. FORBES.

The vitreous bodies of human, dog, and sheep eyes were examined for the presence of fibrinolytic activity by two different methods. In spite of previous conflicting evidence, the results suggest that there is little doubt as to the presence of plasminogen activator in small quantities within the vitreous. Moreover, its behavioral characteristics conform to those of tissue activator as opposed to plasma activator. Its origin within the vitreous and its relationship to intravitreal hemorrhage are discussed.

Fibrinolytic activity in the eye of several species, including man, has been studied extensively during recent years and the degree of activity of any one ocular tissue was related to its vascularity. Thus, the choroid and retina showed high activity, while the cornea, lens, and vitreous showed no activity. A relationship between the...