Retinal Artery Tortuosity in ex-Premature Infants
18-year Follow-up on Eyes of Premature Infants

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Oxygen was first recognized as the main factor in the pathogenesis of retrolental fibroplasia (RLF) in 1951 (Campbell, 1951). By 1955 most newborn centres had restricted the amount of oxygen given to newborn infants in their nurseries, with a rapid decline in the incidence of the disease.


If an immature animal inspired high concentrations of oxygen for long enough, the developing retinal vessels became severely constricted and the capillaries were obliterated and destroyed. When the animal was transferred to air, the constricted vessels reopened and became dilated and tortuous, while new vessels grew haphazardly both into the ischaemic retina and into the vitreous, exactly as in the early stages of RLF. The degree of neovascularization was dependent upon the maturity of the retina, the oxygen concentration, and the duration of exposure (Ashton and Cook, 1954).

Only 25% of infants showing the early proliferative phase of the disease went on to haemorrhage and retinal detachment with fibrous tissue formation behind the lens, and 75% of surviving premature infants developed neither retinal scarring nor complete RLF (Owens, 1953).

Previous studies on surviving infants with lesser grades of retrolental scarring have shown myopia to be a frequent association (Fletcher and Brandon, 1955; Zacharias, Chisholm, and Chapman, 1962). No adequate explanation has been offered for this finding; the possibilities include an excessively

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long axis to the eyeball, excessive corneal curvature, and changes in the refractivity of the ocular media.

In the present study, a group of ex-premature infants have been examined to determine whether there are any persistent ophthalmic changes associated with premature birth, other than retrolental scar formation. Measurements have also been made for refractive error and corneal curvature of this group of patients in an attempt to clarify the association between myopia and RLF.

Methods and Materials

Of 160 surviving premature infants with birthweights of 1500 g or less, admitted between 1950 and 1953 to the University of Colorado Medical Center, 52 were available for follow-up studies. The years 1950–53 were chosen to represent a period of transition with regard to oxygen therapy. Up until 1951 oxygen was used liberally and in high concentrations. Subsequently in this centre its use was severely restricted, more than 40% being used only in infants with respiratory failure and cyanosis.

Each of the 52 young adults seen was studied ophthalmoscopically using a direct ophthalmoscope after dilatation of the pupil with 0.5% cyclopentolate.

Retinal photographs were taken, and refractive errors measured. In a small group of patients the curvature of the cornea was measured by keratometry. In this technique an illuminated object is projected from a fixed distance on to the cornea which acts as a convex mirror. From the size of the reflected image the keratometer computes the curvature of the cornea, which is read off directly in diopters.

From the hospital charts of these patients, data were collected on birthweight, gestational age (where mother’s dates were available and certain), and the amount of oxygen received. This amount was translated into an oxygen score from 0–10 according to the concentration and duration of exposure (Table I).

The retinal findings were recorded at the time of the examination. Grades of tortuosity of the retinal arteries were later confirmed by reviewing the retinal photographs and were expressed on a scale from 0–3 for each eye, giving a maximum score of 6 per patient.

Results

Fifty-two patients were examined. The range of birthweights and gestational ages is shown in Table II. The retinal findings are summarized in Table III.

| TABLE II |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Birthweight and Gestational Age Range of Sample |
| | Birthweight (g) | No. of Patients Seen | Mean | SD | Range |
| | Gestational age (wk) | 52 | 44 | 1168 | 187 | 709–1500 |
| | | | | | 2.7 | 26–39 |

*NOTE: In 12 cases, gestational age was uncertain. In 7 cases, the infants were of small weight for their gestational age (SGA).*

| TABLE III |
|-----------------|-----------------|
| Retinal Findings |
| No. of Patients |
| Bilateral complete RLF | 4 |
| Unilateral complete RLF | 3 |
| Bilateral retinal scarring | 7 |
| Arterial tortuosity* = 1 | 2 |
| 2 | 4 |
| 3 | 1 |
| 4 | 7 |
| 5 | 0 |
| 6 | 21 |
| Normal | 3 |
| Total | 52 |

*Arterial tortuosity was expressed on a scale from 0–3 for each eye, giving a maximum score of 6 for each patient.*

Fourteen patients had some degree of retrolental fibrosis. In 4 cases there was complete bilateral destructive RLF with microphthalmos; and in 3 cases in which RLF was complete unilaterally, the other eye showed retinal scarring with traction of the disc in 2 patients and extreme tortuosity of the retinal arteries in the third. There were 7 patients who showed bilateral retinal scarring with distortion of the retinal architecture, temporal traction of the disc, and patchy retinal pigmentation (Fig. 1). Thirty-five patients showed abnormal tortuosity of the retinal arteries. The arteries were distinctly more tortuous than the veins; the degree of tortuosity was similar in both eyes. In those cases with slight tortuosity the vessels affected were
the superior and inferior temporal arteries. Examples of tortuosity scores 1, 2, and 3 are shown in Fig. 2, 3, and 4. Where there was frank retinal scarring, the vessels appeared unusually straight rather than tortuous (Fig. 1). Three patients had normal retinas.

Forty-three patients were refracted. Where both eyes could be tested, the refractive error was similar. The distribution of refractive errors is shown in Table IV. The patients with retinal scarring showed significant myopia, with refractive errors ranging from −3 to −26 diopters. Patients with tortuosity of the retinal arteries showed no definite pattern of refraction, but had refractive errors ranging from +5 to −6 diopters: 16 of these patients (48.5%) had no refractive error (emmetropic).

Corneal curvature was measured in 10 patients who were myopic and showed extreme arterial tortuosity or retinal scarring (Table V). These measurements of corneal curvature were within the normal limits for adults.
TABLE IV
Refractive Errors in 43 Patients with Either Retinal Scarring or Tortuosity of Retinal Arteries

<table>
<thead>
<tr>
<th>Refractive Error in Diopters</th>
<th>+5</th>
<th>+1</th>
<th>0</th>
<th>-1</th>
<th>-2</th>
<th>-3</th>
<th>-3</th>
<th>-5</th>
<th>-6</th>
<th>-15</th>
<th>-26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with retinal scarring</td>
<td>2</td>
<td>1</td>
<td>16</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Patients with arterial tortuosity</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

TABLE V
Corneal Curvature

<table>
<thead>
<tr>
<th>No. of Cases</th>
<th>Refractive Error Dipters</th>
<th>Corneal Curvature Dipters</th>
<th>Normal Adult Corneal Curvature Dipters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Range</td>
<td>Mean</td>
</tr>
<tr>
<td>Tortuosity 6+</td>
<td>-4.4</td>
<td>-2.75 to -6.0</td>
<td>44.9</td>
</tr>
<tr>
<td>Retinal scarring</td>
<td>-9.6</td>
<td>-4.5 to -26</td>
<td>44.3</td>
</tr>
</tbody>
</table>

(Normal data from 2000 adult patients as measured by the National Eye Research Foundation.) A. Prechtel, 1970, personal communication.

TABLE VI
Correlation Coefficients

<table>
<thead>
<tr>
<th></th>
<th>Birthweight</th>
<th>Gestational Age</th>
<th>SGA/AGA</th>
<th>Oxygen Score</th>
<th>Refractive Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete RLF</td>
<td>-0.38†</td>
<td>-0.118</td>
<td>-0.128</td>
<td>0.276*</td>
<td></td>
</tr>
<tr>
<td>Retinal scarring</td>
<td>0.025</td>
<td>-0.040</td>
<td>0.035</td>
<td>-0.212</td>
<td>-0.382‡</td>
</tr>
<tr>
<td>Tortuosity</td>
<td>0.026</td>
<td>-0.276*</td>
<td>0.343*</td>
<td>-0.012</td>
<td>0.111</td>
</tr>
</tbody>
</table>

* Denotes significance at 5% level.
† Denotes significance at 1% level.
‡ All patients with retinal scarring were myopic. Since myopia is measured in negative diopters the correlation coefficient carries a negative sign.

Tests of correlation were made between complete RLF, retinal scarring, tortuosity score and birthweight, gestational age, oxygen score, and refractive error (Table VI). Complete RLF was significantly associated with low birthweight and high oxygen score; retinal scarring correlated with myopia; and arterial tortuosity was associated with low gestational age but was significantly less evident in those cases known to have been small in weight for their gestational age (SGA).

Discussion

In the early clinical descriptions of RLF, gross dilatation and tortuosity of both the retinal arteries and veins was noted as a common early pointer to the disease (Fig. 5) (Owens and Owens, 1949). Among infants with these changes, only a minority went on to retinal detachment and permanent damage from scarring or complete RLF (Owens, 1953).

Hix (1953) noted an association between the degree of tortuosity of the retinal arteries in the proliferative phase of the disease, and the likelihood of developing destructive RLF. He also observed that tortuosity was most obvious in the temporal arteries and that it persisted up to 3 months of age. Tassman and Annesley (1966) mentioned the presence of persistent tortuosity of the retinal vessels in some cases of non-destructive RLF which went on to retinal tears and detachment in late childhood or early adult life.

In the present group of patients, 4 had bilateral complete RLF; 3 had unilateral complete RLF in association with scarring or vascular tortuosity in the other eye; 7 had bilateral retinal scarring; 35 had some degree of arterial tortuosity; 3 had normal eyes.

It is recognized that there is great biological variation in the susceptibility of premature infants to RLF. Moreover, a retrospective assessment of
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This includes excessive corneal curvature as an explanation for this phenomenon.

Tortuosity of the retinal vessels is a common finding in the early stages of RLF (Fig. 5) (Owens and Owens, 1949). In the majority of published cases, patients with lesser degrees of retinal scarring had lesions located at the temporal periphery (Reese and Stepanik, 1954). It is known that the temporal periphery of the retina is the latest to develop a mature vasculature (Cogan, 1963).

Tortuosity of the retinal arteries has been described as a very rare congenital anomaly (Duke-Elder, 1963). However, from the prevalence of this condition in the group of ex-premature infants studied and from its predominance in the temporal retinal arteries, it seems likely that this represents a forme fruste of RLF. Moreover, the SGA infants had significantly lesser degrees of tortuosity; presumably the retinal vessels would be more mature at birth in this group of patients compared with AGA infants of similar birthweight. It appears that in those cases of proliferative RLF which do not progress to retinal scarring, the early changes in the retinal arteries persist; the retinal veins return to normal. In the present study the condition carried no morbidity.

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REFERENCES


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