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Association of HLA with Eales (Periphlebitis Retinae) and iridocyclitis in South India.

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Abstract
Forty-six patients with Eales disease (periphlebitis retinae) and seventy-eight patients with iridocyclitis (anterior uveitis) were studied for Human Leucocyte Antigen (HLA) -A, -B and -DR by microlympho-cytotoxicity assay. Eales disease was associated with HLA-B51 (relative risk, RR / etiological fraction, EF / corrected P value, PC: 7.2 / 0.32 / 0.00014); A32 (7.17 / 0.26 / 0.001) and DR4 (3.67 / 0.28 / 0.008). Samples from both Tamil Nadu and other States revealed similar associations. Iridocyclitis were associated with HLA-B27 (12.84 / 0.37 / 0.00027), though HLA-A2 (2.26 / 0.23), DR4 (2.58 / 0.18) and DR12 (3.93 / 0.1) showed elevated but insignificant risks. While HLA-DR4 was associated with chronic cases, B27 was associated with acute and chronic diseases. Further B-27 was associated with the disease in different major groups studied. The association of B27 with iridocyclitis in major (ethnic) groups and HLA-B51 with Eales and other diseases like Behcet described elsewhere may have a common HLA genetic predisposition. Nonetheless the target organ may differ based on the nature of etiological agents and the precipitation factors.

Key words: Eales disease, iridocyclitis, HLA, India

Introduction
The association of HLA-B27 in iridocyclitis (anterior uveitis), an inflammation of the iris and ciliary bodies of the eye with known and specific symptomatology but with a multiple aetiology, has been well established in most of the ethnic groups studied except Negroes¹. Apart from HLA-B27, a few other HLA antigens such as HLA A2 among Blacks ² and HLA-A9 among Asian Indians³ has been associated with this disease.

Another eye disease, Eales (Periphlebitis retinae) is an inflammatory condition affecting the peripheral retinal veins mainly in young men between the age of 20-30 years (4-6). The disease passes through inflammatory, obliterative and proliferative phases and affecting the vision by vitreous haemorrhage. This clinical symptom was first described by Eales in 1884⁴ and further documented by many (7-9). Though this disease has a worldwide distribution, it is more common in tropical countries like India ⁶,¹⁰. A study on their aetiology has not thrown definite clue in the causative factors¹¹. It is generally believed that the disease is associated with infections inducing hypersensitivity. Allergic reaction to tuberculo - protein has also been implicated in the initiation of this disease¹². In recent times the role of lymphocytes and macrophages in Eales and neovascularization has been described ¹³,¹⁴. Various serum factors have been implicated in the aetiology of Eales disease ¹⁵,¹⁶. HLA-A & -B antigens in 48 patients with Eales disease have also been studied but no significant association was identified¹⁷.

Our studies on South Indian Pulmonary tuberculosis patients and two others on Russian and Indonesian patients have revealed interesting and strong associations with HLA DR2¹⁸-²⁰. Association of HLA may be identified only in places where the disease is endemic and this can be attributed to epidemiological conditions and genetic factors. A

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study on Eales disease was thus carried out in Madurai, S. India: the patients were drawn from Aravind Eye Hospital, where many cases of Eales disease are referred from all over Tamil Nadu and other States of India. Further the existence sympathetic isolation of ethnic and linguistic groups in the name of caste system warrants to explore any ethnic differences in the HLA association. Iridocyclitis, another eye disease with a well-established HLA association was also studied simultaneously: This would validate the HLA association in Eales, if any.

Materials and methods

Patients attending the outpatient clinics were selected at random with informed consent. Case history and information regarding their nativity, ethnic origin (caste) and socioeconomic statuses were obtained in a precoded questionnaire. 10 ml of peripheral blood from cubital vein was obtained and processed for study.

Patients: Eales disease (periphlebitis retinae): A total of 46 patients attending the Retina clinic of Aravind Eye Hospital, Madurai was selected at random and studied. Most patients were presented with sudden loss of vision in one eye and with different degrees of disease progression in the other eye viz. signs of inflammation consisting of perivascular sheathing, periphlebitis, retinal haemorrhages, venous occlusions, and new vessels in the retina and proliferation of new vessels into the vitreous. The selection criteria included, patients with primary periphlebitis not associated with other ocular diseases such as uveitis, cataract, glaucoma, optic atrophy and corneal opacities of macular degeneration.

Due importance was paid to know the origin of the sample. Among the total 46 Eales patients, 30 belonged to Tamil Nadu and the rest 16 to "other States" of India. The other States included Uttar Pradesh - two (=number of patients), Madhya Pradesh - two, Bihar - three, West Bengal - two, Andhra pradesh - two, Maharashtra - two and Kerala - three. Therefore relative risks were calculated only for the patients from Tamil Nadu comparing the controls from Tamil Nadu. The frequencies of 'others' are also presented in table 2 for comparison.

Iridocyclitis: A total of 78 iridocyclitis patients attending the out patients clinic of the department of ophthalmology, Government Rajaji Hospital, Madurai were selected and studied. The disease was diagnosed based on various symptoms like pain, redness and photophobia. On clinical examination, circum corneal congestion, keratic precipitates, aqueous flare, cells in anterior chamber and posterior synechiae were looked for. All cases were subjected to biomicroscopy, tonometry and funduscopy and cases with systemic diseases, joint diseases, pulmonary diseases and dental carries were excluded. Mantoux (DTH skin test) was tested with 1 TU of PPD-RT28 following the conventional methods. Patients with an average induction diameter of 10 mm and above were considered as Mantoux positive and <10 mm as Mantoux negative. All these patients belonged to Tamil Nadu.

Controls: One hundred and eleven controls matched for major group (more similar caste groups form a major group) were selected from the staff and students of the University and studied for the HLA polymorphism, using the same batch of reagents. Individuals with any eye diseases or any systemic and autoimmune disorders were excluded. The age distributions of the controls and patients are presented in table 1. The HLA profile of the controls compared well with those already published HLA allelic frequencies of random healthy samples reported earlier from this laboratory.

HLA typing: 10 ml of peripheral blood was obtained from each patient and controls and was defibrinated. Lymphocytes were separated on a Ficoll-Conray density gradient. A miniature nylon wool column was used for the separation of T and B lymphocytes. The HLA typing was performed by two stage microlymphocytotoxicity assay. The quality of the reagents used in this study were extensively analysed and reported elsewhere.
Table 1
Distribution of age, sex and eye affected in Eales' and iridocyclitis patients

<table>
<thead>
<tr>
<th>Patients</th>
<th>No.</th>
<th>Age group (in years)</th>
<th>Sex</th>
<th>Eyes affected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>11-20</td>
<td>21-30</td>
<td>31-40</td>
</tr>
<tr>
<td>Eales</td>
<td>46</td>
<td>2</td>
<td>24</td>
<td>18</td>
</tr>
<tr>
<td>%</td>
<td></td>
<td>4.4</td>
<td>52.2</td>
<td>39.0</td>
</tr>
<tr>
<td>Iridocyclitis</td>
<td>78</td>
<td>8</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>%</td>
<td></td>
<td>10.3</td>
<td>25.6</td>
<td>21.8</td>
</tr>
<tr>
<td>Controls</td>
<td>111</td>
<td>4</td>
<td>57</td>
<td>32</td>
</tr>
<tr>
<td>%</td>
<td></td>
<td>3.6</td>
<td>51.4</td>
<td>28.8</td>
</tr>
</tbody>
</table>

M – males, F – females; L – left eye, R – right eye, B – both eyes; n+ – number of patients in each sub group.

Having identified significant association of HLA-B51 and DR4 in Eales and B27, A2 etc. In iridocyclitis, extensive analyses of the HLA phenotyping reagents were performed by serum versus antigen, serum versus serum and serogram using our computer programmes. The r values and antigen assignments in both control and patient groups were highly reliable. The list of specificities thus studied are presented in table 2.

Statistical Analysis: Frequencies of HLA alleles in patients and controls were compared and relative risks calculated. The haplotype frequencies were calculated using our programmes. Allelic frequencies were estimated by Bernstein’s formula, relative risks by a modified method of Woolf and Haldane and aetiological and preventative fractions as described by Green. Patients and controls were compared using chi-square test and value was obtained to learn the significance: corrected p value was obtained by multiplying the p value by the number of alleles studied in each locus (cf. 1).

Results

Sexual preponderance and age-at-onset in Eales

Table 1 present the distribution of patients with Eales disease (periphlebitis retinæ) and iridocyclitis according to age class, sex and the eye affected. While 56.6% of Eales patients were of the age group of <30 years, 95.6% were <40 years. Among iridocyclitis patients 35.8% were <30 years of age and 47.7% were <40 years of age. While the sexes of the patients were considered 95.6% of Eales patients and 65.4% of the iridocyclitis patients were males. The analysis of the eyes affected revealed that while the percentage of left, right and both eyes affected groups in iridocyclitis patients were around 30-35 each. Among Eales patients, the percentage with affected left eye was 13%, right eye 28.3% and both eyes 52.7%.

HLA association in Eales and Iridocyclitis:

Table 2 presents frequencies of HLA-A, B and DR antigen in patients with iridocyclitis and Eales.
Table 2

Association of HLA with iridocyclitis and Eales' disease in south India

<table>
<thead>
<tr>
<th>HLA</th>
<th>Controls</th>
<th>Iridocyclitis</th>
<th>Eales</th>
<th>T.NADU</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=111</td>
<td>78</td>
<td>OTHERS</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>%PF (n+)</td>
<td>%PF (n+)</td>
<td>RR</td>
<td>CHISQ</td>
</tr>
<tr>
<td>A1</td>
<td>34.2 (38)</td>
<td>38.5 (30)</td>
<td>1.20</td>
<td>0.36</td>
</tr>
<tr>
<td>A2</td>
<td>23.4 (26)</td>
<td>41.0 (32)</td>
<td>2.26</td>
<td>6.60d</td>
</tr>
<tr>
<td>A3</td>
<td>14.4 (16)</td>
<td>16.7 (13)</td>
<td>1.19</td>
<td>0.20</td>
</tr>
<tr>
<td>A4</td>
<td>31.5 (35)</td>
<td>28.2 (22)</td>
<td>0.86</td>
<td>0.28</td>
</tr>
<tr>
<td>A10</td>
<td>6.3 (7)</td>
<td>7.7 (6)</td>
<td>1.25</td>
<td>0.17</td>
</tr>
<tr>
<td>A11</td>
<td>28.8 (32)</td>
<td>26.9 (21)</td>
<td>0.91</td>
<td>0.08</td>
</tr>
<tr>
<td>A19</td>
<td>32.4 (36)</td>
<td>15.4 (12)</td>
<td>0.39</td>
<td>6.7bd</td>
</tr>
<tr>
<td>A29</td>
<td>5.4 (6)</td>
<td>2.6 (2)</td>
<td>0.58</td>
<td>0.81</td>
</tr>
<tr>
<td>A32</td>
<td>5.4 (6)</td>
<td>3.8 (3)</td>
<td>0.75</td>
<td>0.19</td>
</tr>
<tr>
<td>Aw33</td>
<td>12.6 (14)</td>
<td>2.6 (2)</td>
<td>0.22</td>
<td>5.43c</td>
</tr>
<tr>
<td>A28</td>
<td>16.2 (18)</td>
<td>20.5 (16)</td>
<td>1.33</td>
<td>0.36</td>
</tr>
<tr>
<td>A-</td>
<td>12.6 (14)</td>
<td>5.1 (4)</td>
<td>0.63</td>
<td>13.3</td>
</tr>
<tr>
<td>HLA</td>
<td>Controls N=111</td>
<td>Iridocyclitis 78</td>
<td>OTHERS 16</td>
<td>T.NADU 30</td>
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<tr>
<td>-----</td>
<td>----------------</td>
<td>------------------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td></td>
<td>%PF (n+)</td>
<td>RR</td>
<td>CHISQ</td>
<td>EF</td>
</tr>
<tr>
<td>5</td>
<td>14.4 (16)</td>
<td>1.77</td>
<td>2.36</td>
<td>0.10</td>
</tr>
<tr>
<td>B51</td>
<td>7.2 (8)</td>
<td>2.74</td>
<td>5.00c</td>
<td>0.11</td>
</tr>
<tr>
<td>Bw52</td>
<td>2.7 (3)</td>
<td>1.87</td>
<td>0.83</td>
<td>0.02</td>
</tr>
<tr>
<td>7</td>
<td>17.1 (19)</td>
<td>0.73</td>
<td>0.61</td>
<td>0.05</td>
</tr>
<tr>
<td>8</td>
<td>1.8 (2)</td>
<td>0.85</td>
<td>0.03</td>
<td>0.00</td>
</tr>
<tr>
<td>2</td>
<td>13.5 (15)</td>
<td>0.85</td>
<td>0.14</td>
<td>0.02</td>
</tr>
<tr>
<td>3</td>
<td>14.4 (16)</td>
<td>0.61</td>
<td>1.20</td>
<td>0.05</td>
</tr>
<tr>
<td>5</td>
<td>0.9 (1)</td>
<td>1.43</td>
<td>0.12</td>
<td>0.00</td>
</tr>
<tr>
<td>1</td>
<td>22.7 (22)</td>
<td>1.22</td>
<td>0.31</td>
<td>0.04</td>
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<tr>
<td>22</td>
<td>4.5 (5)</td>
<td>1.82</td>
<td>1.85</td>
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<tr>
<td>5</td>
<td>26.1 (29)</td>
<td>0.68</td>
<td>1.18</td>
<td>0.08</td>
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<tr>
<td>7</td>
<td>10.8 (12)</td>
<td>0.26</td>
<td>4.19a</td>
<td>0.07</td>
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<td>27.9 (31)</td>
<td>0.84</td>
<td>12.5 (2)</td>
<td>0.07</td>
</tr>
<tr>
<td>HLA</td>
<td>Controls</td>
<td>Iridocyclitis</td>
<td>Eales</td>
<td>OTHERS</td>
</tr>
<tr>
<td>-----</td>
<td>---------</td>
<td>---------------</td>
<td>-------</td>
<td>--------</td>
</tr>
<tr>
<td></td>
<td>N=106</td>
<td>50</td>
<td></td>
<td>16</td>
</tr>
<tr>
<td>%PF</td>
<td>(n+)</td>
<td>%PF (n+)</td>
<td>RR</td>
<td>CHISQ</td>
</tr>
<tr>
<td>R1</td>
<td>13.2</td>
<td>20.0</td>
<td>1.65</td>
<td>1.31</td>
</tr>
<tr>
<td>R2</td>
<td>29.2</td>
<td>34.0</td>
<td>1.25</td>
<td>0.39</td>
</tr>
<tr>
<td>R3</td>
<td>17.0</td>
<td>22.0</td>
<td>1.39</td>
<td>0.64</td>
</tr>
<tr>
<td>R4</td>
<td>14.2</td>
<td>30.0</td>
<td>2.58</td>
<td>5.48b</td>
</tr>
<tr>
<td>R5</td>
<td>24.5</td>
<td>24.0</td>
<td>0.99</td>
<td>0.00</td>
</tr>
<tr>
<td>DRw11</td>
<td>3.8</td>
<td>10.0</td>
<td>2.75</td>
<td>2.58</td>
</tr>
<tr>
<td>DRw12</td>
<td>3.8</td>
<td>14.0</td>
<td>3.93</td>
<td>5.24b</td>
</tr>
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<td>33.0</td>
<td>24.0</td>
<td>0.65</td>
<td>1.25</td>
</tr>
<tr>
<td>w7</td>
<td>22.7</td>
<td>14.0</td>
<td>0.58</td>
<td>1.48</td>
</tr>
<tr>
<td>w8</td>
<td>11.3</td>
<td>6.01</td>
<td>0.56</td>
<td>0.96</td>
</tr>
<tr>
<td>w9</td>
<td>8.5</td>
<td>6.01</td>
<td>0.76</td>
<td>0.20</td>
</tr>
<tr>
<td>w10</td>
<td>15.1</td>
<td>20.0</td>
<td>1.42</td>
<td>0.67</td>
</tr>
</tbody>
</table>

relative risk and other calculations were only for samples belonging to Tamil Nadu.

- Relative risk
- Chi-square
- total number
- number of individuals positive for the given antigen
- percentage phenotype frequency

Values - (uncorrected) a<0.05; b<0.025; c<0.01; d<0.005; e<0.001; f<0.0001; g<0.00001; h<0.000001; i<0.0000001
and their relative risks and attributable risks. In iridocyclitis HLA-B27 showed the highest relative risk (RR) of 12.84 with an attributed risk (= aetiological fractions, EF) of 0.37 and corrected P value (pc) was 0.000016. HLA-A2 (RR=2.26, EF=0.23), B51 (2.74, 0.11), DR4 (2.58, 0.18) and DR12 (3.93, 0.1) showed elevated relative risks and aetiological fractions with the disease, but not significant when corrected for the number of antigens studied.

The data on Eales patients were divided into two groups viz. patients belonging to Tamil Nadu (N=30) and that belonging to other states (N=16) (ref. methods). Relative risks were calculated only for patients belonging to Tamil Nadu comparing the appropriate controls (Table 2). The frequencies of HLA antigens in sample belonging to other States are also presented in Table 2, for comparison. HLA-B51 presented highest RR of 7.18, with an EF of 0.32 and pc=0.00012, followed by HLA-A321 (7.17, 0.26, 0.0012) and HLA-DR4 (3.67, 0.28, 0.12). These antigens were elevated in Eales patients belonging to other States as well. HLA-A10 (RR=3.7, EF=0.15), B8 (7.44, 0.12) and DR2 (2.5, 0.32) showed elevated relative risks and aetiological fractions though statistically insignificant when corrected. HLA-B27 was absent in both the Eales samples studied. Iridocyclitis samples were subdivided and analysed further and reported below, whereas it was not possible to do this with Eales samples due to the sample size.

Table 3

<table>
<thead>
<tr>
<th>HLA</th>
<th>Controls</th>
<th>Patient Subgroup</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>n=111</td>
<td>HLA-B27</td>
</tr>
<tr>
<td></td>
<td></td>
<td>31</td>
</tr>
<tr>
<td>B27</td>
<td>4.5(5)</td>
<td>100(31)</td>
</tr>
<tr>
<td>RR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>X2</td>
<td>23.15</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>EF</td>
<td>23.4(26)</td>
<td>38.7(12)</td>
</tr>
<tr>
<td>A2</td>
<td>2.07</td>
<td>2.41</td>
</tr>
<tr>
<td></td>
<td>3.01</td>
<td>5.83</td>
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<td></td>
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<tr>
<td></td>
<td>0.20</td>
<td>0.25</td>
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<tr>
<td>DR4</td>
<td>14.2(15)</td>
<td>32.0(8)</td>
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<td>2.39</td>
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<td></td>
<td>4.62</td>
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<tr>
<td></td>
<td>0.025</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>0.21</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Primary association in Iridocyclitis

To know the primary association of HLA with iridocyclitis, the samples were subdivided based on HLA-B27 status (present or absent) and DR4 status, the two alleles with highest risk among the class I and class II antigens, and relative risks calculated (Table 3). While HLA-B27 revealed a significant risk in both HLA-DR4 and non-DR4 subgroups, HLA-DR4 revealed only a marginal asso-
### Table 4

Severity of iridocyclitis and the associated HLA

<table>
<thead>
<tr>
<th>HLA</th>
<th>Controls</th>
<th>Patient subgroups based on severity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=111</td>
<td>Subacute 9*</td>
</tr>
<tr>
<td>B27</td>
<td>%PF</td>
<td>4.5 (5)</td>
</tr>
<tr>
<td></td>
<td>RR</td>
<td>6.45</td>
</tr>
<tr>
<td></td>
<td>X2</td>
<td>5.48</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>0.025</td>
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<tr>
<td></td>
<td>EF</td>
<td>0.19</td>
</tr>
<tr>
<td>B51</td>
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<td></td>
<td></td>
<td>0.40</td>
</tr>
<tr>
<td>A2</td>
<td></td>
<td>23.4 (26)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.74</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.69</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.14</td>
</tr>
</tbody>
</table>

|      | n=106    | 3          | 30        | 17         |
| DR4  |          | 14.2 (15)  | 0         | 17.8 (8)   | 29.2 (7)  |
|      |          |            |           |            | 4.22      |
|      |          |            |           |            | 2.82      |
|      |          |            |           |            | NS        |
|      |          |            |           |            | 0.15      |
| DRw12|          | 3.8 (4)    | 0         | 13.3 (8)   | 4.2 (1)   |
|      |          |            |           |            | 6.04      |
|      |          |            |           |            | 8.24      |
|      |          |            |           |            | 0.005     |
|      |          |            |           |            | 0.17      |

Abbreviations as in earlier tables. * = since the sample size is
cation, that too in HLA-B27 subgroup alone. Nonetheless HLA-A2 showed a very strong association in HLA-DR4 subgroup with an attribute risk (EF) of 0.73: 12 out of the 15 HLA-DR4 subgroup possessed HLA-A2 (table 3).

**HLA and severity of iridocyclitis**

The patient samples with iridocyclitis were sub-divided based on the severity of the disease (subacute, acute and chronic), (table 4) and the HLA association was analysed. HLA-B27 was elevated in both acute and chronic disease whereas HLA-DR4 and A2 only with chronic disease (Table 4). Though HLA-B51 showed elevated relative risk with subacute cases (N=9) the finding needs to be confirmed in a larger sample size.

**HLA-B27 association and Mantoux status, sex and age-at-onset**

Table 5 presents the data on Mantoux sensitivity and sex of iridocyclitis patients and its correlation to the HLA-B27 association. HLA-B27 association was equally significant in both Mantoux positive and Mantoux negative patients and patients of both the sex. However the relative risk and EF were high in female patients (RR 32.6 compared to 6.7 in males, Table 5). Analysis of the age at onset of acute and chronic iridocyclitis in different sexes and B27 subgroups (Table 6) revealed that the mean age at onset of chronic disease was always higher (44.4 ± 6.45 yrs to 45.0 ± 2.66) than acute onset (31.27 ± 2.38 to 35.33 ± 3.28) irrespective of the sex and B27 status.

**HLA-B27 association in Major Groups of Tamil Nadu**

In order to know whether there could be any ethnic differences in HLA association of iridocyclitis, samples were sub-divided based on their caste group (ethnic identity) and grouped as ‘Major Groups’ as described elsewhere 21-23 and HLA association studied (Table 7). In both the major groups studied, Major group II (a palaeo Mediterranean related ones) and Major group III (a mixed population of Western Brachycephals, Mediterraneans and others), the association of HLA-B27 was identified (pc 0.016).

**Discussion**

**HLA and heterogeneity of iridocyclitis**

The present study has extended the association of iridocyclitis with HLA-B27 to South Indian patients. It has also brought out that Eales disease was not associated with HLA-B27 but it was associated with HLA-B27 with iridocyclitis (cf. 1), a few HLA-B51. While majority of the studies revealed association others showed association of HLA-B8 in American Blacks, HLA-DR4 in Finland and Netherlands34,35. Further, HLA-DRB1*1104, a split of

---

**Table 5**

**Relative risks of HLA-B27 to develop iridocyclitis in subgroups of Mantoux status and sex**

<table>
<thead>
<tr>
<th>Patient sub groups</th>
<th>B27 in Control</th>
<th>B27 in Patient</th>
<th>RR</th>
<th>X2</th>
<th>p</th>
<th>EF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mantoux</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>5/111</td>
<td>10/23</td>
<td>15.06</td>
<td>21.07</td>
<td>0.000001</td>
<td>0.41</td>
</tr>
<tr>
<td>Negative</td>
<td>5/111</td>
<td>21/55</td>
<td>12.07</td>
<td>24.81</td>
<td>0.000001</td>
<td>0.35</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4/58</td>
<td>18/51</td>
<td>6.69</td>
<td>12.03</td>
<td>0.001</td>
<td>0.3</td>
</tr>
<tr>
<td>Female</td>
<td>1/53</td>
<td>13/27</td>
<td>32.59</td>
<td>18.48</td>
<td>0.000001</td>
<td>0.47</td>
</tr>
</tbody>
</table>

* = Mantoux status of the controls were not considered.
Table 6

Age-at-onset of acute and chronic cases of iridocyclitis

<table>
<thead>
<tr>
<th>Patient subgroup</th>
<th>Acute n=45 Mean ± SE</th>
<th>Chronic n=24 Mean ± SE</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>33.07±2.03</td>
<td>47.67±3.16</td>
<td>0.0001</td>
</tr>
<tr>
<td>Female patients</td>
<td>33.64±4.06</td>
<td>46.17±4.18</td>
<td>0.0001</td>
</tr>
<tr>
<td>Male patients</td>
<td>32.81±2.30</td>
<td>49.17±4.69</td>
<td>0.0001</td>
</tr>
<tr>
<td>HLA-B27+ve</td>
<td>35.33±3.28</td>
<td>44.4±6.45</td>
<td>0.05</td>
</tr>
<tr>
<td>Non HLA-B27</td>
<td>31.27±2.38</td>
<td>50.0±2.66</td>
<td>0.00001</td>
</tr>
</tbody>
</table>

p value by student's t test. Abbreviations as in earlier tables

Table 7

Association of HLA with iridocyclitis in major groups of Tamil Nadu

<table>
<thead>
<tr>
<th>HLA</th>
<th>TotalN *(cont/pts)</th>
<th>Major group II 36/20</th>
<th>Major group III 34/24</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RR 9.38</td>
<td>9.41</td>
</tr>
<tr>
<td></td>
<td>N+ 2/8</td>
<td></td>
<td>2/10</td>
</tr>
<tr>
<td></td>
<td>% 5.6/40.8</td>
<td>5.9/41.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RR 9.12</td>
<td></td>
<td>9.65</td>
</tr>
<tr>
<td></td>
<td>EF 0.36</td>
<td></td>
<td>0.37</td>
</tr>
<tr>
<td></td>
<td>p value 0.001</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Bw22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>N+ 4/1</td>
<td></td>
<td>1/7</td>
</tr>
<tr>
<td></td>
<td>% 11.1/5</td>
<td></td>
<td>2.9/2.2</td>
</tr>
<tr>
<td></td>
<td>RR 0.56</td>
<td>9.57</td>
<td></td>
</tr>
<tr>
<td></td>
<td>X2 0.44</td>
<td></td>
<td>7.19</td>
</tr>
<tr>
<td></td>
<td>EF -</td>
<td>0.26</td>
<td></td>
</tr>
<tr>
<td></td>
<td>p value -</td>
<td>0.005</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations as in earlier tables

* = respective controls belonging to respective major groups were used to compare
HLA-DR5, showed significant association with chronic iridocyclitis and a combination of HLA-A2, DR5 and DR8 is frequently associated with chronic iridocyclitis among the early onset (<5 yrs) juvenile chronic arthritis while late onset pauciarticular disease has an increased frequency of HLA-B27. The present study on the association of HLA-B27 both in acute and chronic diseases, but HLA-DR4 and A2 only with chronic diseases and HLA-B51 in subacute cases, once again points the heterogeneity of the disease and probably the susceptibility. A HLA-B27 association of iridocyclitis in the present study, in two different major groups studied, Major group II (a Palaeo Mediterranean related groups) and Major group III (a mixed population of Western Brachycephals, Mediterraneans and others): has further indicated that the association transcends ethnic barrier. Thus the association of HLA-B27 with iridocyclitis identified in different ethnic groups and countries suggests a HLA dependent aetiology of iridocyclitis common to all the populations: identifying the aetiological agents which induces different form of the disease in different susceptible individuals may throw more light on the immunogenetic predisposition.

**HLA and Immunological mechanisms in iridocyclitis and Eales**

In recent times many immunological mechanism, pathogens and antigens have been implicated in uveitis and B27 related diseases. Sialic acid level is elevated in the serum of idiopathic acute iridocyclitis patients and since inflammation alone cannot elevate serum levels of sialic acid, idiopathic acute iridocyclitis has been suggested to be a multiorgan disease with systemic involvement. Intercellular adhesion molecule-1 (ICAM-1), a cytokine-inducible adhesion molecule expressed on cells of multiple lineages at sites of inflammation has been shown to be elevated in the serum of HLA-B27 negative anterior uveitis, intermediate uveitis and patients with sarcoidosis but not in HLA-B27 positive acute anterior uveitis, Fuch's heterochromic cyclitis and in ocular toxoplasmosis.

Elevated serum antibodies to Klebsiella aerogenosa in patients with iridocyclitis has also been identified in recent times and this suggests an immunological basis for the disease.

Sensitivity to BCG may also have a correlation to many ophthalmic diseases. Antibodies to PPD have been shown to be marginally elevated in Eales patients and a serum protein of 23 kDa with a Pl of 5.9 is unique to Eales patient. In the present study a marginal insignificant association and enhanced etiological fraction of Eales with HLA-DR2, an allele shown to be associated with severe forms of pulmonary tuberculosis in South India, Indonesia and Russia has been identified. It has been reported recently that a 16 year old Caucasian girl developed acute panuveitis progressing to bilateral serous retinal detachment following PPD skin testing on two separate occasions separated by an interval of 8 years. DTH status may be inherent irrespective of chronic exposure. In healthy contacts and this may further depend on tuberculin antigenic preparations studied. The present study on Mantoux status and B27 association in iridocyclitis, however showed equally strong associations both in Mantoux positive patients and in Mantoux negative patients indicating that the tuberculin sensitivity may not be associated with either HLA-B27 or iridocyclitis. A more controlled study, however is required to answer the question of involvement of tuberculosis sensitivity in Eales pathogenesis.

**Association of HLA with Eales and iridocyclitis transcend ethnic barrier**

The present study on Eales patients has revealed an association of HLA-B51, A32 and DR4: thus it differed from iridocyclitis which was associated with HLA-B27. Nonetheless, the indicated HLA antigens HLA-B51 and others in Eales were elevated in patients belonging to Tamil Nadu and ‘other’ state and HLS-B27 in iridocyclitis in both Major group II and III studied. These findings supports the view that HLA alleles as such or a linked genome may be involved in the disease susceptibility and pathogenesis.
HLA-B5 CREG antigens may predispose for vasculitis related ophthalmic disease

It is essential to mention here that the frequency of HLA-B5 and related antigens (CREG) are very high (85%) in south Indian population. Among other eye diseases, HLA-B51 was associated with Behcet’s disease. Recently HLA-B*5101, a subtype of HLA-B51 has been shown to be strongly associated with Behcet’s disease in Japanese patients and a few amino acids differing from other splits of B5 (B*5102, B*5103) has been implicated in susceptibility.

The present study revealing an association of HLA-B51 with Eales disease raised an interesting question whether the HLA-B51 association in Eales, Behcet’s, subacute iridocyclitis and other ophthalmic diseases with vasculitis may have a common genetic predisposition, but manifest in different target organs based on the nature of infection or allergy resulting in a localized pathology: the available literatures referred above indicates such a possibility. Identifying the pathogen and immune mechanism posses a challenge and warrants further indepth study.

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Eye Banking for developing countries in the new millennium

Mr. Raheem Rahmathullah, Dr. M. Srinivasan, Mrs. Alees Rajkumar, Mr. Selvam

Introduction

Corneal Blindness in the developing world has traditionally been attributed to trachoma, xerophthalmia, neonatal ophthalmia, measles and leprosy. In India 1.52% are blind from corneal opacities (National Survey) 86-89. In the Nepal blindness survey, corneal trauma and ulceration were found to be the second leading cause of unilateral vision loss after cataract accounting for 7.9% of all blind eyes. In Malawi, Tanzania and Bangladesh, corneal scarring was found to be responsible for 39-55% of all cases of unilateral blindness. Survey in blind children in Africa have shown that approximately 70% if all blind disability in this group is caused by corneal opacification.

The requirement of corneas in India is about one lakh annually. The number of eyes being procured annually is only about 17,000 of which only about 50 to 60% are utilized. This clearly indicates a gap between the supply and demand. There are about 200 eye banks in the country of which only about 30% are functional. Most of these are functioning more like collection centers rather than eye banks. There are very few Eye Banks, which maintain required quality. There is a need for organizations, and individuals to come forward and work towards promotion of eye donations, and procurement of eyes, in a country where home deaths are common, so as to try and address this need in the next millennium.

Methodology

As soon as a home death occurs, a family member calls the eye bank and informs of the demise and their willingness to donate. The contact is via telephone and details such as donor, name complete address, nearest landmark and telephone number is given to enable the eye bank team to identify the donor address easily. At this time of contact the following instructions are given:

- Raise the head of the donor slightly by placing a pillow.
- Close the eyelids
- Switch off fans.
- Keep Air conditioner on if it is there.

A few minutes later the eye bank calls up the given telephone number just to verify the incoming call. On reaching the house, the eye bank team members first introduce themselves and pay homage to the departed. Then they speak to the senior family members, and obtain the consent of the next of kin with of two witnesses. During this conversation the name and age of donor, cause of death, and information on whether the donor was hospitalized is noted down. If hospitalized, whether the donor was on a ventilator, whether blood transfusion was given and had any neurological problem. All this information is documented prior to enucleation.

The enucleating procedure

Since most of the deaths in India are home deaths, there is need for strict asepsis care, caution and sterility being maintained throughout the procedure. First make a cursory examination of the cornea with a torch. At this time also quickly observe for evidence of drug abuse. Clean the area around the eyes, eyelids, nasal area and forehead several times. This must be done in a centrifugal manner. The cleaning should be done with alcohol pads first and then with betadine. Now drape the donor.

Aravind Eye Hospital & Postgraduate Institute of Ophthalmology, Madurai.
and prepare a sterile field so as to place the instruments and the eye jars. Apply antibiotic drops (approximately 25 to 30 drops).

Open the eyelids using a sterile applicator and a speculum is inserted. Using a small clawed forceps and tenotomy scissors, lift and cut the conjunctiva at the limbus 360°. The four-rectus muscles are successfully looped with a muscle hook except for the lateral rectus. Cut the muscles. Before cutting the lateral rectus, clamp it close to the eye, then cut the muscle distant to the clamp. The two oblique muscles and the optic nerve now remain. When lifting up the clamped lateral rectus muscle, insert the curved enucleation scissors between the conjunctiva and the globe. Locate the optic nerve by feel and cut leaving at least 1/4 inch of the nerve attached to the globe. Now place the globe in the eye jar and note on the jar which contains which eye. Ensure that the chamber is moist. Instill about 25 to 30 drops of antibiotic solution (Neosporin or Gentamicyn) over the cornea before screwing the lid. Now label the eye jar and reconstruct the face socket.

Drawing blood

This has become mandatory for all eye banks. With the prevalence of HIV and HBsAg increase, no one can afford to take risks. Blood should never be drawn downstream from an IV site to avoid hemodilution. Always angle the needle in under the skin, apply a slight back pressure on it by withdrawing the plunger about half an inch. This creates suction to draw in blood when the vessel is found, indicated by the sudden flow of blood into the syringe. When this occurs, withdraw the syringe just enough to fill it completely. Usually gentle probing with the needle is necessary to locate the vessel. Once blood is drawn, insert the syringe into the vacutainer tube. Hold the plunger firmly while piercing the vacutainer. Ensure that the blood is made to drip along the sides of the vacutainer tube slowly during the transfer process from the syringe. Ideally a 10-cc syringe with an 18-gauge needle should do. 5 to 10 cc of blood should be drawn. Let the vacutainer containing blood slant at an angle of about 30° for about 5 minutes to separate the serum thus preventing lysis of blood before being packed. During this process the technician should wear a gown, cap, mask and gloves for their safety.

Blood can be drawn from the Subclavien vein, Jugular Vein, Femoral Vein, or from the heart. Drawing from the femoral vein requires the least amount of training but yields the least amount of blood. Drawing from the jugular vein is most difficult and needs tremendous skill and yields maximum blood.

Packing for transportation

- The ideal container should be a Styrofoam container or any igloo container which maintains the temperature between 2° and 8°C
- Never use dry ice for packing. Place water in a small plastic container and freeze. Before packing remove the container with ice and keep at room temperature until the moisture begins to form on the top of the ice. At this point, close the lid and place the ice pack in a polythene wrapper and seal. In this manner the temperature of the ice will be maintained for longer duration.
- Place the eye jars and the vacutainer containing blood, between these containers of ice in a moist sponge.
- If Styrofoam containers are used just wet the Styrofoam box on the outside to maintain the temperature.
- Ensure that the consent form, evaluation and donor history is sent along with the package. All these precautions are necessary to ensure that the eyes reach their destination safely.

Quality control

This is the key to proper utilization of any cornea. Not only during the enucleation process but even more after the eyes are brought to the eye bank for processing. The entire processing should be performed under sterile conditions. The pro-
cessing that follows once the eyes are received at the eye bank is as follows:

- Tissue evaluation
- Corneal excision and preservation
- Serology
- Documentation
- Distribution
- Preservative mediums

**Tissue evaluation**

As soon as the eyes are received at the eye bank, the whole globe is evaluated and graded. A careful examination of the cornea under a slit lamp is necessary. Examine the epithelium for haze, exposure, sloughing or any other epithelial defects. Then see the stroma if it is clear or cloudy, whether arcus senilis is there and opacities if any. Check for folds in the descemets membrane and an observational evaluation of the endothelium. It after this examination the cornea is found to be good then it is excised.

**Corneal excision**

This procedure should be performed in a sterile environment under aseptic conditions as far as possible. If the environment where the donor is offers these conditions you may do a corneal excision and transfer the cornea to the preservative medium immediately. As most deaths are home deaths and environmental conditions may not be suitable for corneal excisions, it would be safer to enucleate the whole globe and perform the corneal excision in the eye bank, under the Laminar Air Flow (LAF) in sterile conditions, thus improving the quality of the tissue. By using the glove and gown technique we improve the asepsis of the entire procedure thus avoiding contamination.

**Serology**

This is now mandatory for eye banks, due to the increase in the prevalence of diseases such as HIV and HBsAg etc. At least 5 cc of blood must be available for performing serology. The sample should preferably collected in plain silicone coated vacutainer which is inexpensive. There are many test kits that are available to use. Sterility of the procedure should be maintained. Adhere to all the safety measures as indicated. Avoid contamination or direct contact with the serum. Work under a Laminar Air Flow. Decontamination should be done as per the guidelines set. Ensure that the work surfaces are cleaned with 70% alcohol prior to and after use.

**Preservative mediums**

The most commonly used preservative mediums are MK and Optisol. MK medium is easily available in India as it is produced by the support of Rotary at Hyderabad and supplied to only recognized eye banks. Corneas can be preserved in this medium from 72 hours to 96 hours. The other medium is Optisol. This has to be imported and costs approximately US$42/- per vial. Corneas can be stored in this medium for 10 to 14 days. Check to see that the color of the medium has not changed as that would indicate a change in the pH value due to contamination.

**Documentation**

This is absolutely essential for all eye banks. As we are dealing with tissue that is being recovered from cadavers and being grafted to human recipients, this document is a testimony for any medico legal purpose in the future. Also this is a document for all the processing and procedures that is preformed to maintain the standards and hence is an invaluable document.

**Distribution**

Corneal tissues may be distributed to ophthalmic institutions, corneal surgeons and other eye banks. The emphasis here is in the packing and transportation. Ensure that the corneas are maintained between 2 and 8° during the transportation process. Also see that the various documents such as tissue evaluation, serology, and donor information reports are enclosed. Use of Styrofoam containers...
are advisable, as these will maintain the tempera-
tures as well as withstand the journey. However
even gas sterilized empty film roll container can
also be used as the globe fits snugly into the con-
tainer.\textsuperscript{7,8}

Quality
From the quality control aspects for eye bank-
ing, a regular regimen for cleaning of the eye bank
should be maintained. Disinfection of instruments
must be performed very meticulously and as per
the disinfecting procedure. The sterility of the eye
bank will be maintained, if the cleaning procedures
are maintained as per the procedure. It is important
to maintain this in similar fashion to an OR, except
that you should UV radiate and not fumigate.

Regulatory body
The regulatory body (Non Governmental) in our
country is the Eye Bank Association of India (EBAI)
which Headquarters at Hyderabad and has its zonal
offices. The other regulatory body is the Interna-
tional Federation of Eye Banks (IFEB) which is for
International Eye Bank and is situated in the US.
International eye banks are affiliated to both, re-

gional and international body.

Discussion
Good Eye Banking practices depends on proper
quality control. This can be further bifurcated in
clinical and non-clinical practices. In the clinical,
practices details such as sterile procedures, cor-
rect evaluation, good documentation procedures,
proper disaffection methods being used and proper
packing are important. On the non-clinical side,
courteous telephonic conversation, documentation
doctor information, prompt and immediate ac-
tion, and sensitivity to the situation are all very
important. Corneal retrievals could be either di-
rectly from the donor home or from a hospital. In
our country where home deaths are common, it is
important that we try and maintain asepsis of the
procedure as far as possible to maintain quality, at
the same time is sensitized to the situation of the
donor family.

From our data for 1998 we found that the nearly
62\% of the eyes that we received were from donors
in the age group of 60 to 80 years, most of the
causes of death being respiratory failure. With the
prevalence of HIV and HBsAG on the increase, it
has become mandatory for all eye banks to perform
serology tests for the above as well as syphilis.
Despite the documentation of HIV in tears\textsuperscript{9}
and donor corneal tissue\textsuperscript{10-14}, the potential for trans-
mision via corneal transplant is very low. There
have been no reports so far of sero conversion
after corneal transplant. Some patients who re-
ceived corneas from HIV infected donors, showed
no evidence of sero conversion\textsuperscript{15-16}. Nevertheless
the potential of transmission is too great to take
undue risks.

Transmission HBV through corneal transplant
has been documented in the case of two different
donors\textsuperscript{17}. Recipients from one cornea from each
donor developed clinical and serological evidence
of HBV infection, 14 weeks after keratoplasty per-
formed, without prior serological testing. The other
recipient of the other donor, developed clinical con-
ditions but tested positive, two years after pen-
etrating keratoplasty. However there have been no
reported cases of syphilis having been transmitted
through corneal transplant.

Recent studies indicate that there is a poor cor-
relation between reactive syphilis and HIV testing
in potential cornea donors\textsuperscript{18}. However every test
has a cost associated not only in terms of money
but also in false positives and tissue wastage.
Implementation or abandoning tests should be
based on strong scientific data. In developing
countries attention must be paid to the cost factor
and hence it is necessary to use the most suitable
and appropriate equipments.

Conclusion
With the demand for corneas on the increase and
the limited supply, it is imperative that the corneas
received must be utilized to the maximum. Currently
the utility rate ranges between 25\% and 60\%. In
developing countries where the demand is so great,
it is imperative that quality is maintained at all the
various stages of the process to ensure a higher utility and lower wastage. In teaching Institutions there is no wastage. The sclera are also preserved in absolute alcohol and utilized for orbit surgeries. The focus in eye banking in the developing countries in the next millennium will have to be towards increase in corneal procurement, high quality and better utilization of all the donor corneas received and lower costs.

References
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Intravitreal injection of fluorescein for clear-vitreous vitrectomy

Dr. R. Kim*, Dr. George F. Hilton**, Dr. P. Namperumalsamy*

Abstract
Aim
In clear-vitreous vitrectomy the peripheral vitreous gel is very difficult to visualise. To identify this invisible tissue we used intravitreal fluorescein which was found to facilitate the excision of the gel.

Method
We studied 43 eyes with clear vitreous undergoing vitrectomy for various causes. After core vitrectomy a dilute solution of fluorescein was injected into the central vitreous followed by an almost complete vitrectomy of the peripheral vitreous gel.

Results
The use of intravitreal fluorescein decreased the vitrectomy time and made the procedure easier. There were no significant complications.

Conclusion
Intravitreal fluorescein in clear-vitreous vitrectomy helps in identifying the normally invisible vitreous gel, with no apparent complications.

Key Words: Fluorescein, Vitrectomy, Vitreous gel

Introduction
The indications for vitrectomy continue to expand with each passing year. Diseases traditionally considered to be incurable may now be managed with vitrectomy techniques. These include vitrectomies done in clear vitreous for conditions such as macular hole, giant retinal tear detachment, diabetic traction detachment and macular pucker.

In all these conditions it is very difficult to do a complete vitrectomy as the clear vitreous gel cannot be adequately visualised. In this study we used an intravitreal injection of fluorescein solution with which to stain the vitreous gel. We have found it easy to identify the gel and thereby a more complete vitrectomy could be readily accomplished.

Our review of the literature disclosed no reports on the use of intravitreal fluorescein.

Materials and methods
Forty-three patients with clear vitreous underwent three port pars plana vitrectomy, with other associated procedures, for various indications as shown in the Table 1.

Table 1
Clear – Vitreous vitrectomy cases managed with Intravitreal injection

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Surgical Indication</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Macular hole</td>
<td>12</td>
</tr>
<tr>
<td>2</td>
<td>Macular pucker</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>RD with Giant Retinal Tear</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>RD with posteriorly located breaks</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>RD due to macular hole</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>PDR with traction RD of macula</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>RD with PVR</td>
<td>8</td>
</tr>
<tr>
<td>8</td>
<td>Removal of posteriorly dislocated IOL and crystalline lens</td>
<td>4</td>
</tr>
</tbody>
</table>

RD Retinal Detachment
PDR Proliferative Diabetic Retinopathy
PVR Proliferative Vitreoretinopathy

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** Department of Ophthalmology, University of California, San Francisco,
After core vitrectomy, one ml of fluorescein solution was injected into the central vitreous. The procedure was then continued with a high-flow wash out of the dye from the fluid in the central core. The wash out was accomplished with mid vitreal suction 250 mm Hg and with elevation of the infusion fluid bottle. The vitreous gel was then easily seen with the fluorescent stain. This enhanced visibility greatly and facilitated the more complete removal of peripheral vitreous instead of a blind search for the invisible gel. It was found to be a time saving procedure.

In our earlier cases we used a few drops of 20% fluorescein, such as is commonly used for fluorescein angiography, in the syringe of Balanced Salt Solution (BSS) or Ringer Lactate solution. This concentration was too high and the time taken to wash out the stained fluid was greatly prolonged. Subsequently we shifted to sterile fluorescein strips and dipped them in the BSS, but this method proved to be unpredictable. Thereafter we investigated the use of 2% fluorescein solution (2% fluorescein sodium 1 ml droppette IOLAB Pharmaceuticals Division of IOLAB Corporation (Claremont CA 91711, USA) in 2 ml of BSS in the strength of one, two or three drops. We found that 3 drops in the 2 ml of BSS was the optimal concentration for adequate staining of this gel. Of this, only one ml was injected into the vitreous. From our experience we have equivalent doses for different fluorescein concentration as given below in Table 2.

Table 2

<table>
<thead>
<tr>
<th>Intraocular Fluorescein</th>
<th>Commercial fluorescein</th>
<th>Drops</th>
<th>Volume</th>
<th>Intravitreal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2%</td>
<td>3</td>
<td>2.0ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10%</td>
<td>2</td>
<td>6.5ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20%</td>
<td>1</td>
<td>6.5ml</td>
</tr>
</tbody>
</table>

Discussion

This study was performed to identify yet another use of fluorescein in ophthalmology by determining the optimal concentration of fluorescein for injection into the vitreous and to identify any possible side effects.

Sodium fluorescein is an inexpensive water-soluble dye that produces an intense green fluorescent color in alkaline solution. This color is detectable in concentration as dilute as one part per million.

The most frequent indication in our series for clear-vitreous vitrectomy was idiopathic macular hole. After the injection of intravitreal fluorescein the removal of the peripheral vitreous gel was much easier. In case of giant retinal tear with rolled-over flap, it was easy to identify the fluorescein stained gel behind the flap.

We had four cases of macular pucker in which intravitreal fluorescein was used for a more complete vitrectomy. Subsequently we have learned that it is not usually necessary to do an extensive vitrectomy for the peeling of these epiretinal membranes of the macula.

The use of intracocular fluorescein did not hinder any or the subsequent procedures, nor did we observe staining of any other tissues. Postoperatively no complications were encountered which could be attribute to the use of intravitreal fluorescein.

The most common ophthalmic use of fluorescein is for applanation tonometry, contact lens fitting and for the diagnosis of corneal abrasions. It has also been used for intracameral injection to demonstrate aqueous leakage. Intravenous injection for fluorescein angiography is well known. A Letter to the Editor reported the use of "intracameral subcapsular" fluorescein injection for improved visualisation during capsulorhexis in mature cataracts.
We now suggest yet another use of fluorescein; to be used as an aid in vitreous surgery. Fluorescein is readily available, it may be given with a simple technique, and is effective in staining the vitreous gel. We suggest the routine use of intravitreal fluorescein in clear-vitreous vitrectomies.

References
Polymerase chain reaction in ophthalmology

C. Gowri Priya¹, Dr. Lalitha Prajna¹, Dr. N. Venkatesh Prajna²

As we approach the new millennium, newer strategies are required to counter the ever-versatile armamentarium of microorganisms. Polymerase Chain Reaction (PCR) invented by Kary Mullis in 1985¹, serves as one such tool which helps physicians to diagnose and treat disease at the molecular level. Briefly, PCR is a rapid procedure for in vitro amplification of a specific region of DNA and thus facilitates accurate diagnosis even in the presence of an extremely small sample. It was first used in clinical ophthalmology in 1990 and is now being used in all ophthalmic subspecialties².

Organisms are conventionally identified either directly by staining and culture or indirectly by serology. Though these techniques each have clinical value, PCR has the greatest sensitivity as it can detect even if a single copy of the DNA is present in the sample and can convert it into millions of copies.

Although PCR is both simple and rapid, it should be used like any other molecular biological tool, appropriately, and has the following strengths and weaknesses. It can be used to analyze extremely small amounts of DNA and once standardised, it is specific and can be used to analyze large numbers of samples rapidly. It is outstanding in its ability to detect mutations as small as a single base pair or point mutations. The speed of the reaction is faster, and quicker results can be obtained as compared to the conventional results obtained through culture. However, the following weaknesses remain. The establishment of this technique takes time and investment. The extremely high degree of sensitivity obtained also leads to confounding contamination problems and hence false positivity may be reported. For an ophthalmologist to derive maximum benefit, knowledge of these techniques and their advantages and limitations are essential.

Principles of PCR

Every microorganism has DNA sequences, which are unique to it, a situation somewhat similar to the uniqueness of fingerprinting. The procedure of PCR uses this principle to arrive at a diagnosis. It is essential to have a provisional suspicion of a clinical diagnosis before ordering a PCR, since each organism to be detected requires a specific primer.

What are primers?

Every microorganism, at the molecular level has certain regions comprising of specific nucleotides, which are specific to that particular organism. A primer is usually composed of 8-20 nucleotides flanking each side of these regions and is available in a customized fashion.

E.g. of a primer: Insertion sequence - IS6110 specific for tubercle bacilli with

IS1 5' CCTGCGAGCGTAAGCGTACGG 3'
IS2 5' CTCTGCAGCGCGCGCTTCGG 3'

as the flanking sequence for a 123bp region.

Procedure of PCR

The initial step for performing PCR is to extract the DNA from the biological sample to be analyzed like, the lacrimal gland, conjunctiva, tear film, cornea, aqueous humor, vitreous, retina etc. The process of DNA extraction involves the following sequential steps:

1. Department of Microbiology and Immunology, Aravind Eye Hospital
2. Department of Cornea and Refractive Surgery, Aravind Eye Hospital
a) Lysis of the cell wall using lysozymes
b) Deproteinization using proteinases and phenol:chloroform extraction
c) Precipitation of DNA using ethanol

Apart from the sample DNA obtained by the above steps, the other requisites are:
- Taq DNA polymerase (enzyme required for DNA synthesis)
- Forward and reverse primers (already described)
- Deoxyribonucleotide triphosphates-dNTPs (which are the building blocks for DNA synthesis) and
- PCR buffer (which aids as a buffering agent).

After adding these components into sterile PCR tubes, they are subjected to 35-40 cycles of amplification in a pre-programmed thermal cycler. Each cycle consists of three steps (Fig. 1).

1. **DENATURATION** - Separation of double stranded DNA into single stranded DNA by heating (94°C).
2. **ANNEALING** - By cooling (55°C-65°C), the short fragment of DNA-primers, by virtue of their defined sequence, bind to the complementary region in the separated strands. Since annealing occurs only if the single stranded DNA has the complementary sequence for the primers, this step guarantees the specificity of the reaction.
3. **EXTENSION/ELONGATION** - In the presence of DNA polymerase and dNTPs, nucleotides complementary to the separated strand are added, extending the primer.

This results in amplification of a single copy of the DNA into two copies of the DNA. The repetition of this cycle by n times will lead to amplification of target sequence $2^n$ times.

The next step is to identify the amplified product and this is accomplished by gel electrophoresis. Further confirmation can be done by blotting the gel onto a membrane of nitrocellulose or nylon for

**Fig-1 Schematic representation of PCR**
hybridization with a known probe. For permanent documentation of the results, these can be photographed by gel documentation system (Fig.2).

![Gel photograph showing the amplified products of PCR](image)

**Variations of PCR**
Different variations of PCR have been developed to maximize its utility in specific applications.

1. **NESTED PCR** is a frequently used modification for improving specificity and sensitivity. In this, an inner and outer set of primers are used. PCR is first performed using the outer set. A portion of the first amplification is reamplified using the inner set of primers.

2. **RT-PCR** - The starting material is a messenger RNA. The specific mRNA sequences are detected by first reverse transcribing the mRNA to cDNA using reverse transcriptase (RT). RT-PCR has tremendous potential in differentiating active from latent infection.

   1. Molecular weight marker
   2 & 3 - Positive control
   4 - Sample 1
   5 - Sample 2
   6 - Negative control

**Application to ophthalmology**
The PCR has been used for diagnosis of ocular infections from multiple sites including the lacrimal gland, conjunctiva, tear film, cornea, aqueous humor, vitreous and retina (Fig.3). Because of the very small sample volumes available and the fastidious nature of many of the organisms known to cause ocular disease, PCR is well suited for the diagnosis of ocular infections. It is particularly useful in uveitis and retinitis patients who present atypically.

**Conjunctiva**
- VZV, HPV
- Chlamydia
- *Rochalimaea henselae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*

**Cornea**
- HSV, HHV-6
- HIV - 1
- Hepatitis C
- HSV-mRNA
- *Acanthamoeba*, Fungus

**Aqueous**
- CMV, HSV, EBV, VZV
- *Toxoplasma gondii*
- *Mycobacterium tuberculosis*, *Leptospira*

**Vitreous**
- HIV - 1
- CMV, HSV, EBV, VZV
- *Propionobacterium acnes*, *Borrelia burgdorferi*

**Subretinal fluid**
- HSV, CMV, EBV

*Fig-3 Infectious organisms identified by PCR from various ocular locations*
Multiple infections

Studies have shown the possibility of multiple concurrent infections being diagnosed by PCR that cannot be diagnosed on clinical grounds. Rummelt et al.⁵ reported one patient found to have retinitis secondary to CMV, HSV, and HIV on histopathology. They concluded that multiple viral infections of the retina, mimicking classic CMV retinitis, should be considered in the clinical diagnosis of necrotizing retinitis in AIDS patients. Concurrent retinitis secondary to CMV and Toxoplasma gondii has also been reported. The incidence of plasmid microbiological infectious retinitis is unknown but may play a role in differences in progression of retinitis.

In suspected cases of endophthalmitis, it is crucial to determine whether the pathological process is due to infection or inflammation. Recently, two PCR-based kits have been developed to rapidly distinguish infection from inflammation and to identify the pathogen. The “endophthalmitis kit” can detect 14 species of bacteria, Candida spp., and Aspergillus spp., using multiplex PCR technology⁶. A similar kit for keratitis is also available.

Newer diseases

Newer and emerging agents can be easily identified by PCR, which can be missed by other conventional techniques. Laboratory diagnosis of Borrelia burgdorferi, the agent for Lyme disease, is based on serology with known limitations⁷. Karma et al.,⁸ report a case where antibody testing delayed the diagnosis but a positive result by PCR helped in the diagnosis. Similarly, in cat-scratch disease, the causative organism, Rochalimaea henselae has been identified by PCR where staining and culture were negative⁹. Leptospiral uveitis, a common uveitic entity in South India has been demonstrated in 80% of the uveitis patients by PCR whereas, only 72% could be identified by serology¹⁰.

Virology

Numerous researchers have applied the technique of PCR to aid in the diagnosis of specific viruses. Martinez et al.¹¹ in the study to correlate clinical feature of herpetic keratitis with virological studies, concluded that viral isolation and PCR were equally sensitive in epithelial keratitis, but in stromal keratitis only PCR could detect the virus. A recent study by Kim et al.,¹² reported the development of a multiplex PCR, which would aid in the diagnosis of adenovirus, HSV and VZV in cases of conjunctivitis. Boley et al.,¹³ also have developed multiplex PCR for detection of posterior uveitis pathogens.

Human Papilloma Virus is gaining center stage in ocular disease due to its high prevalence in lid and lacrimal gland tumors¹⁴, conjunctival papilloma as well as in conjunctival dysplasia and carcinoma¹⁵. In HIV infected patients on multi-drug therapy, the viral load can be determined to see efficacy of treatment.

Bacteriology

PCR has been proved to be very sensitive and specific in infections of Chlamydia. Elnifro et al.,¹⁶ analyzed the relative merits of antigen detection with PCR and found PCR to have a better role than direct fluorescent antibody (DFA) test that requires meticulous examination of stained smear for interpretation. Moreover, Chlamydia can be identified up to species level by PCR while DFA is only genus-specific¹⁷. A PCR procedure without the extraction of DNA, identified Pseudomonas aeruginosa within 4 hours¹⁸. A single assay using multiplex PCR to simultaneously identify ocular isolates of Staphylococcus aureus, Pseudomonas aeruginosa and Streplococcus pneumoniae within hours has been reported by Chan et al.¹⁹.

The diagnosis of mycobacterial infection remains a challenge in ophthalmology as ocular complications of tuberculosis presents a variable array of symptoms throughout the course of illness. PCR is of great help to the ophthalmologists faced with a case of suspected ocular tuberculosis with no evidence of systemic tuberculosis where it is difficult to be certain whether the infection is truly tuberculous in origin. The identification of tubercle bacilli from different ocular specimens by PCR has helped in confirming the diagnosis²⁰,²¹.
Mycology
PCR is proving to be a useful tool in fungal infections as shown by the work of Alexandrakis et al.\textsuperscript{22}, in his work on Fusarium panophthalmitis. Okhravi et al.\textsuperscript{23}, have shown that PCR-RFLP analysis has a great potential in the rapid detection and identification of Candida spp. A rapid identification of pathogenic fungi (Aspergillus spp., Candida spp., and Fusarium spp.) which share a common target sequence has been reported\textsuperscript{24}.

Parasitology
Protozoan infections due to Acanthamoeba and Toxoplasma are difficult to diagnose both directly and in the laboratory. PCR is again very useful in these infections. Acanthamoeba, an uncommon cause of corneal infection was amplified by PCR from corneal epithelial and tear samples enabling prompt diagnosis and treatment\textsuperscript{25}. Norose et al.\textsuperscript{26}, have shown that PCR can be used to diagnose with certainty and to quantify the number of Toxoplasma gondii in vitreous humor in a patient with recurrent toxoplasmosis. Recently, a O-150 PCR has been developed to differentiate the blinding and nonblinding strains of Onchocerca volvulus an endemic parasite in Nigeria\textsuperscript{27}.

Genetics
Although the main focus of PCR is in the diagnosis of infection, there are other applications especially in genetic disorders and in pathology. Our understanding of the genetics of the eye diseases has benefited tremendously from the advances in molecular genetics. The genes for many inherited disorders including retinitis pigmentosa,\textsuperscript{28} retinoblastoma, gyrate atrophy, congenital cataract and juvenile glaucoma\textsuperscript{29} have been cloned and characterized. As in other areas of clinical medicine, these discoveries have led to new methods of diagnosis, more effective preventive counseling and have suggested novel therapeutic modalities including gene therapy.

Pathology
Any fresh ocular tissue, formalin fixed or paraffin embedded tissue and even stained or unstained cytology slide or tissue sections can be used for DNA extraction. This aids not only in the identification of pathogenic organisms but also in the pathophysiology of ocular diseases. The first diagnostic application of PCR was in the prenatal diagnosis of sickle cell anemia. The pathogenesis of Diabetes mellitus, Pemphigus vulgaris, Myasthenia gravis and multiple sclerosis have been clarified by PCR. Using PCR, a possible link between the iridocorneal endothelial syndrome and HSV has been reported\textsuperscript{30}. Also an association between virus and cancer has been shown by PCR as in HTLV-I and leukemia.

Immunology
Autoimmune diseases and other immune-mediated diseases are increasingly recognised. The association between the HLA types and various ocular diseases such as VKH syndrome, Behcet's disease\textsuperscript{31}, Sympathetic ophthalmia etc., has been confirmed by PCR.

Conclusion
Thus, in addition to its certain impact in our care of patients with infections that involve the eye, it appears that PCR is here to stay as part of our cultural and medical vocabulary. From a technique "in evolution", it has come a long way where it is used as the diagnostic aid in many ocular diseases.

Increasing numbers of immunosuppressed patients with intraocular infections and improvements in antibiotic therapy for specific organisms require a more accurate diagnosis. PCR is capable of providing such requirements. This technique is evolving rapidly and in cooperation with clinicians and molecular biologists a number of applications are being developed, which contribute to the growing demands on microbiological testing.

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Iridocorneal Endothelial (ICE) Syndrome - A case report

Dr. Ramesh Moorthy, Dr. Krishnadas

Introduction

As early as 1903, Harms recognised ICE syndrome as a discrete entity. The acronym ICE stands for the 3 subsyndromic types - Iris naevus syndrome, Chandler's syndrome and Essential Iris atrophy. Campbell et al in 1978 postulated that all three are linked by a common endothelial dysfunction with production of an abnormal basement membrane. The exact etiology is however unknown, this being acquired after birth, though a possible role of EBV infection or HSV has been proposed. This is a case report of ICE syndrome.

Case Report

A 28 year old female came to our hospital with complaints of discoloration, redness and blurring of vision in the right eye for a duration of 3 months. There was no preceding history of trauma and none of the other family members were similarly affected. The best corrected visual acuity in the RE was 6/9 and LE 6/6. Slit lamp examination showed circumcorneal congestion, cornea had bullae with edema and a stromal opacity inferotemporally. Anterior chamber was of irregular depth with peripheral anterior synchiae extending nearly circumferentially. Iris had a stretch hole at 7 O'clock and melting holes at 12 and 1 O'clock. There was corectopia and ectropion uveae, the pupil was oval with a sluggish reaction to light. Both fundi were normal. Intraocular pressure by applanation tonometry was 14 mm Hg in the RE and 10 mm Hg in the LE. Specular microscopic analysis of the RE showed pleomorphism and polymegathism. The co-efficient of variation of cell size (cv) value was 44.61 in the RE and 36.32 in the LE.

Fig-1 Slit lamp photo showing iris holes, ectropion uvea, corectopia and corneal edema

Fig-2 Specular microscopic analysis showing pleomorphism and polymegathism

Discussion

This case merits presentation because of its rarity in the Indian setting. The predominant feature of Chandler's syndrome is corneal edema. Iris changes are minimal and confined to the stroma with no hole formation, although nodules are seen. Our patient had corneal edema and bullae along with holes in the iris suggesting a mixed picture of Chandler's syndrome and essential iris
atrophy. This could be explained as an intermediate transitional stage of one variation into another. Shields et al have reported in a study of 37 patients of ICE syndrome, that 2 cases initially diagnosed as Chandler's syndrome developed iris holes thus changing the diagnosis to essential iris atrophy. Even in cases of Essential iris atrophy, corneal edema may occur. Therefore instead of strictly compartmentalising this condition into specific sub-syndromic types, it should be considered as different manifestations of the same spectrum of disease.

Specular microscopy provides the strongest evidence that the variations represent a spectrum of disease. The earliest change is a loss of the uniform hexagonal shape of the endothelial cells, with pleomorphism and polymegathism. Analysis of the endothelium of the unaffected fellow eye is mandatory as it may show subclinical abnormalities. This was true in many cases where the RE had a CV value of 44.61 and the left eye 36.32 which is much higher than the normal range of 25-30. Even though the endothelial cell density was not drastically reduced, polymegathism and pleomorphism were noted.

The ICE syndrome is a progressive disorder. It is important to recognise and establish the diagnosis early especially in India so that the patient may have realistic expectations as glaucoma usually develops early or late. Specular microscopy proves to be an invaluable tool for early and confirmatory diagnosis.

References
Cavernous hemangioma causing luxated globe

Dr. Preethy Rangan, Dr. Siva Prasad, Dr. Usha Kim

Introduction
Luxation of the globe, the ultimate stage of proptosis can be caused by various tumours including cavernous hemangioma. Luxation does not produce permanent damage to vision, the slack of the optic nerve (Intra orbital part) being so considerable so as to avoid damage. Expanding orbital tumours may cause marked proptosis, but actual luxation of the globe is exceedingly rare. We report a case of luxation in cavernous hemangioma of the orbit.

Case Report

A 40 year old male came to our hospital with complaints of protrusion of right eyeball for the past 7 years. Examination revealed an eccentrically luxated RE down and in with a mass in the superotemporal quadrant. The mass was globular with a bluish hue and smooth surface and was 3.5 x 3 cm in size. Venous dilatations were seen on the skin of upperlid. Orbital margins could be palpated fully. All extraocular movements were restricted. Pupil was reactive to light. Fundus was normal. Both anterior and posterior segments were normal in left eye. Visual acuity was 6/9 in RE and 6/6 in LE. General and systemic examination was within normal limits except for severe anaemia. He was treated with anthelmintics and 3 pints of blood transfusion before taking him for orbitotomy. CT scan revealed a soft tissue lesion in the right orbit with bony orbital expansion in the superotemporal and retrobulbar region. Probable diagnosis of a slow growing benign vascular tumour was made which was causing the luxation of globe.

Right superolateral orbitotomy was done and a well-encapsulated mass of about 5x5x3 cm was removed in toto. On immediate postoperative period patient had a complete ptosis probably due to long term stretch of levator palpebra superiors and sudden loss of support given by the luxated globe. Vision was 6/9 and fundus was normal postoperatively. Histopathological examination confirmed a diagnosis of cavernous hemangioma. On the 40th postoperative day the ptosis had improved considerably and he had a pinhole vision of 6/9 RE.

Discussion
When the eyeball protrudes out of the orbit and lids close behind the eyeball causing pain and discomfort, it is called Luxation. A shallow orbit and laxity of fascia and muscles are the predisposing factors. Luxation has been reported in...
1. Space occupying lesions like lacrimal gland tumour, hemangioma etc.,
2. Haemorrhages into orbit
3. Acute cellulitis
4. Endocrine exophthalmos
5. Voluntary and traumatic luxation has also been reported.

Fig-3 CT Scan picture showing mass in the retrobulbar and superspace

Postoperative picture of same patient

Cavernous hemangioma is the most common benign orbital tumour of adults. They are development hamartomas. It causes slowly developing proptosis. It occurs as a well-encapsulated mass in the retrobulbar space causing axial proptosis. Tumour has a bluish hue due to stagnant and poorly oxygenated blood with in it. Histopathologically the tumour shows large closely packed congested vascular spaces separated by fibrous septa. Vascular channels are lined by endothelial cells. Ultrasoundogram shows well defined round tumour with moderate sound transmission and multiple high internal echoes on.

A-scan CT scan shows bone displacement due to the mass and slow enhancement of the mass with contrast. MRI shows lesions hypo intense to fat on T1 weighted images and hyperintense to fat and isointense to vitreous on T2 weighted images. Surgical excision is easy due to the well encapsulation of the tumour.

References
Purtscher's Retinopathy - a case report

Dr. Meena Gopinath, Dr. Ravi Gandhewar, Dr. R. Kim

Introduction

A characteristic ophthalmoscopic picture, variously called Traumatic Retinopathy of Purtscher, or Traumatic Liporrhagia (Lymphorrhagia) Retinal or Traumatic Retinal Angiopathy has long been known to follow accidents, particularly those involving extensive crushing or fractures in various parts of the body. Ophthalmological reports of the condition have been relatively infrequent, perhaps because the symptoms are often transient and specialist examination is not requested in cases of this type. This is the case report of a 26 year old male with purtscher's retinopathy.

Case report

A 26 year old male presented with the complaints of defective vision in both eyes of 3 weeks duration following a fall from a bullock cart. He had been under the influence of alcohol at the time of injury. There was loss of consciousness for half an hour following the injury and he had sustained scalp and facial injuries.

On examination, there was a healing wound over the right frontoparietal area. Scar marks and multiple abrasions were seen over the right temporal region and over the face. On palpation of left side of the face, zygomatic fracture was felt. The visual acuity was 1/60 not improving with correction in both eyes.

Slit lamp examination showed subconjunctival haemorrhage in the temporal bulbar conjunctiva and sluggishly reacting pupil in the left eye. The right eye pupil also showed a sluggish reaction to both direct and consensual light reflexes. Ophthalmoscopic examination of both eyes revealed multiple superficial haemorrhages, islands of whitish grey opacities and localised milky patches of edema that were closely associated with the retinal vessels and involving the macular area. (Fig 1 and Fig 2)
Computed tomography scan demonstrated fracture of posterolateral wall of both orbits with blood in ethmoidal sinus. There was fracture of cribiform plate and a bone chip was present in the left maxillary antrum. Bifrontal contusion was seen in the brain scan.

Fundus fluorescein angiography was performed and had the following findings: Area of resolved edema with residual hard exudates; area of leakage and capillary non perfusion.

**Discussion**

In 1912, Purtsher described traumatic retinal angiopathy in 5 patients who had suffered severe head injuries. This bilateral condition is associated with head injuries, compression of the chest, compression of the abdomen with rupture of the liver, following acute pancreatitis, fat embolism, Scleroderma, Dermatomyositis and amniotic fluid embolism. In its classic form, Purtsher’s retinopathy is characterised by marked generalised retinal edema, macular edema, multiple patches of peripapillary superficial retinal whitening, intraretinal and disc edema and haemorrhages. The nerve fiber layer infarcts follow the distribution of the major temporal vessels, are 1 disc diameter or smaller in size and are accompanied by a few intraretinal or periretinal haemorrhages or both. The fundus changes begin immediately following the injury. Visual acuity is variably affected and may range from 6/6 to finger counting. Dense paracentral or central scotomas may be present. Fluorescein angiography may show leakage of dye in the region of the white retinal patches, retinal and disc edema, venous staining and areas of capillary nonperfusion. Indocyanine green angiography performed in a 19 year old male 4 days, 3 months and 5 months after sustaining an injury showed an area of choroidal hypofluorescence. Possible mechanisms for the pathogenesis of Purtsher’s retinopathy include:

1. Arteriolar occlusions from embolisation such as air or fat.
2. Retinal venous wall trauma from increased intravenuous hydrostatic pressure.
3. Arteriolar endothelial damage as a consequence of sudden increase in retinal arterial and venous pressure.
4. Local retinal vascular coagulopathy or granulocytic aggregation leading to multiple arteriolar occlusions.
5. Retinal angiospastic response following sudden increase in venous pressure.

The course of the disease is that the fundus changes typically resolve over a 4 month period. Visual acuity and fundus appearance may return to normal or there may be permanent visual loss associated with optic atrophy and RPE changes at the macula. The condition is usually self-limiting. Late visual recovery after intravenous methyl prednisolone at a dose of 1g/day was reported in a 25 year old man by Atabay-C et al. Further research only can confirm the rationality in using systemic corticosteroids to treat this condition.

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Neurocysticercosis presenting as secondary optic atrophy- a case report

Dr. B. Manohar Babu, Dr. G. Ramachandran, Dr. P. Subburam, Dr. G. Natchiar

Introduction
Cysticercosis caused by Taenia solium (pork tapeworm) is a disease of epidemic proportions in regions where free-range pig farming is practiced by communities lacking in adequate sanitation and appropriate education. In endemic areas, neurocysticercosis is a possibility in any person from that region who develops neurologic signs or symptoms.

Case report
8 year old girl from a village near Madurai presented with complaints of headache, defective vision both eyes of 5 days duration. Parents give history of headache with fever a month ago, following which she developed visual loss. H/O one episode of fits a few year ago. No H/O vomiting, eye pain, transient obscuration of vision, giddiness. No past H/O primary complex, any other treatment taken.

On examination visual acuity in right eye was 1/60 and in left eye was perception of light only. There was relative afferent pupillary defect in the right eye, afferent pupillary defect in the left eye. Anterior segment was otherwise normal.

Fundus examination of both eyes, by distant direct ophthalmoscopy showed good red glow with no opacities in ocular media and by direct ophthalmoscopy showed an elevated disc with indistinct blurred margins and filled up cup, the disc surface had a greyish hue. Vessels appeared attenuated with minimal sheathing close to their origin. Exudates were found on the macula. Systemic examination was within normal limits.

A provisional diagnosis of bilateral papilledema with early secondary optic atrophy was arrived at, and we proceeded to investigate the patient.

Investigations
- X ray chest – PA view – was normal.
- ESR was 17mm in 1 hour.
- X ray skull lateral view showed
  - Erosion of posterior clinoid process
  - Sutural separation
  - Silver beaten appearance of skull vault
- CT scan Brain with contrast was done:
Multiple ring enhancing lesions with surrounding severe edema

- Scolex seen in a few of the lesions as evidenced by a dense central focus in the lesion
- Present in the cerebral hemispheres, cerebellar hemispheres and brainstem.

Based on the CT findings a final diagnosis of Neurocysticercosis presenting as bilateral papilledema with early secondary optic atrophy.

**Discussion**

Cysticercosis is a fluid filled sac, containing the invaginated head or scolex of the larval form of Taenia solium – the common Pork Tapeworm. It is usually acquired by inadvertent ingestion of eggs produced by adult tapeworms that have taken residence within the human intestine. Patients may be infected by eggs from a tapeworm they themselves carry, or ingestion of egg bearing segments discharged from another's tapeworm -contaminating food or drink. The ingested segments (eggs→larva) then penetrate intestinal wall and are borne via blood stream and lymphatics to muscle, central nervous system or eye, where they encyst.

Most common presenting symptom of neurocysticercosis is a seizure diathesis, in endemic areas, neurocysticercosis causes more than half of all adult onset seizure disorders. Headache is common, hydrocephalus (secondary to chronic meningitis) and ensuing ventricular obstruction are frequent. Acute obstruction of the ventricular system is perhaps the greatest threat to the patient, and so papilledema is seen with ensuring optic atrophy and loss of visual acuity if left untreated. Less common manifestations include cranial neuropathies, an inflammatory endarteritis (causing vascular occlusive disease) or the presentation of a mass within the suprasellar or preopticine cisterns, masquerading as a pituitary or dorsal mid brain lesion. Cysticerci can be present in brain parenchyma, ventricles, spinal cord, subarachnoid space, optic nerve.

Commoner ocular manifestations include subconjunctival, anterior chamber, extraocular muscle cysticerci, and in the posterior segment cysticerci are seen in subretinal area and in the vitreous. There has been a case report of a patient having superior orbital fissure syndrome consisting of a complete 3rd nerve palsy and partial 4th +6th nerve palsies.

Diagnosis of Neurocysticercosis is based on a combination of

1. Blood and cerebrospinal fluid analysis for larval antigen
2. Neuro imaging studies
   a) Immune studies like ELISA, or preferentially, enzyme linked immuno electro-transfer blot assay is done.

   The second test is both highly sensitive and specific, it detects antibodies to the major glyco proteins representative of lentil-lectin affinity - purified Taenia solium. It can be performed on both serum and CSF. CSF is examined for possible lymphocytic pleocytosis (and eosinophilia) as well as measurement of CSF protein.
   b) CT scan studies show multiple areas of infiltration, cystic in quality, which contain a small dense central focus, presumably corresponding to the larva’s scolex. These are commonly associated with calcification (if the cysticerci have died) and contrast enhancement (if they degenerate). Lesions may be associated with edema and ring enhancement.

Treatment is with anticysticercal medication. Albendazole (an imidazole) 15 mg/kg/day x 2weeks and praziquantel (an isoquinoline) 50-100ml/kg/day x 2weeks are used extensively in treatment of parenchymal cysticercosis infections. Each agent frequently eliminates cysticerci from brain albeit incompletely, yet treatment with either agent is associated with adverse reactions that seem to be generated by the host’s inflammatory response to dying parasites. Albendazole is the drug of choice in parenchymal brain cysts, giant subarachnoid cysts and ventricular cysts. Corticosteroids alleviate the host’s inflammatory response to the parasite (brain
edema). Surgery is required if diagnosis is uncertain, cysts exhibiting tumor like behaviour, pseudotumor (edema refractory to medical treatment), intraventricular cysticercosis (V-P shunt), and when there is acute or subacute rise in ICT.

Epidemiological management include screening of all members of the household for infection of adult tapeworms, so that appropriate treatment could be given to reduce risk of additional cysticerci infection. Family members are at risk for cysticercosis because of close contact with a known infected proband, they should be evaluated serologically and treated if serologies are positive.

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   Dayanand Medical College, Ludhiana
Bilateral macular coloboma following congenital toxoplasmosis

Dr. A. Maghizh, Dr. S. R. Mamatha

Bilateral macular coloboma has been considered one of hallmarks of congenital disease, where as acquired infections are generally thought to result in unilateral disease. Most cases are now recognized to be due to intrauterine infection with Toxoplasma gondii. We herein report a case of bilateral macular coloboma with satellite lesion probably due to congenital toxoplasmosis.

Case report

A 32 year old man, presented with a history of blurring of vision in both eyes since childhood. There was no contributory medical or family history.

Examination of the patient revealed the best corrected visual acuity as 20/200 in Right Eye and 20/80 in Left Eye. The anterior segments were normal. Ophthalmoscopy showed well circumscribed, excavated and pigmented macular colobomas of 8x8 disc diameter in right eye and 6x6 disc diameter in left eye, with ectatic sclera at the base. A few large choroidal vessels were visible at the base. Right optic disc was dragged temporally towards the coloboma. There was lot of pigment aggregation in the lesion, more so in the periphery. Another similar, smaller lesion, of one disc diameter, just below the left macular coloboma, over the infero temporal arcade was seen. (Fig 1 and 2)

Color vision by Ischiara's test chart showed defective color vision in right eye. Fields by Goldman's perimeter revealed central scotoma in both eyes.

Ultrasonography showed a bilateral ectatic lesion with overhanging margins in the macular region with a normal axial length. A systemic evaluation, including complete blood count, erythrocyte sedimentation rate and VDRL test were non contributory. Serum for Toxoplasma IgG antibodies showed a high titre.

Discussion

Mann classified macular colobomas into three types, namely pigmented macular coloboma, non pigmented macular coloboma and macular coloboma...
associated with abnormal vessels. The above case can be fitted into the pigmented variety.

Macular coloboma is known to develop from an intrauterine inflammation or rarely as a developing abnormality of the eye. The infective process does not produce macular coloboma in families or in association with other ocular or systemic abnormalities. Maternal immunity protects against fetal transmission; thus women infected before pregnancy are at little or no risk for delivering a child with congenital toxoplasmosis, and women who deliver one child with congenital toxoplasmosis are at little or no risk of having a second infected child. There are, however, rare reports of congenital toxoplasmosis in more than one sibling. Thus if macular coloboma occurs in two siblings of different ages, it is unlikely to be due to infection.

The majority of macular colobomas are due to intrauterine toxoplasma infection. Toxoplasmosis is a progressive and recurring disease. When it is congenital, toxoplasmosis is a major cause of visual loss. Toxoplasmosis is a common infection acquired by ingestion of undercooked meat containing T. Gondii cysts or material contaminated with T. Gondii cysts excreted by cats. When an immuno competent pregnant woman acquires the infection for the first time—that is, before she is immune—she transmits the infection transplacentally to her fetus in utero.

The most common eye finding in congenital toxoplasmosis is retinochoroidal scars. In a study of 94 children with congenital toxoplasmosis (76 of whom were treated with pyrimethamine and sulfadiazine for at least one year), Mets and associates found chorioretinal scars in 79% of patients, and bilateral scars in 65%. Peripheral retinal scars were present in 64% of patients, whereas macular scars were present in 58%. Considering the much smaller area of the macula, these results suggest a definite predilection for macula in patients with congenital toxoplasmosis. This predilection may be due to the fact that posterior pole is vascularized earlier than other portions of the retina, or to the unique vasculature of the fetal macula, which contains end arterioles. Other ocular manifestations of congenital toxoplasmosis are strabismus, nystagmus, microphthalmia, microcornea, cataract, vitritis (active), retinitis (active), retinal detachment and optic atrophy. Signs of active infection in infants are white-yellow chorioretinal lesions with vitreous cells and other systemic findings like meningoencephalitis, hepatitis and thrombocytopenia.

The goals of management of ocular toxoplasmosis include eradication of the parasite and suppression of the inflammatory response. Mostly, Toxoplasma gondii infection is self limited and asymptomatic. Currently available drugs do not eliminate tissue cysts and therefore cannot prevent chronic infection. Treatment is therefore not warranted for the majority of Toxoplasma gondii infections. Due to these reasons, many clinicians do not treat small, peripheral retinal lesions that are not immediately vision-threatening, so as to avoid drug-associated side effects. The classic treatment regimen combines pyrimethamine with sulfadiazine. Both medications inhibit the folic acid metabolism, vital for the survival of the parasite. Corticosteroids are used to decrease problems associated with inflammation, such as macular edema, vitreous inflammatory reaction and retinal vasculitis. Their use is felt to be especially important for lesions that threaten the macula or optic disc.

Hereditary macular coloboma, on the other hand is a developmental abnormality producing bilateral atrophic excavated and well-circumscribed macular centered lesions with a clear hereditary or familial origin. Mann calls them “macular dysplasia”. Hereditary macular coloboma, usually caused by localised neuroectodermal or mesodermal maldevelopment are less frequently observed than the acquired types, which are usually of infectious origin. Hereditary bilateral macular coloboma have been reported as an isolated entity or combined with retinal aplasia, Leber’s congenital amaurosis, retinal detachment, skeletal abnormalities or with idiopathic hypercalciuria. The inheritance of Hereditary macular colobomas are thought to be autosomal dominant.
Similar round or oval sharply punched out macular centered lesions, simulating macular coloboma can be seen in cytomeglovirus inclusion diseases, central aerolar choroidal dystrophy, dominant progressive focal dystrophy, and autosomal dominant central pigment epithelial and choroidal degenerations. The above mentioned lesions are characterized by a progressive retinal pigment epithelial and choroidal atrophy in macular area showing the underlying choriod. These lesions are differentiated clinically by, slow development of an important loss of central vision. Color vision is usually poor in advanced cases. On the contrary, in this case patient had defective vision from birth. Defective color vision in right eye could be attributed to the massive size of the lesion and severe loss of visual acuity.

Unfortunately, there is no way to prove that these lesions are in fact due to congenital rather than acquired infection without serological examination for toxoplasmosis at the time of birth or early infancy. The only way to make a definitive diagnosis of congenital toxoplasmosis is the demonstration of Toxoplasma gondii in the diseased tissue. This unfortunately is impracticable. Hence the probable diagnosis depends on clinical features and serological studies. We presume the diagnosis to be congenital toxoplasmosis because the patient had bilateral macular lesion and a positive titre for IgG. Moreover, we believe that the retinal striations that radiate from disc to the lesion in right eye representes retraction of tissue after an inflammatory disease and would not be seen in a purely developmental lesion.

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Central corneal guttae and age-related macular degeneration- Are they co-existent?

Dr.D.Chitra, Dr.Babu Rajendran, Dr.P.Janakiraman

Introduction
The corneal endothelium and the retinal pigment epithelium are located on basement membranes, i.e. Descemet's & Bruchs respectively. They both have tight junctions and also active cell transport systems involving Na-K ATPase & anionic pumps. Both are derived from neuro-ectoderm. Drusen are a hallmark of AMD just as Corneal Guttae are of corneal endothelial degeneration. Both are seen as excrescences on a membrane [Bruch's and Descemet's].

The similarities between the corneal endothelium & the RPE in terms of their embryology, barrier function and predilection to age-related degeneration prompted this investigation into a possible association between Central Corneal Guttae and Age related Macular Degeneration.

Materials and methods
This is prospective study of the corneal endothelium on 100 eyes of 63 patients, at The Eye Research Foundation, Chennai.

50 eyes from 28 patients with Age-related Macular Degeneration were taken as the study group. 50 eyes from 35 age matched patients who were selected at random from our out-patient department after ruling out the presence of AMD were taken as the control group.

All patients in the study group had Fundus Fluorescein Angiography done in an attempt to avoid underestimation of macular changes that can occur with clinical examination alone.

All 100 eyes had Specular Microscopy done. Patients were excluded if they had glaucoma, evidence of uveitis, history of previous intra-ocular surgery, history of contact lens wear or history of long term use of topical medications. A detailed ophthalmic examinations was done with the indirect ophthalmoscope after full dilatation of the pupil with 0.5% tropicamide or 1% cyclopentolate drops. All 28 patients (50 eyes) in the study group had Fundus Fluorescein Angiography done. 31 eyes had Indocyanine Green Videoangiography done. Fundus Fluorescein Angiography and Indocyanine Green Videoangiography were done using the Topcon Fluorescein Angiography/ICG Image Net System which is based around the Topcon TRC-50 IA fundus camera. To perform ICGV, we used a Topcon T.V. relay lens (for 50 IA) Model XC-75 CE mounted within the view finder of the camera back and connected to a black and white monitor National Electronics Inc, M900X.

Specular microscopy
All cases (100 eyes) had specular microscopy done with the Topcon SP 2000P non-contact specular microscope in conjunction with the IMAGEnet for Windows Endothelial Cell Analysis System which is an advanced image analysis software which automatically determines density and hexagonality of the endothelial cell images and reports statistical information regarding cell area. The salient features of the Topcon SP 2000P specular microscope are:
- Field of coverage 0.2X0.5 mm
- Photographic points _5 (central cornea and 4 in the perimeter, each approximately 3mm from the center of the cornea)

Results
± The total no. of patients in this study were 63. The total no. of eyes were 100. The age range of
the 28 patients in the study group was 50-85 years with a mean of 68.3 and a standard deviation of \( \pm 9.4 \). The age range of the 35 patients in the control group was 52-80 years with a mean of 68.42 and a standard deviation of \( \pm 8.69 \). There were 22 males and 6 females in the study group and 25 males and 10 females in the control group.

**Distribution Of Guttae**

The distribution of Guttae among the AMD cases and in the controls is given below in Table-2

<table>
<thead>
<tr>
<th>No. of guttae</th>
<th>No. of Eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
</tr>
<tr>
<td>0</td>
<td>25(50%)</td>
</tr>
<tr>
<td>1 TO 10</td>
<td>23(46%)</td>
</tr>
<tr>
<td>11 TO 20</td>
<td>1(2%)</td>
</tr>
<tr>
<td>&gt;21</td>
<td>1(2%)</td>
</tr>
</tbody>
</table>

25 of the 50 eyes (50%) from patients with AMD showed presence of Central Corneal Guttae. 10 of the 50 eyes (20%) from patients in the control group showed presence of central corneal guttae. There was no statistical significance in the distribution of guttae (p=0.50)

**Type of AMD and Guttae**

In the study group, of the 21 eyes with non-exudative AMD, 10 eyes (47.6%) had central corneal guttae. Among the 29 eyes with exudative AMD, 15 eyes (51.7%) showed presence of central guttae, as shown below in Table - 3

<table>
<thead>
<tr>
<th>AMD</th>
<th>Guttae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-exudative AMD(21)</td>
<td>10</td>
</tr>
<tr>
<td>Exudative AMD (29)</td>
<td>15</td>
</tr>
</tbody>
</table>
There was a significant association between the type of AMD and the occurrence of central corneal guttae (p=0.05)

![Graph showing association between type of AMD and occurrence of central corneal guttae](image)

**Discussion**

Age-related macular degeneration is defined as the presence of some degree of visual loss in association with drusen & geographic atrophy of Retinal Pigment Epithelium (RPE) or changes associated with subretinal neovascularization in individuals over the age of 50.1

AMD is the leading cause of legal blindness in patients over 65 years of age and the commonest overall cause of blindness in the western world.2 10% of AMD patients have exudative form which accounts for 88% of legal blindness attributable to AMD.3

The various features that have been described in AMD are drusen, geographic atrophy, RPE changes, Choroidal neovascularization and disciform degeneration. Hyashi & co.4 reported that ICG angiography was useful to detect occult CNV & showed that the ICG dye leak from the CNV into the subretinal space is slower and of a lesser magnitude than Fluorescein leak of CNV. Yannuzzi & associates.4 showed that occult CNV can be converted into classic CNV in 39% of the 129 patients in their series, because of the information obtained through digital ICG video angiography. In our study, 5 (26.3%) of the 19 eyes that had ICG angiography done showed CNV which was not seen with Fundus Fluorescein Angiography.

Vogt5 was the first to use the term corneal guttae to describe the slit lamp appearance of small excrescences on the posterior corneal surface.

**Incidence**6

31.5% - 10-39 years  
70.4% - 40-99 years

Lorenzetti et al.6 have demonstrated an increased incidence of corneal guttae in early life.

Rodriguez and others7 have shown by electron microscopy that the changes in Descemet's Membrane are seen as early as the first two decades.

Corneal guttae are often seen as a primary condition in patients of middle to older age. Progressive bilateral accumulation of guttae usually seen in the fifth or sixth decade & somewhat more commonly in females, is typical of hereditary endothelial dystrophy of Fuchs. As guttae become numerous and central the endothelial cells are compromised. Then stromal edema followed by bullous epithelial edema occurs. Increasing stromal edema pushes the relatively inelastic Descemet's Membrane posteriorly, resulting in multiple wrinkles and folds.8

Wilson et al.9 found no significant difference in endothelial permeability between patients with mild guttae, patients with confluent guttae and increased corneal thickness and those with normal cornea. Radioactive labeling of endothelial Na+/K+ATPase pump site has shown an increase in pump site density and pump function in eyes with corneal guttae.10

In a study conducted by Prasad Rao and associates11, patients with severe AMD had an increased prevalence of central corneal guttae (p=0.013 &p=0.061 for right and left eyes). They found no correlation between the severity of central corneal guttae and AMD (p=0.34).

In our study, we found a 50% incidence of central corneal guttae in cases with AMD and a 20% incidence of central corneal guttae in the control group. We also found a significant association between the type of AMD and the occurrence of central guttae (p=0.05). However, we did not find any significance in the distribution of central corneal guttae among the 100 eyes in our study.
Conclusion
When a patient requiring cataract extraction or anterior segment surgery, presents with central corneal guttae, the successful outcome of the surgery may be compromised due to presence of AMD. Hence the presence of central corneal guttae may be used as a prognostic indicator. We also found that ICG videoangiography is useful in diagnosing occult CNV in 26.3% of the eyes that underwent the procedure.

References
Bilateral acute retinal necrosis with retinal detachment - a case report

Dr. Anand Rajendran, Dr. S.R. Rathinam

Introduction

Acute Retinal Necrosis (ARN) is a unique ocular inflammatory syndrome, one which has a propensity to involve the fellow eye and develop graver complications like retinal detachments, despite aggressive therapy. Hence, in this era of scientific advancement, it still presents a challenge to the modern ophthalmologist.

In 1971, Urayama and colleagues described ARN for the first time. Their report involved 6 patients with retinal vasculitis, vitritis and necrotizing retinitis. All these patients subsequently developed rhegmatogenous retinal detachment, the final visual acuity being poor. Initially termed “Kirisawa’s Uveitis”, the current nomenclature was derived from Young and Bird’s description of 2 cases of “Bilateral Acute Retinal Necrosis” or “BARN”.

We present a case report of a 63 year old immunocompetent male who presented to us initially with unilateral ARN which progressed to bilaterality and subsequently developed a rhegmatogenous retinal detachment in the first involved eye, despite optimal medical management.

Case report

The patient presented to us with rapid onset, progressive, mildly painful defective vision in the right eye of 15 days duration, associated with floaters and colored haloes. His previous ailment included - joint pains (for which he had been on chloroquine and steroids), low back pain, painful mouth ulcers, hearing defects and he had undergone thyroidectomy and appendicectomy in the past. The fellow eye was asymptomatic.

An ocular examination revealed visual acuity in the right eye of 1/60 NIGH (the left eye 6/24 improving to 6/6). The intraocular pressures were within normal limits. A slitlamp examination showed pigmented keratic precipitates; an anterior chamber of normal depth with a 1+ flare, 1+ cells; iris of normal color pattern; pupil of normal size and reacting to light and minimal lens changes. The posterior segment had - severe vitritis (3+), retinal vasculitis in all quadrants and peripheral circumferential confluent retinal infilrates.

A clinical diagnosis of acute retinal necrosis of the right eye led us to the following investigations – the blood counts, hemoglobin and ESR values were within normal limit. The VDRL titre was non-reactive and Mantoux negative. His previously recorded T3, T4, TSH, serum values of uric acid, calcium, phosphorous were normal. Other titres of HSV1, HSV2, HIV, RA factor, CRP, ANA factor were negative in yield. However, the HZV titre showed a positive result.

Acute retinal necrosis of Varicella Zoster etiology prompted us to augment I/V Acyclovir 500 mg, 3 doses for 3 days. The patient was discharged on request with subjectively improved vision [(R) eye -2/60] on a maintenance dose of oral Acyclovir 800 mg 5 times/day with tapered topical steroids.

First follow-up (2 weeks later)

Onset of mild blurred vision of fellow eye (left) with persistence of right eye status was reported despite strict compliance. Ocular examinations detected bilateral acute retinal necrosis (BARN), ARN being incipient in the left eye while the right eye showed mild resolution. I/V acyclovir 500 mg, 3

Aravind Eye Hospital and Postgraduate Institute of Ophthalmology
doses / day for 4 days and tapered over another 3
days. A corrected visual acuity of right eye – 6/60;
and left eye – 6/9 after a week of therapy justified
discharge on the same maintenance regimen.

Second follow-up (2 weeks later)
Significant amelioration in both eyes noted. Cor-
rected visual acuities of right eye -6/18, left eye -6/
9 was noted to be concomitant with improved fund-
dal pictures. The same regimen was continued.

Third follow-up (1 month later)
A dramatic loss of vision in the right eye (finger
counting) with maintained left eye status noted.
An extensive shallow rhegmatogenous retinal detac-
tachment involving the macula with 3 retinal holes
in the superior nasal sector of the right eye seen.
Although scleral buckling with pars plana
vitrectomy and silicon oil infusion was advised,
patient refused surgery and continued the same
medical therapy.

Last Visit (1 month later)
The patient’s visual acuity in the right eye had
deteriorated to faint perception of light with a total
retinal detachment. The left eye remained status
quo.

Discussion

Epidemiology
Widely reported now, ARN may occur in either
sex and has a bimodal age distribution peaking at
20 and 50 years. Although initially reported in the
immuno-compentent, ARN has now been docu-
mented in AIDS cases.

Aetiology
Culbertson and coworkers, in 1982, first demon-
strated herpes virus in retinal cells by electron mi-
croscopy. Varicella zoster virus, proven by culture,
serology, and immunohistochemical staining from
various ocular fluids, tissues is one of the chief
pathogens along with HSV1, HSV2 and rarely
CMV.4,5 Causation is probably by mutations in the
virus or changes in host susceptibility. Holland et
al proved a 50% association of HLA DQW7 with
ARN. Other HLA types implicated are BW62, DR4.

Clinical Features
Initially, mild ocular or periorbital pain
accompanied a partial loss with floaters. The anterior
segment may present with flare, cellular reaction,
keratic precipitates, posterior synechiae, iris
nodules, rarely a hypopyon and raised intraocular
pressures.

The posterior segment presents the diagnostic
clinical triad of retinal necrosis, vitritis and vasculitis.
Initially small retinal lesion begins as necrotic
“thumb prints” coalescing circumferentially in the
periphery.

Complications and Sequelae
Rhegmatogenous retinal detachments and pro-
liferative vitreo-retinopathy occur in 75% of cases.
Retinal tears consequent to vitreo-retinal traction
due to organization of the vitreous debris leads to
the retinal detachments.

Typically these retinal breaks occur in the regres-
sive phase even in cases of successful treatment
with antivirals.

Other sequelae – retinal branch arterial or venous
occlusion, retinal holes, macular edema, retinal op-
tic disc neovascularization, vitreous haemorrhage.

Differential Diagnosis
Progressive outer retinal necrosis (PORN), CMV
retinitis and large cell lymphoma vasculitis may
contribute to the diagnostic dilemma. The clinical
picture may be complimented by the investiga-
tions

• complete blood counts
• acute and convalescent serum titres to HSV 1 &
2, CMV, VZV.
• HIV titre
• Other tests – VDRL, Mantoux.

Aqueous, vitreous and endoretinal biopsy is indi-
cated in cases of poor therapeutic responses. FFA
to detect blockage of choroidal fluorescence in foc-
of retinitis, “cut off” intravascular patterns and USG
to detect retinal detachments in severe vitritis may
be used. CT & MRI for optic nerve sheath enlarge-
ment in optic neuritis.
Therapy
Medical – intravenous acyclovir is the drug of choice in an adult dosage of 1500 mg/m²/day in 3 divided doses for 5 to 10 days. A maintenance dose of 400 – 600 mg, 5 times a day up to 6 weeks is recommended, since most fellow eye affections, as in our case, occurs within this period. As proven in this case, the use of acyclovir lessen but does not abolish the development of ARN in the fellow eye. Systemic steroids 60 – 80 mg/d with topical steroids and cycloplegics counters the inflammation.

Lasers and surgical management
Prophylactic laser photoocoagulation posterior to areas of active retinitis precludes development of retinal detachment. Pars plana vitrectomy with or without scleral buckling has been used to treat retinal detachments.

Modern vitreous-retinal surgical technique proposed by Blumenkranz et al – Peyman et al have improved visual outcome in such cases.

References
Role of preservatives in Ophthalmology

Dr. A. Maghizh, Dr. N. Venkatesh Prajna

In ophthalmology the term preservative designates an agent that is added to a preparation to inhibit the growth of microorganisms, whereas in general pharmacology preservatives are considered agents that are added to prevent decomposition. Preservatives should not be used for single-dose solutions because they may cause severe irritation. They should be employed only in multiple-dose solutions, which tend to become contaminated with time. We herein present a case report to highlight the importance of preservatives in Ophthalmology.

Case report

A 35 years old male patient, diagnosed 5 years back as a case of dry eye and responding amicably to treatment as observed on routine follow ups, presented to our clinic with complaints of acute onset of redness, photophobia and defective vision over a period of 15 days.

Ocular examination showed circumcorneal congestion and increased punctate epitheliopathy. Suspecting a reaction to possible contamination from his medications, we examined the bottle and its contents. He had been using a preservative free sterile ophthalmic irrigating solutions for the past 5 years, since he found them more comfortable than artificial tear substitutes, which were later prescribed. The contents, as expected were turbid, with particulate and organized free floating debris. On subjecting these to a microbiological examination, unidentified dermataceous fungi and citrobacter species were cultured.

This brings to attention the significance of preservatives in ophthalmic solutions and the need to examine the dropper and bottle at every visit.

Fig-1 showing contaminated ophthalmic solution with organised free floating debris

Discussion

Topically applied tear supplements are the mainstay of therapy for aqueous tear deficiency, although other methods like preservation of existing tears and stimulation of tears are available. All the current treatment of aqueous tear deficiency are directed at providing symptomatic relief. Presently, there are no true therapeutic tear replacements with biological activity.

Most of the commercially available lubricating drops are aqueous solutions containing a polymeric agent such as polyvinyl alcohol, methylcellulose or dextran to increase viscosity.

The ideal means for preparing and distributing sterile ophthalmic solutions would be by marketing them in a single dose container without any preservative, after proper sterilization.
Several inherent problems accompany the use and distribution of single dose containers like the inconvenience of handling the containers for each application and high cost involved in manufacturing and distributing the individual items. It is for these reasons that most ophthalmic solutions in use are available in convenient multiple dose vials with added preservative.

The common preservatives used in ophthalmic solutions include Benzalkonium chloride, Chlorbutanol, Esters of hydroxy benzoic acid, Phenyl mercuric nitrate, Polymyxin, Thimerosal. Benzalkonium, the most common preservative is a cationic detergent which contains bacteriostatic rather than bactericidal activity.

**Objections to use of preservatives include**

1. Surface active quaternary ammonium germicide are unreliable against pseudomonas aeruginosa.
2. Inactivation by high molecular anionic detergents and soap and by natural rubber.
3. Incompatibility with certain ophthalmic drugs.
4. Antibacterial activity is interfered with by changes in PH.

Along with these the preservatives in artificial tear solutions can elicit contact sensitivity reactions. Some patients with dry eye must instill lubricating drops several times per hour to keep their symptoms tolerable. This frequency of instillation combined with reduced tear turnover makes these patients susceptible to ocular surface epithelial toxicity from preservatives in lubricating solutions particularly Benzalkonium chloride.

A study conducted by Hughson and Styron compared solution with and without Benzalkonium chloride. They were kept in open containers at room temperatures for 19 days during which time they were examined for the presence of viable organisms. All of the solutions without preservative were contaminated while those with the preservatives remained sterile.

As in our case, microbial contamination can be expected once the container is opened, which further increases when the dropper has been removed from the prescription vial. Contamination can also be expected through contact of dropper with an infected surface of eyelid/eye of the patient or another person who had previously used the same application. Contamination is evidenced by the ophthalmic solution becoming turbid, due to bacterial or fungal growth.

The advantages inherent with the preservative free solution, has made the ‘single dose disposable’ preparation more popular. This has allowed the patients to use these solutions as frequently as they desire, without experiencing ocular surface epithelial toxicity. Preservative free lubricants must be considered for all patients who feel they must instill their medications more than four times a day to relieve their symptoms. Thus wherever practicable, ophthalmic solutions should be dispensed in individual sterile single dose containers without an added chemical preservative.

The ophthalmologist should be aware that eye medications formulated with antiseptic “Preservatives” contain bacteriostatic rather than bactericidal concentrations of these drugs. Hence, appropriate precautions against contamination of the solution (with preservatives) during use are still necessary.

Since known chemical agents have certain shortcomings, in their antimicrobial spectrum or certain chemical incompatibilities and undesirable irritating effects, the search for the chemical agent that can fulfill the requirement of the “ideal” preservative must be continued.
Abstract from other Journals
Contributed by Dr. Vasu

Reversal of Optic Disc cupping after Glaucoma Surgery Analyzed with a Scanning Laser Tomograph
(Ophthalmology 1999; 106: 1013-1018)
Mark. R. Lesk. MD, George IL Spach. M.D.,
Augurto Azyuaro Blanco, M.D, Silvana V. et al

Objective
To detect and quantitate changes in optic nerve morphology after glaucoma surgery using the Heidelberg Retina Tomograph.

Participants and intervention
The authors prospectively enrolled 21 adult patients undergoing incisional glaucoma surgery for progressive glaucoma damage. Quantitative analysis of the optic nerve head by scanning laser tomography and automated perimetry were performed before and after glaucoma surgery.

Main outcome measures
Changes in optic nerve parameters were subjected to linear regression analysis with respect to percent of postoperative reduction of IOP, as well as with respect to age, refraction, pre-operative Cup: disc ratio, and change in visual field parameters.

Results
17 patients had pre and post-operative images suitable for analysis. Mean IOP at the time of image acquisition before surgery was 30.5 ± 12mmHg, and after surgery 11.8±5.2mm Hg (mean follow – up 26±7 weeks) 11of 13 (85%) patients having IOP reduction of greater than 40% showed improvement in optic disc parameters.

All four patients with less than 25% reduction in IOP showed worsening of most parameters. Changes in optic disc parameters were highly correlated with percent changes of IOP were cup area, rim area,

Cup: disc ratio, and mean cup depth (each, p<0.005) The age of the patient correlated highly with change in maximum cup depth (p<0.005). Refraction and clinical improvement in visual fields was correlated with the degree of improvement of cup: disc ratio (p=0.025)

Conclusion
Most patients showing a 40% lowering of IOP after glaucoma surgery show improved optic nerve morphology as measured by HRT. The amount of improvement correlated highly with the percent reduction of I.O.P.

Cataract Surgery with Ciliary Sulcus Fixation of IOL in patients with Uveitis

Purpose
To describe intentional placement of IOL haptics in the ciliary sulcus of patients with Uveitis who are at high risk for postoperative posterior synechiae and lens dislocation.
Methods
16 eyes of 12 patients with uveitis who underwent cataract surgery with ciliary sulcus fixation of IOL were reviewed. Patients were followed for a median of 16.5 months (range, 9 to 44 months) after surgery. Eyes were evaluated for surgical technique and the following preoperative and postoperative factors: best-corrected visual acuity, IOP, anterior chamber cells, and posterior synechiae. The following additional postoperative factors were sought: lens dislocation, lens edge capture, and evidence of pigment dispersion.

Results
- Posterior synechiae were present in 13 eyes before surgery; postoperative posterior synechiae developed in only three of these eyes. These adhesions resulted in lens edge capture in one eye and limited lens decentration in another. Scant pigment was present on the lens optic or in the anterior chamber, suggesting pigment dispersion, in four eyes. There was no evidence of consistently increased anterior segment inflammation or IOP after surgery when compared with preoperative levels for this group of patients. Postoperative posterior synechiae were seen most after in eyes that had can-opener anterior capsulotomy than in eyes that had continuous curvilinear capsulorrhexis.

Conclusions
Ciliary sulcus fixation allows the IOLs to serve as a physical barrier between the iris and the lens capsule remnants. This technique may be useful for reducing the risk of postoperative posterior synechiae in patients with uveitis without increasing the risk of other postoperative problems.

Mitomycin – C in combined or Two stage procedure Trabeculectomy Followed by penetrating keratoplasty
Itay Chowers, MD, and Uriel Ticho, MD. (Journal of Glaucoma 8: 184-187; 1999)

Purpose
To evaluate the efficacy and safety of application of mitomycin - C in combined and separate trabeculectomy and penetrating keratoplasty for the treatment of coexisting corneal disease and glaucoma.

Methods
A retrospective evaluation of 11 eyes of 10 patients was conducted. A combined trabeculectomy with MMC and penetrating keratoplasty procedure was performed in eight eyes (group 1) and keratoplasty was performed after a previous trabeculectomy with MMC in 3 eyes (group 2).

Results
In group 1, 7 of the 8 eyes had controlled IOP and clear corneal graft at the end of the follow-up period (range, 5-60 months, mean duration - 16.7 months). In group 2, all three eyes had controlled IOP at the end of the follow-up period (range, 4-30 months; mean duration, 14 months) two of these patients had clear corneal grafts, and graft failure occurred in the remaining patient. Complications included transient flat anterior chamber and progressive cataract, which occurred in a single eye in group 2.
Conclusions
Mitomycin – C was found to be safe and efficacious in the present series, controlling IOP in 10 of 11 eyes (91%) with coexisting Corneal disease and glaucoma. The transplanted corneas remained clear in 9 of 11 eyes (82%). Complications related to MMC included a reversible epithelial defect that occurred in one eye.

Tolerance of Extended - Term Vitreous Replacement with perfluoro-N-Octane and perfluoroperhydrophenanthrene Mixture (Phenoctane)
(Chaning Liang, M.D., Gholam. A. Peyman, M.D. Retina 19: 230-239, 1999)

Purpose
To improve the surface visibility of perfluoroperhydrophenanthrene, various percentages of perfluoro-N-Octane were added.

Methods
20 New Zealand white rabbit eyes underwent gas vitrectomy. One milliliter of balanced salt solution was injected into each group1 eye as control. Perfluoro-N-Octane was added to Perfluoroperhydrophenanthrene in ratios of 15:85, 25:75, and 50:50; 1ml of each mixture was injected into the vitreous cavities of Groups 2, 3 and 4, respectively. Eyes were examined clinically and electrotetrograms were performed before and 4 and 8 weeks after injection, when the rabbits were killed. Eyes were processed for light and transmission electron microscopy.

Results
The indices of refraction of the 15:85, 35:75 and 50:50 mixtures were 1.3275, 1.3191 and 1.3026, respectively, and the mixtures were visible in the vitreous cavity. Emulsification and mild to moderate dust – like opacities were observed in eyes from groups 2 through 4; vitreous strands formed in four of the group 4 eyes. The retinae were attached. ERG responses were normal, except in one eye with cataract. Light microscopy showed normal retinal architecture, with some macrophages with intracytoplasmic vacuoles on the surface of the inferior retina or in the vitreous cavity. Fingerprint disfigurement of photoreceptor outer segments were seen in some group 3 and 4 eyes under TEM.

Conclusions
Minimal changes were induced by the 15:85 mixture in the rabbit eye. The mixture of 25:75 and 50:50 produced some ultrastructural changes of the retina. The mixtures were visible under water.

Split thickness buccal mucous membrane grafts and B Irradiation in the treatment of recurrent pterygium

Background
Pterygium is a common problem and after surgical removal may recur in up to 80% of cases, depending on the technique of primary excision. Recurrent pterygia may result in severe conjunctival scarring and shortening, resulting in insufficient conjunctiva to perform further grafting and lid surgery. When there is insufficient autologous conjunctiva, mucous membrane grafts have been described, but they may result in a beefy red appearance, with graft contraction and a poor tear film.
Method
The use of split thickness buccal mucous membrane grafts is described in three patients with recurrent pterygium, two in combination with lamellar keroplasty. β irradiation was used as adjuvant therapy in all cases.

Results
In all three cases an acceptable cosmetic appearance was achieved, with no recurrence of the pterygium, and a good range of eye movements.

Conclusions
It is recommended that split thickness buccal mucosal grafts, combined with b irradiation, should be considered in complex cases of pterygium recurrence when there is insufficient autologous conjunctiva and conjunctival shortening with restricted eye movements.