**DEWS DRY EYE: DIAGNOSTIC TEST TEMPLATE**

**RAPPORTEUR**
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**TEST**
Grading staining: Oxford Schema

**TO DIAGNOSE**
The scheme is used to estimate surface damage in dry eye.

**VERSION of TEST**
[ V 1 ]

**DESCRIPTION**
Surface damage to the exposed eye, assessed by staining, is graded against standard charts.

**NATURE of STUDY**
N. A.

**CONDUCT of TESTS**
Grading Schema:
Staining is represented by punctate dots on a series of panels (A-E). Staining ranges from 0-5 for each panel and 0-15 for the total exposed inter-palpebral conjunctiva and cornea. The dots are ordered on a log scale

<table>
<thead>
<tr>
<th>PANEL</th>
<th>GRADE</th>
<th>CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0</td>
<td>Equal to or less than panel A</td>
</tr>
<tr>
<td>B</td>
<td>I</td>
<td>Equal to or less than panel B, greater than A</td>
</tr>
<tr>
<td>C</td>
<td>II</td>
<td>Equal to or less than panel C, greater than B</td>
</tr>
<tr>
<td>D</td>
<td>III</td>
<td>Equal to or less than panel D, greater than C</td>
</tr>
<tr>
<td>E</td>
<td>IV</td>
<td>Equal to or less than panel E, greater than D</td>
</tr>
<tr>
<td>&gt;E</td>
<td>V</td>
<td>Greater than panel E</td>
</tr>
</tbody>
</table>

Conduct of Test:
- Dye is instilled.
- Slit-lamp is set (eg. 16 magnification with x10 oculars with Haag-Streit).
- Cornea: The upper eyelid is lifted slightly to grade the whole corneal surface,
- Conjunctiva: To grade the temporal zone, the subject looks nasally; to grade the nasal zone the subject looks temporally.
- (The upper and lower conjunctiva can also be...
Selection of dyes:
A list of dyes can be found in the original paper. With fluorescein, staining must be graded as quickly as possible after instillation, since the dye then diffuses rapidly into the tissue and its high luminosity blurring the stain margin.

Staining after rose bengal or lissamine green, persists at high contrast and may therefore be observed for a considerable period. This is convenient for both grading and photography.

Fluorescein sodium
1. Quantified drop instillation
   eg 2 μl of 2 % sterile fluorescein instilled into each conjunctival sac with a micro-pipette (using a sterile tip). In very dry eye, larger volumes risk the possibility of inadequate dilution into the fluorescent range.

2. Unquantified instillation – impregnated paper strips
   This is a convenient approach in the clinic using the following method of application:
   - A single drop of unit dose saline is instilled onto a fluorescein-impregnated strip.
   - When the drop has saturated the impregnated tip, the excess is shaken into a waste bin with a sharp flick.
   - The right lower lid is then pulled down and the strip is tapped onto the lower tarsal conjunctiva. A similar procedure is carried out on the left.

   If too large a volume is delivered then the concentration in the tear film will be too high, and the tear film and staining pattern will be non-fluorescent.

3. Timing
   The fluorescein break-up time (FBUT) is usually performed prior to grading. Since fluorescein diffuses rapidly into tissues, punctate staining blurs after a short period. It is therefore essential to assess staining rapidly, in sequence, in the right and then the left eye, so that the staining patterns observed are equally crisp.

   If it is intended to photograph the staining pattern for grading, then photography should follow immediately after each instillation.

Exciter and Barrier Filters
The absorption peak of fluorescein sodium occurs between 465 - 490 nm and the emission peak between 520 - 530 nm. A suggested filter pair for detection of fluorescein staining is a yellow, Kodak Wratten 12 barrier filter (transmitting above 495 nm) or an orange Wratten 15 filter (transmitting above 510 nm) in combination with a blue Wratten 47 or 47A exciter filter. The 47A shows greater transmittance than the Wratten 47 over the absorption range. The ‘cobalt’ filter of many slit-lamps is suitable to use with a Wratten 12 or 15
barrier.

Where more light is required for photographic purposes, narrow band-pass, interference filters can be used.

The use of both exciter and barrier filters allows both the cornea and conjunctiva to be assessed using a single stain. This is a major advantage in clinical trials where it is otherwise customary to employ fluorescein to grade corneal staining and rose bengal or lissamine green to grade conjunctival staining.

Disadvantages of Fluorescein Staining
Blurred pattern if reading is delayed. Delay in photographing fluorescein staining results in blurred images of the staining pattern.

Rose Bengal
The intensity of rose bengal staining is dose dependent. If drop size or concentration is reduced to minimize stinging, the amount of staining is also reduced. Use of impregnated strips will give weaker staining than use of a full drop of 1% solution. Best results are achieved with, eg. 25 µl 1%, instilled into the conjunctival sac. Because rose bengal stings, instillation is best preceded by a topical anesthetic.

Instillation Technique
1) eg. A drop of Proxymetacaine is instilled into the conjunctival sac followed, after recovery, by;
2) A drop of rose bengal 1.0%. This is instilled onto the upper bulbar conjunctiva with the upper lid retracted and the patient looking down.
3) Since both anaesthetic and drop may stimulate reflex tearing, the test should follow measurement of the FBUT and of the Schirmer test. (Conjunctival staining due to insertion of the Schirmer paper can usually be distinguished from that due to dry eye disease).

Both eyes may be stained prior to grading, since there is no risk of the staining pattern in the first eye being obscured by the time the second eye is graded.

The cited paper gives advice about avoidance of overspill.

Visibility
Rose bengal staining on the conjunctiva shows up well against the sclera and may be enhanced using a red-free (green) light source. Corneal staining may show up well against a blue iris, but is difficult to see against a dark brown iris.

Phototoxicity
Photo-activation of rose bengal by sunlight increases post-instillation symptoms, especially in severe dry eye with heavy staining. This post-instillation pain can be minimised
Lissamine green stains the eye in a similar manner to rose bengal but is as well tolerated as fluorescein. Visibility and dose-dependency are the same as rose bengal and staining is persistent so that photography need not be performed immediately after instillation. Lissamine green is available as impregnated strips or may be ordered as a pre-prepared solution. A 25 μl 1% drop will give more intense staining. Because the drop is well tolerated, no anaesthetic is required.

Visibility
As with rose bengal, lissamine green staining is easily visible on the conjunctiva. On the cornea, staining is seen well against a light blue iris background but is poorly visible against a dark brown iris background. For both rose bengal and lissamine green, because the dyes are poorly seen within the tear film, the dye in the tear film does not obscure the staining pattern. Also, since both dyes do not diffuse into the substantia propria of the conjunctiva, the staining pattern is retained for longer.

Visibility of staining may be enhanced using a white light source and a red barrier filter, to give a black pattern on a red ground. A suitable filter is a Hoya 25A, or a Kodak Wratten 92.

Repeatability
A small intra-interobserver study was carried out in 1986 and was presented but not published:

**Intra-observer study:** This study asked two trained ophthalmologists to grade a series of standard slides, showing corneal and conjunctival fluorescein staining, on 2 separate occasions. [note: -this study is only relevant to grading photographic records not patients.]

<table>
<thead>
<tr>
<th></th>
<th>Cornea</th>
<th>Conjunctiva</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observer 1</td>
<td>0.86</td>
<td>0.69</td>
</tr>
<tr>
<td>Observer 2</td>
<td>0.65</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Not that values are in the good to excellent range.

**Inter-observer study:** In this study, the same 2 observers
graded fluorescein staining (blue exciter; yellow filter) in 13 dry eye patients at an interval within 2-3 weeks.

Inter-observer κ for grading patients with dry eye, using the Oxford scheme. Two observers. Fluorescein; bengal rose

<table>
<thead>
<tr>
<th>Observer 1 v 2</th>
<th>Cornea</th>
<th>Conjunctiva</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluorescein</td>
<td>0.88</td>
<td>0.48</td>
</tr>
<tr>
<td>Bengal rose</td>
<td>0.87</td>
<td>0.54</td>
</tr>
</tbody>
</table>

It is of interest that observations are in the excellent category for cornea, with either stain and in the fair category for conjunctiva.

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>(true positives)</th>
<th>[ - ]</th>
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<tbody>
<tr>
<td>Specificity</td>
<td>(100 – false positives)</td>
<td>[ - ]</td>
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References: