

<b>DEWS</b>	<b>DRY EYE: DIAGNOSTIC TEST TEMPLATE</b>	
<b>RAPPORTEUR</b>	A.J.Bron	18 <sup>th</sup> Oct 2004
<b>TEST</b>	<b>Mixed tests</b>	
<b>TO DIAGNOSE</b>	Ocular Irritation / Dry Eye	REFERENCES
<b>VERSION of TEST</b>	Multiple tests	Pflugfelder et al. 1998
<b>DESCRIPTION</b>	Evaluation of Subjective and Objective tests for diagnosing tear-film disorders known to cause ocular irritation.	
<b>NATURE of STUDY</b>	<p>40 adults with ocular irritation: (SSATD (11); NSATD (9); inflamm MGD (<b>rosacea</b>) (10); atrophic MGD (10). 10 normals</p> <p>Controls and SSATD were of younger age. SSATD less males than controls or inflamm MGD</p> <p><b>Summary of Results:</b></p> <p>Symptoms more severe in the SS group.</p> <p>FBUT shorter in ATD, MGD groups than controls.</p> <p>Schirm. Lower in ATD than MGD or controls.</p> <p><b>Tear Clearance</b> delayed in ATD and MGD</p> <p>Non-invasive grid distortion in ATD not MGD or controls.</p> <p>SS group More: loss of nasolacrimal reflex Schirmer; lower clearance, greater F and RB stain.</p> <p><b>Schirmer scores</b> correlated inversely with RB stain, corneal fluoresce stain, grid distortion.</p> <p><b>RB stain</b> correlated with grid distortion and loss of nasolacrimal reflex but not with MGD.</p> <p><b>Statistical Tests used were:</b> Among group Kruskal wallis; Wilcoxon/Mann-Whitney; ANOVA; Fisher's least significant difference; Fisher's exact test; t-test; Kendall's <math>\tau</math> non parametric correlation analysis; Spearman correlation analysis.</p> <p>Schirmer test: worse and fellow eye</p> <p>BUT, Stain, corneal sensation: Scores averaged for two eyes</p>	Pflugfelder et al. 1998
<b>CONDUCT of TESTS</b>	<p>Various Tests.</p> <p>On the day of examination, subjects rated their symptoms;</p> <p><b>Symptom of ocular irritation:</b></p> <p>Burning/stinging</p> <p>Mucus discharge</p> <p>Itching</p> <p>FB sensation</p> <p>Blurred vision</p> <p>Dryness</p> <p>Soreness (pain)</p> <p>Photophobia</p> <p><b>5 point Scale of Symptoms:</b></p> <ul style="list-style-type: none"> <li>▪ 0 = No discomfort</li> <li>▪ 1 = trace</li> <li>▪ 2 = mild</li> <li>▪ 3 = moderate</li> </ul> <p>4 = severe</p> <p><b>TESTS</b></p> <p><b>Biomicroscopy</b></p> <ul style="list-style-type: none"> <li>▪ Inferior meniscus debris, mucus,</li> </ul>	Pflugfelder et al. 1998

	<ul style="list-style-type: none"> <li>▪ Lid irreg</li> <li>▪ Lid/bulb hyperaemia</li> <li>▪ Corneal PEE/ adherent mucus/ filaments</li> </ul> <p><b>MGD</b>  <b>METAPLASIA:</b> white protruding shaft  Expression from 5 central lower glands:  0 = all 5 expressible                      Quality not graded  1 = 3-4 expressible  2 = 1-2 expressible  3 = no glands expressible</p> <p><b>MEIBOGRAPHY</b> of nasal and temporal <b>halves</b> of the lower lid:  <ul style="list-style-type: none"> <li>▪ 0 = no drop out                      eye values averaged</li> <li>▪ 1 = ≤33%</li> <li>▪ 2 = 34-66% drop out</li> <li>▪ 3 = 67-100% drop out</li> </ul> </p> <p><b>XEROSCOPY</b>  Masked evaluation of videotaped NIBUT</p> <p><b>FLUORESCEIN BUT</b>  Infero-temporal bulbar conjunctiva touched with Fluoret wetted with preservative free saline, then blink. Eyes averaged.</p> <p><b>FLUORESCEIN STAINING</b>  Staining observed with a blue light without a yellow filter  4 point scale: 'Standardized for cornea and conjunctiva'</p> <p>0 = none                      for temp/nasal/inferior bulbar + cornea  1 = mild                      Max possible score was 12  2 = moderate  3 = severe</p> <p><b>ROSE BENGAL STAINING</b>  20µl of 1% rose bengal instilled. <b>No source or details of instillation provided.</b>  4 point scale: 'Standardized for cornea and conjunctiva'</p> <p>0 = none                      for temp/nasal/inferior bulbar + cornea  1 = mild                      Max possible score was 12  2 = moderate              (Minus inferior score = van Bijsterveld0  3 = severe</p> <p><b>SCHIRMER TEST</b>  Standard:  Without anaesthesia  Eyes open  Short part placed over lower lid margin at junction of middle and lateral third  Read at 5 minutes</p> <p><b>FLUORESCEIN CLEARANCE TEST</b>  Instill 5µl of Fluress (concn not stated)</p>	<p>Pflugfelder et al.  1990 E B virus</p>
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	<p>Standard Schirmer strip over lateral lower lid margin for 1 min at 10, 20 and 30 minutes. Strip removed and evaluated for fluorescence under a blue light.</p> <p><b>NASAL-LACRIMAL REFLEX TEARING</b>  Method:  After removing the Schirmer strip following the 30 min clearance test :  Nasal mucosa stimulated with a dry cotton swab (time?) on the side with the lowest Schirmer value.  Then <b>Schirmer strip inserted for 1 minute.</b>  A Schirmer value greater than 1 mm more than the 30 min value.</p> <p>Serum tests  ANA ≥ 1: 160; RhF ≥1:160; +ve Anti Ro and Anti La</p>	Tsubota 1991 AJO
<b>RESULTS of STUDY</b>	<p>Many symptoms were experienced by subjects in al 4 groups.</p> <p><b>Film:</b> SSATD : Greater debris and mucus than all other groups  <b>Lid hyperaem</b> All dis except SSATD had &gt; hyperaemia (p≤0,033) than control. Inflamm MGD &gt; SSATD (p≤0,008)  <b>Lid irreg:</b> Inflamm MGD . SSATD or control (p≤0,009; and p≤0,023)  <b>Tarsal injn:</b> Inflamm MGD&gt; SSATD (p=0.03)  <b>Tarsal injn:</b> InflammMGD&gt;atrophMGD (p≤0.020) or control (p≤0.003)  <b>Mucus adher:</b> SSATD &gt; MGD or control  <b>MGMetaplas:</b> NSATD and MGD &gt; controls (p≤0.033)  MGD &gt; SSATD (p≤0.03)  <b>MGExpressn:</b>  <b>Lower lid:</b> All disease group had fewer expressible glandsthan controls (p≤0.006).  <b>Upper lid:</b> All but SSATD had fewer expressible. (p≤0.009) (note younger age of SS pts)  Both lids: InflammMGD fewer expressible than SSATD  Upper lid: Atroph MGD fewer expressible MG than SSATD</p> <p><b>Drop out:</b> All nasal and temp drop out values greater for MGD than for controls (p≤0.0001) and nonSSATD (p=0.004).  <b>InflammMGD</b> greater loss than nonATD (p=0.05)  NonSSATD and MGD more med lat loss than SSATD (p≤0.03)</p> <p>Grid distortion: number assessed from each group unclear?</p> <p><b>FBUT:</b>  All ATD and MGD shorter BUT than controls (p≤0.001)  SSATD shorter BUT than atrophMGD(p≤0.016) and nonSSATD was shorter than inflame (p≤0.049) and atrophMGD(p≤0.011)</p> <p><b>FLUORESCCEIN STAIN:</b> Scores were meaned for each site</p>	

for 2 eye  
 SSATD staining > all other groups. (p≤0.009)  
 Global staining: NonSSATD > CONTROLS. (p≤0.021)  
 Global staining: InflammMGD > controls. (p≤0.021)  
 Nasal Stain: SSATD >all groups staining > all other groups.  
 (p≤0.009)  
 Infer Stain: SSATD > MGD and controls staining > all other  
 groups. (p≤0.045)  
 Cornea Stain: SSATD > all other groups. (p≤0.034) (Controls  
 less than nonSSATD and inflammMGD

**ROSE BENGAL STAIN:** 2 eye Scores were meaned for  
 each site.

Global score: SSATD > all groups (p≤0.038)  
 Infer stain: nonSSATD > control (p≤0.032)  
 Corn stain: nonSSATD > control (p≤0.001)  
                   inflammMGD > control (p≤0.015)  
                   atrophMGD > control (p≤0.032)

Van Bijsterveld score:  
 Global score: nonSS > controls (p≤0.037)

Group	Conjunctiva			Cornea	Total
	Nasal	Temp	Inf		
SSATD					7.8±2.67
NSSATD					2.2±1.95
InflMGD					1.4±1.53
AtrMGD					1.3±1.70
Control					0.5±0.50

Rose bengal data:

“Total” scores out of 12.

**STAIN CORRELATIONS:** (Fig 11)

Global Fluor score strongly correlated with RB score  
 (Spearman correlation coeff = 0.807; p , 0.001).

RB score correlated with grid distortion (p≤0.001 t-test)

RB score correlated with loss of naso-lacrimal reflex  
 (p≤0.001 t-test)

RB score not correlated with MGD features.

**SCHIRMER TEST:**

Worse eye Schirmer scores lower for nonSS- and SSATD  
 groups than for MGD and controls (p≤0.001)

Fellow eyes similar, but SSATD fellow eyes scores lower  
 than for nonSSATD (p=0.02).

Inflam Sch scores < atrophicMGD scores (p=0.04)

**SCHIRMER CORRELATIONS:**

Schirmer scores correlated inversely with:  
 Total fluorescein scores (Kendall’s τ – 0.505; p< 0.001)

(Pflugfelder et al.  
 1997)

	Total Rose bengal scores (Kendall's $\tau = 0.474$ ; $p < 0.001$ ) (Stain and Schirmer scores meaned from both eyes?)  <b>MUCIN</b> Previous study showed normal goblet cell densities and epithelial mucin (Pflugfelder et al. 1997) <b>CLEARANCE</b> <b>Controls: Zero % showed retention at 20 minutes</b> <b>SSATD :100%</b> <b>NonSSATD :77.8%</b> <b>AtrMGD :70%</b> <b>InflMGD :40%</b>	
<b>Video need</b>	Yes: [ ] No: [ ] .	
<b>Materials:</b>	<ul style="list-style-type: none"> <li>• Wech Allyn Finhoff transilluminator for meibography</li> <li>• Xeroscope</li> <li>• Smith and Nephew Fluorets (now Chauvin)</li> <li>• Unisol Alcon Preservative-free saline</li> <li>• Schirmer papers: Iolab Corporation</li> <li>• Fluress fluorescein soln: Sola Barnes-Hind</li> </ul>	
<b>Standardization</b>	Different requirements for each test.	
<b>Repeatability</b>	Intra-observer agreement. [ - ] Inter-observer agreement. [ - ]	
<b>Sensitivity</b>	<b>(true positives)</b> [ - ]	
<b>Specificity</b>	<b>(100 – false positives)</b> [ - ]	
<b>Test problems</b>	Note: simple staining scoring. Note: averaging of non-parametric data. SS patients younger than other groups	
<b>Glossary</b>	ATD = aqueous tear deficiency SSATD = Sjogren's Syndrome ATD MGD = here used for Meibomian gland disease, not dysfunction	

## References

Pflugfelder S C, Tseng SC, et al. (1990). Epstein-Barr virus infection and immunologic dysfunction in patients with aqueous tear deficiency. *Ophthalmology* 97(3): 313-23.

Pflugfelder SC, Tseng SC, et al. (1997). Correlation of goblet cell density and mucosal epithelial membrane mucin expression with rose bengal staining in patients with ocular irritation. *Ophthalmology* 104(2):223-35.

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