DEWS	**DRY EYE: DIAGNOSTIC TEST TEMPLATE**	
RAPPORTEUR	A.J.Bron	21st Oct 2004
TEST	**A preferred sequence of tests**	
TO DIAGNOSE	Dry Eye	REFERENCES
VERSION of TEST	[V 1]	Bron et al. 2003
DESCRIPTION	A general approach to the sequence of tests employed	
NATURE of STUDY	N. A.	
SEQUENCE of TESTS	The order of tests used in dry eye diagnosis is critically important since each test may influence the next. In general it is good practice to work from the least invasive to the most invasive test. The following clinical tests are presented in order of increasing invasiveness. This is not a comprehensive list, but simply a representative sample of tests frequently performed. Since some of the tests are mutually exclusive, it is not suggested that all tests in each section should be performed. Some tests may have to be performed on separate days. **1. Symptoms and History** A record is required of clinical history and ocular symptoms. A number of authors have developed validated questionnaires for the assessment of dry eye.[24,25,26,27,28,29] None of these questionnaires attempt to distinguish symptoms arising specifically from the lids (as might occur in blepharitis) from those arising solely from the ocular surface. **2. Non-invasive tests** A number of tests are regarded as non-invasive although since they involve patient positioning and examination with a light source it must be accepted that there may be a minimally invasive element. It is likely too, that timing of the tests may determine whether they are conducted in steady-state conditions. Standardization of the environment and conditions of measurement are most likely to reduce such variation. ▪ The non-invasive tear break up test (NIBUT) was created to measure the stability of the pre-corneal tear film.[30] It involves projection of a target onto the convex, mirror surface of the tear film and recording the time taken for the image to break up after a blink. The test was originally performed with a custom-built 'Toposope', but has also been performed using the keratometer.[31] TearscopePlus™ .[32] and Xeroscope which is commercially available.# ▪ Tear film lipid layer interferometry examines and grades tear film lipid thickness on the basis of the observed	Bron et al. 2003 Reference numbers refer to the above paper.

	interference colours and patterns. Currently available apparatus includes the TearscopePlus™ and the Kowa DR-1 (specular reflection video recording system).[33] ▪ Reflective meniscometry is used to measure the curvature of the lower tear meniscus, from which meniscus volume can be approximately calculated and total tear sac volume inferred.[34,35] **3. Minimally invasive tests.** The following tests may be performed immediately after the performance of non-invasive tests. **Tear sampling:** The degree of invasiveness depends on the size of sample taken and the amount of lid manipulation which occurs. Some samples (eg. for osmolarity measurements) can be extremely small, eg. 200 nL. **Fluorescein instillation:** Certain tests involve the instillation of fluorescein. As noted earlier the amount instilled can be controlled using a micro-pipette. ***Fluorescein tear break-up time is a measure of tear film stability.[36,37] The timing of break-up of the pre-corneal tear film after the blink is recorded*** ***Grading staining after fluorescein instillation has already been discussed. As noted, the FBUT and staining patterns should be recorded in sequence first on one eye and then on the fellow eye, recording the FBUT first.*** ***Meniscus profile can be photographed after fluorescein instillation and used to estimate meniscus volume and related parameters following a suitable interval after fluorescein instillation.[38]*** ***Instillation of fluorescein is required for the measurement of tear turnover using fluorophotometry and other methods of tear fluorescein clearance. [39,40,41,42,43]*** Studies of the inferior tear meniscus have indicated that, in normal eyes, without punctal occlusion, tear meniscus height is restored to normal within 5 minutes after the instillation of a 5µl drop of normal saline. [44] *On the basis of this, a 5 minute gap is recommended before the next tests.* **4. Mildly invasive tests** ▪ Meibometry is a quantitative method for the measurement of the basal, or casual, meibomian lipid levels on the lid margin. It involves application of a plastic loop to the middle third of the slightly everted lower lid. The change in optical density produced by the lipid imprint is used as an index of the casual lipid	

level.[45] Modification of this technique to measure lipid delivery involves baseline removal of lipid using a lipid solvent.[46] This will induce reflex tearing and is moderately to markedly invasive.

A 5 minute gap is recommended before the next set of tests.

5. Moderately invasive tests.

A number of tests involve the insertion of a wick into the lower conjunctival sack and measurement of wetting length over a defined period of time.

- The phenol red thread test (PRTT) is acknowledged to be less invasive than the Schirmer test. The wetting of a cotton thread was originally regarded as an index of tear volume[47,48], probably influenced by the balance between negative hydrostatic pressure in the meniscus and the capillary action of the thread [49,50].

6. Markedly invasive tests

- The Schirmer I test without anesthetic uses standard filter papers to assess reflex tear production.[51,52] Insertion of the filter paper causes surface epithelial damage at the site of insertion, which will stain with dyes (e.g. rose bengal). This damage also results in the leakage of plasma proteins into the tear fluid.[53]
- The Schirmer I test of basal tear secretion with anaesthetic resembles the test without anaesthesia except that it involves the instillation of an unspecified volume of topical anaesthetic prior to the test, which is mopped out of the conjunctival sac prior to the test.[54] The efficiency of the latter maneuver in removing fluid is not known and no validation of the Schirmer test with anaesthetic appears to have been reported.

The Schirmer II test measures the tear response to nasal stimulation.[55,56]

7. Additional Invasive Tests

Lissamine green and rose bengal dyes, using either drops or impregnated strips, may be regarded as moderately to markedly invasive tests since, they induce reflex tearing. Instillation of rose bengal, as discussed earlier, must be regarded as a highly invasive test, which, in the absence of anaesthesia, induces pain and marked reflex tearing

8. Lid assessment and meibometry

Clinical assessment of the lid margins, oil glands and tarsal conjunctiva involves significant lid manipulation, which must be assumed to induced reflex tearing. This

	applies to a lesser extent, to the performance of meibography.[57] Therefore such tests must be performed at the end of an examination sequence. A similar argument applies to the assessment of tear oil quality, which involves expression of the oil by pressure through the lids.[58] **9. Other Ocular Assessments** For clinical trials purposes it is usual to include a full assessment of the anterior segment (including eversion of the upper lids), measurement of the intraocular pressure and an assessment of the media and fundus oculi, with or without mydriasis. These tests would normally be performed at the end of the 'dry eye' sequence, or at a separate visit.	
RESULTS of STUDY	N. A.	
Web Video	NA	
Materials:	according to cited test	
Standardisation	according to cited test	
Variations of technique	according to cited test	
Diagnostic value	NA	
Repeatability	NA	
Sensitivity	NA	
Specificity	NA	
Other Stats	NA	
Test problems	NA	
Test solutions	NA	

References:

Bron AJ, Evans VE, et al. (2003). Grading of corneal and conjunctival staining in the context of other dry eye tests. *Cornea* 22(7): 640-50.