

DEWS	DRY EYE: DIAGNOSTIC TEST TEMPLATE	
RAPPORTEUR	Alan Tomlinson	10 th Jan 2006
TEST	Fluorophotometry (Fluorimetry) - Tear Flow	
DIAGNOSES	Changes in tear flow in aqueous tear deficiency (ATD).	REFERENCES
VERSION of TEST	[Version 1] Scanning automated fluorophotometry (Fluorotron Master, Coherent Inc, Palo, Alto, CA)	
DESCRIPTION	<u>To calculate tear flow from measurements of tear volume and turnover.</u>	
CONDUCT of TEST	<p><u>Tear Turnover Rate</u></p> <ol style="list-style-type: none"> 1) Subject is seated at the chin rest of the Fluorotron (with the anterior segment adapter fitted). Horizontal and vertical adjustments are made to align the subject's eye in the instrument's optic beam. 2) Three scans are conducted to establish the intrinsic corneal autofluorescence. 3) A 1 µl drop of 2% sodium fluorescein is instilled into the lower fornix with a pipette. 4) Initial scans are taken 1 minute post instillation, then at 2 minute intervals for a further 20 minutes. 5) The intrinsic corneal autofluorescence value is subtracted from all values obtained from tear film fluorescence, prior to data analysis. 6) Fluorescein concentration at each time point is calculated from the Fluorotron scans obtained at all time points beyond 4 minute post instillation, to avoid initial reflex tearing caused by instillation. 7) The decay in fluorescence is calculated from the log of the curve obtained from the formula: $T_0(t_0) = 100 \frac{[C_t(t_0) - C_t(t_0+1)]}{C_t(t_0)} \quad (\%/min)$ <p>Where $C_t(t)$ = fluorescein concentration in tear film at time t(min).</p> <p>Assuming a monophasic decay of fluorescence from 5 mins post instillation with a decay time constant β (min^{-1}):</p> $C_t(t) = C_t(0).e^{\beta t} \quad (ng/ml)$ <p>the following is obtained:</p> $T_t(t_0) = 100 (1 - e^{\beta t_0}) \quad (\%/min)$ <p>This calculation can be carried out using the software package ANT_SEGMENT tear.</p> <p><u>Tear Volume</u></p> <ol style="list-style-type: none"> 1) Subject is seated at the chin rest of the Fluorotron (with the anterior segment adapter fitted). Horizontal and vertical adjustments are made to align the subject's eye in the instrument's optic beam. 	<p>Kuppens, 1992 Van Best, 1995</p> <p>Van Best, 1995</p> <p>Kuppens, 1992</p>

	<p>2) Three scans are conducted to establish the intrinsic corneal autofluorescence.</p> <p>3) One μl of 2% sodium fluorescein is instilled into the lower fornix with a pipette.</p> <p>4) Initial scans are taken 1 minute post instillation, then at 1 minute intervals for a further 4 minutes.</p> <p>5) The intrinsic corneal autofluorescence value is subtracted from all values obtained from tear film fluorescence, prior to data analysis.</p> <p>6) Fluorescein concentration at each time point is calculated from all the Fluorotron scans obtained.</p> <p>7) The decay in fluorescence is calculated from the log of the curve obtained from the formula:</p> $T_0(t_0) = 100 \frac{[C_i(t_0) - C_i(t_0+1)]}{C_i(t_0)} \quad (\%/min)$ <p>Where $C_i(t)$ = fluorescein concentration in tear film at time t(min).</p> <p>Assuming a monophasic decay of fluorescence from 5 mins post instillation with a decay time constant β (min^{-1}):</p> $C_i(t) = C_i(0) \cdot e^{-\beta t} \quad (\text{ng/ml})$ <p>the following is obtained:</p> $T_i(t_0) = 100 (1 - e^{-\beta t_0}) \quad (\%/min)$ <p>This calculation can be carried out using the software package ANT_SEGMENT tear.</p> <p>Tear volume is then calculated from:</p> $V_t = (C_d \cdot C_m^{-1} \cdot k^{-1} - 1) V_d$ <p>Where C_d = fluorescein concentration in the drop C_m = initial fluorescein concentration calculated by back extrapolation with the Fluorotron in ng/ml. k = correction factor ($k = 250$) for the limited spatial resolution of the Fluorotron and V_d = drop volume in ml.</p> <p>Calculation of tear flow:</p> $\text{Tear flow} = \frac{V_t}{T_0(t_0)} \quad (\mu\text{l}/min)$	<p>Van Best, 1995</p> <p>Kuppens, 1992</p> <p>Mishima, 1965</p>
Web Video	Not available	
Materials:	<p>Fluorotron Master 2% sodium fluorescein Mimims (Chauvin, UK) Air displacement pipette P2 Pipetman (Gilson, Villiers-le-Bel, France)</p>	

	Disposable sterile tips (Gilson, Villiers-le-Bel, France).	
Variations of technique	Varying concentrations and instillation volumes of fluorescein can be used, e.g. 1% and 0.5 -2 µl.	
Standardization	Time of day [X] Temperature [] Humidity [] Air speed [still] Illumination [low ambient] Other:[Blink is initiated immediately prior to scan to ensure uniform tear thickness]	Pearce et al, 2000
Diagnostic value	This version : [] Determination of tear flow an indication of aqueous tear deficiency. To obtain estimate of tear drainage from eye. Other version: []	Mathers, Daley, 1996 Mathers et al, 1996 Gobbels et al, 1992
Repeatability	Intra-observer variation. [Not significant] Inter-observer variation. [Not significant]	Mishima et al, 1966 Van Best, 1995
Sensitivity	[NA]	
Specificity	[NA]	
Other Stats		
Test problems	High cost of basic equipment. Time required for measurement. Indirect (surrogate) measures of tear outflow and volume as it is assumed that fluorescein and aqueous tear are eliminated at the same rate from the eye. Absorption of fluorescein into the ocular tissue may be a factor in dry eye patients and may decrease apparent rate of decay.	
Test solutions	Use of high molecular weight conjugates.	McNamara et al, 1998
FORWARD LOOK	Production of a cheaper automated scanning fluorophotometer. Development of reduced test incorporating 6 measurements for total of 10 minutes (tear turnover). Combination of tear flow (µl/min) with evaporation rate (µl/min) gives a value of “total tear flow” in the eye and an estimate of total tear production. This allows analysis of the proportion of tears eliminated by evaporation and/or drainage in various forms of dry eye.	Pearce et al, 2000 Mathers, Daley, 1996 Mathers, 2004
Glossary		

References

Gobbels N, et al. Tear secretion in dry eyes as assessed by objective fluorophotometry. *German J Ophthalmol* 1992; 1:350-353.

Kuppens EVMJ, et al. Basic tear turnover and topical timolol in glaucoma patients and healthy controls by fluorophotometry. *Invest Ophthalmol Vis Sci* 1992; 33:3442-3448.

Mathers WD, Daley TE. Tear film and evaporation in patients with and without dry eye. *Ophthalmology* 1996; 103:664-669.

Mathers WD, et al. Tear film changes associated with normal ageing. *Cornea* 1996; 15:229-334.

Mathers WD. Evaporation from the ocular surface. *Exp Eye Res* 2004; 78:389-394.

McNamara NA, et al. Fluorometry in contact lens research: The next step. *Optom Vis Sci* 1998; 75:316-322.

Mishima S, et al. Determination of tear volume and tear flow. *Invest Ophthalmol* 1966; 5:264-275.

Pearce EI, et al. An improved fluorophotometric method for tear turnover assessment. *Optom Vis Sci* 2001; 78:30-36.

Van Best JA, et al. Measurement of basal tear turnover using a standardised protocol. *Graefes Arch Clin Exp Ophthalmol* 1995; 233:1-7.