Assessment of Tear Film Dynamics: Quantification Approach

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ABSTRACT **The dynamics of the tear film are reviewed with specific reference to the biophysical aspects: distribution, turnover and elimination through evaporation, drainage, and absorption. The review concentrates on quantitative assessments and is confined to aspects of the dynamics that can be fully and directly measured. The techniques of fluorophotometry, fluorescein clearance, lacrimal scintigraphy, evaporimetry and osmometry are described. Reports in the literature for values of tear turnover (flow), evaporation and osmolarity for normal and dry eyes are collated. Indices of tear film dynamics based on these measurements, including tear function index, total tear flow, and osmolarity, are discussed in relation to their potential in the differential diagnosis of dry eye and new referent values for the disease suggested. The limitations of derivation and application of these indices are discussed.**

KEYWORDS **absorption, distribution, evaporation, osmolarity, tear dynamics, tear indices, tear turnover**

I. INTRODUCTION

A complete tear film is essential for the health and function of the eye. Normal tear film dynamics require adequate production of tears, retention on the ocular surface, and balanced elimination. Disruption of any of these components can lead to the condition of dry eye. This review will focus on the biophysical aspects of tears. The approach will be essentially quantitative and will concentrate on the aspects of tear film dynamics that can be most fully and directly measured; therefore, it will consider the distribution, turnover (and drainage), evaporation, and absorption of tears (Figure 1). It will address laboratory techniques for the assessment of the tear film rather than the more conventional clinical approaches found in much of the literature. In addition, the dynamic balance of these elements will be considered through a single parameter—that of tear film osmolarity. Consideration will be given to this and other indices of tear film dynamics. The indices will be used in an attempt to define dynamics in the normal healthy eye and differentiate them from those in the dry eye.

II. TEAR DISTRIBUTION

Tears are produced principally by the lacrimal gland under the influence of the parasympathetic and sympathetic nerves.[1] Traditional methods of measuring tear production are based on absorption of tears[2] by Schirmer strips[3] or cotton threads.[4] Both tests are poor quantifiers of tear production; the Schirmer test is marred by low specificity and sensitivity,[2,5] and the exact parameter measured with the cotton thread test has been questioned.[6] Although such tests have clinical utility, particularly in the diagnosis of aqueous deficienct dry eye from the normal,[7] they offer only an indirect measure of tear production[8] and are of limited use in the quantification of tear dynamics.

The distribution of tear fluid on the ocular surface is dependent on the lid blink.[9] Lid closure on blinking proceeds from the temporal to the nasal side of the eye, spreading tears across the ocular surface and facilitating drainage through the lacrimal puncta.[10] The interblink time in normal individuals averages 4 ± 2 secs and is significantly decreased in patients with dry eye (1.5 ± 0.9 secs),[9] the blink rate being increased in dry eye patients to maximize the tear supply to the ocular surface.[11] In concentrated, close reading tasks, the blink rate drops under relaxed conditions by about one half (from 22.4 ± 8.9/mins to 10.5 ± 6.5/mins).[12]

The distribution of tear film can be observed dynamically with use of thin film interferometry. This technique, originated by Doane,[13,14] allows observation of the in vivo tear film through the application of the principle of thin film interferometry. Interference fringes are produced by light reflected at the air-lipid and at the lipid-aqueous

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Abbreviations are printed in **boldface** where they first appear with their definitions.

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OUTLINE

boundaries of the tear film, due to the changes in refractive index. Specular reflection from the lipid layer precludes a clear view of the aqueous layer of the precorneal tear film, although where the lipid layer is very thin or absent, fringes can be observed from the aqueous phase.[15]

Lipid layer interferometry was developed through the work of McDonald,[16] Hamano et al,[17] Norn,[18] and Guillon.[19] A dynamic interferometry system was first described by Doane.[13] A number of clinical instruments have been developed based on this optical principle, including the Tearscope described by Guillon and Guillon,[20] and instruments developed by Doane[13] and by Goto and Tseng.[21,22] A number of qualitative grading systems for the tear film have been proposed for these instruments.[20,23,24] These are useful for looking at structure of the tear film, and they offer some insight into its stability.[24] Significant differences in appearance (and grade) have been observed in dry eye conditions, with the partial or complete absence of the lipid layer being a feature (Figures 2 and 3).[25]

The development of a quantitative approach to the analysis of interferometric images from the tear film of normal and dry eye patients owes much to the work of Goto and Tseng.[22] Goto and Tseng, with the use a kinetic analysis of sequential interference images, were able to record the lipid spread time of tears in normal and dry eye patients. This spread time, defined by the interval necessary for the lipid film to reach a stable interference image, was 2.17 ± 1.09 secs in the aqueous tear deficiency state, significantly slower than that recorded for normal eyes (0.36 ± 0.22 secs [Figures 2 and 3]).[21,22] Because of this slower spread time, the resultant lipid film was found to be thicker on the inferior cornea

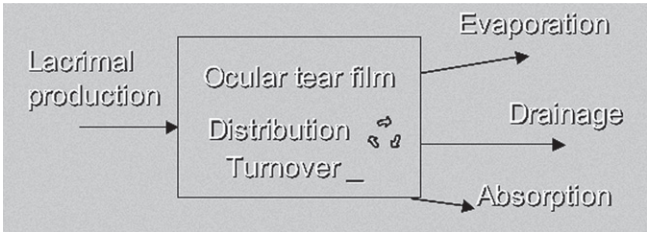

Figure 1. Diagrammatic representation of the input and output components of the tear system.

than on the superior cornea,[22] the thickness being measured from a "look-up" simulated color chart obtained from the reflectance of thin film interference generated by a white light source.[26] Tear film particle movement, as an indicator of the time necessary to obtain stability of the tear film after the blink, had previously been used by Owens and Philips.[27] Almost 90% of Goto and Tseng's patients with aqueous tear deficiency showed vertical streaking, rather than a normal horizontal propagation of the interferometric pattern on the superior cornea.[22] Owens and Philips measured the displacement of tear film particles just after a blink and found the time necessary to reach zero velocity (tear stabilization time) to be 1.05 ± 0.3 secs.[27] The observed particles were thought to be accumulations of newly secreted lipid from the meibomian glands.

A commercial thin film interferometer (DR-1, Kowa Co Ltd, Japan) was developed by Yokoi and Komuro.[28] In this apparatus, the specular reflection from the tear surface is imaged with a video camera, observed on a TV monitor, and recorded digitally. Yokoi et al have developed a classification system for grading interference pat-

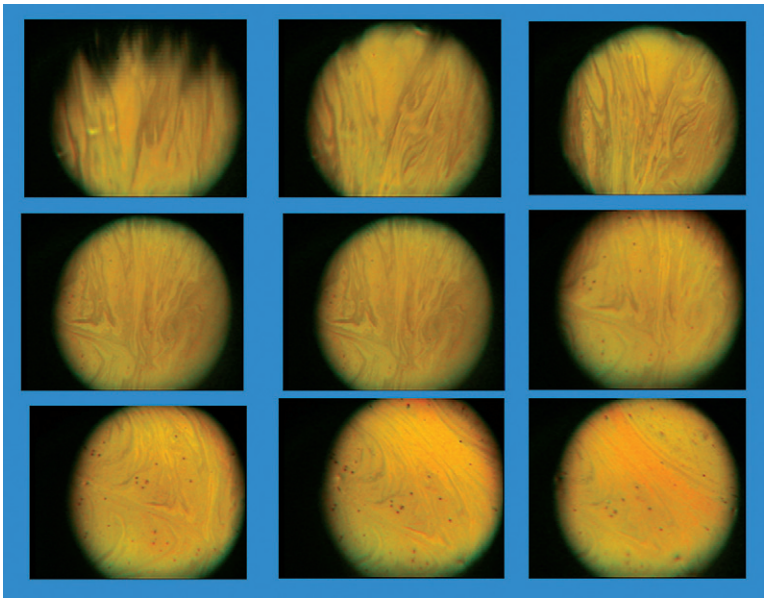

Figure 2. Series of thin film interferometry images obtained by the dynamic technique of Doane[13] from a normal asymptomatic subject. The images are obtained at 1 sec intervals, following a blink. The lipid layer of the normal tear film reaches a relatively stable pattern within the first second after the blink (consistent with the lipid spread time measurements of Goto and Tseng[22]). This pattern is then stable for about 6 secs.