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**PUBLISHED 5 MAY 2015** 

# A Stepwise Approach To Acute Dry Eye

How to approach the occasional situation in which this chronic condition suddenly becomes acute.

Dry-eye disease is well-recognized as a complex, chronic disease that needs chronic therapy. Superimposed on the intricate landscape of oxidative processes, immunological priming, autoimmunity and inflammatory responses are bouts of acute distress brought on by a constellation of extrinsic and intrinsic factors. Dry-eye-associated discomfort typically waxes and wanes, based on behavior and environment, as well as diurnal and seasonal biorhythms. Dry-eye subjects also use behavioral modification to optimize comfort and visual function.



Nevertheless, a few times a year, dry-eye subjects can fall off the wagon: an extended stay in the sauna; cleaning the attic; painting the house; an airplane trip; or hiking, skating or mountain biking on a dry, windy day. This is reckless behavior for a dry-eye subject who, like a Flying Wallenda, has to climb gingerly back up on the high wire after falling off.

Non-environmental factors can also bring about an acute attack of dry eye. We need to ask questions: Did the patient have a recent bout of the flu, a gastrointestinal virus, a fever or episodes of vomiting that may have led to dehydration? Alternatively, is the patient experiencing the onset of menopause, which may have exacerbated a previously milder type disease? The introduction of new medications, such as an antihistamine, or a new antidepressant or antihypertensive therapy may also be responsible for acute worsening of dry eye.

These acute episodes require not only stepping up the maintenance therapy, but also additional pulses of more robust therapeutic options to bring the patient back from the precipice. This month we'll speak to the acute versus chronic presentations of dry eye and discuss how to recognize and treat them, as well as how to educate the



patient in recognizing and pre-empting the downward cycle of ocular surface discomfort and damage.

#### **Clinical Presentation**

When a dry-eye patient presents with an abrupt worsening of her disease, what she's feeling is acute, severe discomfort.



When patients begin to suffer from acute dry eye, environmental factors often play a role. An airplane trip alone can be enough to bring on an acute episode of the disease.

Innate protective blink mechanisms are overwhelmed by these acute challenges, and normal blink patterns are therefore altered, resulting in compromised visual function that is perceptible to the patient.<sup>1</sup> To the clinician, the eyes are very red, with prominent horizontal vessels in the interpalpebral fissure as well as under the lid. These are



signs that the discomfort is not only environmental, but also endogenous in origin. There is occasionally scleritis, and there is profuse rose bengal and fluorescein staining.

What has occurred is acute damage juxtaposed on the baseline chronic inflammatory state of dry eye. The body responds to this damage with a wound-healing process that is remarkably the same in all tissues: mounting of an inflammatory response; clearing away of the dead cells and tissues; and gradual mitotic renewal of the epithelial surface. This reparative process is impaired in the dry-eye patient due to a dysfunctional tear film in which the balance of tear constituents such as mucins and lipids is disrupted,<sup>2</sup> a situation that can prolong the reparative process and delay the biological cleanup to the point that it lasts weeks in the dry-eye patient instead of hours or days as in a normal subject.

Most research in the past decade on dry-eye disease points to inflammatory processes at its origin. Even if we limit our discussion to non-systemic, non-Sjögren's activation of dry eye, local inflammation plays a significant role. As with all inflammation, there are chronic and acute pathways that converge and diverge with different signals, but all must begin with an initiating, immunologically



priming event. The most challenging aspect of dry-eye research has been to pull apart these threads and try to identify which cell or pathway may be the initial instigating player. By the time the patient is bothered enough to go to the doctor, his or her clinical dry-eye disease is usually in its chronic stages and the continuous cycles of tear film instability are causing mounting inflammation. However, in the case of a dry-eye attack or exacerbation, the clinician has a chance to observe the disease in its acute, early stage. Understanding what happens at the inception of dry eye can give us greater insight on how best to manage acute exacerbations of the disease.

## **Initial Steps in Acute Cases**

One of the earliest players in dry-eye disease is interleukin 17 (IL-17), found in a subset of T cells called CD4+ T cells because they express the CD4 glycoprotein on their surface.  $^{3-6}$  CD4+ T cells mature along four distinct paths determined by the pattern of signals they receive during antigen presentation; these are defined as Th1, Th2, Th17 and regulatory T or  $T_{regs}$  cells. This nomenclature is based on the primary cytokine secreted by each cell population: Th1 cells secrete interferon-gamma (IFN- $\gamma$ ); Th2 cells secrete interleukin-4, IL-5 and IL-13; and Th17 cells



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