



## Allergic conjunctivitis and dry eye syndrome

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### ABSTRACT

**Background:** Allergic conjunctivitis (AC) and dry eye syndrome (DES) are 2 of the most common anterior inflammatory disorders of the ocular surface and one does not preclude the coexistence of the other.

**Objectives:** To examine the potential overlap between AC and DES as comorbidities.

**Methods:** Using the validated questionnaire known as Subjective Evaluation of Symptom of Dryness, we studied self-reported itchiness, dryness, and redness. In an outpatient optometric setting, 689 patients treated from January 1, 2007, to January 1, 2011, were surveyed for their ocular history and categorized according to their reported level of discomfort of itchiness, dryness, and redness.

**Results:** Patients ranged in age from 5 to 90 years (median age, 25 years; 39.5% male; 60.5% female). In the studied 689 patients, clinically significant itchiness was found in 194 (28.2%), dry eyes in 247 (35.8%), and redness in 194 (28.2%). Symptom overlap was demonstrated in many of the patients. Of the 194 patients with itchiness, 112 (57.7%) had clinically significant dryness. In the 247 patients with dry eyes, 112 (45.3%) had clinically significant itch. Redness was apparent in 120 of the 194 patients with itch (61.9%) and 122 of the 247 patients with dryness (49.4%). Statistical analysis demonstrated that self-reported itchiness, dryness, and redness were not independent of each other ( $P < .001$ ; Pearson  $\chi^2$  test). The odds of patients with “itchy eyes” also experiencing dry eyes were 2.11 times and the odds of these patients also experiencing redness were 7.34 times that of patients with nonitchy eyes.

**Conclusions:** Most patients with “itchy eyes” consistent with AC also have dry eyes and redness. These results suggest that some symptomatic patients concomitantly have features of AC and DES.

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### Introduction

Allergic conjunctivitis (AC) and dry eye syndrome (DES) are 2 of the most common anterior inflammatory disorders of the eye. These disorders have been regarded to be the epidemics of the 21st century.<sup>1</sup> Depending on the study, the prevalence of dry eyes has been reported to range from 5% to 35% of the population.<sup>2</sup> Up to 40% of the general US population has reported ocular symptoms consistent with AC.<sup>3</sup> Both conditions have a strong effect on quality of life. When measured with questionnaires reflecting quality of life, dry eye disease and allergic rhinoconjunctivitis can have the same effect on quality of life as moderate angina.<sup>4</sup> Approximately 46% of patients with AC display significant impairment of their overall quality of life during an acute episode.<sup>5</sup>

Traditionally, DES and AC are regarded as 2 different diseases. However, recent literature has shown both conditions share similar characteristics, including several of their signs and symptoms.<sup>6–8</sup> However, the literature has not shown similarities in the same

group of patients. We examined the clinical similarities using a simple questionnaire that included itchiness, dryness, and redness in patients with AC and DES.

### Methods

A total of 689 patients randomly selected from an ambulatory optometric practice were surveyed for their ocular history and categorized for their discomfort level of itchiness, dryness, and redness. The study population was located at a single site in Southern California. The ethnic makeup of the surrounding neighborhoods was approximately 68% Hispanic and 20% white. The patients were seen from January 1, 2007, to January 1, 2011. AC was diagnosed by symptoms (itch, redness, tearing, or swelling), papillary response, and patient history. Inclusion criteria were males or females with a history of AC. AC was diagnosed by symptoms (itch, redness, tearing, or swelling), papillary response, and patient history.

Patients excluded from the study were those who had undergone intraocular, corneal refractive surgery or ocular laser surgery within 6 months and those with any active ocular infection, such as infectious, viral, chlamydial, or immunologic conjunctivitis that may potentially confound the results of this study.

Age and sex were noted for each patient. Oral informed consent was obtained. Institutional review board exemption was

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**Table 1**  
Subjective evaluation of symptom of dryness or frequency of dryness score definitions<sup>10–14</sup>

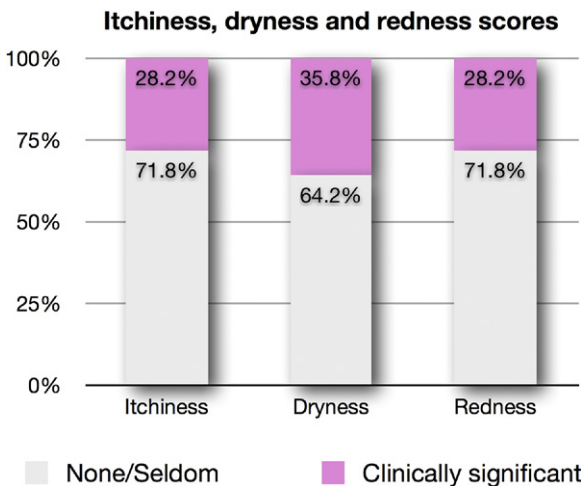
Score	Definition
Never or none (0)	I do not have this symptom.
Seldom or trace (1)	I seldom notice this symptom, and it does not make me uncomfortable.
Sometimes or mild (2)	I sometimes notice this symptom; it does make me uncomfortable, but it does not interfere with my activities.
Frequently or moderate (3)	I frequently notice this symptom; it does make me uncomfortable, but it sometimes interferes with my activities.
Always or severe (4)	I always notice this symptom; it does make me uncomfortable, but it usually interferes with my activities.

granted by the institutional review board of California State University at Fullerton (application HSR-11-0199). The validated Subjective Evaluation of Symptom of Dryness (SESoD) questionnaire or Frequency of Dryness Score previously used in several studies was used to collect information on self-reported itchiness, dryness, and redness<sup>9–13</sup> (Table 1). The instrument had been used to detect racial differences in dryness in Hispanic populations<sup>10</sup> and to determine a link between family history of diabetes mellitus and dryness.<sup>11</sup>

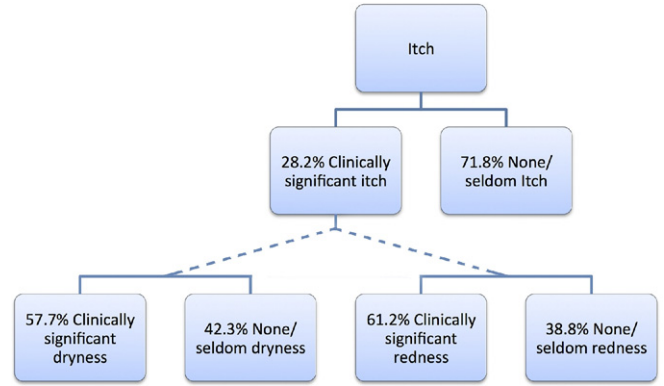
Pearson  $\chi^2$  tests ( $df=1$ ) were used to determine whether the 3 variables (itchiness, dryness, and redness) were independent of each other, along with the corresponding *P* values. After the independence was established, the relationships among the variables were explored. Binary logistic regression analysis was used to determine the nature of the relationship with odds ratios.

**Results**

In this study, patients ranged in age from 5 to 90 years (median age, 25 years), and most were female (60.5% female and 39.5% male). Approximately 35.2% of the patients were taking medications that may have an effect on the ocular surface (oral, topical, and inhaled antihistamines or corticosteroids). This percentage was roughly equally distributed in the itchiness, redness, and dryness subsets: 28.2% (194/689) self-reported clinically significant itchiness, 35.8% (247/689) dry eyes, and 28.2% (194/689) redness (Fig 1).



**Fig. 1.** Itch, dryness, and redness scores. For 689 patients, the percentages of clinically significant itch, dryness, and redness scores are shown. A total of 28.2% of the 689 patients screened reported clinically significant itch, 35.8% had self-reported dryness, and clinically significant redness was seen in 28.2%.



**Fig. 2.** Clinically significant itch. A total of 194 of 689 patients (28.2%) had itchiness. Of those 194 patients, 112 (57.7%) had dryness and 120 (61.9%) had redness. The flowchart indicates that most patients with itch have dryness and redness.

The flowchart (Fig 2) depicts the relationships between redness and dryness within the subgroup of 194 patients reporting clinically significant itchiness. Within the clinically significant itch subgroup, 112 of 194 patients (57.7%) had clinically significant dryness, whereas 120 of 194 (61.9%) had clinically significant redness. Most patients with itch also have dryness and redness.

Within the subgroup of 247 patients with dryness, 112 (45.3%) had clinically significant itch and 122 (49.4%) had clinically significant redness. For the self-reported redness subgroup, 120 of 194 (61.9%) also had significant itchiness and 122 (62.9%) had dryness. Table 2 gives the numbers of patients within each group and subsequent overlap (Table 2). The overlap among itch, dryness, and redness is shown in Figures 3, 4, and 5. The overall overlap between all subgroups is shown in Figure 6.

The Pearson  $\chi^2$  tests demonstrated that self-reported itchiness, dryness, and redness were not independent of each other ( $P<.001$ ) Between dryness and itchiness, the Pearson  $\chi^2$  was 56.227 ( $P<.001$ ). Between redness and itchiness, the Pearson  $\chi^2$  was 151.593 ( $P<.001$ ). Lastly, between redness and dryness, the Pearson  $\chi^2$  was 85.836 ( $P<.001$ ).

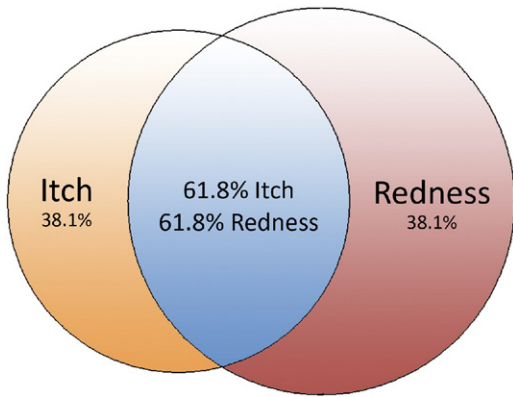
With binary logistic regression analyses, the odds of patients experiencing itchy eyes and also dry eyes were 2.11 times that of patients with nonitchy eyes. For redness, the odds were 7.34 times. The odds of patients with redness vs nonredness experiencing dryness were 3.65, and the odds for itchiness were 7.34. Finally, the odds of patients with dry eyes vs nondry eyes experiencing itchiness were 2.11 and the odds for redness were 7.34 (Table 3).

**Discussion**

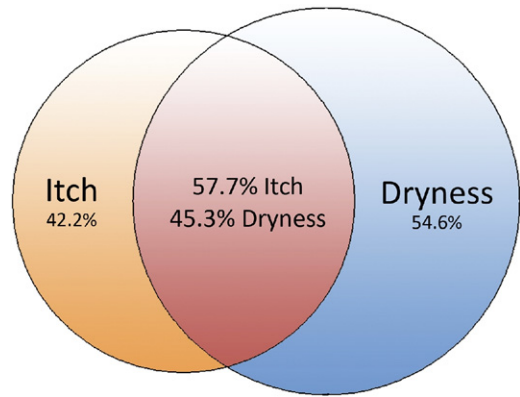
The results of the study reveal several overlapping self-reported symptoms between AC and DES. Itch has been and continues to be a significant differentiator for AC from other types of conjunctivitis.<sup>14</sup> When the itch symptoms are clinically significant, the odds are high that the eyes will be symptomatically red and dry. On the flip side, this study demonstrates that even patients with dry eyes have higher odds for itch and erythema and adds further support to

**Table 2**  
Numbers of patients in each subgroup (N=689)

Clinically significant score	Total No. of clinically significant patients
Itch	194
Dryness	247
Redness	194
Itch and dryness	112
Itch and redness	120
Dryness and redness	122



**Fig. 3.** Itch and redness. Venn diagrams show the overlap between itch and redness. A total of 61.8% of the patients experienced both itch and redness.



**Fig. 5.** Itch and dryness. The overlap between clinically significant itch and dryness was 57.7% of the self-reported itch patients and 45.3% of the self-reported dryness patients.

the existence of a large symptomatic crossover between the 2 diseases.

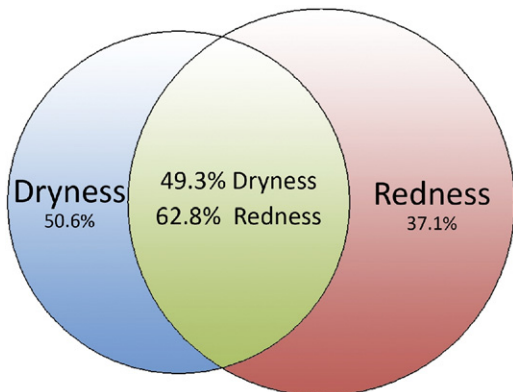
Self-reported dryness has been shown to correlate with dry eye disease.<sup>9,12</sup> Subjective instruments, such as questionnaires, are used extensively in dry eye studies. Frequently used subjective instruments include the McMonnies Dry Eye Questionnaire, the Ocular Surface Disease Index (OSDI), the Dry Eye Questionnaire, and the National Eye Institute–Visual Function Questionnaire (NEI-VFQ). The McMonnies Dry Eye Questionnaire is 15 questions and used as a screening instrument. Introduced in 1997, the OSDI is a validated 12-item scale for the assessment of symptoms related to dry eye disease and their effect on vision. The OSDI is the most commonly used questionnaire in dry eye studies. The questions are divided into 3 subscales: symptoms (3 questions), environmental triggers (3 questions), and vision-related function (6 questions). The Dry Eye Questionnaire is 21 items on prevalence, frequency, diurnal severity, and intrusiveness of symptoms. The NEI-VFQ is a 25-item questionnaire with 2 ocular pain subscale questions.<sup>2</sup> Although these tools have been criticized because of a lack of correlation with clinical signs of dry eye, they have the power to identify patients with early to moderate dry eyes who lack many signs of more advanced cases similar to the instrument used in this study.

Much of the following discussion surrounds risk factors, environmental triggers, and objective tests not covered by the SESoD questionnaire. The SESoD focuses on frequency of symp-

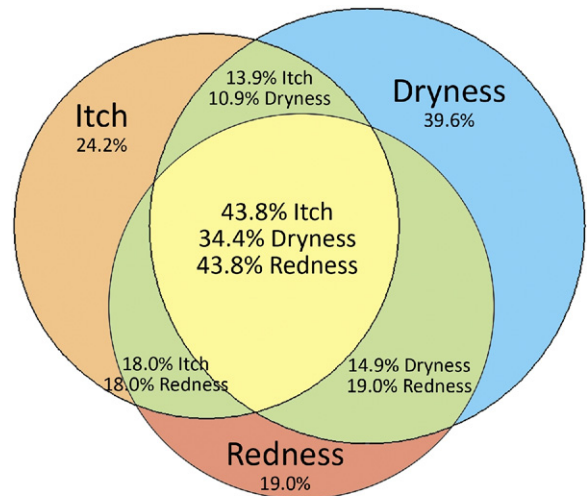
toms and is designed more as a screening questionnaire. Frequency has been highly correlated with intensity of symptoms. Frequency is also relevant to clinical trials because it is difficult to demonstrate a change in infrequent symptoms. For clinical studies, it is appropriate to use SESoD during the study qualification visit and another questionnaire, such as the OSDI, to cover risk factors and monitor treatment efficacy.<sup>2</sup> Examination of the literature reveals many of the underlying potential connections between AC and DES. Clinically, AC has been shown to be associated with changes in tear film composition, structures that are associated or perhaps predispose the patient to dry eyes. Itching can bring on eye rubbing, which can disrupt the corneal epithelium and lead to worsening of the inflammation on the ocular surface.<sup>15</sup>

DES and AC are usually regarded as 2 separate entities. Differential diagnosis is difficult because the signs and symptoms as demonstrated in this study are very similar.<sup>7,8,15</sup>

There are many instances in the literature connecting tear film dysfunction with AC. One study theorizes that tear film dysfunction is thought to be a possible complication of ocular allergic disease.<sup>16</sup> In patients with chronic forms of AC, such as patients with atopic keratoconjunctivitis and vernal conjunctivitis, decreased tear film break-up times,<sup>17</sup> decreased conjunctival mucins in the tear fluid layer,<sup>18</sup> and conjunctival goblet cell density<sup>19–20</sup> have also been



**Fig. 4.** Dryness and redness. A total of 50.6% of the self-reported dryness patients also have redness, and 62.8% of the redness patients also have dryness.



**Fig. 6.** Itch, dryness, and redness. The Venn diagram shows the relationship among all 3 subgroups.



**Table 3**  
Odds ratios for self-reported itch, dryness, and redness

Symptom	Odds ratio
Itch vs nonitch	
Dryness	2.11
Redness	7.34
Redness vs nonredness	
Itch	7.34
Dryness	3.65
Dryness vs nondryness	
Itch	2.11
Redness	7.34

noted in animal models. Reduced tear break-up times are known to be associated with significantly fewer goblet cells. One study suggests a mechanism in which AC reduces goblet cell density and sets the patient up for dryness.<sup>19</sup> In another study, the intensity of the allergic inflammation ocular surface was correlated to the tear film (dry eye) effect.<sup>21</sup>

Reduced tear break-up times is a significant objective sign of DES.<sup>2</sup> In one study, seasonal and perennial forms of AC have been shown to reduce tear break-up time (3.4 vs. 12.4 seconds;  $P < .05$ ) and increased tear film lipid layer. A total of 78% had grade 3 or higher dry eye change in tear film lipid layer interferometry, consistent with DES. Overall, seasonal AC appears to be associated with advanced tear instability and thickening of the tear film lipid layer.<sup>22</sup> In a study of international airline crewmembers during the time when smoking had been permitted, atopy was also a factor in the development of ocular DES symptoms.<sup>23</sup> One of the atopic risk factors that is associated with DES may be related to the long-term use of antihistamines that have anticholinergic properties due to their intrinsic high muscarinic receptor binding.<sup>24</sup> The exposure to perennial allergens such as dust, as studied in an environmental chamber, was associated with a significantly decreased tear film break-up time. A correlation analysis showed that perceived “air quality” was significantly correlated with “dry eyes” and “eye irritation” and that nonindustrial office dust may cause physiologic changes and sensory symptoms in eyes and nose that clinically overlap with allergy.<sup>25</sup> Interestingly, the association of atopy to tear film dysfunction may also be due to the development of hyperosmolar tears associated with chronic inflammation that may initiate a spiraling cycle.

Studies exist that would support the observation that AC establishes an environment that generates a dry ocular surface.<sup>19</sup>

Current classification systems divide DES into 2 major categories: aqueous deficient (tear volume insufficiency) and evaporative dry eye (meibomian gland dysfunction and posterior blepharitis).<sup>2,26</sup> The discussion so far generally refers to an aqueous deficient dry eye. The other major category, evaporative dry eye, has also been connected to AC. Some have referred to evaporative dry eye as having an allergic component.<sup>6,27</sup>

One question arises regarding AC and dryness: does one condition predispose to the other? Our discussion of the literature seems to lead to AC existing as the first condition and predisposing to DES. Epidemiology may offer more clues. A closer look at ocular allergy shows it to be more common in the pediatric population, whereas DES is uncommon. DES is more likely to occur in older individuals.

Despite these ways of differentiating the 2 conditions, AC and DES clinically manifest similar symptoms and readily mimic each other. Symptoms of redness or erythema, burning, and tearing suggest that individual patients may have both conditions at the same time.<sup>6,27,28</sup> The symptom overlap is similar to the one seen between allergic or nonallergic rhinitis and asthma.

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