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SUPPLEMENT

Blepharitis in the United States 2009: A Survey-based Perspective on Prevalence and Treatment

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Blepharitis in the United States 2009: A Survey-based Perspective on Prevalence and Treatment

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ABSTRACT Like dry eye disease 15 years ago, blepharitis today is a poorly defined condition about which there is considerable misunderstanding. For a variety of reasons, there is little good data on either the prevalence of blepharitis or how eyecare practitioners currently treat it. The work reported herein consists of two recent studies: a telephone survey of a representative sample of the adult US population (n = 5,000) whose purpose was to discover the frequency of common ocular surface symptoms associated with blepharitis; and a study that queried a selected group of ophthalmologists (n = 120) and a similarly selected group of optometrists (n = 84) about the frequency of blepharitis in their practices, the existence of comorbid conditions, and their management strategies. This data suggests that blepharitis symptoms are very common in the US population, with younger individuals reporting more, and more frequent, symptoms than older people, contrary to clinical dogma. Ophthalmologists and optometrists report that blepharitis is commonly seen in clinical practice in 37% and 47% of their patients, respectively, and it is widely agreed that meibomian gland dysfunction (MGD) is the most common cause of evaporative dry eye disease. In addition, management paradigms are shifting away from more traditional management with antibiotic ointment and warm compress therapy to prescription therapy for anterior and posterior blepharitis.

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I. INTRODUCTION

Eyecare practitioners recognize blepharitis as a common presenting condition. However, there has been no reliable population-based survey of its prevalence, nor is there wide consensus on its treatment. Discussion of blepharitis is complicated by the absence of a simple, widely accepted definition for the condition, as well as by terminology that is outdated and commonly misused.

Dry eye disease, an ocular surface condition related to blepharitis, was in a similar state in the early 1990s, when the National Eye Institute and members of the ophthalmic industry sponsored a meeting of clinicians and researchers that produced a consensus definition and classification of dry eye disease that formed the basis for more than a decade of research.[1] That research not only shed considerable light on dry eye disease, but also led to the development of an important therapeutic agent (cyclosporine) and ongoing efforts to develop additional agents. Since then, two other major group reports on dry eye disease have been produced, and today there is a widely accepted international definition and treatment protocol for the condition.[2,3]

This paper reports on two recent studies that shed light on the prevalence and treatment of blepharitis. We see this effort as a step in a larger process that aims to bring to blepharitis the same degree of scrutiny and consensus that now exists for dry eye disease.

A. Definition of Blepharitis

Blepharitis has been classified and subclassified in a variety of ways over more than a century.[4-6] Consequently, multiple and overlapping naming conventions exist. This no doubt reflects the number and complexity of the states and conditions that can produce eyelid inflammation. As currently used, the term “blepharitis” encompasses conditions that result from pathology associated with the pilosebaceous unit of the anterior lid and the meibomian

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glands of the posterior lid. Recent work has shown that these seemingly disparate etiologies have at least some common threads.[7,8]

Clearly, multiple pathogenetic mechanisms are involved in the group of conditions we call blepharitis. For example, meibomian gland dysfunction (**MGD**), a subset of the conditions that fall under the rubric "blepharitis," can be the result of a number of associated factors that lead to different subclinical and clinical effects.

The simplest and perhaps most clinically useful classification of blepharitis subdivides the condition into anterior and posterior. The former is most often a product of bacterial overgrowth and/or sebaceous gland activity, whereas the latter is almost always associated with dysfunction of the meibomian glands. MGD is the most common cause of evaporative dry eye. Foulks and Bron detailed this relationship in 2003 and proposed a classification system of meibomian gland disease (Figure 1).[7]

The study of blepharitis has unique challenges, as it often coexists with and masquerades as other related conditions, most frequently dry eye disease; seborrheic dermatitis, acne rosacea, and atopy are other common comorbidities.[4] Dry eye disease is a condition in which the tear film cannot adequately protect the ocular surface due to insufficient tear production and/or excessive tear evaporation. Blepharitis is a condition that may affect the normal functioning of the lashes and meibomian glands through bacterial products, inflammation, altered meibomian gland secretions, or a combination of these factors.

B. Review of Prior Studies

In a review of meibomian gland disease, Driver and Lemp surveyed the history of blepharitis.[4] They noted that some of the earliest reports of what is now called blepharitis or meibomian gland dysfunction date back to the 19th century, referring to conditions such as conjunctivitis meibomianae and meibomian seborrhea. In 1942, Scobee concluded, based on his review of the anatomy and physiology of the meibomian glands, that staphylococci residing in the meibomian glands play a predominant role in the recurrence of conjunctivitis.[4] It was not until 1982 that McCulley and coworkers concluded that meibomitis was not primarily an infectious entity but rather a product of gland dysfunction, often found in association with seborrheic dermatitis or acne rosacea; this set the stage for treatments that focused on restoring normal function to the meibomian glands.[9]

After further research, in 1984, McCulley divided blepharitis into multiple groups, including four seborrheic types, a primary meibomianitis type, and a staphylococcal and a mixed seborrheic-staphylococcal type.[10] He suggested the use of antibiotics to treat the staphylococcal group (typically younger, female patients) in the form of bacitracin, erythromycin, and aminoglycoside ointments. In research published in 1992, Raskin further supported the use of antibiotic ointments and advocated their use for seborrheic blepharitis as well.[11] However, many researchers, including McCulley, suggested that, aside from staphylococcal blepharitis, there was no cure for blepharitis, and that only management of the condition could be achieved. Thus, some practitioners may have shied away from treating blepharitis because of uncertainty about the efficacy of available agents.

By 1995, researchers had deemed blepharitis a "diagnostic and therapeutic enigma."[12] Eyecare providers were frustrated with the condition, as were patients, who were often overlooked or misdiagnosed. Smith and Flowers attributed the pathogenesis of blepharitis to changes in tear film dynamics and underlying dermatologic abnormalities.[12] They cited the lid margins as the primary site for symptoms, which included itching and burning. They reported that there was no long-term cure for blepharitis, even the staphylococcal forms, because individuals with the condition were likely to be highly susceptible to the causative organism and, hence, to chronic recurrences. They suggested lid hygiene measures, topical or systemic antibiotics, and tear supplementation as the most effective regimen, stressing that ongoing treatment would be necessary.

In 2004, recognizing that clinical diagnosis and treatment of blepharitis were, overall, failing to gain good treatment outcomes, Mathers and Choi used cluster analysis

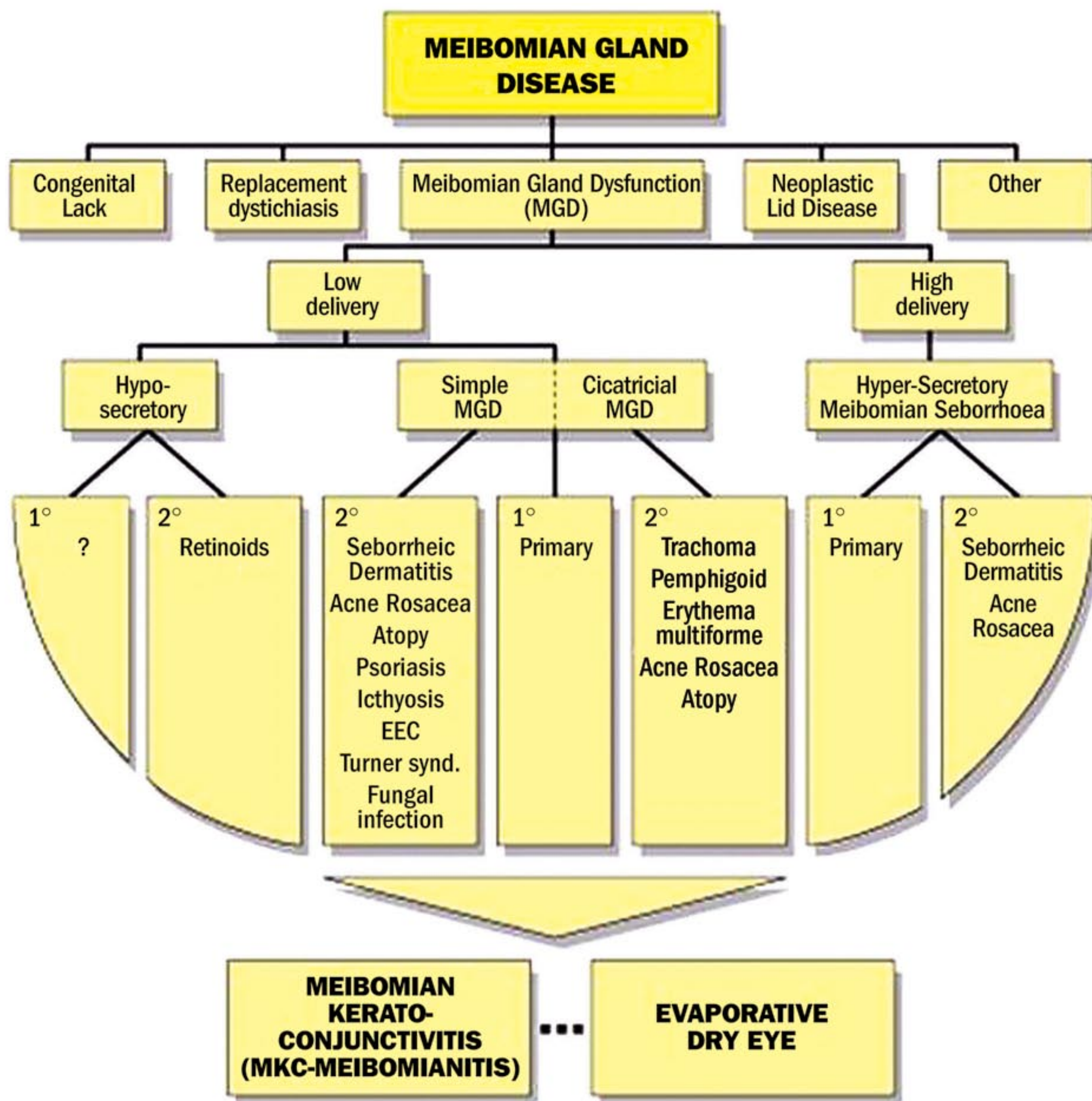


Figure 1. Classification system for meibomian gland disease. Source: Foulks GN, Bron AJ. Meibomian Gland Dysfunction: A Clinical Scheme for Description, Diagnosis, Classification, and Grading. *Ocul Surf.* 2003 Jul;1(3):107-126.

to create a classification tree of blepharitis and dry eye.[13] In addition to creating nine clinically relevant blepharitis groups, the analysis served to further establish the central role meibomian gland dysfunction plays in blepharitis.

How far have we come in our knowledge of blepharitis since then? The most recent studies offer similar information about blepharitis, albeit a distinction is now often made between the anterior or posterior forms in recent literature and, to some extent, in clinical practice. According to a 2008 Canadian consensus statement on the identification and management of blepharitis, blepharitis of the lids and lashes (anterior blepharitis) tends to be staphylococcal in nature, and blepharitis involving the meibomian glands (posterior blepharitis) may be seborrheic, obstructive, or mixed (Table 1).[14] That being said, there is much overlap between what is called anterior and posterior blepharitis,

Table 1. Features of blepharitis

Features of blepharitis
Abnormal functioning of the meibomian glands caused by: Bacteria Inflammation Altered meibomian gland secretions Combination of factors
Comorbid conditions: Dry eye Acne rosacea Seborrheic dermatitis
Anterior blepharitis often staphylococcal in nature
Posterior blepharitis may be seborrheic, obstructive, or mixed in origin

and, indeed, staphylococcal bacteria could, and likely do, affect both anterior and posterior structures. The consensus statement recommends lid hygiene, along with topical or systemic antibiotics and topical steroids (as indicated), as primary treatment strategies for blepharitis.[14]

C. Prevalence of Blepharitis

As reports over the past 100-plus years have shown, there has been substantial confusion regarding the definition of blepharitis and mechanisms of symptom formation. In part because of this definitional uncertainty, we still lack a precise idea of the prevalence of the condition.

We have population data on the incidence of dry eye disease, primarily from the Women's Health Study and Physician's Health Study.[15-17] These and other studies of the epidemiology of dry eye disease are discussed in the *2007 Report of the International Dry Eye WorkShop*.[3] Based on data from the Women's Health Study and the Physicians Health Study, it has been estimated that dry eye disease affects approximately 3.23 million women and 1.68 million men aged 50 years or older.[3] These studies, however, used a fairly stringent definition of dry eye disease, which may not have included people with milder symptoms or episodic cases.[3] Data from large epidemiological studies suggests prevalence of dry eye disease in a range from 5% to 35%, depending on age and disease definition.[3] These studies also suggest that the number of women with dry eye generally exceeds that of men, especially at younger (ie, < 60) ages.

Randomized, controlled studies are not the only sources of information regarding dry eye disease. Incidence estimates or trends can also be gleaned from data residing in federal or public databases. In 2002, Ellwein et al found that Medicare claims data showed that the dry eye disease case incidence per 100 fee-for-service beneficiaries increased from 1.22 in 1991 to 1.92 in 1998 (a 57.4% increase), suggesting that dry eye disease is becoming more prevalent in the Medicare population.[3]

Regarding blepharitis specifically, there is extremely little prevalence or incidence data available in the literature, despite clinical awareness that blepharitis is one of the most common disorders encountered in eyecare practice.[18,19] Hom and coworkers performed meibomian gland expression on 398 randomly selected "apparently normal" patients presenting for routine vision examinations. One hundred fifty-five patients (39%) were judged to have MGD, based upon absent or cloudy meibomian gland secretions.[20] In this study, prevalence increased with age but was not correlated with other factors.

In 2003, Venturino and colleagues prospectively collected and analyzed data from 1,148 consecutive patients seeking an eye examination because of ocular discomfort or irritation.[21] They found that posterior blepharitis was the most commonly diagnosed condition among the patients studied (24%), followed by dry eye disease (21%), and anterior blepharitis (12%). They further noted that, overall, treatment in use was not specific to the diagnosis and gave poor clinical results.

As with the Hom and Venterino studies, most of the data available to estimate the prevalence of blepharitis is based on a relatively small number of clinical samples. Furthermore, comparing studies of blepharitis prevalence is confounded by inconsistency in terminology and contextual issues related to overlap with dry eye disease.

Table 2. Steps to determine the prevalence of blepharitis
Define blepharitis
Standardize lid examination technique
Quantify changes in lid condition

Indeed, in clinical practice many practitioners may not record every case of blepharitis they see, assuming that some blepharitis is incidental or expected, particularly when patients are being seen for other reasons, such as a spectacle examination, or if the blepharitis has been long-standing and/or asymptomatic.

Future efforts to determine prevalence of blepharitis will require: a stringent definition of blepharitis and/or specific subtypes of blepharitis; a well-accepted, standardized technique for examining lids; and a method to quantify changes in lid condition (Table 2). Only with these conditions met can we assess the true prevalence of blepharitis in the United States.

II. PATIENT SURVEY: PREVALENCE OF BLEPHARITIS-RELATED SYMPTOMS

A. Introduction

To gain a clearer understanding of the prevalence of blepharitis symptoms in the general population, Inspire Pharmaceuticals, Inc. engaged the Mattson Jack Group (St. Louis, MO) to conduct a computer-assisted telephone interview survey of adults in the United States.[22]

B. Methods

Random-digit dialing was used to contact 5,019 adults aged 18 years and older living in private households in the United States of America during July 2008. Completed interviews were weighted by age, gender, geographic region, and race to obtain a study population representative of the adult US population. A weighted sample of 5,000 individuals was used for the report.

Survey questions were designed to elicit information on the frequency of symptoms associated with lid margin disease (Table 3). Subjects were asked about the frequency with which they had experienced the following symptoms over the last 12 months: itching or burning of eyelids; eye irritation after using a computer for more than 3 hours; eyelids feeling heavy or puffy; crust or flakes on eyelashes upon waking; eye dryness or irritation; eyelids sticking together upon waking; eyes feeling watery, especially in the morning; and eye redness upon waking (Table 4). For each symptom, subjects were asked to rate the frequency of occurrence as *all of the time*, *most of the time*, *half of the time*, *some of the time*, or *never*.

Subjects were also asked whether there was any history of red bumps on eyelids, styes, thinning of eyelashes,

Table 3. The Mattson Jack Telephone Survey Instrument

1 Thinking about the PAST 12 MONTHS, please tell me if you have experienced any of the following eye conditions all of the time, most of the time, half of the time, some of the time, or never.

01 All of the time
02 Most of the time
03 Half of the time
04 Some of the time
05 Never
98 DON'T KNOW
99 REFUSED

A. Itching or burning of your eyelids
B. Your eyelids felt heavy or puffy
C. Your eyes felt dry or irritated
D. Your eyes teared or were watery, especially in the morning
E. Your eyes felt irritated after computer sessions of more than 3 hours
F. You noticed crust or flakes on your eyelashes when you first woke up
G. Your eyelids stuck together when you first woke up
H. Your eyes or eyelids looked red when you first woke up

2 Now, thinking about your eye history, please tell me which, if any, of the following you have EVER experienced? [READ AND ROTATE LIST. RECORD AS MANY AS APPLY. WAIT FOR YES OR NO FOR EACH]

01 Red bumps on your eyelids
02 Sties on your eyelids
03 Eyelashes have become thinner over the past few months or year
04 NONE OF THESE
98 DON'T KNOW
99 REFUSED

3 Have you worn contact lenses in the PAST 12 MONTHS?

01 YES
02 NO
98 DON'T KNOW
99 REFUSED

[ASK IF 3 (01)]

4 How often do you have trouble wearing contact lenses? Would you say . . . [READ LIST. RECORD ONE ANSWER]

01 All of the time
02 Most of the time
03 Half of the time
04 Some of the time
05 Never
98 DON'T KNOW
99 REFUSED

5 Have you ever been told by a family physician, ophthalmologist or optometrist that you have any of the following? [READ AND ROTATE LIST. RECORD AS MANY AS APPLY. WAIT FOR YES OR NO FOR EACH]

01 Blepharitis
02 Dry eye
97 NONE OF THESE
98 DON'T KNOW
99 REFUSED

Table 4. Symptoms experienced in the last 12 months by survey responders

Symptom	%
Itching/burning eyelids	32%
Eyelids heavy/puffy	35%
Eyes dry/irritated	53%
Eyes teared/watery, especially in morning	36%
Eyes irritated after computer sessions of more than 3 hours	38%
Crust or flakes on eyelashes when first woke up	33%
Eyelids stuck together when first woke up	15%
Eyelids red when first woke up	28%

or contact lens use, and whether or not they had ever received a diagnosis of blepharitis or dry eye disease. All reported findings are subject to the accurate recall of the participants.

C. Results

1. Prevalence and Frequency of Symptoms

Among respondents, 79.3% reported experiencing at least one of the symptoms listed in Table 4 within the past 12 months, and 63% reported experiencing more than one symptom in the past 12 months (Figure 2). Respondents to this survey reported experiencing 2.7 symptoms in the previous 12 months. The most commonly reported symptoms were dry or irritated eyes (53%), eye irritation after computer sessions of more than 3 hours (38%), and watery eyes (36%) (Figure 3).

About one-third (32%) of respondents reported experiencing at least one symptom at least half the time within the past 12 months (Figure 4). Also, 15% of respondents reported having experienced at least one of the three symptoms that clinicians associate specifically with anterior blepharitis (crust or flakes on eyelashes upon waking, eyelids sticking together upon waking, and redness of the eyes or eyelids on waking) at least half of the time in the past 12 months, and 1% of respondents had experienced all three symptoms in the last 12 months (Figure 5). Nine percent of respondents experienced crust or flakes on eyelashes at least half of the time, 7% experienced eye or eyelid redness, and 3% experienced eyelids sticking together (Figure 6).

Finally, since the majority of symptomatic respondents experienced multiple symptoms, the data was analyzed to determine how symptoms were grouped (Figure 6). This analysis

showed that patients who reported their eyelids sticking together upon waking always reported itching and burning of eyelids and eye dryness and irritation as well. Similarly, as a cluster, symptoms of eye irritation after long computer sessions, eye dryness and irritation, heaviness and puffiness of eyelids, and watery eyes tended to be reported when multiple symptoms were mentioned.

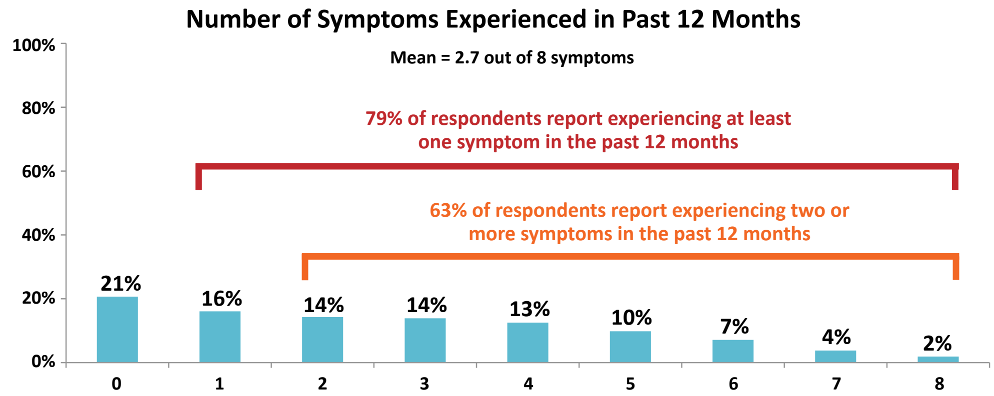


Figure 2. A large majority of survey respondents (79%) reported experiencing at least one symptom in the past 12 months. (Adapted with permission from The Mattson Jack Group, Inc. "Epidemiology of Blepharitis." September, 2008.)

2. Age and Gender Distribution

In addition to examining the overall prevalence and frequency of symptoms in the surveyed individuals, respondents were also subdivided by age and gender to determine which subjects were most likely to experience symptoms. While the number of symptoms experienced in the past 12 months did not vary by gender, certain symptoms were found to be reported more frequently among either men or women. Men were more likely to have experienced eyelid crusting or flakes upon waking or eye/eyelid redness upon waking, while women were more likely to report other symptoms, such as eye dryness and irritation, heavy and puffy eyelids, and eye irritation after prolonged computer use (Figure 7). Women were also more likely to have experienced red bumps, styes, and thinning of the eyelashes.

Younger respondents were more likely to report having experienced symptoms in the past 12 months. Among respondents aged 18 to 49 years (n = 2,890), 83% reported experiencing at least one symptom in the past 12 months, compared to 78% of individuals 50 to 64 (n = 1,240), and 70% of individuals 65 and older (n = 801). On average, younger respondents also had a higher proportion of symptoms occurring at least half the time than did older respondents (65 years and older, n = 801). Among respondents aged 18 to 49 years, the mean number of symptoms experienced at least half of the time in the past 12 months was 0.7, compared to 0.5 for respondents 50 years or older.

While symptoms were generally more common among younger individuals, some symptoms were more common in older adults. The likelihood that respondents reported thinning

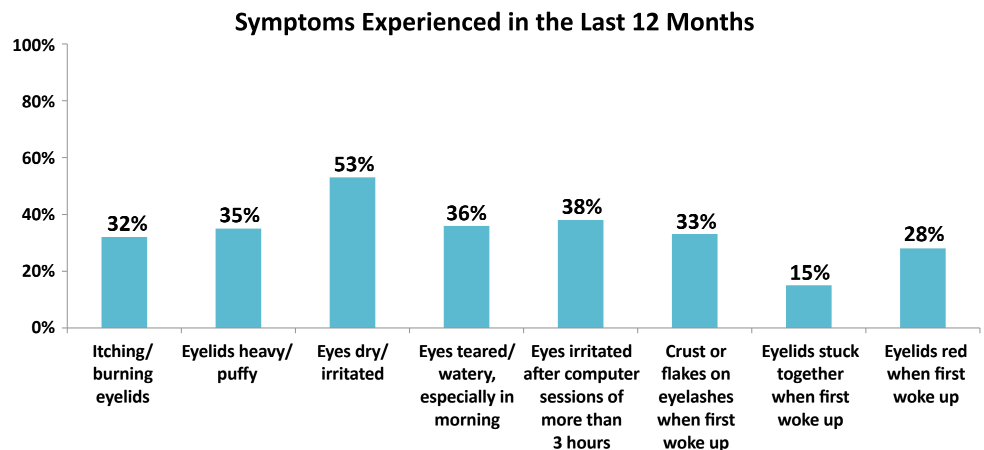


Figure 3. Percentage of patients who experienced each of the above symptoms at least some of the time in the last 12 months. (Adapted with permission from The Mattson Jack Group, Inc. "Epidemiology of Blepharitis." September, 2008.)

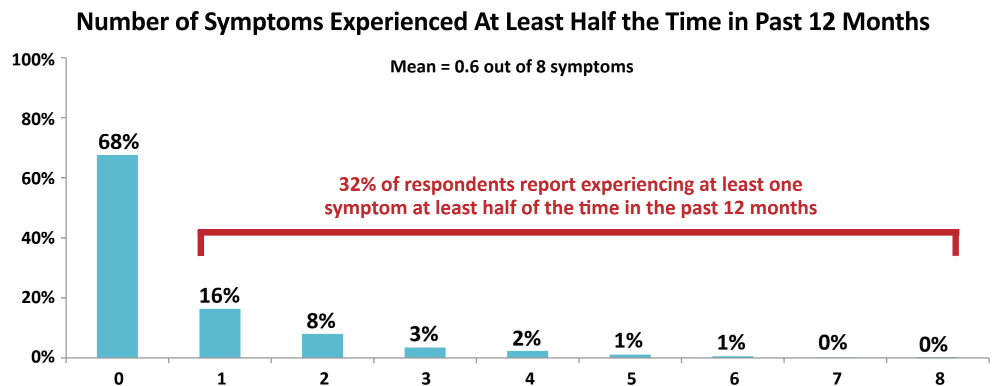


Figure 4. Thirty-two percent of survey respondents reported experiencing at least one symptom *at least half the time* in the past 12 months. (Adapted with permission from The Mattson Jack Group, Inc. "Epidemiology of Blepharitis." September, 2008.)

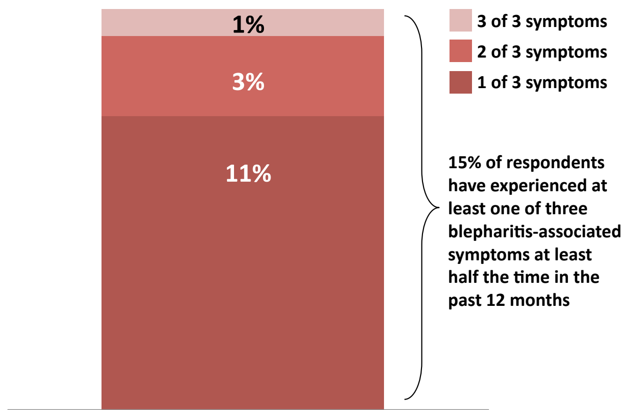


Figure 5. Fifteen percent of respondents experienced at least one blepharitis-associated symptom at least half the time in the past 12 months. (Adapted with permission from The Mattson Jack Group, Inc. "Epidemiology of Blepharitis". September, 2008.)

of eyelashes increased with age, and styes were reported most frequently among respondents between 50 and 64 years of age.

3. Blepharitis and Dry Eye Disease

In addition to symptoms commonly found in blepharitis, some of the symptoms about which respondents were queried are typical of dry eye disease (eg, eye irritation after more than 3 hours of computer use, eyelids itching or burning, feeling of dry or irritated eyes, watery eyes). Many of the symptoms typical of dry eye were reported by one-third or more of respondents.

Of the sample population, 1% of respondents had been diagnosed with blepharitis and 11% had been diagnosed with dry eye disease. Overlap was observed between these two groups; approximately 40% of the respondents diagnosed with blepharitis had also been diagnosed with dry eye disease. Of those with a previous diagnosis of blepharitis, symptoms were similar to those with dry eye, although eyelids stuck together on waking, eyes or lids red on awakening, and thinning of lashes may be more indicative of blepharitis and warrant further evaluation.

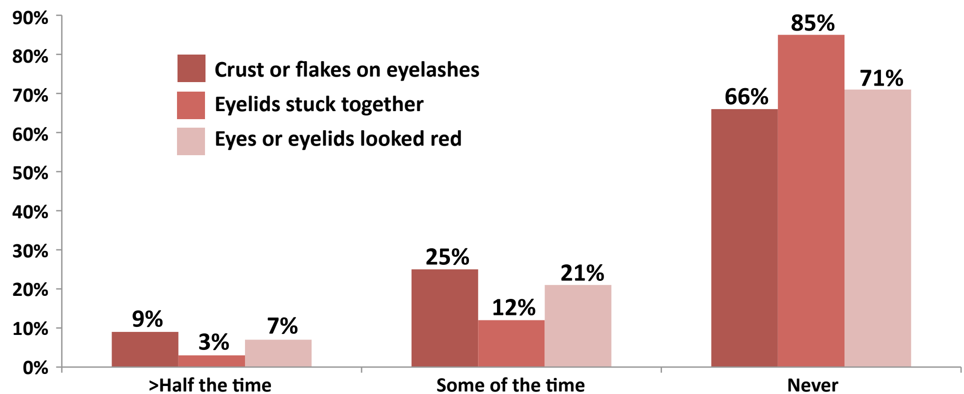


Figure 6. Blepharitis-associated symptoms include crust or flakes on eyelashes, eyelids sticking together, and eye or eyelid redness. (Adapted with permission from The Mattson Jack Group, Inc. "Epidemiology of Blepharitis." September, 2008.)

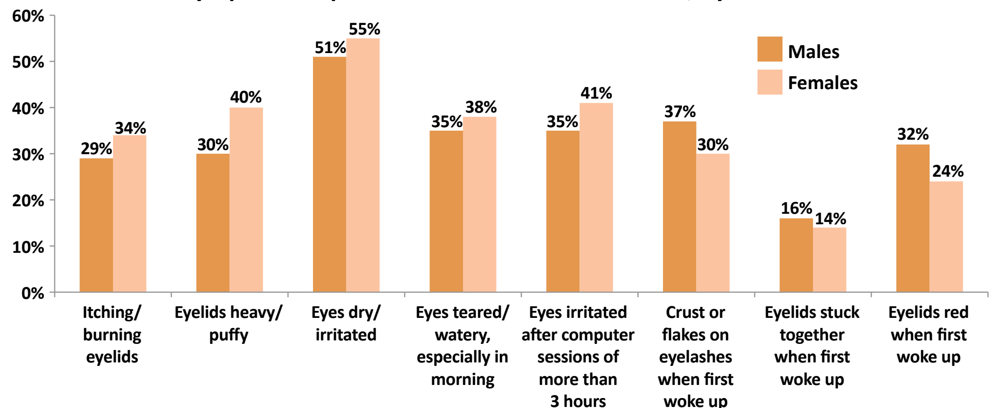


Figure 7. The occurrence with which respondents reported certain symptoms varied slightly by gender. (Adapted with permission from The Mattson Jack Group, Inc. "Epidemiology of Blepharitis." September, 2008.)

D. Discussion

As the first large-scale population-based survey to address symptoms that clinically are blepharitis-related, this study provides a valuable perspective on symptoms associated with both blepharitis and dry eye disease.

In addition to showing that many individuals experience ocular symptoms often associated with blepharitis, this data reveals somewhat surprising patterns in the distribution of these symptoms. Although most clinicians view blepharitis and dry eye disease as conditions that more commonly affect older rather than younger individuals, this survey found that younger individuals reported the highest frequency of symptoms. In part, this finding may reflect that younger people have greater consciousness of symptoms. Because older people often grow to accept a variety of insults as part of aging, over time a moderate level of ocular irritation may come seem normal. In addition, blepharitis and dry eye disease are chronic conditions, and over time the disease process itself may cause changes that affect pain-signaling. Younger people, too, may spend more time in

front of computer screens, thus provoking ocular dryness symptoms. Moreover, many of these young people may also be contact lens wearers, in whom symptoms of ocular dryness and irritation are common.[23,24]

Because the people interviewed were not examined by eyecare practitioners, we cannot extrapolate from reported symptoms to diagnosis. Diagnosis is further complicated by the fact the symptoms about which patients were queried can point to multiple conditions. For example, itching or burning eyelids could be a symptom of ocular allergy or dry eye disease, as well as blepharitis.

Indeed, some of the symptoms queried (itching/burning; eyes dry/irritated; eyes irritated after prolonged computer use) are more typically associated with dry eye disease than blepharitis. However, the majority of dry eye disease has an evaporative component that is typically the result of meibomian gland dysfunction, or posterior blepharitis.[7,25]

The fact that 11% of the adult population claims to have been diagnosed with dry eye disease is surprising in that the value is similar to prevalence reports, indicating that the general public has a significant awareness of the term dry eye. Some of these diagnoses may represent eyecare practitioners using the term "dry eye" to explain ocular discomfort, especially in contact lens wearers. The fact that only 1% remembered a diagnosis of blepharitis may represent practitioners' reluctance to diagnose the condition or patients' inability to recall an unfamiliar word. If the blepharitis is asymptomatic, the practitioner simply may not mention it. In addition, some of the diagnosed dry eye cases may include MGD (posterior blepharitis). Further studies to delineate differences in specific symptoms of dry eye in contrast to blepharitis, as well as prevalence studies of blepharitis, and of mixed dry eye and blepharitis, are needed.

E. Conclusions

Symptoms of ocular irritation and dryness are common within the general population—more than half (53%) of the study population reported eyes feeling dry or irritated during the last 12 months. In addition, 32% of survey respondents experienced at least one symptom at least half of the time, indicating frequency more indicative of ocular disease. Ocular irritation following more than 3 hours of computer use was also a common symptom (38%). These irritative symptoms are frequently associated with dry eye disease, which is thought to be highly correlated with meibomian gland dysfuntion.

Symptoms associated with anterior blepharitis (crust or flakes on lashes, eyelids stuck together on awakening, eyelids red on awakening) were also relatively common and often reported together. Based on these findings, we can say that symptoms associated with both blepharitis and dry eye disease affect a very substantial proportion of the adult population, and there is considerable overlap in diagnoses of dry eye disease and blepharitis. In addition, symptomatic respondents frequently reported difficulty in wearing contact lenses, which can lead to lens discontinuation and possibly adverse contact lens outcomes. Blepharitis is an often-overlooked condition of the ocular surface that warrants further research.

III. SURVEY: EYECARE PRACTITIONERS' EXPERIENCE WITH BLEPHARITIS

A. Introduction

The high prevalence of blepharitis-like symptoms found in the Mattson Jack survey suggests that ophthalmologists and optometrists are likely to encounter this condition frequently in practice. To gain further insight into the frequency with which eyecare practitioners encounter the signs and symptoms of blepharitis and how they manage them, Inspire Pharmaceuticals organized several "summit" meetings, during the course of which eyecare providers were surveyed about a range of issues related to the evaluation, diagnosis, and treatment of blepharitis.

B. Methods

A paper questionnaire was given to 120 ophthalmologists attending one of the summit meetings in July 2008. The doctors in attendance were a selected group with a skew toward innovators, high prescribers, and physicians thought likely to be interested in the treatment of blepharitis. Prior to taking the questionnaire, the physicians heard a noted researcher present a talk on the subject of blepharitis. The physician responses were analyzed and reported by Campbell Alliance Group (Raleigh, NC).[26] Another summit meeting, held in September 2008, asked similar (but not identical) questions of 84 similarly selected optometrists; data from the optometrist group was analyzed in the course of preparing this report. As with the phone survey reported here, practitioner responses are subject to the accurate recall of individual practice patterns and preferences and are not based on billing and coding or prescription data.

C. Results

1. Diagnosis

Ophthalmologists were asked how often they observed blepharitis in their practices. Respondents were instructed that for the purposes of the survey, blepharitis was defined as a range

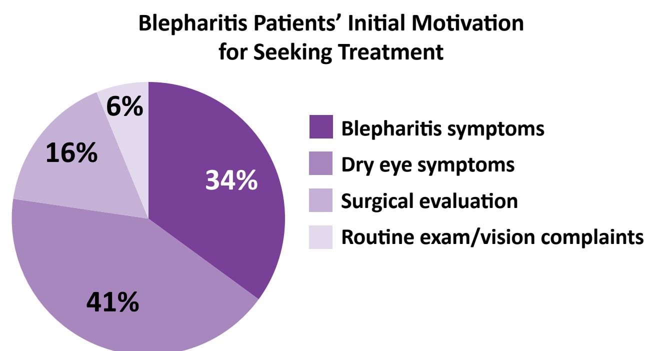


Figure 8. Blepharitis patients had many reasons for initially seeking treatment. (Adapted with permission from Campbell Alliance Group. Patterns of Practice and Prevalence Rates for Lid Margin Disease. July-August 2008.)

of acute and chronic disorders involving the lid margin, with anterior blepharitis primarily affecting the region at the base of the eyelashes and posterior blepharitis affecting meibomian orifices. Overall, ophthalmologists estimated that 37% of the patients they saw presented with some form of blepharitis.

Of the patients diagnosed with blepharitis, only 34% had sought treatment for blepharitis symptoms; the rest initially sought treatment because of dry eye symptoms (41%), surgical evaluations (16%), or routine exams/vision complaints (6%) (Figure 8). Ophthalmologists estimated that approximately 22% of the patients they diagnosed with blepharitis did not present with ocular surface symptoms as a chief complaint.

Ophthalmologists were also asked whether they attempted to differentiate between anterior and posterior blepharitis. While symptoms of the two conditions overlap—and some patients may have both conditions—60% of ophthalmologists reported that they routinely attempt to distinguish anterior from posterior blepharitis.

2. Clinical Presentation

In addition to questioning ophthalmologists about the prevalence of blepharitis in clinical practice, this survey sought to identify which patients were most likely to be diagnosed with blepharitis by the clinicians surveyed. When the ophthalmologists were asked which clinical features are most commonly associated with posterior blepharitis/MGD, they noted change

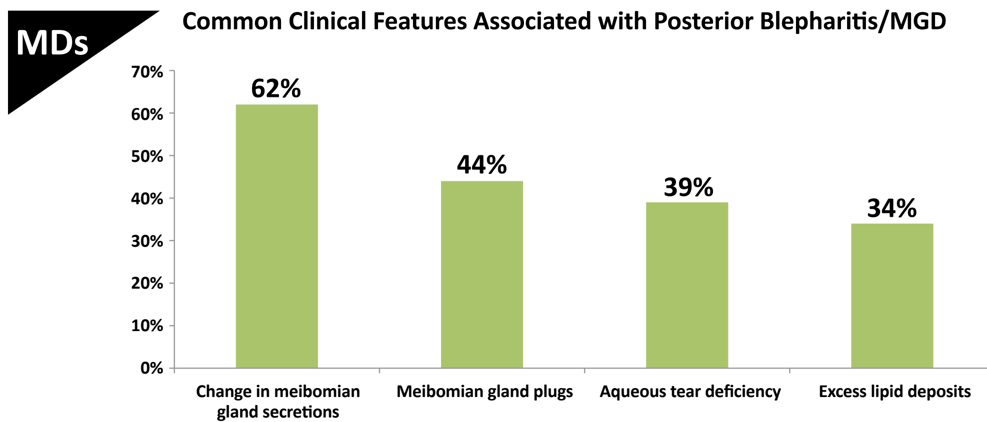


Figure 9. Ophthalmologists reported multiple clinical features commonly associated with posterior blepharitis/MGD. (Adapted with permission from Campbell Alliance Group. Patterns of Practice and Prevalence Rates for Lid Margin Disease. July-August 2008.)

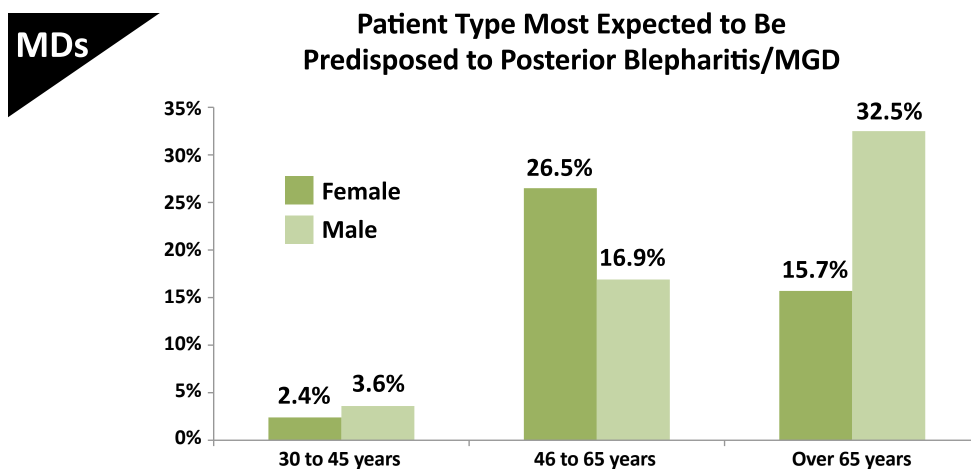
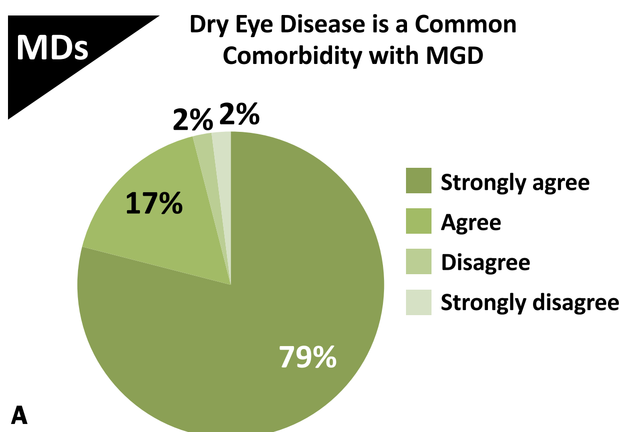


Figure 10. Ophthalmologists identified men over 65 as the patient group most likely to be predisposed to posterior blepharitis/MGD. (Adapted with permission from Campbell Alliance Group. Patterns of Practice and Prevalence Rates for Lid Margin Disease. July-August 2008.)



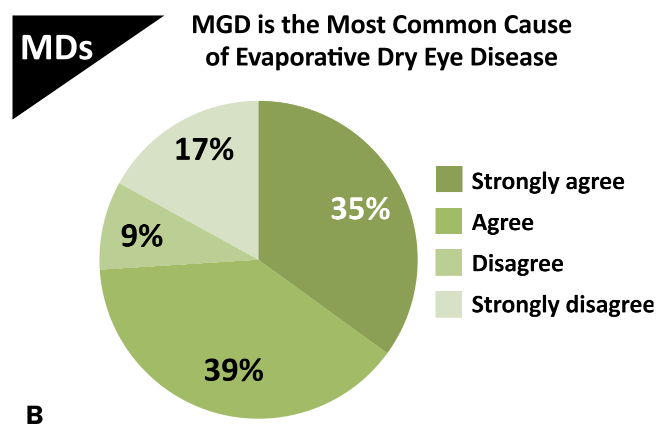


Figure 11. The majority of ophthalmologists agreed that dry eye disease is a common comorbidity with MGD (A) and that posterior blepharitis/MGD is the most common cause of evaporative dry eye disease (B). (Adapted with permission from Campbell Alliance Group. Patterns of Practice and Prevalence Rates for Lid Margin Disease. July-August 2008.)

in meibomian gland secretions (62%), meibomian gland obstruction (44%), aqueous tear deficiency (39%), and excess lipid secretion (39%) (Figure 9).

When asked about the age and gender of patients most expected to be predisposed to posterior blepharitis/MGD, 33% of ophthalmologists identified men over age 65, followed by women between the ages of 46 and 65 years (27% of respondents) (Figure 10). In a write-in answer, ophthalmologists also noted patient factors they associated with posterior blepharitis/MGD, which included rosacea, light skin, and poor lid hygiene.

3. Comorbidity with Dry Eye Disease

Ninety-six percent of the ophthalmologists who participated in the survey agreed or strongly agreed that dry eye disease is a common comorbidity with MGD, and 74% agreed or strongly agreed that MGD is the most common cause of evaporative dry eye (Figures 11A and B). When asked to identify comorbid conditions commonly seen with blepharitis, 77% of respondents mentioned dry eye disease, 31% mentioned allergic conjunctivitis, and 31% mentioned rosacea.

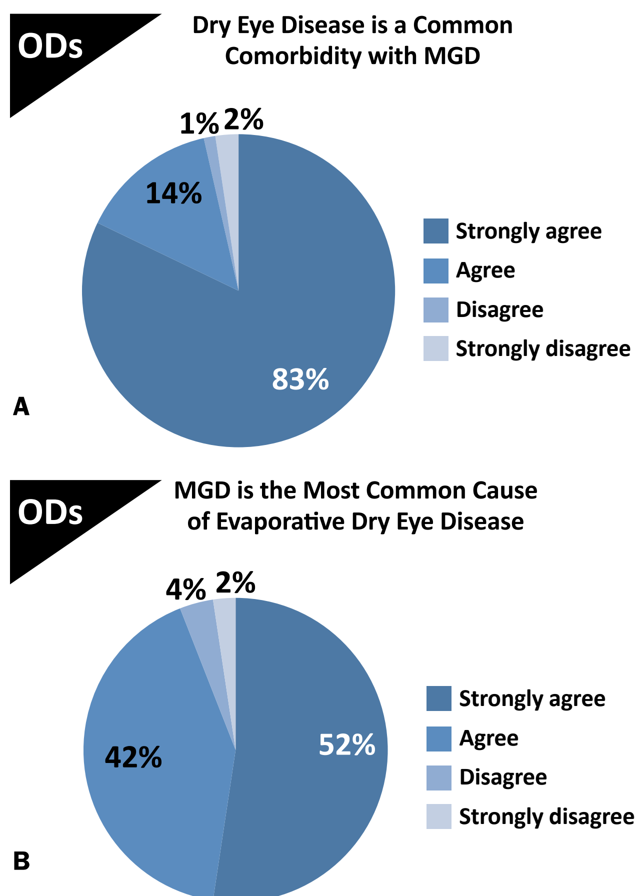


Figure 12. Optometrists also agreed that dry eye disease is a common comorbidity with posterior blepharitis/MGD (A) and that posterior blepharitis/MGD is the most common cause of evaporative dry eye disease (B). (Adapted with permission from Campbell Alliance Group. Patterns of Practice and Prevalence Rates for Lid Margin Disease. July-August 2008.)

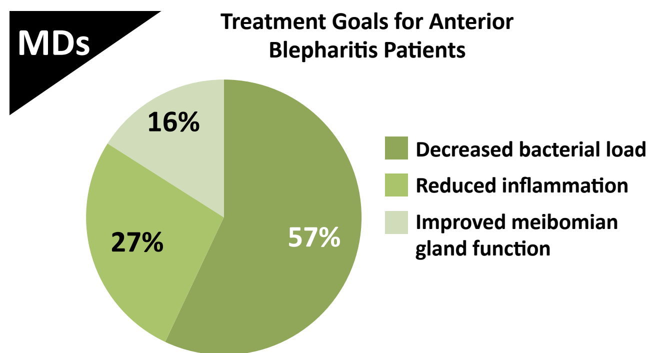


Figure 13. Ophthalmologists reported having multiple treatment goals for anterior blepharitis patients. (Adapted with permission from Campbell Alliance Group. Patterns of Practice and Prevalence Rates for Lid Margin Disease. July-August 2008.)

D. Comparison between Ophthalmologists' and Optometrists' Approaches to Management of Blepharitis

In addition to surveying ophthalmologists, optometrists (n = 84) were surveyed in a similar manner to determine their views about blepharitis/MGD presentation, diagnosis, and comorbidity. Overall, both groups had similar responses, although some differences were observed.

On average, optometrists reported that 47% of the patients they saw presented with some form of blepharitis, compared to a prevalence of 37% in the ophthalmology survey. The percentage of optometrists who reported routinely differentiating between anterior and posterior blepharitis (83%) was higher then the percentage of ophthalmologists who reported making this distinction (60%).

With respect to patient characteristics associated with blepharitis/MGD, optometrists and ophthalmologists reported similar beliefs. In addition, optometrists and ophthalmologists reported (in a write-in question) that they encountered similar comorbidities, with optometrists indicating that blepharitis and MGD were frequently associated with allergy (12%) and rosacea (12%). In addition, both groups believed MGD was a major contributing factor to contact lens intolerance.

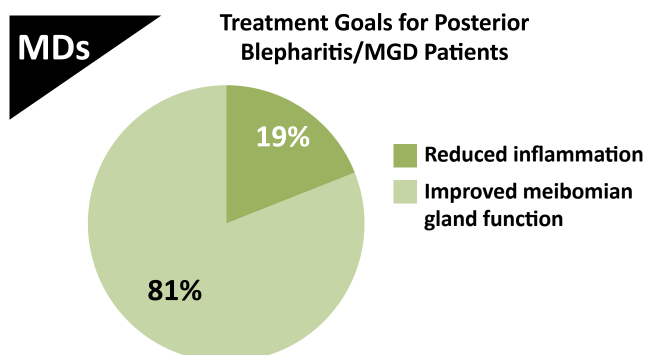


Figure 14. For posterior blepharitis patients, the majority of ophthalmologists listed improved meibomian gland function as their most important treatment goal. (Adapted with permission from Campbell Alliance Group. Patterns of Practice and Prevalence Rates for Lid Margin Disease. July-August 2008.)

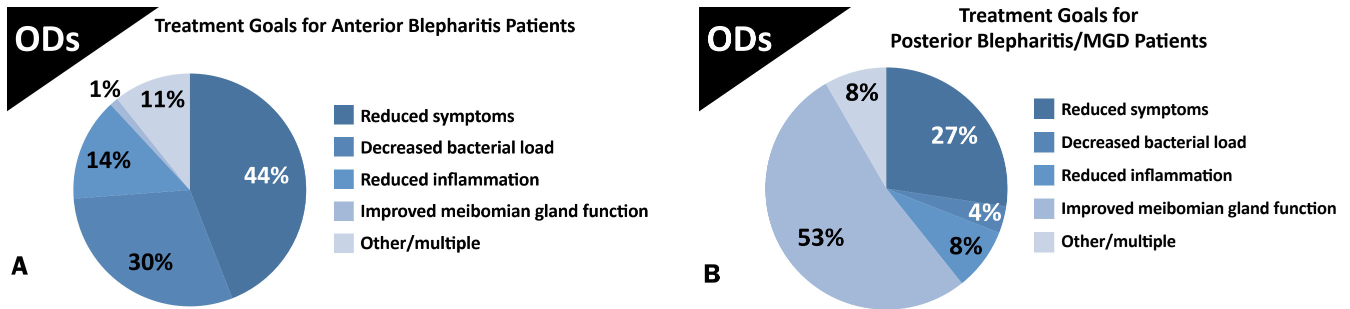


Figure 15. Optometrists reported multiple treatment goals for both anterior blepharitis (A) and posterior blepharitis (B). (Adapted with permission from Campbell Alliance Group. Patterns of Practice and Prevalence Rates for Lid Margin Disease. July-August 2008.)

Similarly, when asked about associations between blepharitis and dry eye disease, the vast majority of optometrists (97%) agreed or strongly agreed that dry eye disease is a common comorbid condition with posterior blepharitis/MGD, and 94% agreed or strongly agreed that posterior blepharitis/MGD is the most common cause of evaporative dry eye disease (Figure 12A and B).

1. Treatment Considerations

Among the ophthalmologists surveyed, 69% of blepharitis patient visits result in some form of treatment. Of those patient visits that require treatment, 53% will result in a prescription as part of the overall treatment plan.

Ophthalmologists reported having different treatment goals for anterior and posterior blepharitis. When asked which treatment goal is of primary importance in the management of anterior blepharitis, they reported that their most important treatment goals (in addition to reducing symptoms) were decreasing the bacterial load (57%), reducing inflammation (27%), and improving meibomian gland function (16%) (Figure 13). For posterior blepharitis, the most important treatment goals (in addition to reducing symptoms) were improving meibomian gland function (81%) and reducing inflammation (19%) (Figure 14).

For anterior blepharitis, optometrists reported that their primary goals, in addition to symptom reduction (44%), were decreased bacterial load (30%) and reduced

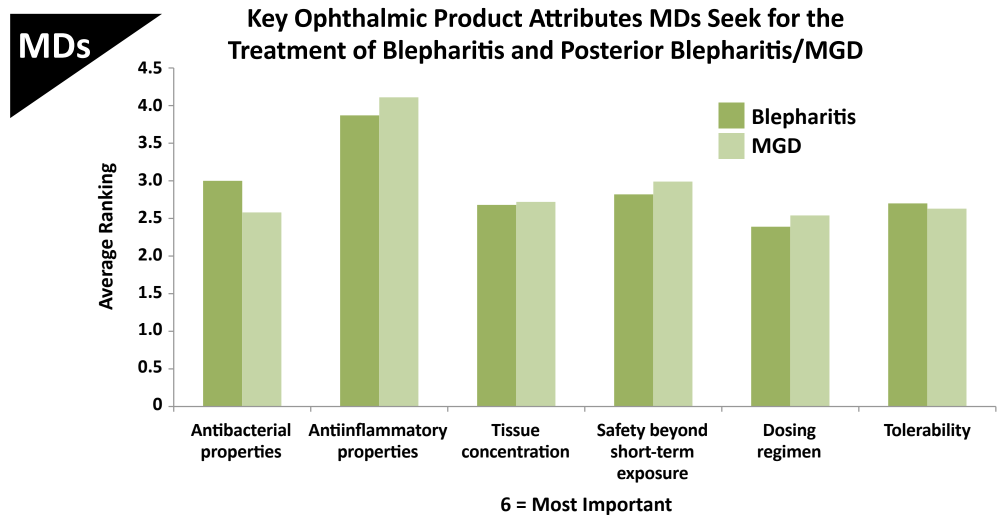


Figure 16. Among ophthalmologists, antiinflammatory activity was the most desired drug attribute for the treatment of both blepharitis and posterior blepharitis/MGD, followed by antibacterial activity, safety, and tissue concentration. (Adapted with permission from Campbell Alliance Group. Patterns of Practice and Prevalence Rates for Lid Margin Disease. July-August 2008.)

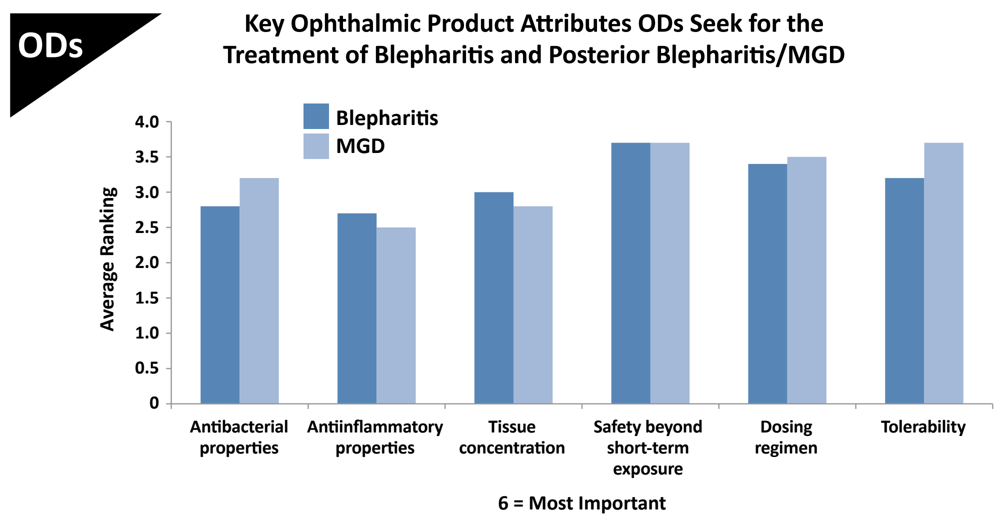


Figure 17. Among optometrists, safety, tolerability, and dosing regimen were the most important attributes of a drug for the treatment of both blepharitis and posterior blepharitis/MGD. (Adapted with permission from Campbell Alliance Group. Patterns of Practice and Prevalence Rates for Lid Margin Disease. July-August 2008.)

inflammation (14%) (Figure 15A). For posterior blepharitis, optometrists reported goals of improved meibomian gland function (53%), reduced symptoms (27%), and reduced inflammation (8%) (Figure 15B).

2. Pharmacological Treatment

Despite having reported different treatment goals for anterior and posterior blepharitis, ophthalmologists sought similar product attributes for both blepharitis (all) and posterior blepharitis/MGD treatments, with antiinflammatory activity being the most important attribute mentioned in both questions. For blepharitis (all), the next most important attributes were antibacterial activity, safety, and tissue concentration (Figure 16). For posterior blepharitis/MGD, the second, third, and fourth most important attributes were safety, tissue concentration, and tolerability. When asked about the most important product attributes for blepharitis (all) and posterior blepharitis/MGD, optometrists placed more emphasis on safety, tolerability, and dosing regimen, with less emphasis placed on antiinflammatory activity (Figure 17).

When asked about the drugs they use to achieve these goals, both ophthalmologists and optometrists reported similar preferences, with azithromycin ophthalmic solution 1% being the top choice for both blepharitis (all) and posterior blepharitis/MGD patients and oral doxycycline being a second choice (Figures 18 and 19). Antiinflammatory agents (cyclosporine, loteprednol etabonate, and the combination agent dexamethasone/tobramycin) ranked just behind azithromycin and doxycycline. Following them were bacitracin and erythromycin ointments. Ranking lowest, were the fluoroquinolones (moxifloxacin, gatifloxacin, and ciprofloxacin).

E. Discussion

We are in a period during which the treatment of ocular surface disorders is changing. The data reported herein provides a valuable snapshot of the current clinical situation among innovative doctors interested in and currently managing blepharitis.

The two sets of practitioner survey data have certain limitations. As with any study in which a limited number of individuals is invited to participate, respondents may not be representative of a larger population of optometrists and ophthalmologists. In this case, the sponsorship of the study (which was known to participants) may have attracted eyecare practitioners with a particular interest in blepharitis and/or individuals who were early adopters of topical azithromycin (which is marketed by the survey's sponsor). As a result, this survey could have overestimated the prevalence of blepharitis and clinicians' preference for azithromycin treatment. In addition, recall can limit or bias study results. Therefore, the findings presented here probably cannot be extrapolated to eyecare practitioners at large.

Nonetheless, the optometrists and ophthalmologists surveyed here make efforts to differentiate blepharitis and MGD and are educating patients and prescribing therapies for the condition. While slight differences in the two surveys limit direct statistical comparisons, the fact that both the ophthalmologist and optometrist surveys found similar trends indicates an encouraging level of consensus among

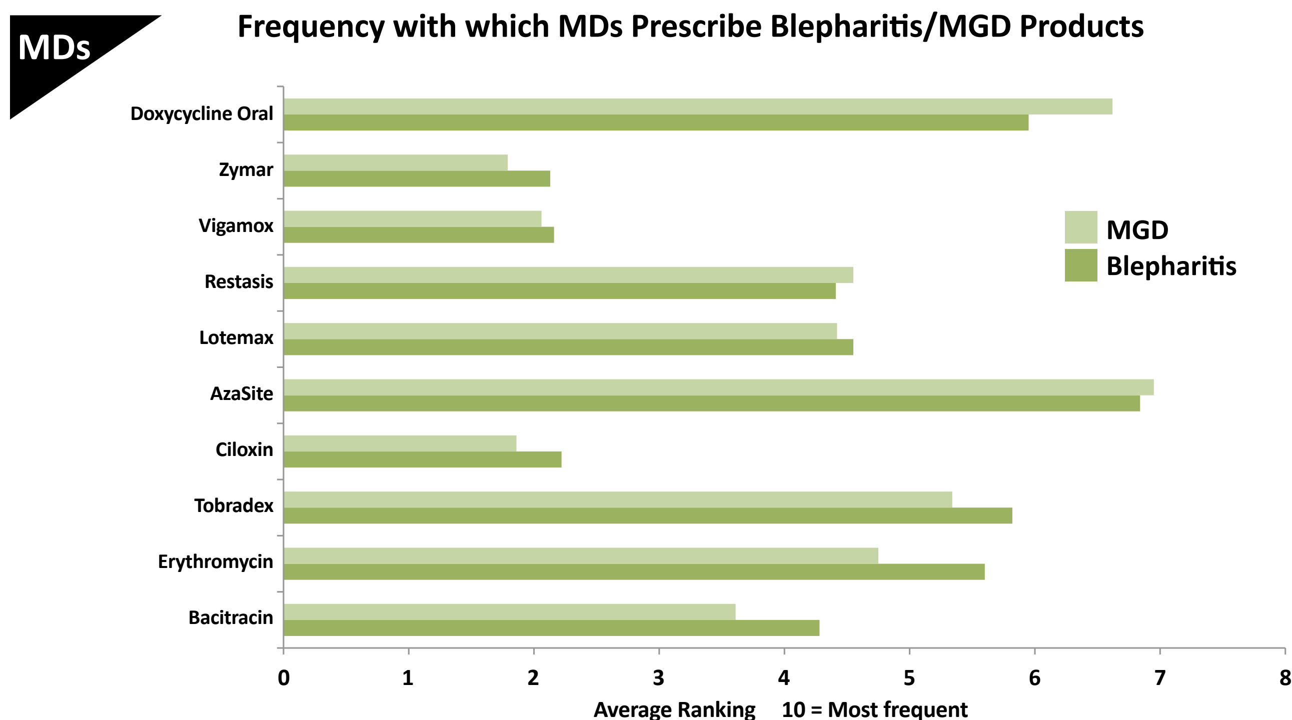


Figure 18. Among ophthalmologists, topical azithromycin was the most frequently prescribed treatment for both blepharitis and MGD. (Adapted with permission from Campbell Alliance Group. Patterns of Practice and Prevalence Rates for Lid Margin Disease. July-August 2008.)

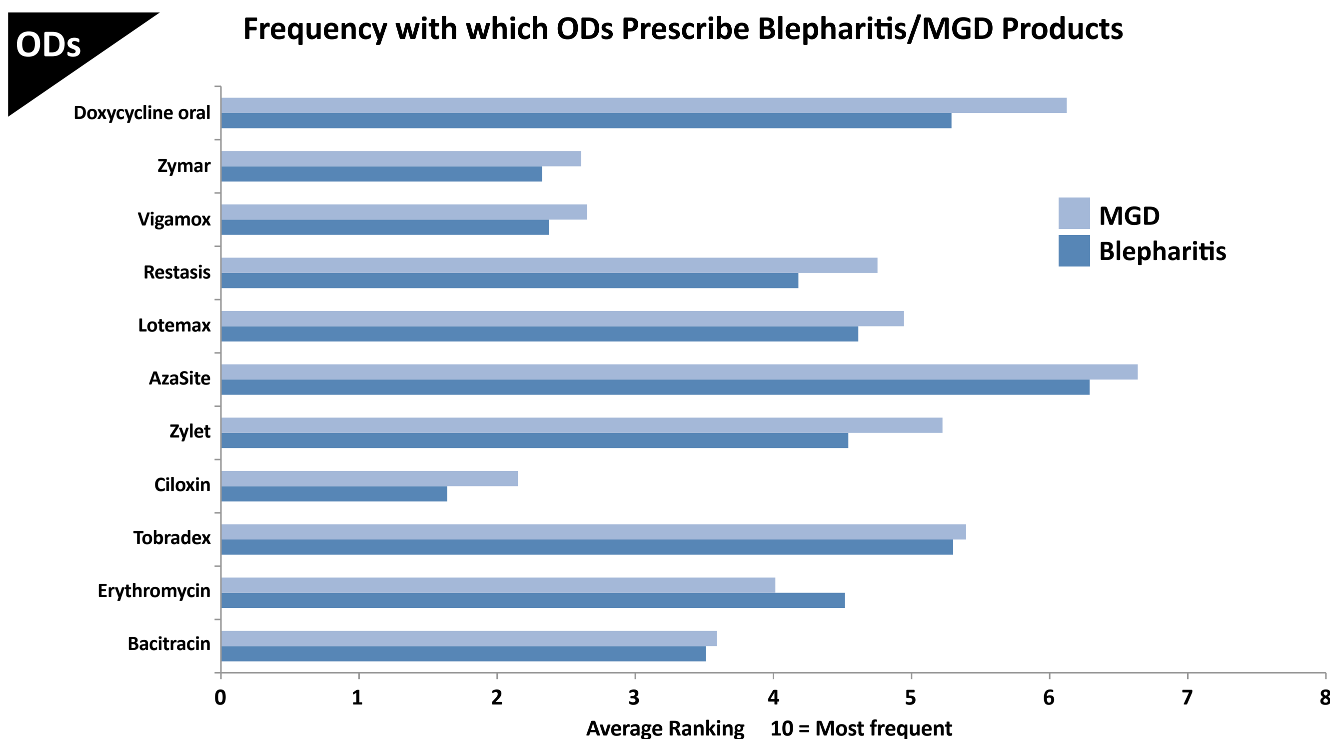


Figure 19. Among optometrists, topical azithromycin was the most frequently prescribed treatment for both blepharitis and MGD. (Adapted with permission from Campbell Alliance Group. Patterns of Practice and Prevalence Rates for Lid Margin Disease. July-August 2008.)

eyecare practitioners who may be considered expert clinicians or early adopters.

Both surveys show that blepharitis and dry eye are prevalent conditions for which practitioners use a multitude of therapies. In addition, many practitioners report dry eye and blepharitis are comorbid, although there is lack of agreement as to the true relationship between the conditions. There is agreement that lid margin inflammation is an element that needs treatment in both posterior and anterior blepharitis. There is also consensus among the ophthalmologists and optometrists surveyed that MGD is is a major component of dry eye disease and contact lens intolerance; however, it is unclear if the opinion is that MGD is a comorbid condition or an underlying causative factor.

With respect to treatment reported by the practitioners in this survey, while lid hygiene measures (including warm compresses for MGD) are currently used and traditionally have been the mainstay of blepharitis treatment, the eyecare practitioners surveyed are currently recommending prescription drug therapy and are moving away from traditional antibiotic ointment therapy in favor of new ophthalmic pharmaceuticals.

IV. SUMMARY OF ALL SURVEY FINDINGS

The data presented here represents a snapshot of the ocular surface disease landscape. A large segment of the public is affected by blepharitis-associated symptoms, and ocular surface diseases are of importance to practitioners. As with all eye diseases, practitioners are looking for tools to more effectively manage patients and prevent adverse outcomes. It is our hope that this data will be an additional step in engaging researchers to further the understanding of the epidemiology and etiology, comorbid conditions, presenting symptoms, associated factors, clinical diagnosis, and management of blepharitis.

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Commentary

Enhancing Our Knowledge of Blepharitis*

GARY N. FOULKS, MD, FACS†

Blepharitis is one of the most common, and yet most commonly overlooked, clinical conditions affecting our patients. Information about the true prevalence of the condition is limited, derived predominantly from studies of contact lens wearers or those considering contact lens wear. The survey data presented in this supplement to *The Ocular Surface* takes an important and useful step toward correcting that deficiency in our understanding of blepharitis by assessing both the patient and practitioner populations.

SCOPE OF THE PROBLEM

Many practitioners have viewed blepharitis more as a nuisance than as a significant clinical problem, particularly since treatment options were limited, as was the success of those treatments. Like dry eye disease, blepharitis is not a life-threatening (nor, in its milder forms, a sight-threatening) condition, which has made it easier to dismiss. Blepharitis, again like dry eye disease, is multifactorial in nature, which has complicated classification and treatment of the disease.

However, new research regarding the impact of blepharitis, as well as encouraging reports of the effectiveness of new treatment options, has increased awareness of and interest in this condition. More intensive investigation of blepharitis identifies it not only as a frequent cause of irritating and cosmetically unappealing symptoms, but also as a major cause of evaporative dry eye disease and contact lens intolerance. Blepharitis, we now know, can impair visual function, and that has important implications with respect to surgical outcomes and underscores the need for effective treatment prior to surgery.

A chronic condition, untreated blepharitis can over time result in lid alterations, including eyelid notching and scarring, loss of eyelashes, and in-turning of eyelashes. These structural changes are not easily reversed and may be permanent. Chronic blepharitis can also lead to destruction of the meibomian gland architecture and closure of the orifices by scar tissue.

RESEARCH AIMS

The multifactorial nature of blepharitis and our still incomplete understanding of its etiology have hampered the development of a consensus definition and classification. Beyond culturing to determine microbial colonization, there have been few diagnostic tests that shed light on blepharitis. New methods of measuring tear function, new understandings of the composition of meibomian gland secretions, and new means of evaluating visual function are changing that picture.

From the patient perspective, it is important to identify and characterize the symptoms and signs of the disease, so that the appropriate diagnosis and management can be achieved. From the practitioner perspective, it is imperative to develop reliable and efficient diagnostic techniques, and to expand effective treatment options.

SURVEY DATA

The survey data identified and discussed in this supplement comprises an important step toward a better understanding of blepharitis. The data set has limitations, including lack of confirmatory physical examination of the subjects and selective recruitment of practitioners in the physician study. That said, the survey provides a good start in pursuing both improved instruments for survey and enhanced perception of blepharitis by practitioners.

The eyecare practitioner survey is one of the first surveys of practitioner attitudes toward blepharitis. Its results provide insight into the perceptions of a select group of treating practitioners, a knowl-

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edge of what they use to manage blepharitis, the range of treatments available, and an understanding of what these practitioners would like to have available for blepharitis management in the future. The data provides important information on the perceived effectiveness of azithromycin ophthalmic solution 1%, an exciting avenue for further exploration. The computer-assisted telephone survey provides a fairly large population-based look at symptoms of blepharitis, and at the prevalence of those symptoms.

CONCLUSION

The study data provides us with information that will further the development of other research efforts. In fact, this supplement comes at an ideal time. In May, the Tear Film and Ocular Surface Society will hold an international workshop on meibomian gland dysfunction immediately following the annual Association for Research in Vision and Ophthalmology meeting. Aims of this workshop include developing a contemporary understanding of the definition and classification of meibomian gland dysfunction; assessing methods of diagnosis, evaluation, and grading of severity; and developing recommendations for management and therapy of the condition.

I look forward to the outcome of this workshop, which, combined with data from this supplement and a newly heightened interest in blepharitis within the eyecare community, will doubtless deepen our understanding of this historically enigmatic condition and its optimal treatment.

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Commentary

The Patient's Experience of Blepharitis*

MARGUERITE B. MCDONALD, MD†

Blepharitis is one of the most common conditions affecting patients presenting to ophthalmic practices. Blepharitis can occur in both sexes, all races, and at any age, although light-skinned individuals over the age of 40 of northern European extraction appear to be disproportionately affected.[1] Despite the frequency with which eyecare practitioners see blepharitis in their patients, there is little reliable epidemiologic data on its prevalence.

While the exact prevalence of blepharitis in the general population is uncertain, what those of us who treat blepharitis patients know with certainty is the negative impact this condition has on the quality of patients' lives—blepharitis can affect patients' physical appearance, comfort, visual function, and even social interactions. Blepharitis causes bright red, bleary, puffy eyes that itch and burn, making patients feel both uncomfortable and unattractive. Blepharitis patients' vision is often affected and, after a time, patients' eyelids may be permanently disfigured.

Unfortunately, many older patients with the disease assume that puffy, red, irritated eyes are just one more of the many insults of aging. Similarly, eyecare practitioners see so much blepharitis that it can come to seem almost "normal," at least in certain groups. If the patient is asymptomatic—or at least not complaining—the practitioner may be tempted to ignore it. Until recently, our options for treating blepharitis were inconvenient for the patient, only partially effective, and, in some cases (eg, oral tetracyclines) prone to unpleasant side effects. When we had little in the way of effective treatments, ignoring low-grade blepharitis was understandable.

CHRONIC AND PROGRESSIVE

Although its intensity may wax and wane, untreated blepharitis is a chronic condition, with symptoms becoming more pronounced with the passing of time. Red-rimmed, notched lids and loss of cilia are not uncommon—battle scars from years of chronic inflammation and bouts with the chalazia and hordeola to which these patients are prone. Preventing progression to irreversible lid damage is one of the strong arguments in favor of treating blepharitis, even if the patient is able to tolerate the symptoms at the time of the visit.

The eyes are an important part of our "body language," and red, puffy eyes can have social implications for patients. Friends, family, and coworkers may assume that the patient has insomnia or has spent some time crying, or even suspect a drinking or drug problem. In short, blepharitis is a distressing and uncomfortable condition for many patients.

POSTERIOR BLEPHARITIS

Blepharitis frequently takes the form of posterior lid margin disease or meibomian gland dysfunction. Since the meibomian glands are the source of the lipid portion of the tear film that protects the ocular surface, meibomian gland dysfunction can have both direct and indirect effects on the tear film. Some of the abnormal lipids produced by patients with meibomian gland dysfunction are directly irritating to the ocular surface; other lipid changes affect tear film stability.[2] Reduced tear film break-up time is the chief sign of tear film instability. An unstable tear film loses water to evaporation, raising the concentration of solutes in the tears and, therefore, the osmolarity of the tear film. Hyperosmolarity is thought to be an important cause of ocular surface inflammation and the chief instigator of the pathogenetic chain of events that leads to the symptoms of evaporative dry eye.[3]

Many patients with posterior blepharitis complain of ocular irritation on awakening. Presumably, this is due to irritation from the abnormal tear lipids that have built up in the tear film overnight, when there was little production of aqueous tears to wash the irritants away. Later in the day, the

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symptoms may resurface, as the ocular surface is repeatedly exposed to the environment because the unstable tear film cannot protect it for the entire interval between blinks.

In addition to discomfort, evaporative dry eye symptoms secondary to meibomian gland dysfunction may also reduce patients' ability to tolerate contact lens wear. Having to reduce wearing time, or not being able to wear contact lenses at all, is frustrating for the many patients who would much rather wear contact lenses than glasses.

Refractive surgery patients with posterior blepharitis are at high risk of postoperative dry eye symptoms. In addition, these patients want (and, indeed, expect) to have high-quality vision after surgery. Compromised postoperative acuity due to posterior blepharitis is unacceptable. Treating lid disease before and after refractive surgery will improve outcomes and make us better surgeons.

STAPHYLOCOCCAL BLEPHARITIS

Blepharitis associated with the anterior lid margin is typically a product of bacterial overgrowth. Patients with anterior blepharitis tend to be more aware of the lid's involvement, as they can see scurf and collarettes at the base of the lashes, whereas patients with meibomian gland dysfunction tend to experience more generalized ocular symptoms and may not realize that the source of their problem is a group of tiny glands inside the lids.

In addition to cosmetic and comfort issues, untreated chronic blepharitis can do irreversible damage. Chronic inflammation within the meibomian glands over many years destroys the gland architecture, and cicatricial changes at the meibomian orifice seal off the gland. With time there may be enough scarring to change the position of the lid relative to the surface of the globe (ectropion or entropion). At this point, there is virtually no meibomian function and no means to restore that function. One good reason to treat blepharitis is to ensure that it never progresses to a stage where the damage is irreversible.

CONCLUSION

Although often neglected by both patients and physicians, blepharitis is an extremely common condition, that negatively impacts appearance, comfort, and visual function. Treating blepharitis improves patients' comfort and quality of life. Early treatment may also prevent progression to irreversible lid damage. It is important to pretreat any blepharitis patient who is headed for ocular surgery.

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The Effects of Blepharitis on Ocular Surgery*

Richard L. Lindstrom, MD†

A significant number of patients who present for ocular surgery have signs or symptoms of blepharitis. I estimate that blepharitis affects approximately a third of my cataract surgery patients; including all ocular surface disease brings the total to close to half. Since most of these patients are 60 years of age or older, these numbers do not necessarily reflect the prevalence of blepharitis in other patient groups; however, as the data presented in this supplement shows, blepharitis is also common in younger people.

For ocular surgery patients with blepharitis, proper preoperative treatment is essential for achieving optimal surgical outcomes. In addition to reducing the risk of complications related to bacterial infection, proper blepharitis treatment helps to ensure that patients achieve the best possible postoperative vision.

NEED FOR DIAGNOSIS

Although diagnosing blepharitis is fairly straightforward if one looks for it, surgeons too often give only a cursory glance at the lids and adnexa. Because a healthy ocular surface is essential for good visual outcomes, surgeons should be alert to signs and symptoms of blepharitis and related ocular surface diseases when performing the preoperative examination.

In taking a history, I listen for complaints of burning, grittiness, or itchiness, any of which can be indicative of blepharitis. Many blepharitis patients will also report crusting in the morning, and they may have a history of recurrent styes or hordeola.

On examination, lid erythema is a classic finding for both anterior and posterior blepharitis. Patients with anterior blepharitis may also have collarettes and scurf along the anterior lid margin, while patients with posterior blepharitis may exhibit foamy tears, inspissation of the meibomian glands, and telangiectasia of the lid vessels.

Finally, because blepharitis is frequently associated with dry eye disease, I also pay attention to the ocular surface and the tear film. Because the diglycerides and free fatty acids that are often present in the tears of blepharitis patients can irritate the ocular surface, posterior blepharitis may produce symptoms of ocular dryness. When this occurs, patients may need dry eye therapy in conjunction with blepharitis treatment.

MY TREATMENT APPROACH

Once blepharitis has been diagnosed, treatment should be initiated promptly. In the past, many surgeons overlooked blepharitis, particularly mild cases, because of the ubiquity of the condition and the lack of effective treatments. With the availability of new antibiotics, however, treatment should be recommended in every case; not only can proper therapy relieve symptoms and optimize surgical outcomes, it may also prevent the eyelid scarring, loss of eyelashes, and other sequelae of chronic untreated blepharitis.

Although lid hygiene has traditionally been the mainstay of blepharitis treatment, hygiene measures have shown limited success when used alone. However, adding new antibiotics to the treatment regimen can significantly improve signs and symptoms, so I recommend both lid hygiene measures and antibiotic treatment.[1] Specifically, I instruct patients to instill a drop of topical azithromycin 1%, close their eyes for 30 seconds, and then massage the drop into the lid margins.

While blepharitis treatment will usually provide some improvement within a few days, I typically wait at least 1-2 weeks before performing surgery to ensure that the blepharitis has completely

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resolved. I also add this blepharitis treatment to the postoperative drug regimen to promote ocular surface rehabilitation following surgery.

BENEFITS OF TREATMENT

Although relieving the patient's symptoms and preventing the potential sequelae of chronic blepharitis comprise reason enough to institute treatment, ocular surgery patients gain additional benefits from therapy.

First, by reducing the bacterial load on the surface of the eye, blepharitis treatment may reduce the risk of surgical infections. Although we do not have good data documenting the degree to which blepharitis may increase the risk of ocular infection, we do know that the bacteria that cause ocular infections generally originate in the normal ocular flora. Ensuring that this bacterial population is well controlled before surgery is a prudent step to reduce the risk of infection.

Second, if patients are to achieve the best possible postoperative vision, a healthy tear film is essential. Postoperative quality of vision is a key aspect of patient satisfaction—particularly for premium intraocular lens (IOL) patients. Also, since I sometimes choose a slightly different refractive target or even a different IOL for the second eye based on the visual results achieved in the first eye, I want to be able to evaluate a patient's vision as soon as possible after surgery—without its being affected by ocular surface problems.

CONCLUSION

Although often overlooked, blepharitis treatment should be viewed as an essential component of ocular surgery. Treatment before surgery may help to reduce the risk of surgical infection, and pre- and postoperative treatment can improve the quality of vision following surgery. Since cataract surgery and other procedures are increasingly being judged by their refractive results, such treatment is an important part of a successful procedure.

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Commentary

The Role of Bacteria in Blepharitis*

TERRENCE P. O'BRIEN, MD†

Clinicians suspect that bacteria play an important role in blepharitis, but many questions remain about the precise nature of that role in the pathogenesis of clinical disease. Since some bacterial colonization of the eyelids is normal and typically benign, possibly even beneficial, the presence of bacteria alone does not cause blepharitis. Instead, ongoing research suggests several possibilities; the condition may be due: to the wrong types of bacteria becoming established on the eyelids, too many bacteria colonizing this area, or an imbalance among the various bacterial species present.

Further investigation of these possibilities is needed to fully elucidate the etiology of the most common forms of blepharitis, but our growing understanding of this condition has already helped to identify promising avenues for therapy. Since some of the symptoms of blepharitis result from inflammation, a drug with an immunomodulatory effect is likely to prove beneficial. In addition, since bacterial byproducts contribute to this inflammation, using mild lid scrubs to remove this material in combination with a broad spectrum antibiotic active against common lid flora will likely continue to play a role in treatment of these pervasive conditions.

HOW BACTERIA CAUSE SYMPTOMS

In anterior blepharitis, sometimes called staphylococcal blepharitis, the lid margin exhibits excessive bacterial colonization—typically with coagulase-negative staphylococcus (CoNS), particularly *Staphylococcus epidermidis* and, to a lesser degree, *Staphylococcus aureus*. CoNS can cause symptoms by releasing various toxic bacterial products into the tear film; this stimulates the production and release of proinflammatory cytokines and leads to recruitment of inflammatory cells triggering host-induced in addition to organism-induced inflammation.

The role of bacteria in posterior blepharitis is less clear. *Propionibacterium acnes* and *S. epidermidis* are both present in patients with meibomian gland dysfunction, but these bacteria may only indirectly contribute to patients' symptoms.[1] One hypothesis is that these bacteria release lipases that break down the meibum into free fatty acids and soaps, which in turn irritate the eye and disrupt the tear film.[2]

In both anterior and posterior blepharitis, the cause of inflammation appears to be bacterial byproducts rather than the bacteria themselves. To understand blepharitis, then, we must answer the question: What prompts bacteria to release these toxic agents? While some strains may be inherently virulent, research suggests that many species alter their behavior based on environmental factors. CoNS, for example, are normally harmless flora, but under certain conditions they become opportunistic pathogens that produce the signs and symptoms of staphylococcal blepharoconjunctivitis.

QUORUM SENSING

The specific environmental triggers that influence bacterial behavior are the subject of current investigations; one emerging possibility is that production of bacterial byproducts may be related to a breakdown in the normal balance of bacterial species on the surface of the eye and lids.

Normally, bacterial populations use a mechanism called *quorum sensing* to alter colony size in response to various factors. In quorum sensing, signaling molecules called autoinducers allow bacteria to sense the concentration of their own and other species in the same environment. In a healthy eye, this mechanism seems to help different species of bacteria colonize the same area without producing symptoms.[3] When this mechanism malfunctions, however, one or more bacterial populations can become overgrown—a situation that may then lead to blepharitis.[4,5]

What triggers such an imbalance is also under study, but the introduction of foreign bacteria is a

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possible cause. By touching his or her eyes, a person could accidently introduce bacteria that are not part of the normal ocular flora, and growth of these foreign bacteria could upset the bacterial balance on the eye. Disease states that increase individuals' overall risk of infection might also predispose them to blepharitis, as could infestation with parasites such as *Demodex* mites—which could trigger an inflammatory response that in turn upsets the eye's normal bacterial homeostasis.

TREATMENT IMPLICATIONS

As we come to understand how bacteria cause symptoms in blepharitis, we are led to conclude that antibiotic therapy alone may be insufficient. In fact, chronic use of an antibiotic in the absence of other therapeutic measures could create an imbalance in the ocular flora that induces another set of problems. Instead, we need to combine topical antibiotics, and possibly systemic antibiotics, with other measures such as lid hygiene, which can help reduce excessive colonization and remove some of the toxic bacterial byproducts.

Also, because inflammation plays an important role in producing blepharitis symptoms, the ideal treatment should have an antiinflammatory component. Topical macrolide antibiotics such as azithromycin—which are known to be antiinflammatory as well as antibacterial—may have a useful therapeutic role in blepharitis.

CONCLUSION

While many questions remain about the etiology of blepharitis, bacterial overgrowth appears to be an inciting event in anterior blepharitis, and it may play an important role in posterior blepharitis as well. However, because some level of bacterial colonization of the eyelids is normal, our approach to treatment must focus on restoring the normal colonization of the eyelids rather than indiscriminate potentially cytotoxic efforts to sterilize the lid margin area. Modulating the immune responses triggered by these bacteria under certain conditions may be beneficial in regaining control of symptoms and improving patient comfort.

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