Risk Factors for the Development of Corneal Infiltrative Events Associated with Contact Lens Wear

Philip B. Morgan,1 Nathan Efron,1 Noel A. Brennan,2 Elizabeth A. Hill,1 Matthew K. Raynor,3 and Andrew B. Tullo5

PURPOSE. To identify risk factors for the development of corneal infiltrative events (CIEs) associated with contact lens wear, and to report other relevant clinical characteristics.

METHODS. A series of symptomatic contact lens wearers presenting consecutively to a large hospital clinic over a 1-year period were examined. The clinical severity of any CIE was determined with a scoring system, and general and lens-specific information was captured with a questionnaire. Logistic regression analyses were performed to investigate the association between a range of risk factors and the occurrence of any CIE and the subset of cases categorized as severe keratitis. Three quasi-independent control groups were used for this analysis: hospital, lens-matched, and population. The relationship between clinical severity and the delay in attending the hospital was investigated. The prevalence of symptoms and initial actions taken by patients are reported.

RESULTS. Factors identified as being associated with an increased risk of development of a CIE include: wearing modality/lens type (greatest risk for extended-wear hydrogel lenses of 7.1 vs. daily wear hydrogel lenses), male gender (relative risk 1.4), smoking (1.4), the absence of relevant ocular (1.8) and general health (2.4) problems, and the late winter months (greatest risk in March of 3.6 vs. July). The overall predictive value of these risk factors for a given individual was low. Shorter time delays in hospital attendance were associated with increasing severity of keratitis. Eye soreness was the most common initial symptom (prevalence 69%), and the most frequent initial course of action taken by the patient was lens removal (prevalence 50%).

CONCLUSIONS. Risk factors for the development of contact lens keratitis were identified that, although being of limited predictive value for individual patients, highlight general associations that may assist in the management of contact lens wearers. Such risk factors may also assist in the development of a more complete understanding of the etiology of contact-lens-associated CIEs. 

In a recent paper,1 we described the incidence of severe and noncevere keratitis among patients wearing all current forms of contact lenses designed for both daily and extended wear. We adopted the novel approach of considering contact lens-related corneal infiltrative events (CIEs) as a continuous spectrum of disease severity. This approach represents an alternative to the more traditional one of attempting to differentiate between so-called microbial and sterile keratitis.2,4 A CIE is defined as a clinical event characterized by an aggregation of inflammatory cells in the cornea, irrespective of etiology.3

The identification of the type and magnitude of risk in relation to the development of CIEs is a useful adjunct to clinical practice if the risk factors are capable of predicting outcomes. Numerous investigators have identified risk factors for the development of either sterile or microbial keratitis for daily and extended contact lens wear (Tables 1, 2, 3). Few authors have addressed the question of risk of CIEs in association with silicone hydrogel lens wear. McNally et al.6 reported that those who wear silicone hydrogel lenses on an extended-wear basis have an increased risk of infiltrative events other than microbial keratitis if they are under the age of 30 years. The risk increases if they smoke tobacco.

As part of the design of our earlier study,1 we collected information on a range of factors ancillary to lens type (including silicone hydrogel lenses) and modality of wear that may have had an influence on the incidence of the full spectrum of CIEs. The purpose of this study was to identify which of these factors show significant associations with the development of CIEs and to consider possible clinical implications.

METHODS

A survey was undertaken of contact lens wearers consecutively attending the acute service of the Royal Eye Hospital (Manchester, UK), irrespective of their reason for coming to the hospital, between January 25, 2003, and January 24, 2004. The study patients were asked to complete a patient survey questionnaire to provide information pertaining to their contact-lens-wearing experience and circumstances relating to their coming to the hospital.

Table 4 lists the variables extracted from the questionnaire that were entered into the analysis. Occupation was scored on a scale from 1 to 10 by three of us, according to our perception of socioeconomic standing based on the description provided by the patient. A score of 10 corresponded to an occupation of a highly professional nature with strong intellectual demands. A score of 1 corresponded to an occupation of an unskilled and/or menial nature with minimal intellectual demands. Health problems deemed to be relevant are those that were judged by three of us to have implications with respect to contact lens wear. For example, chronic abdominal pain was considered to be unrelated to lens wear, whereas diabetes was deemed to be of relevance. Eye problems thought to be relevant are those that were judged by three of us to have implications with respect to contact lens wear. For example, retinal detachment was judged to be unrelated to lens wear, whereas dry eye was taken to be of relevance. Seasonal influence was investigated by considering the month in which the patients attended the hospital.

Because of the small number of patients in certain categories of lens wear, we classified wearing modality/lens type for the purposes of this analysis into the following five groups: daily wear rigid lenses; daily wear hydrogel daily disposable lenses; daily wear hydrogel lenses (i.e.,
all daily wear hydrogel lenses excluding daily disposable lenses); ex-
tended wear hydrogel lenses (including daily disposable lenses that
were used on an extended-wear basis in a noncompliant manner); and
extended-wear silicone hydrogel lenses.

For each study patient examined, the attending clinician made a
judgment as to whether there was any form of CIE, which may or may
not have been associated with corneal ulceration. If there was no
evidence of a CIE, no further information was captured for the pur-
poses of this study. If there was a CIE, the attending clinician com-
pleted a clinical survey form (on the reverse side of the patient survey
questionnaire) which enabled the severity of the CIE to be assigned a
score (from 2 to 22) based on a clinical severity matrix described by
Aasuri et al.17 and subsequently modified by us.1 For the purposes
of discussion, these patients are referred to as the CIE group. For certain
aspects of our analysis, cases of severe keratitis were identified as those
having a clinical severity score >8.

Three quasi-independent control groups were used in the analysis,
the justification for which is considered in the Discussion section. First,

### Table 1. Some Previously Reported Risk Factors for CIEs in Contact Lens Wear

<table>
<thead>
<tr>
<th>Factor</th>
<th>Relative Risk</th>
<th>Referent</th>
<th>Caveats</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>×3.2</td>
<td>Not smoking</td>
<td>For extended wear</td>
<td>5</td>
</tr>
<tr>
<td>Age 18–50 years</td>
<td>×2.2</td>
<td>Age &gt; 50 years</td>
<td>For silicone hydrogel extended wear; risk increases to ×2.7 for smokers</td>
<td>6</td>
</tr>
<tr>
<td>Previous inflammatory episodes</td>
<td>×4.1</td>
<td>No previous inflammatory episodes</td>
<td>For silicone hydrogel extended wear</td>
<td>6</td>
</tr>
<tr>
<td>Previous acute red eye</td>
<td>×6.9</td>
<td>No previous acute red eye</td>
<td>For silicone hydrogel extended wear</td>
<td>6</td>
</tr>
<tr>
<td>Previous sterile keratitis</td>
<td>×6.1</td>
<td>No previous sterile keratitis</td>
<td>For silicone hydrogel extended wear</td>
<td>6</td>
</tr>
</tbody>
</table>

### Table 2. Some Previously Reported Lens-Related Risk Factors for Microbial Keratitis in Contact Lens Wear

<table>
<thead>
<tr>
<th>Factor</th>
<th>Relative Risk</th>
<th>Referent</th>
<th>Caveats</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily wear</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conventional soft</td>
<td>×1.0</td>
<td>Hydrogel daily wear</td>
<td>By definition</td>
<td>7</td>
</tr>
<tr>
<td>Conventional EW lenses*</td>
<td>×1.178</td>
<td>Hydrogel daily wear</td>
<td>Not worn overnight</td>
<td>7</td>
</tr>
<tr>
<td>Hard (PMMA†)</td>
<td>×0.50</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>×0.45</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>×1.00</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>×1.5</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>×0.3</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>×0.95</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>×0.90</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>×0.45</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>×2.37</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>×0.68</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>Disposable</td>
<td>×2.46</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>×0.31</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>×0.90</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>Extended wear</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conventional soft</td>
<td>×5.15</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>×3.5</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>×5.8</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>×3.89</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>×1.87</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>×2.5</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>×6.12</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>×6.13</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>Daily wear soft lenses§</td>
<td>×8.08</td>
<td>Hydrogel daily wear</td>
<td>Worn overnight</td>
<td>7</td>
</tr>
<tr>
<td>RGP‡</td>
<td>×4.6</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Disposable</td>
<td>×7.73</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>×14.34</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>×8.18</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>×4.6</td>
<td>Hydrogel daily wear</td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>Consecutive nights sleeping in lenses</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>×3.6</td>
<td>Daily wear</td>
<td>Population control</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>×2.4</td>
<td>Daily wear</td>
<td>Hospital control</td>
<td>7</td>
</tr>
<tr>
<td>2–7</td>
<td>×6.8</td>
<td>Daily wear</td>
<td>Population control</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>×10.0</td>
<td>Daily wear</td>
<td>Hospital control</td>
<td>7</td>
</tr>
<tr>
<td>8–14</td>
<td>×11.8</td>
<td>Daily wear</td>
<td>Population control</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>×37.9</td>
<td>Daily wear</td>
<td>Hospital control</td>
<td>7</td>
</tr>
<tr>
<td>&gt;15</td>
<td>×14.5</td>
<td>Daily wear</td>
<td>Population control</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>×45.0</td>
<td>Daily wear</td>
<td>Hospital control</td>
<td>7</td>
</tr>
<tr>
<td>≥7</td>
<td>×4.6</td>
<td>&lt;7 nights</td>
<td></td>
<td>4</td>
</tr>
</tbody>
</table>

* Lenses recommended by the manufacturer for extended wear (EW).
† Polymethyl methacrylate.
‡ Rigid gas permeable.
§ Lenses recommended by the manufacturer for daily wear.
data relating to patients presenting to the hospital who were contact lens wearers but did not have any form of CIE formed the basis of a hospital control group. Second, we sought to create a matched control group of contact lens wearers without CIEs, consisting of the same number of patients in each of the wearing modality/lens type groups as that found in the CIE group. This control group was assembled by recruiting patients from the Eurolens Research subject database whose records of contact lens wear matched the required wearing modality/lens type criteria. Third, the control described in our previous publication1 constituted a population control group, which comprised projections of the number of those in the hospital catchment population who were prescribed the various wearing modality/lens types. Because of the distinct nature of each of these control groups, different variables were available for entry into the logistic regression models (see Table 4 and the description of the statistical analysis in the following text for more details).

Descriptive statistics relating to features of interest within the CIE group were collated. Further analyses that did not require a control group, such as correlation between factors relating to patients who had CIEs, were undertaken in an attempt to define associations of clinical interest.

The research adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients surveyed in this study. Ethics approval to conduct the study was obtained from

### Table 3. Some Previously Reported Non–Lens-Related Risk Factors for Microbial Keratitis in Contact Lens Wear

<table>
<thead>
<tr>
<th>Factor</th>
<th>Relative Risk</th>
<th>Referent</th>
<th>Caveats</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-professional workers</td>
<td>×3.3</td>
<td>Professional workers</td>
<td>For extended wear</td>
<td>4</td>
</tr>
<tr>
<td>Living in Boston, MA</td>
<td>×4.6</td>
<td>Living in New Hampshire</td>
<td>For extended wear</td>
<td>8</td>
</tr>
<tr>
<td>Living in southern UK</td>
<td>×9.3</td>
<td>Living in northern UK</td>
<td>For AK*</td>
<td>15</td>
</tr>
<tr>
<td>Young age (12–19 years)</td>
<td>×2.2</td>
<td>Old age (&gt;40 years)</td>
<td>For extended wear</td>
<td>8</td>
</tr>
<tr>
<td>Male gender</td>
<td>×2.0</td>
<td>Female gender</td>
<td>For daily wear</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>×2.2</td>
<td>Female gender</td>
<td>For daily wear</td>
<td>4</td>
</tr>
<tr>
<td>Hard domestic water</td>
<td>×5.4</td>
<td>Soft domestic water</td>
<td>For AK</td>
<td>15</td>
</tr>
<tr>
<td>Traveling abroad</td>
<td>×2.9</td>
<td>Not traveling abroad</td>
<td>For AK</td>
<td>15</td>
</tr>
<tr>
<td>Swimming</td>
<td>Magnitude not specified</td>
<td>Using disinfection</td>
<td>For AK</td>
<td>16</td>
</tr>
<tr>
<td>Lack of disinfection</td>
<td>×55.9</td>
<td>Using disinfection</td>
<td>For AK</td>
<td>16</td>
</tr>
<tr>
<td>Chlorine-based disinfection, used optimally</td>
<td>×14.6</td>
<td>Using other chemical system</td>
<td>For AK</td>
<td>16</td>
</tr>
<tr>
<td>Chlorine-based disinfection, used suboptimally</td>
<td>×41.1</td>
<td>Using other chemical system</td>
<td>For AK</td>
<td>16</td>
</tr>
<tr>
<td>Smoking</td>
<td>×2.7</td>
<td>Not smoking</td>
<td>Population control</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>×4.2</td>
<td>Not smoking</td>
<td>Hospital control</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>×3.5</td>
<td>Not smoking</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Noncompliance with cleaning procedures</td>
<td>×6.8</td>
<td>Compliance with cleaning procedures</td>
<td>For AK</td>
<td>2</td>
</tr>
</tbody>
</table>

* Acanthamoeba keratitis.

### Table 4. Factors Derived from Patient Survey Questionnaires Entered into the Logistic Regression Analysis

<table>
<thead>
<tr>
<th>Factor</th>
<th>Method of Categorization/Designation</th>
<th>Hospital Control</th>
<th>Matched Control</th>
<th>Population Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>Number of years</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Occupation score</td>
<td>Score from 1 to 10 based on perceived socioeconomic standing, where 1 is unskilled, menial labor; 10 is senior professional.</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Smoking</td>
<td>Yes</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relevant eye problems</td>
<td>Yes</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relevant health problems</td>
<td>Yes</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wearing modality/lens type</td>
<td>Daily wear rigid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Daily wear hydrogel disposable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Daily wear hydrogel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Extended wear hydrogel</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Extended wear silicone hydrogel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contact lens care solution</td>
<td>Multipurpose solution</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hydrogen peroxide</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swimming in last 14 days without goggles</td>
<td>Yes</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Season</td>
<td>12 months of the year</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>
the Local Research Ethics Committee (Central) of Manchester Health Authority.

A series of stepwise logistic regression models (JMP; SAS Institute, Inc., Cary, NC) were constructed using possible risk factors as the independent variables and the binary outcome of the presence or absence of CIEs as the dependent variable. This series of models comprised an analysis for two categories of CIE (all CIEs and severe keratitis) tested against the three control groups (hospital, matched, and population), giving a total of six separate logistic regression models.

The logistic regression models enabled estimates of statistically significant odds ratios; however, for ease of data interpretation, these ratios were converted to relative risks with appropriate 95% confidence intervals. Statistical outcomes generating odds ratios were converted to relative risks with appropriate 95% confidence intervals. The statistic “lack of fit” was considered to be statistically significant and probabilities 0.05 and 0.10 were considered to be weakly significant. The statistic “lack of fit” was assessed as a precaution against overmodeling of the data. The strength of the overall associations accounted for by the model was assessed by considering pseudo-$r^2$ values generated by the software.

**RESULTS**

A total of 415 contact lens wearers attended the study center over the 12-month survey period. Useable responses to the patient survey questionnaire were obtained from 410 of these lens wearers. Of these, 118 were observed to have a CIE, and a clinical survey form was completed by the attending clinician for each of these patients. The remaining 292 patients who completed the survey questionnaire forms constituted the hospital control group. The matched control group comprised 116 subjects. The number of population controls has been presented previously. Table 5 gives a breakdown of the number of subjects in the CIE group and the three control groups, stratified for wearing modality/lens type.

Table 6 presents a matrix of the relative risk, 95% confidence intervals and probabilities for levels of the significant factors as identified in the six logistic regression models. Essentially, each of the columns with numerical data represents the result of a separate logistic regression. As can be seen from this table, the following six factors were identified as statistically significant in at least one of the logistic regression models: wearing modality/lens type, gender, smoking, relevant eye problem, relevant health problem, and month of year. A comparison of particular interest is the risk of developing CIEs while wearing hydrogel lenses versus silicone hydrogel lenses on an extended-wear basis. In the hospital control group, there was a higher risk of severe keratitis in the extended-wear hydrogel group versus the extended-wear silicone hydrogel group (relative risk; 95% CI: 3.78; 1.07–13.35) but no difference for all CIEs (1.28; 0.71–2.33). For the population control, there was also a higher risk of severe keratitis in the extended wear hydrogel group versus the extended-wear silicone hydrogel group (4.87; 1.10–21.69) but again, there was no difference for all CIEs (0.82; 0.33–2.05).

The number of contact lens wearers attending the hospital clinic with nonsevere keratitis, severe keratitis, and other ocular problems is displayed in Figure 1 for the 12 months of the study survey. Also plotted on this graph, for interest, is the number of consultations for influenza-like illness to the UK National Health Service Helpline per 100,000 persons aged 15 to 64 in England during this same period. The significance of this latter plot is considered in the Discussion.

Tables 7 and 8 describe the percentage frequency of reported symptoms and the immediate course of action taken, respectively, among the CIE group. A higher severity of CIE was significantly associated with a shorter delay between the onset of symptoms and attendance at the hospital (Spearman Rank Correlation, $z$ [corrected for ties] = −2.7, $P < 0.01$); this relationship is illustrated in Figure 2.

**DISCUSSION**

Obtaining a representative control group in epidemiologic studies usually presents a considerable challenge. In this work, three quasi-independent control groups were used. Use of the hospital control group was based on the assumption that attendance at the hospital was independent of the risk factors associated with contact lens wear. Of course, this control group of contact lens wearers reported to the hospital because they were symptomatic, and as such, they may not represent an accurate cross section of contact lens wearers within the population as a whole. We believe that a disproportionately high number of extended-wear lens users may be represented in this control group because of the greater physiological impact of this modality of lens wear; however, the proportions of the different lens types (i.e., rigid versus daily disposables versus hydrogels versus silicone hydrogels) probably represent a reasonable reflection of lens wear within the general community.

We also assembled an external control group of contact lens wearers, matched for wearing modality/lens type, who had not had a CIE. A limitation of this matched control group is that it restricted assessment to risk factors other than wearing modality/lens type and seasonal effects. In addition, the formation of a matched control group from a different demographic population (in this case, subjects participating in university-based contact lens clinical trials) may have influenced the results.

**Table 5. Number of Patients within CIE and Control Groups Stratified by Wearing Modality/Lens Types**

<table>
<thead>
<tr>
<th>Wearing Modality</th>
<th>Lens Type</th>
<th>Nonsevere Keratitis</th>
<th>Severe Keratitis</th>
<th>Hospital Control</th>
<th>Matched Control</th>
<th>Population Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily wear</td>
<td>Rigid</td>
<td>4</td>
<td>2</td>
<td>38</td>
<td>6</td>
<td>6,996</td>
</tr>
<tr>
<td></td>
<td>Hydrogel daily disposable</td>
<td>15</td>
<td>8</td>
<td>64</td>
<td>23</td>
<td>16,413</td>
</tr>
<tr>
<td></td>
<td>Hydrogel</td>
<td>42</td>
<td>19</td>
<td>142</td>
<td>61</td>
<td>29,876</td>
</tr>
<tr>
<td></td>
<td>Silicone hydrogel</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>179</td>
</tr>
<tr>
<td>Extended wear</td>
<td>Rigid</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Hydrogel daily disposable</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Hydrogel</td>
<td>2</td>
<td>4</td>
<td>9</td>
<td>4</td>
<td>415</td>
</tr>
<tr>
<td></td>
<td>Silicone hydrogel</td>
<td>15</td>
<td>3</td>
<td>31</td>
<td>18</td>
<td>1,517</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>80</td>
<td>38</td>
<td>292</td>
<td>116</td>
<td>55,414</td>
</tr>
</tbody>
</table>

* Subclassification based on a threshold diagnostic score of nonsevere keratitis <8 < severe keratitis.
The population control, which was used to derive incidence figures for CIEs in our previous study,\(^1\) essentially constituted a third control group. These data consisted of projections of the number of wearers in the hospital catchment population based on earlier survey data relating to prescribing habits of wearing modality/lens type. Therefore, information was not available in relation to factors such as age, gender, smoking, and relevant eye and health problems, which limited the number of risk factors that could be analyzed in the relevant logistic regressions. A further limitation of the population control group is that actual patterns of lens wear in the population may not be in precise concordance with what was prescribed. Because the estimate of prescribed extended wear in hydrogel lens wearers is low, the relative risk of a CIE associated with this form of lens wear is sensitive to small fluctuations in this estimate. We were therefore interested in observing that the statistically significant finding of higher risk for severe keratitis associated with extended-wear hydrogel lenses compared with that of extended-wear silicone hydrogel lenses found in the population control (relative risk, \(\times 4.87\)) was replicated when using the hospital control (\(\times 3.78\)), notwithstanding the potential lack of robustness of both of these control groups.

Several observations can be made regarding the risks of CIEs with various wearing modalities and lens types. Irrespective of the control group, daily wear of rigid lenses was found to cause a lower risk of CIEs compared with daily wear of hydrogel lenses. Sleeping in hydrogel and silicone hydrogel contact lenses was associated with a higher risk of CIEs than was daily hydrogel lens wear. These findings are consistent with the general sentiment expressed by numerous investigators of the risks of sleeping in contact lenses. Males have different attitudes and perceptions relating to health risks than do females, in that they receive health risks. Males have a 30% to 40% increased risk of the occurrence of CIEs compared with females. This gender difference has been reported previously for microbial keratitis.\(^4,8\) The reason for this association is not obvious, but it may be related to perceived health risks. Males have different attitudes and perceptions relating to health risks than do females, in that they

### Table 6. Relative Risk, 95% CI, and Probabilities for Various Levels of Significant Factors for the Logistic Regression Models

<table>
<thead>
<tr>
<th>Factor</th>
<th>Referent</th>
<th>All CIEs</th>
<th>Severe Keratitis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Hospital Control ((r^2 = 0.088))</td>
<td>Matched Control ((r^2 = 0.068))</td>
</tr>
<tr>
<td>Wearing modality/lens type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily wear rigid</td>
<td>Daily wear hydrogel</td>
<td>0.46</td>
<td>0.42</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.21-0.99)</td>
<td>(0.18-0.97)</td>
</tr>
<tr>
<td>Daily wear daily disposable</td>
<td></td>
<td>0.89</td>
<td>0.69</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.59-1.34)</td>
<td>(0.43-1.11)</td>
</tr>
<tr>
<td>Extended wear hydrogel</td>
<td></td>
<td>1.53</td>
<td>0.124</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.92-2.53)</td>
<td>(3.08-16.29)</td>
</tr>
<tr>
<td>Extended wear silicone hydrogel</td>
<td></td>
<td>1.19</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.77-1.84)</td>
<td>(3.44-9.81)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>Female</td>
<td>1.41</td>
<td>1.31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.03-1.95)</td>
<td>(1.02-1.69)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>Non smoker</td>
<td>1.35</td>
<td>1.19</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.05-1.75)</td>
<td>(0.77-1.84)</td>
</tr>
<tr>
<td>Relevant eye problem</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>Present</td>
<td>1.77</td>
<td>2.35</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.08-2.88)</td>
<td>(1.07-5.12)</td>
</tr>
<tr>
<td>Relevant health problem</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>Present</td>
<td>2.35</td>
<td>0.43</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.07-5.12)</td>
<td>(1.04-1.31)</td>
</tr>
<tr>
<td>Month of year(\dagger)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>January</td>
<td>July</td>
<td>2.29</td>
<td>NA2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.97-5.39)</td>
<td>(1.03-5.12)</td>
</tr>
<tr>
<td>February</td>
<td></td>
<td>2.42</td>
<td>NA2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.03-5.65)</td>
<td>(1.04-1.31)</td>
</tr>
<tr>
<td>March</td>
<td></td>
<td>3.63</td>
<td>NA2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.68-7.80)</td>
<td>(1.04-1.31)</td>
</tr>
</tbody>
</table>

NA1, not applicable, because groups were matched for wearing modality/lens type; DNA, data not available for the control population of lens wearers; FNS, factor not significant; NA2, not applicable, because collection of control data was not dependent on time of year.

\(\dagger\) For ease of presentation, selected examples only are provided for the 66 possible factor/referent combinations.

\(r^2\) estimating the proportion of variance accounted for by the logistic regression model containing the significant factors.
perceive risks as much smaller and much more acceptable.\textsuperscript{18} For example, males may be more inclined to undervalue the importance of personal hygiene with respect to contact lens care.

Smoking was found to be associated with a 35\% greater risk of CIEs, and this was increased to twofold for severe keratitis. Others have reported similar findings.\textsuperscript{2,7} Smoking may be a risk factor for several reasons. It is generally considered that smoking is an unhealthy pursuit, which may be linked to a general lack of hygiene with respect to matters relating to contact lens wear and care. Toxins from smoke may either irritate the eyes directly\textsuperscript{19} or become absorbed into the contact lens and act as an irritant that compromises the health of the ocular surface\textsuperscript{20} and predisposes the eye to a CIE. Smoking is known to have an immunomodulatory effect, and in that way cigarette smokers may have the secondary effect of precluding a CIE. An alternative explanation is that compromised ocular health may be associated with a general upregulation of the innate defense status of the eye, so that there is an ever-present resistance to extraneous challenges to the ocular surface which could result in a CIE. These principles can be extended to explain why compromised general health also serves to protect the eye from a CIE.

The notion that adverse ocular conditions related to contact lens wear can be influenced by the time of year (seasonal effect) is well established; for example, Begley et al.\textsuperscript{22} reported that the onset of contact lens–associated papillary conjunctivitis was seasonal, in that the incidence of this condition peaked during the allergy seasons in the midwestern United States. It may be supposed in the present study that the incidence of CIEs is related to seasonal variations in ocular or general health. We found a two to fourfold increased risk of CIEs in late winter (January to March) in the United Kingdom, compared with the risk in midsummer (July). We accessed the number of consultations for influenza-like illness to the UK National Health Service Helpline by people aged 15 to 64 years in England during the same time period as our study and found that this number peaked around October and November 2003,\textsuperscript{23} which is in discordance with the peak incidence of CIEs in our study from January to March 2003 (Fig. 1). Of interest, this observation is consistent with the finding described earlier of a lower incidence of CIEs in association with compromised general health.

A noteworthy statistic in our logistic regression analyses is the pseudo-$r^2$ values. These are analogous to the $r^2$ values generated in conventional linear regression models, which indicate the amount of variance within the dataset that can be accounted for by the identified significant factors. For the six regression analyses reported herein, the pseudo-$r^2$ values were all less than 10\%. This suggests that any given risk factor (or, indeed, group of risk factors) is of limited value in predicting the likelihood of a given individual’s having a CIE, notwithstanding the general associations that we have demonstrated. Although numerous investigators have also identified risk factors associated with keratitis among contact lens wearers (Ta-

### Table 7. Reported Symptoms of Patients with CIEs

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sore eyes</td>
<td>69</td>
</tr>
<tr>
<td>Discomfort (54%)</td>
<td></td>
</tr>
<tr>
<td>Pain (15%)</td>
<td></td>
</tr>
<tr>
<td>Redness</td>
<td>59</td>
</tr>
<tr>
<td>Laceration</td>
<td>19</td>
</tr>
<tr>
<td>Photophobia</td>
<td>9</td>
</tr>
<tr>
<td>Discharge</td>
<td>4</td>
</tr>
<tr>
<td>Reduced vision</td>
<td>3</td>
</tr>
</tbody>
</table>

### Table 8. Immediate Course of Action Taken by Patients with CIEs

<table>
<thead>
<tr>
<th>Action</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Removed lenses</td>
<td>50</td>
</tr>
<tr>
<td>Professional advice</td>
<td>43</td>
</tr>
<tr>
<td>Bathed eye</td>
<td>24</td>
</tr>
<tr>
<td>Drops/ointments</td>
<td>16</td>
</tr>
<tr>
<td>Other remedy</td>
<td>5</td>
</tr>
</tbody>
</table>

Many patients reported more than one immediate course of action.
bles 1, 2, 3), they have failed to report the strength of those associations. If such associations are weak, then the predictive capacity of the risk factors for an individual patient is potentially exaggerated. In view of the benefit of knowing these associations, we suggest that future studies would be enhanced by citing $r^2$ or pseudo-$r^2$ values.

In our analysis, several of the factors listed in Table 4 were not found to be statistically significant—nämlich: age, occupation, contact lens care solutions, and swimming. Our failure to establish significance is due to either (1) there being insufficient power in our dataset to enable a demonstration of statistical significance or (2) there being sufficient power, but the factor was genuinely not associated with the development of a CIE. It is for these reasons that we have been unable to verify the findings of previous studies of an association of age,$^6$ occupation,$^4$ contact lens care solutions,$^{16}$ and swimming$^{15}$ with CIEs among contact lens wearers.

It is not surprising that ocular discomfort was the symptom that was first noticed by patients who had CIEs. This symptom was reported by 69% of patients. The other prominent symptom noticed at onset was eye redness. These onset symptoms are similar to those previously reported by patients who have nonsevere$^3$ or severe$^2$ keratitis.

From a clinical perspective, it is comforting to note that the most common immediate course of action for a patient who experiences a CIE is to remove the contact lenses, and that the second most common action is to seek professional advice. Patients consulted a variety of professionals, including optometrists, opticians, general medical practitioners, pharmacists, and emergency hospital staff. Some of the more unusual courses of immediate action included going to sleep and placing cold cucumber slices or moist tea bags on the closed eye.

We found an inverse relationship between the clinical severity score and the time of delay in attending the hospital. It is interesting that there is considerable variance in the data. For example, three patients with clinical severity scores $>8$ (severe keratitis) delayed their attendance at the hospital by more than 1 week. It may be that these patients had only mild symptoms in the first week and their symptoms became more severe immediately before attending the hospital, which would explain their delayed attendance. In general, if it is assumed that the level of ocular discomfort is similar irrespective of the delay in attending the hospital (due to a pain-intolerance threshold having been crossed), then a more severe condition that might be expected to progress more rapidly is associated with a shorter delay in attending the hospital. Conversely, a more slowly progressing condition of lower severity might be associated with a longer delay in attending the hospital.

When dealing with CIEs in practice, contact lens clinicians may wish to consider the information presented in this article relating to risk factors, reported symptoms, actions taken by patients, and their delay in attending the hospital. Factors identified as being associated with an increased risk of a CIE include wearing modality/lens type (greatest risk for extended wear hydrogel lenses), being male, smoking, the absence of relevant ocular and general health problems, and the late winter months. As highlighted in this article, such risk factors may also assist in the development of a more complete understanding of the etiology of contact lens-associated corneal infiltrative events.

Acknowledgments

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References


