

# Risk factors for aerobic bacterial conjunctival flora in preoperative cataract patients

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## Abstract

**Purpose** To investigate the relationship between the background of preoperative cataract patients and bacterial conjunctival flora.

**Methods** A total of 990 cataract patients who had completed preoperative examinations in 2007 and 2008 were included. Patients using topical antibiotics at the preoperative examination or having a history of intraocular surgery were excluded. Conjunctival cultures had been preoperatively obtained. Patient characteristics were investigated via medical records. Risk factors for conjunctival flora of seven typical bacteria were analyzed by univariate and multivariate analyses.

**Results** The detection rate of alpha-hemolytic streptococci and *Enterococcus faecalis* increased with age ( $P = 0.044$  and  $P = 0.002$ , respectively). The detection rate of Gram-negative bacilli was higher among patients with oral steroid use or lacrimal duct obstruction ( $P = 0.038$  and  $P = 0.002$ , respectively). The detection rate of *Corynebacterium* species was higher among older patients and men, and lower among patients with glaucoma eye drop use ( $P < 0.001$ ,  $P = 0.012$  and  $P = 0.001$ , respectively). The detection rate of methicillin-susceptible coagulase-negative *Staphylococci* was higher among men and lower among patients with a surgical history in other departments ( $P = 0.003$  and  $P = 0.046$ , respectively). The detection rate of methicillin-resistant coagulase-negative *Staphylococci* (MR-CNS) was higher among patients with oral steroid use, a visit history to ophthalmic facilities, or a surgical history in other departments ( $P = 0.002$ ,  $P = 0.037$  and  $P < 0.001$ , respectively).

**Conclusions** Elderly patients, men, patients with lacrimal duct obstruction or immunosuppressed patients are more likely to be colonized by pathogens that cause postoperative endophthalmitis. Moreover,

**MR-CNS colonization was associated with healthcare-associated infection.**

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## Introduction

Bacterial conjunctival flora may be the causative organism in postoperative endophthalmitis.<sup>1</sup> Endophthalmitis caused by *Staphylococcus aureus*, *Enterococcus faecalis* and gram-negative bacilli such as *Pseudomonas aeruginosa* is likely to be severe.<sup>2</sup> Moreover, multidrug resistance of conjunctival bacterial flora has become a serious problem.<sup>3</sup> Recently, it was reported that multidrug-resistant coagulase-negative *Staphylococci* (MR-CNS) are detected from conjunctiva.<sup>4</sup>

To combat the threat of postoperative endophthalmitis, it is necessary to clarify the epidemiological characteristics of bacterial conjunctival flora. Studies on risk factors for conjunctival bacterial colonization have reported higher detection rates of conjunctival bacteria in elderly or male patients.<sup>5–8</sup> In addition, there was a positive correlation between the dose of prednisolone and the number of bacterial isolates.<sup>9</sup> There are also reports that atopic dermatitis and diabetes affected the bacterial conjunctival flora.<sup>8,10–12</sup> Our study design was constructed in consideration of the following two points. First, we focused on the detection rate of each bacteria separately rather than that of total bacterial isolates because of variations in the pathogenicity, auxotrophy and transmission route in each type of bacteria. Next, we focused on the possibility of healthcare-associated infection. Multidrug-resistant bacteria such as methicillin-resistant *Staphylococci* often become a problem as causative organisms of healthcare-associated infection. Therefore, the visit history to ophthalmic facilities and the surgical history in other departments were adopted in our study as an indicator of healthcare-associated infection.

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In the present study, we investigated the patient background associated with each type of conjunctival bacteria by using univariate and multivariate logistic regression analyses and revealed that preoperative cataract patients had specific risk factors for each type of conjunctival bacteria.

## Materials and methods

### Investigation of patient background

Approval for this study was obtained from the Institutional Review Board at Machida Hospital. All cataract patients from July 2007 to August 2008 who satisfied the selection criteria and gave informed consent were included in this study. Patients using topical antibiotics at the preoperative examination or having a history of intraocular surgery were excluded. The numbers of included patients and potential patients were the same. All patients who fit the inclusion criteria had completed all of the preoperative examinations. Conjunctival swab collection, lacrimal irrigation test, blood pressure measurement and blood tests were performed before cataract surgery. The following patient characteristics were collected from medical records: age, sex, hypertension, diabetes, oral steroid use, lacrimal duct obstruction, glaucoma eye drop use, visit history to ophthalmic facilities within 6 months and surgical history in other departments within 3 years. The 6-month and 3-year periods were set for convenience as ranges that could be collected from medical records as accurately as possible. If the subject was previously treated in the internal medicine department or started treatment after the preoperative examination, we determined the presence of hypertension or diabetes. After collecting the conjunctival swab, the presence of lacrimal duct obstruction was determined.

### Bacterial identification from conjunctival swabs

Conjunctival swabs were collected from one eye for which surgery had been scheduled for the first time. The lower fornix of the conjunctiva was swabbed with a cotton swab that was first soaked in sterile saline. The swab was placed into transport medium (BBL CultureSwab Plus, Nippon Becton Dickinson, Co., Ltd., Tokyo, Japan) and sent to the microbiological laboratory. Specimens were incubated under aerobic and enrichment conditions at 35 °C for 3 days by using sheep blood agar, chocolate agar, BTB agar and thioglycollate broth. Methicillin resistance of the *Staphylococcus* species was determined according to Clinical and Laboratory Standards Institute guidelines (M100-S17, 2007, and M100-S18, 2008).

### Analysis of risk factors for bacterial conjunctival flora

First, univariate analysis was performed to determine whether conjunctival carriage of each of the seven types of bacteria (methicillin-susceptible *Staphylococcus aureus* (MSSA), alpha-streptococci, *Enterococcus faecalis*, gram-negative bacilli, *Corynebacterium* species, methicillin-susceptible coagulase-negative *Staphylococci* (MS-CNS) and MR-CNS) were associated with nine background factors (age, sex, hypertension, diabetes, oral steroid use, lacrimal duct obstruction, glaucoma eye drop use, visit history to ophthalmic facilities and surgical history in other departments). The Mann-Whitney *U*-test was used for analysis of age, and Fisher's exact test was used for the analysis of other background factors. *P*-values < 0.05 were considered statistically significant.

Next, each of the seven types of bacteria were set as objective variables, nine background factors were set as explanatory variables, and multivariate analysis was performed. The female sex was set as 0, and the male sex was set as 1 to transform variables. Correlation of seven objective variables and nine explanatory variables was examined by using Spearman's correlation coefficient prior to multivariate analysis. It was confirmed that the correlation coefficient of all variables was < 0.3, and the correlation was not as strong with each other. Logistic regression analysis was performed by using the forced entry method. It was confirmed that the significance probability was < 0.05 by the omnibus test of model coefficients for all adopted models. All statistical analyses were performed by using IBM SPSS Statistics version 19 for Windows (IBM Japan, Ltd., Tokyo, Japan).

## Results

### Patient background

A total of 990 cataract patients were included in this study. The male:female ratio was 1 : 1.5. The average age was  $73.9 \pm 10.1$  years (range, 15 to 97 years), and 83.3% of patients were over 65 years of age. Among the eligible patients, 533 had hypertension (53.8%), 206 had diabetes (20.8%), 29 used oral steroids (2.9%), 31 had lacrimal duct obstruction (3.1%), 97 used glaucoma eye drops (9.8%), 725 visited ophthalmic facilities within the past 6 months (73.2%) and 74 had surgery in other departments within the past 3 years (7.5%).

### Composition of bacterial isolates

Positive culture results were obtained from 719 of 990 cases. Table 1 shows the details of bacterial isolates from the conjunctival sac. Two strains of *Streptococcus pneumoniae* are included in the group of other gram-positive cocci. Four strains of *Haemophilus* species are

**Table 1** Composition of the bacterial species isolated from conjunctival sac

Bacteria	Number of strains	Proportion (%)
<i>Corynebacterium</i> species	462	44.8
Methicillin-susceptible coagulase-negative <i>Staphylococci</i>	230	22.3
Methicillin-resistant coagulase-negative <i>Staphylococci</i>	136	13.2
Methicillin-susceptible <i>Staphylococcus aureus</i>	44	4.3
Methicillin-resistant <i>Staphylococcus aureus</i>	6	0.6
<i>Enterococcus faecalis</i>	36	3.5
Alpha-hemolytic streptococci	31	3.0
Other gram-positive cocci	28	2.7
Gram-negative bacilli	55	5.3
Gram-negative cocci	4	0.4
Total	1032	100

included in the group of gram-negative bacilli. Both bacteria of CNS and *Corynebacterium* species accounted for 80.3% of the total bacterial isolates. Furthermore, the addition of MSSA, alpha-hemolytic streptococci, *Enterococcus faecalis* and gram-negative bacilli accounted for 96.4% of total isolates. Thus, these seven bacteria were considered the main isolates from conjunctiva of preoperative cataract patients.

#### Risk factors for each bacterial conjunctival flora

For MSSA, none of the background factors showed statistical significance in the univariate analysis (Table 2a), and there were no obvious risk factors for carriage of MSSA in the multivariate logistic regression analysis (Table 3a).

Alpha-hemolytic streptococci and *Enterococcus faecalis* showed a significant association with age in univariate analysis ( $P=0.008$  and  $P=0.001$ , respectively; Tables 2b and c), and age was a risk factor of alpha-hemolytic streptococci and *Enterococcus faecalis* in multivariate logistic regression analysis ( $P=0.044$  and  $P=0.002$ , respectively; Tables 3b and c). The adjusted odds ratio for 1 additional year of age in alpha-hemolytic *Streptococci* and *Enterococcus faecalis* was 1.049 (95% confidence interval (CI), 1.001–1.100) and 1.077 (95% CI, 1.029–1.128), respectively.

Gram-negative bacilli showed a significant association with lacrimal duct obstruction in univariate analysis ( $P=0.004$ ; Table 2d). In addition to lacrimal duct obstruction, oral steroid use was also a risk factor in multivariate logistic regression analysis ( $P=0.038$  and  $P=0.002$ , respectively; Table 3d). The adjusted odds ratio was 3.294 for oral steroid use (95% CI, 1.017–10.134) and 4.745 for lacrimal duct obstruction (95% CI, 1.778–12.665). These two factors increased the carriage rate, and the carriage rate of gram-negative bacilli was increased up to 20.0% from 4.5% depending on the two factors (Figure 1a).

*Corynebacterium* species showed a significant association with age, male sex, hypertension and glaucoma eye drop use in univariate analysis ( $P<0.001$ ,  $P=0.044$ ,  $P=0.015$  and  $P=0.003$ , respectively; Table 2e). These factors, except for hypertension, were risk factors in multivariate logistic regression analysis ( $P<0.001$ ,  $P=0.012$  and  $P=0.001$ , respectively; Table 3e). The adjusted odds ratio for 1 additional year of age was 1.042 (95% CI, 1.027–1.057), and the adjusted odds ratio for men was 1.410 (95% CI, 1.080–1.841); these two factors increased the carriage risk. The adjusted odds ratio for glaucoma eye drop use was 0.457 (95% CI, 0.288–0.727); thus, it decreased the carriage risk. The carriage rate of *Corynebacterium* species varied from 11.8 to 55.9% depending on these three factors (Figure 1b).

MS-CNS showed a significant association with sex in univariate analysis ( $P=0.001$ ) (Table 2f). Surgical history in other departments along with the male sex were risk factors in multivariate logistic regression analysis ( $P=0.003$  and  $P=0.046$ , respectively) (Table 3f). The adjusted odds ratio for the male sex was 1.580 (95% CI, 1.163–2.147), and the adjusted odds ratio for surgical history in other departments was 0.495 (95% CI, 0.248–0.988). The carriage rate of MS-CNS varied from 9.3 to 29.3% depending on these two factors (Figure 1c).

MR-CNS showed a significant association with oral steroid use, visit history to ophthalmic facilities and surgical history in other departments ( $P=0.003$ ,  $P=0.036$  and  $P=0.001$ , respectively; Table 2g). Oral steroid use, visit history to ophthalmic facilities and surgical history in other departments were risk factors in multivariate logistic regression analysis ( $P=0.002$ ,  $P=0.037$  and  $P<0.001$ , respectively; Table 3g). The adjusted odds ratios were 3.651 (95% CI, 1.628–8.185) for oral steroid use, 1.650 (95% CI, 1.032–2.639) for visit history to ophthalmic facilities and 2.800 (95% CI, 1.592–4.923) for surgical history in other departments. These 3 factors increased the carriage rate, and the MR-CNS carriage rate varied from 7.8 to 33.3% depending on these three factors (Figure 1d).

**Table 2** Univariate analysis for each bacteria

Factor	a. MSSA			b. Alpha-hemolytic streptococci		
	Positive N = 44	Negative N = 946	P-value	Positive N = 31	Negative N = 959	P-value
Age	74.9 ± 10.4	73.8 ± 10.1	0.431	77.5 ± 9.0	73.7 ± 10.1	0.008**
Sex (male)	19/25	377/569	0.753	14/17	382/577	0.579
Hypertension	24/20	509/437	1.000	21/10	512/447	0.143
Diabetes	6/38	200/756	0.261	10/21	196/763	0.117
Oral steroids	2/42	27/919	0.373	2/29	27/932	0.229
Lacrimal duct obstruction	2/42	29/917	0.644	2/29	29/930	0.253
Glaucoma eye drops	6/38	91/855	0.431	5/26	92/867	0.218
Visit history to ophthalmic facilities	33/11	692/254	0.863	22/9	703/256	0.837
Surgical history in other departments	3/41	71/875	1.000	1/30	73/886	0.723
	c. Enterococcus faecalis			d. Gram-negative bacilli		
	Positive N = 36	Negative N = 954	P-value	Positive N = 52	Negative N = 938	P-value
Age	79.0 ± 7.7	73.7 ± 10.1	0.001**	76.6 ± 7.7	73.7 ± 10.2	0.083
Sex (male)	12/24	384/570	0.489	21/31	375/563	1.000
Hypertension	21/15	512/442	0.614	33/19	500/438	0.198
Diabetes	9/27	197/757	0.531	13/39	193/745	0.482
Oral steroids	1/35	28/926	1.000	4/48	25/913	0.061
Lacrimal duct obstruction	2/34	29/925	0.312	6/46	25/913	0.004**
Glaucoma eye drops	3/33	94/860	1.000	4/48	93/845	0.811
Visit history to ophthalmic facilities	26/10	699/255	0.850	39/13	686/252	0.873
Surgical history in other departments	4/32	70/884	0.337	6/46	68/870	0.271
	e. Corynebacterium species			f. MS-CNS		
	Positive N = 460	Negative N = 530	P-value	Positive N = 223	Negative N = 767	P-value
Age	75.9 ± 8.5	72.1 ± 10.9	0.000**	73.0 ± 10.2	74.1 ± 10.0	0.095
Sex (male)	200/260	196/334	0.044*	110/113	286/481	0.001**
Hypertension	267/193	266/264	0.015*	122/101	411/356	0.819
Diabetes	92/368	114/416	0.583	53/170	153/614	0.224
Oral steroids	15/445	14/516	0.577	5/218	24/743	0.653
Lacrimal duct obstruction	17/443	14/516	0.365	6/217	25/742	0.828
Glaucoma eye drops	31/429	66/464	0.003**	15/208	82/685	0.096
Visit history to ophthalmic facilities	337/123	388/142	1.000	159/64	566/201	0.492
Surgical history in other departments	39/421	35/495	0.277	10/213	64/703	0.060
	g. MR-CNS					
	Positive N = 135	Negative N = 855	P-value			
Age	75.3 ± 10.2	74.4 ± 9.9	0.228			
Sex (male)	52/83	344/511	0.777			
Hypertension	75/60	458/397	0.711			
Diabetes	29/106	177/678	0.820			
Oral steroids	10/125	19/836	0.003**			
Lacrimal duct obstruction	7/128	24/831	0.177			
Glaucoma eye drops	16/119	81/774	0.435			
Visit history to ophthalmic facilities	109/26	616/239	0.036*			
Surgical history in other departments	20/115	54/801	0.001**			

Abbreviation: N, number of patients.

The data indicate real or mean ± SD.

Mann-Whitney U-test was used for age, Fisher's exact test was used for others.

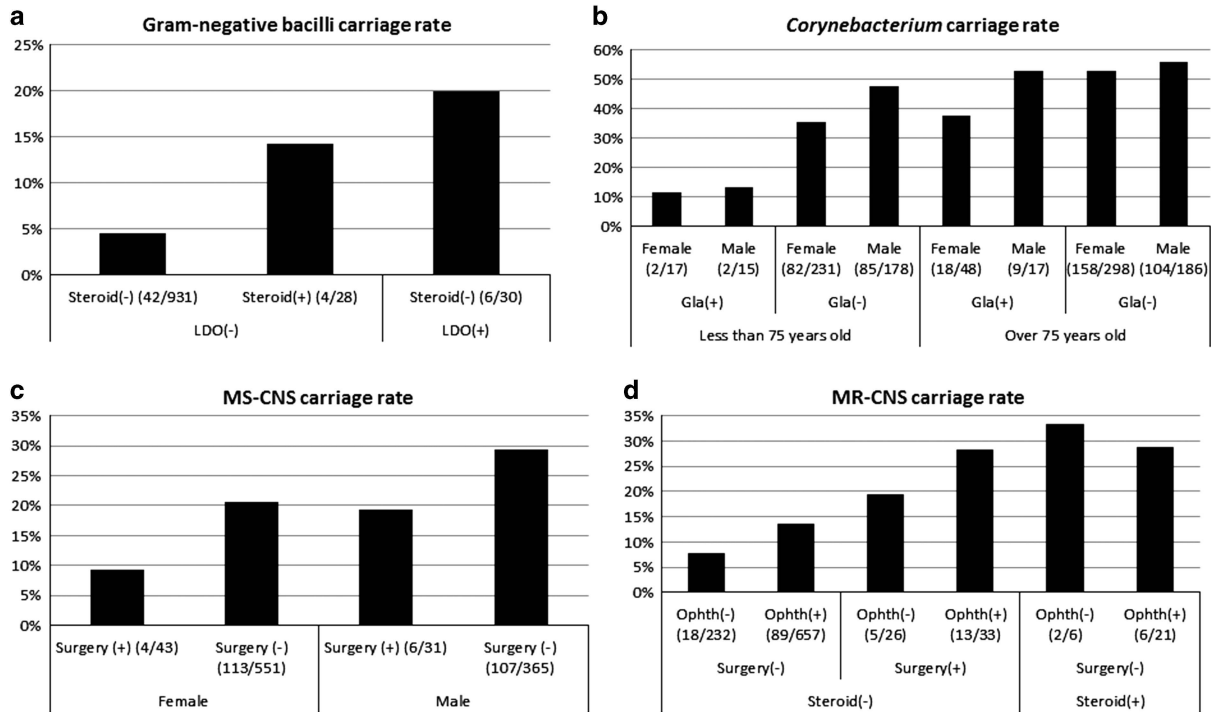
\*P < 0.05, \*\*P < 0.01.

**Table 3** Multivariate analysis for each bacteria

Factor	a. MSSA			b. Alpha-hemolytic streptococci		
	Adjusted odds ratio	95% CI	P-value	Adjusted odds ratio	95% CI	P-value
Age	1.007	0.975–1.041	0.671	1.049	1.001–1.100	0.044*
Sex (male)	0.803	0.432–1.494	0.489	1.287	0.613–2.704	0.505
Hypertension	0.971	0.513–1.837	0.928	1.473	0.665–3.261	0.340
Diabetes	1.673	0.683–4.096	0.260	2.189	0.972–4.930	0.059
Oral steroids	0.648	0.147–2.852	0.566	2.665	0.582–12.200	0.207
Lacrimal duct obstruction	0.703	0.158–3.116	0.642	2.227	0.485–10.231	0.303
Glaucoma eye drops	0.685	0.274–1.709	0.417	1.898	0.677–5.325	0.223
Visit history to ophthalmic facilities	0.954	0.465–1.957	0.898	0.749	0.328–1.714	0.494
Surgical history in other departments	1.089	0.326–3.639	0.889	0.349	0.046–2.621	0.306
	c. Enterococcus faecalis			d. Gram-negative bacilli		
	Adjusted odds ratio	95% CI	P-value	Adjusted odds ratio	95% CI	P-value
Age	1.077	1.029–1.128	0.002**	1.026	0.991–1.062	0.144
Sex (male)	0.795	0.387–1.631	0.531	1.098	0.609–1.981	0.756
Hypertension	0.891	0.443–1.793	0.747	1.355	0.735–2.497	0.330
Diabetes	1.682	0.753–3.758	0.205	1.496	0.755–2.967	0.249
Oral steroids	0.882	0.114–6.806	0.904	3.294	1.071–10.134	0.038*
Lacrimal duct obstruction	1.468	0.326–6.610	0.617	4.745	1.778–12.665	0.002**
Glaucoma eye drops	0.772	0.225–2.651	0.680	0.752	0.258–2.188	0.600
Visit history to ophthalmic facilities	0.954	0.444–2.050	0.903	1.074	0.553–2.086	0.834
Surgical history in other departments	1.372	0.464–4.061	0.567	1.604	0.649–3.964	0.306
	e. Corynebacterium species			f. MS-CNS		
	Adjusted odds ratio	95% CI	P-value	Adjusted odds ratio	95% CI	P-value
Age	1.042	1.027–1.057	0.000**	0.993	0.978–1.008	0.355
Sex (male)	1.410	1.080–1.841	0.012*	1.580	1.163–2.147	0.003**
Hypertension	1.180	0.901–1.545	0.230	1.114	0.810–1.533	0.507
Diabetes	0.948	0.684–1.313	0.747	1.125	0.777–1.630	0.532
Oral steroids	1.121	0.525–2.392	0.768	0.725	0.270–1.946	0.523
Lacrimal duct obstruction	1.196	0.570–2.509	0.636	0.951	0.380–2.382	0.915
Glaucoma eye drops	0.457	0.288–0.727	0.001**	0.621	0.346–1.114	0.110
Visit history to ophthalmic facilities	1.100	0.818–1.479	0.530	0.935	0.665–1.316	0.701
Surgical history in other departments	1.148	0.705–1.868	0.579	0.495	0.248–0.988	0.046*
	g. MR-CNS					
	Adjusted odds ratio	95% CI	P-value			
Age	1.004	0.984–1.025	0.667			
Sex (male)	0.970	0.660–1.425	0.877			
Hypertension	1.010	0.683–1.492	0.961			
Diabetes	1.111	0.699–1.766	0.656			
Oral steroids	3.651	1.628–8.185	0.002**			
Lacrimal duct obstruction	1.922	0.788–4.685	0.151			
Glaucoma eye drops	1.209	0.671–2.178	0.528			
Visit history to ophthalmic facilities	1.650	1.032–2.639	0.037*			
Surgical history in other departments	2.800	1.592–4.923	0.000**			

Logistic regression analysis.

\* $P < 0.05$ , \*\* $P < 0.01$ .



**Figure 1** Changes in bacterial carriage rate in conjunctiva. The numbers in parentheses indicate the number of carriers. Gla, glaucoma eye drops; LDO, lacrimal duct obstruction; Ophth, visit history to ophthalmic facilities; Surgery, surgical history in other departments. (a) Gram-negative bacilli carriage rate varied depending on Steroid and LDO. (b) *Corynebacterium* carriage rate varied depending on sex, Gla and age. (c) MS-CNS carriage rate varied depending on Surgery and sex. (d) MR-CNS carriage rate varied depending on Ophth, Surgery and Steroid.

**Discussion**

With respect to the carriage of alpha-hemolytic streptococci and *Enterococcus faecalis*, age was a risk factor. Acute postoperative endophthalmitis due to *Enterococcus faecalis* and alpha-hemolytic streptococci has a poor prognosis.<sup>13,14</sup> In our results, in patients over the age of 80 years, the conjunctival detection rate of each species was >5%. Therefore, in cases of serious postoperative endophthalmitis in elderly patients, the possibility of infection due to enterococci and streptococci should be considered.

With respect to the carriage of gram-negative bacilli, oral steroid use and lacrimal duct obstruction were independent risk factors. Many gram-negative bacilli detected in our study were bacteria inhabiting the humid environment. Conjunctivitis caused by *Haemophilus* species is seasonal in nature. However, because there was a small number of these species, features of the gram-negative bacilli group in our study would not represent the characteristics of *Haemophilus* species alone. It was suggested that the immune system function needed to eliminate environmental bacteria from the conjunctiva is diminished among patients who use oral steroids. Miller and Ellis<sup>9</sup> reported a positive correlation between the dose

of prednisolone and the number of bacterial isolates from conjunctiva. Therefore, it is believed that immunosuppressed patients can be easily infected by environmental bacteria. The relevance of lacrimal duct obstruction and gram-negative bacilli is easily understood, because gram-negative bacilli grow easily in stagnant tears unable to flow through the blocked duct. To control infection in intraocular surgery, it is important to consider that bacterial conjunctival flora may be changed among mild lacrimal duct obstruction patients without remarkable clinical findings. Kam *et al*<sup>15</sup> reported that the incidence of postcataract endophthalmitis among nasolacrimal duct obstruction patients was significantly higher than in the control group. Therefore, it is preferable to confirm the lacrimal duct obstruction prior to intraocular surgery regardless of epiphora. If lacrimal duct obstruction is present, it is preferable to wash the lacrimal duct just before cataract surgery, or if possible, to perform lacrimal duct reconstruction before cataract surgery.

With respect to the carriage of *Corynebacterium* species, age, male sex and glaucoma eye drop use were independent risk factors. The male sex and increased age increased the risk of conjunctival carriage of

*Corynebacterium*, but glaucoma eye drop use decreased the risk of conjunctival carriage. Fernández-Rubio *et al*<sup>8</sup> reported that increased age and the male sex were associated with the *Corynebacterium* detection rate in conjunctiva. *Corynebacterium* grows easily in lipid-rich environments.<sup>16</sup> Therefore, it is possible that the amount or properties of lipids in the ocular surface of male patients and elderly patients are convenient for the growth of *Corynebacterium*. It is unclear why the detection rate of *Corynebacterium* was reduced by glaucoma eye drop use. The conjunctival detection rate of *Corynebacterium* in preoperative glaucoma patients was significantly decreased as compared to preoperative cataract patients.<sup>17</sup> Because preoperative glaucoma patients should have used glaucoma eye drops, our result might be consistent with this previous report. However, it has also been reported that the use of glaucoma eye drops did not affect the bacterial detection rate.<sup>18</sup> Therefore, the influence of glaucoma eye drops on the detection rate of *Corynebacterium* requires further study.

The proportion of CNS in our study is quite different from that of these bacteria in Europe or the United States. The length of the incubation period is considered to be one of the causes. In the case of 7–10 days of culture period, the proportion of CNS is 64.7–74.0%.<sup>6,9,17</sup> On the other hand, the incubation period is 2 days in previous Japanese papers, and the proportion of CNS is 24.7–57.2%.<sup>4,7</sup> These Japanese data are similar to our data (35.5%). The risk factors for CNS were different according to the presence or absence of methicillin resistance. First, in MS-CNS, the male sex and surgical history in other departments were independent risk factors. The MS-CNS conjunctival carriage rate was increased in men. Fernández-Rubio *et al*<sup>8</sup> reported that the male sex was one of the risk factor for colonization of CNS in conjunctiva. Although the reason is unclear, as in the case of *Corynebacterium*, it is possible that the lipids necessary for the growth of MS-CNS are more abundant in men. In MR-CNS, oral steroid use, visit history to ophthalmologic facilities and surgical history in other departments were independent risk factors. As in the case of gram-negative bacilli, it may be considered that MR-CNS in the conjunctiva is difficult to eliminate in the immunocompromised state caused by systemic steroids. It has not been previously reported that MR-CNS in conjunctiva is associated with visit history to ophthalmic facilities or surgical history in other departments. Our results suggest that MR-CNS conjunctival carriage is strongly affected by healthcare-associated infection. Moreover, the reduction of MS-CNS and the increase of MR-CNS in patients with surgical history appear to be two sides of the same coin. Many surgical patients receive systemic antibiotics in the perioperative period. As a result, the patients affected by antibiotics may be

susceptible to MR-CNS infection. Moreover, MR-CNS could be spread to other patients by physical contact with medical staff in ophthalmic facilities. Therefore, the ophthalmologist must strictly adhere to infection prevention measures to prevent MR-CNS infection among ophthalmic patients. Hand hygiene by alcohol antiseptic or hand washing before contact with the patient's eye is critically important.

With respect to the carriage of *Staphylococcus aureus*, there were no statistically significant risk factors in preoperative cataract patients. A high detection rate of *Staphylococcus aureus* in the conjunctiva in atopic dermatitis patients was previously reported.<sup>10</sup> In the present study, we could not perform a statistical analysis of patients with atopic dermatitis because the number of patients with atopic dermatitis was too small (nine cases). *Staphylococcus aureus* primarily inhabits the nasal vestibule, and about 30% of people have asymptomatic colonization in the nasal vestibule.<sup>19</sup> Alexandrou *et al*<sup>20</sup> reported that prophylactic use of mupirocin nasal ointment significantly reduced the bacterial detection rate in conjunctiva. Therefore, it is possible that nasal *Staphylococcus aureus* colonization affects conjunctival bacterial flora.

The limitations of our study are that some patient background factors, such as atopic dermatitis, autoimmune disease and use of immunosuppressive agents other than steroids, could not be considered because the numbers of patients with these factors were too small. A high detection rate of conjunctival bacteria among patients with systemic disease has been previously reported.<sup>6,8</sup> The reason why diabetes was not a risk factor in our study is unknown. In an epidemiological study of Japan (the Hisayama study), the prevalence of diabetes at 40–79 years was 24.0% for men and 13.4% for women.<sup>21</sup> Since the prevalence of diabetes in our study was 20.8%, our result was similar to that of the Hisayama study. Although diabetes was not a risk factor in our study, there are several reports that diabetes increases the conjunctival bacterial detection rate.<sup>8,11,12</sup> Therefore, care must be taken when performing surgery on patients with severe systemic disease. In addition, it is necessary to further study the risk factors of anaerobic bacteria, such as *Propionibacterium acnes*, which cause late-onset endophthalmitis.

In conclusion, preoperative cataract patients had different risk factors for each type of conjunctival bacteria. Elderly patients, men, patients with lacrimal duct obstruction or immunosuppressed patients were most likely to be colonized by pathogens causing postoperative endophthalmitis. In particular, MR-CNS conjunctival carriage was associated with healthcare-associated infection. To prevent the spread of MR-CNS in

ophthalmologic departments, the strict observance of standard precautions is critically important.

### Summary

#### What was known before

- It is known that advanced age, male sex, immunosuppressive state, atopic dermatitis and diabetes affect bacterial colonization of conjunctiva. However, specific colonization factors for each bacterial species have not been sufficiently studied.

#### What this study adds

- For some bacterial species, there were specific factors that affect colonization of conjunctiva.
- Lacrimal duct obstruction was associated with colonization with gram-negative bacilli.
- Colonization of methicillin-resistant coagulase-negative *Staphylococci* was associated with healthcare-associated infection.

### Conflict of interest

The authors declare no conflict of interest.

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