

## Continuing Medical Education:

# Microbial profile and antibiotic susceptibility of culture-positive bacterial endophthalmitis

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### Learning objectives

Upon completion of this activity, participants will be able to:

1. Identify the most common causes of infectious endophthalmitis.
2. Describe the prevalence of culture-positive bacterial endophthalmitis.
3. Identify the most common causative organisms for infectious endophthalmitis.
4. Describe the antibiotic susceptibility pattern for infectious endophthalmitis.

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# Microbial profile and antibiotic susceptibility of culture-positive bacterial endophthalmitis

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## Abstract

**Purpose** To assess the distribution of microorganisms isolated from patients with bacterial endophthalmitis and their antimicrobial susceptibility.

**Methods** Retrospective analysis of medical and microbiological records of patients with suspected diagnosis of endophthalmitis. The following information was assessed: number of presumed and culture-positive endophthalmitis cases, source of infection, microbiological result (aqueous and/or vitreous culture and Gram staining), microbial characterization and distribution, and antimicrobial susceptibility.

**Results** A total of 107 (46%) of 231 patients with bacterial endophthalmitis showed positive results by gram stain or culture. Of these, 97 (42%) patients were positive for culture only. Most of them (62%) were secondary to a surgical procedure (postoperative), 12% were posttraumatic and 26% were secondary to an unknown source or the data were unavailable. A total of 100 microorganisms were isolated (38 aqueous and 67 vitreous samples) from the 97 culture-positive cases (91% were gram-positive and 9% were gram-negative). Coagulase-negative *Staphylococcus* (CoNS) (48%) were the most frequently isolated, followed by *Streptococcus viridans* (18%), and *Staphylococcus aureus* (13%). The antimicrobial susceptibility for CoNS was as follows: amikacin—91.6%, cephalothin—97.9%, ceftriaxone—50%, ciprofloxacin—62.5%, chloramphenicol—91.8%, gatifloxacin—79.5%, gentamicin—72.9%, moxifloxacin—89.5%, ofloxacin—70.8%, oxacillin—58.3%, penicillin—33.3%, tobramycin—85.4%, and vancomycin—100%.  
**Conclusion** Gram-positive bacteria were the major causes of infectious endophthalmitis

in this large series, usually following surgery. CoNS was the most common isolate. Of interest, susceptibility to oxacillin and fourth-generation quinolones was lower than previously published.

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**Keywords:** endophthalmitis; microbial; antibiotic susceptibility; laboratory investigation

## Introduction

Infectious endophthalmitis following cataract surgery still is a devastating condition, despite major improvements in surgical techniques in the last decades. Most series report on an incidence rate ranging from 0.05 to 0.4% in different studies worldwide.<sup>1</sup>

Most cases are caused by microorganisms from the conjunctiva and the eyelid. They might be secondary to surgery (postoperative endophthalmitis) or to trauma (posttraumatic endophthalmitis). Other microorganisms reach the eye through hematogenous spread (endogenous endophthalmitis).<sup>1–3</sup>

Acute postoperative endophthalmitis is commonly caused by gram-positive bacteria, especially by coagulase-negative *Staphylococcus* (CoNS), *Staphylococcus aureus*, and *Streptococcus viridans*.<sup>3–5</sup> Low virulence microorganisms, such as *Propionibacterium acnes*, some species of *Streptococci*, and fungi, are usually causatives of late postoperative endophthalmitis.<sup>6</sup>

'Posttraumatic endophthalmitis' is caused by the same microorganisms as postoperative cases, as well as other environmental agents.<sup>7</sup>

Endogenous endophthalmitis accounts for 2–6% of all cases. Previously published

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causative organisms include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus agalactiae*, *Clostridium perfringens*, *Moraxella* spp., *Neisseria meningitidis*, *Escherichia coli*, *Klebsiella* spp., *Serratia marcescens*, and *Candida albicans*.<sup>3,8</sup>

Its management requires a prompt intervention, such as vitreous tap or vitrectomy followed by intravitreal injection of antibiotics for postoperative and posttraumatic endophthalmitis.<sup>9</sup> Endogenous endophthalmitis requires that the main cause be treated, usually meaning systemic therapy with antibiotics in addition to ocular therapy.

Taking this into account, this study aimed at assessing the distribution of microorganisms isolated from patients with bacterial endophthalmitis and their antimicrobial susceptibility from 2006 to 2009 and compare them with the data previously published by our group (2000–2005).<sup>3</sup>

### Patients and methods

This was a retrospective study based on medical records from the Departments of Ophthalmology and Ocular Microbiology Laboratory at the Federal University of São Paulo, Brazil.

Data from all patients with presumed infectious endophthalmitis from 1 January 2006 to 31 October 2009 were analyzed. Presumption of endophthalmitis was based on a well-characterized clinical diagnosis.

The following information was assessed: number of presumed and culture-positive endophthalmitis cases, source of infection (postoperative, posttraumatic, endogenous, and unknown), microbiological result (aqueous and/or vitreous culture and gram staining), microbial characterization and distribution, and antimicrobial susceptibility testing of the positive cases for amikacin, cephalothin, ceftriaxone, ciprofloxacin, chloramphenicol, gatifloxacin, gentamicin, moxifloxacin, ofloxacin, oxacillin, penicillin, tobramycin, and vancomycin.

The patients were submitted either to vitreous/aqueous tap or vitrectomy followed by intravitreal injection of antibiotics. Intraocular specimens were collected and cultured on blood agar, chocolate agar, fastidious anaerobic thioglycolate broth, and Sabouraud agar for aerobic and anaerobic bacteria, and fungi. Gram stain and acid-fast stain tests were performed immediately. A positive culture was defined as either separate colonies of the same organism on two or more separate culture plates or confluent growth at the site of inoculation. Antimicrobial susceptibility testing was performed by the disc diffusion method. Current version of CLSI document M-100, published annually, was used for zone diameter interpretation.

### Results

Aqueous and vitreous samples from 231 patients with presumed endophthalmitis of different origins were sent to our laboratory of ophthalmic microbiology throughout the period of this study. A total of 107 (46%) of 231 patients with bacterial endophthalmitis showed positive results by gram stain or culture. Of these, 97 (42%) patients were positive for culture only. Smears were positive for bacteria in 10 culture-negative and in 47 culture-positive cases. Culture was positive in 41 samples obtained from the aqueous humor, 34 from vitreous tap, and 33 from vitrectomy samples. There was overlap among them in 15 cases.

A total of 100 microorganisms were isolated (38 from aqueous and 67 from vitreous samples) from the 97 culture-positive cases (91% were gram positive and 9% were gram negative). Table 1 shows detailed microbial distribution. Coagulase-negative *Staphylococcus* (CoNS) (48%) were the most frequently isolated, followed by *Streptococcus viridans* (18%), and *Staphylococcus aureus* (13%). Three cases were diagnosed with two microorganisms. CoNS was identified in each of them. Contamination from the lid microbiota might have happened.

Most culture positive cases (62%) were secondary to a surgical procedure (postoperative), 12% were posttraumatic and 26% were secondary to an unknown source or the data were unavailable (Table 2). CoNS was the most common microorganism regardless the predisposing factor. Of note, the two cases caused by *Bacillus* sp. were secondary to trauma.

Antibiotic susceptibility for the five more prevalent groups of microorganisms is disclosed in Table 3. It should be pointed out that 33% of the cases of CoNS resistant to gatifloxacin were sensitive to oxacillin (methicillin-sensitive) and 67% were also resistant to oxacillin (methicillin-resistant). All CoNS moxifloxacin-resistant cases were also methicillin-resistant.

### Discussion

To achieve effective prophylaxis and treatment of endophthalmitis, it is important to know the most common etiological agents involved and their response to the major classes of antibiotics routinely used.

The data in this are quite similar to those from our previous report (155 positive samples). From 2000 to 2005, CoNS (42%), *Streptococcus viridans* (14%) and *Staphylococcus aureus* (8%) prevailed. Postoperative infection was, as well as in this series, the most prevalent source (61%). Regarding antibiotic susceptibility, CoNS was 83%-sensitive to oxacillin and 100%-sensitive to the fourth-generation quinolones and vancomycin.<sup>3</sup>

**Table 1** Microbial distribution by species

Isolated microorganisms	Number of isolates
CoNS	48
<i>Streptococcus viridans</i>	18
<i>Staphylococcus aureus</i>	13
<i>Pseudomonas aeruginosa</i>	5
<i>Streptococcus pneumoniae</i>	3
<i>Corynebacterium</i> sp	3
Other Streptococci	2
Gram-positive Bacillus	2
<i>Moraxella nonliquefaciens</i>	2
<i>Serratia</i> sp	1
<i>Propionibacterium acnes</i>	1
<i>Nocardia</i> sp	1
<i>Weeksella virosa</i>	1
Total	100

**Table 2** Microbial distribution according to the source of the infection

Isolated microorganisms	Post-operative	Post-traumatic	Endogenous	Unknown/unavailable
CoNS	32	4	—	12
<i>Streptococcus viridans</i>	14	1	—	3
<i>Staphylococcus aureus</i>	5	3	—	5
<i>Pseudomonas aeruginosa</i>	2	—	—	3
<i>Streptococcus pneumoniae</i>	2	1	—	—
<i>Corynebacterium</i> sp	1	1	—	1
Other Streptococci	1	—	—	1
Gram-positive Bacillus	—	2	—	—
<i>Moraxella nonliquefaciens</i>	2	—	—	—
<i>Serratia</i> sp	1	—	—	—
<i>Propionibacterium acnes</i>	1	—	—	—
<i>Nocardia</i> sp	—	—	—	1
<i>Weeksella virosa</i>	1	—	—	—
Total	62	12	0	26

**Table 3** Antimicrobial susceptibility to the most frequent isolated microorganisms

	CoNS		Staphylococcus aureus		Streptococcus viridans		Streptococcus pneumoniae		Pseudomonas aeruginosa	
	n	%	n	%	n	%	n	%	n	%
Amikacin	48	91.6	13	84.6	—	—	—	—	5	100
Cephalothin	48	97.9	13	69.2	18	94.4	3	100	—	—
Ceftriaxone	48	50	13	69.2	18	83.3	3	100	5	0
Ciprofloxacin	48	62.5	13	92.3	18	50	3	100	5	100
Chloramphenicol	48	91.8	12	100	18	94.4	3	100	5	20
Gatifloxacin	44	79.5	11	100	14	92.8	2	100	5	100
Gentamicin	48	72.9	12	100	—	—	—	—	5	100
Moxifloxacin	48	89.5	12	91.6	13	100	3	100	5	100
Ofloxacin	48	70.8	12	100	18	100	3	100	5	100
Oxacillin	48	58.3	12	75	18	50	3	66.6	—	—
Penicillin	48	33.3	12	8.3	18	94.4	3	100	—	—
Tobramycin	48	85.4	12	83.3	—	—	—	—	5	100
Vancomycin	48	100	13	100	18	100	3	100	—	—

Abbreviations: n, total number of samples assessed; %, percentage of susceptibility.

In the present series of 231 infectious endophthalmitis cases, 46.3% were found to have a positive gram-stain or culture result. The remaining cases did not have a conclusive microbiological culture. The low sensitivity of this technique may be because of different factors, such as small amount of available microorganisms or previous use of antibiotics.<sup>10</sup> Molecular biology techniques, especially PCR, disclose sensitivities from 90 to 100% in most studies.<sup>11,12</sup>

Culture and gram-staining positivity were similarly distributed among aqueous, vitreous tap, and vitrectomy specimens. In all, 15% were simultaneously identified from two different sources (aqueous and vitreous tap or vitrectomy samples). These data were different from our previous study in which vitreous tap specimens made up 51% of all positive cases. As clinical data, such as visual acuity, were not available for this analysis, this difference could simply be explained by a different severity at presentation. Assuming this hypothesis, vitrectomy might have been more used in the present series because of more severe cases and, therefore, disclosed more positive cases than previously.

Gram-positive bacteria were responsible for 91% of culture-positive cases whereas gram negative caused 9% of them. Most published articles show a predominance of gram-positive microorganisms, ranging from 63 to 86%.<sup>13–15</sup> In a previous report from our laboratory (2000–2005), gram-positive bacteria comprised 79% of the culture-proven endophthalmitis isolates.<sup>3</sup> In our present and previous analyses, CoNS, *Streptococcus viridans*, and *Staphylococcus aureus* were the three most common bacteria in a descending order. This is in agreement with the most common microorganisms in the conjunctival flora.<sup>16</sup>

As expected, most cases were secondary to a surgical procedure (62%) and to trauma (12%). The microorganisms profile in the postoperative and posttraumatic groups is that present in conjunctival flora in both and from the environment in the latter. It should be remarked that *Bacillus* sp. was only present in the posttraumatic group.

The most relevant information of this study refers to the antimicrobial susceptibility. In our previous report, comprising data from 2000 to 2005, all CoNS were susceptible to both moxifloxacin and gatifloxacin.<sup>3</sup> From 2006 to 2009, 79.5 and 89.5% of CoNS were sensitive to gatifloxacin and moxifloxacin, respectively. Other studies in the literature have shown this rate to vary from 65 to 96%.<sup>17,18</sup> Additionally, most fourth-generation quinolone-resistant samples were also found to be methicillin resistant in our study. A recently published article showed that most methicillin-resistant samples from the conjunctiva were also quinolone resistant.<sup>19</sup> Betanzos-Cabrera *et al* have just shown how this resistance mechanism occurs.<sup>20</sup> All strains of CoNS resistant to quinolones (gatifloxacin and moxifloxacin) presented mutations at Ser84Phe for the *gyrA* gene, and Ser80Phe for the *parC* gene in their series.

As the fourth-generation quinolones are routinely used in the prophylaxis of many surgical procedures, this increasing trend of CoNS resistance is of concern. Besides that, because of their vitreous penetration above MIC, oral moxifloxacin is used in some settings as an additional treatment of endophthalmitis.

The fourth-generation quinolones showed good *in vitro* results against *Staphylococcus aureus*, *Streptococci*, and *Pseudomonas*. All gram-positive microorganisms were susceptible to vancomycin.

In summary, gram-positive bacteria were the major causes of infectious endophthalmitis in this large series, usually following surgery. CoNS was the most common isolate. Of interest, susceptibility to oxacillin and fourth-generation quinolones was lower than previously published.

## Summary

### What was known before

- Gram-positive microorganisms are the main causes of infectious endophthalmitis—Most of them (if not all) have always been susceptible to fourth-generation quinolones.

### What this study adds

- Recent samples of infectious endophthalmitis, especially CoNS, have shown resistance to fourth-generation quinolones.

## Conflict of interest

The authors declare no conflict of interest.

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1. A 65-year-old patient is diagnosed with infectious bacterial endophthalmitis in the emergency department. Which of the following is the most likely etiology of his condition?
  - A Hematogenous spread
  - B Postoperative infection
  - C Traumatic infection
  - D Idiopathic cause
2. The patient from question one is submitted to a vitreous and aqueous tap. What is the likelihood that the culture will show a positive result by culture or gram stain?
  - A <20%
  - B 32%
  - C 46%
  - D 85%
3. Which of the following best describes the likely organisms cultured in a patient with bacterial endophthalmitis from highest to lowest frequency?
  - A Coagulase-negative *Staphylococcus*; *Streptococcus viridans*; *Staphylococcus aureus*
  - B *Streptococcus pneumoniae*; *Staphylococcus aureus*; coagulase-positive *Staphylococcus*
  - C *Staphylococcus aureus*; *Mycoplasma pneumoniae*; *Streptococcus viridans*
  - D *Streptococcus viridans*; *Staphylococcus aureus*; coagulase-negative *Staphylococcus*

4. The culture for a patient with bacterial endophthalmitis is positive for coagulase-negative *Staphylococcus*. To which of the following antibiotics is the infection most likely to be resistant?
  - A Cephalothin
  - B Ciprofloxacin
  - C Tobramycin
  - D Penicillin

## Activity evaluation

1. The activity supported the learning objectives.

Strongly Disagree				Strongly agree
1	2	3	4	5

2. The material was organized clearly for learning to occur.

Strongly Disagree				Strongly agree
1	2	3	4	5

3. The content learned from this activity will impact my practice

Strongly Disagree				Strongly agree
1	2	3	4	5

4. The activity was presented objectively and free of commercial bias.

Strongly Disagree				Strongly agree
1	2	3	4	5