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## Identification and medical importance of coagulase-negative staphylococci species

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### ABSTRACT

A total of 126 coagulase-negative staphylococci strains (CNS) were isolated from blood samples and from the intravenous catheters and cerebrospinal fluid of 103 patients admitted to the University Hospital of Ribeirão Preto. *Staphylococcus epidermidis* (68.2%), *S. haemolyticus* (11.1%) and *S. hominis* (3.2%) were the most frequent species. The last two CNS showed greater resistance to antimicrobial agents than *S. epidermidis*. CNS were the agents of infection in 10.7% of the patients and the agents of intravenous catheter colonization in 18.4% of the cases.

**Keywords:** Coagulase-negative staphylococci. Septicemia. Bacteremia. Hospital infection.

### INTRODUCTION

*Staphylococcus epidermidis* and other coagulase-negative staphylococci (CNS) represent the major components of the microflora of human skin and mucosae. These microorganisms are commonly isolated in clinical microbiology laboratories and are prevalent in blood cultures and intravascular catheters. Although in medical practice they are considered to be contaminants of specimens collected from patients, CNS have been acquiring increasing importance in the etiology of hospital infections. This fact probably results from the large number of debilitated and immunosuppressed hospitalized patients, and also from the large-scale employment of invasive procedures.<sup>2</sup> An additional problem is the resistance of CNS to multiple antimicrobial agents, which varies according to species.<sup>1,3</sup>

Both microbiologists and the medical team have difficulty in distinguishing the true agents of infection among isolated CNS. The system of species identification, the test of sensitivity to antimicrobial agents and the standardization of clinical-microbiological criteria permit the detection of individual cases of infection and of outbreaks of hospital infection caused by CNS.<sup>4,5</sup>

The objective of the present study was to identify at the species level the CNS isolated from normally non-colonized body fluids and to determine their susceptibility to antimicrobial agents. The microbiological data were correlated with the clinical data in an attempt to determine the role of CNS in the clinical context.

## METHODS

We evaluated CNS isolated from blood cultures, intravascular catheters and cerebrospinal fluid (CSF). The materials were collected between March 1995 and August 1996 from patients admitted to the University Hospital, Faculty of Medicine of Ribeirão Preto, University of São Paulo.

Bacteria isolated from these materials were identified as *Staphylococcus* by classical microbiological tests. The differentiation of CNS species was performed using a tube test for free coagulase and a slide test for bound coagulase (Difco, USA). API 20 Staph and ID 32 Staph galleries (BioMérieux, France) were also used to identify CNS species, using the following additional tests in some cases: PYR (pyrrolidonyl arylamidase, Difco, USA), oxidase and tests of resistance to polymixin and novobiocin (Difco, USA).<sup>6</sup> Quality control was performed using standard CNS strains (ATCC, USA). The test of susceptibility to antimicrobial agents was carried out by the disk diffusion method (Cecon, Brazil) on Müller-Hinton agar plates.<sup>6</sup>

The medical records of the patients were reviewed retrospectively. CNS were considered

to be the cause of infection when the following criteria were satisfied: 1) patient with fever and other alterations suggestive of infection, 2) isolation of CNS from two or more cultures of the same or of different clinical specimens which had been collected separately during the same episode of infection, and 3) no isolation of other microorganisms.

## RESULTS

A total of 126 CNS were isolated from 103 patients, 79.3% from blood cultures, 18.3% from intravenous catheters and 2.4% from CSF. API 20 Staph identified 86 species with precision, but ID 32 Staph and additional tests were necessary to identify 40 other strains. The species identified showed the following distribution: 68.2% *Staphylococcus epidermidis*, 11.1% *S. haemolyticus*, 3.2% *S. hominis*, 2.4% *S. caprae*, 2.4% *S. capitis*, 1.6% *S. chromogenes*, 1.6% *S. lugdunensis* and 0.8% *S. simulans*, *S. saprophyticus* and *S. sciuri*. Three strains (2.4%) were identified by ID 32 Staph as *S. aureus*, although they were coagulase negative. For 6 other CNS (4.8%) we did not reach the precision required to identify the species. Thus, it was possible to recognize 95% of the CNS with the commercial systems used, which are also accessible to small clinical microbiology laboratories.

## DISCUSSION

CNS are the microorganisms most

**Table 1 - Percent sensitivity to antimicrobial agents by the disk diffusion method for the 3 species most frequently isolated**

Species	n <sup>#</sup>	Antimicrobial agents*																		
		OX	PN	AP	CF	CXM	CFO	IPM	VC	TC	EI	CL	CO	TT	GN	TB	AM	PEP	CIP	SFT
<i>S. epidermidis</i>	86	42.2	7.2	9.6	63.8	64.9	57.8	54.2	100	100	79.5	85.4	51.8	79.5	54.2	41.0	90.2	69.1	72.2	30.5
<i>S. haemolyticus</i>	14	40.0	0.0	0.0	40.0	46.7	53.3	60.0	100	100	33.3	53.3	53.3	46.7	26.6	46.7	80.0	46.7	46.7	6.7
<i>S. hominis</i>	4	0.0	0.0	0.0	75.0	25.0	25.0	25.0	100	100	75.0	100	0.0	75.0	50.0	0.0	100	0.0	33.3	0.0

\*: OX - oxacillin; PN - penicillin G; AP - ampicillin; CF - cephalothin; CXM - cefuroxime; CFO - cefoxitin; IPM - imipenem; VC - vancomycin; TC - teicoplanin; EI - erythromycin; CL - clindamycin; CO - chloramphenicol; TT - tetracyclin; GN - gentamicin; TB - tobramycin; AM - amikacin; PEP - pefloxacin; CIP - ciprofloxacin; SFT - trimetoprim-sulfamethoxazole.  
#: number of strains

commonly isolated from blood and their full identification has been recommended.<sup>5, 6</sup> *S. epidermidis*, *S. haemolyticus* and *S. hominis* were the species most often detected, as also observed in other studies.<sup>4, 5</sup> Of the 86 strains of *S. epidermidis*, 7 were causative agents of infection, and the same occurred with 3/14 (21.4%) of the *S. haemolyticus* strains. The difference between these percentages may suggest that *S. haemolyticus* is more pathogenic than *S. epidermidis*.

Vancomycin and teicoplanin showed *in vitro* activity against 100% of the CNS. The percentage of susceptibility of the three most common species to amikacin, clindamycin, tetracyclin and erythromycin was usually elevated, permitting the therapeutic use of these drugs (Table 1). The CNS presented intermediate or low sensitivity to  $\beta$ -lactams and other antibiotics, especially *S. haemolyticus* and *S. hominis*. Resistance to multiple antimicrobial agents is being noted in hospital strains of CNS,<sup>3</sup> with the prediction of future difficulties in the treatment of infections caused by *S. epidermidis* and *S. haemolyticus*.

The 103 cases showed the following distribution according to cause of hospitalization: 17 (16.5%) premature newborn infants or infants with other complications, 16 (15.5%) patients with AIDS, 14 (13.6%) cases of bone marrow transplantation, 10 (9.7%) patients with cancer, 6 (5.8%) patients with multiple trauma, and 40 (38.8%) patients with various problems, including neurological, cardiac and rheumatic diseases, and diabetes mellitus.

In 11 (10.7%) patients, CNS were considered to be the agent of infection, producing septicemia in 4 cases, infection of the central nervous system in 2 and peritonitis in 1. These patients with true CNS infection had serious diseases and had been previously submitted to invasive procedures. Another group of 19 patients (18.4%) presented no infection but had been implanted with a venous catheter for parenteral nutrition and/or administration of medications for a long period of time. The isolation of CNS was attributed to the

colonization of the implanted catheter since the same microorganism had been isolated from the blood of patients during the preceding weeks, some of them with multiple positive cultures. Bacteremia and septicemia induced by CNS have been reported to occur in premature newborn infants and in patients with neoplasias or submitted to surgeries or parenteral nutrition, and especially in intravascular catheters.<sup>2, 3</sup> In the third and largest group of patients there was insufficient evidence to consider CNS to be the cause of infection. These were cases of transitory bacteremia with no consequences or of contamination during the collection of clinical specimens.

In conclusion, a significant proportion of the CNS isolated in this tertiary care hospital was the cause of hospital infection or of colonization of the intravascular catheter. The identification of the species and the test of susceptibility to antimicrobial agents contribute to the understanding of the role of CNS in the clinical context.

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## RESUMO

Foram identificadas 126 amostras de estafilococos coagulase negativos (ECN) isolados de amostras de sangue, catéter endovenoso e líquido cefalorraquiano de 103 pacientes do Hospital das Clínicas de Ribeirão Preto. *Staphylococcus epidermidis* (68,2%), *S. haemolyticus* (11,1%) e *S. hominis* (3,2%) foram as espécies mais frequentes. As duas espécies de ECN mostraram maior resistência aos antimicrobianos do que *S. epidermidis*. ECN foram agentes de infecção em 10,7% dos pacientes e de colonização de catéter endovenosos em 18,4% dos casos.