Coagulase-Negative Staphylococcal Infections

Kathie L. Rogers, PhD[a], Paul D. Fey, PhD[a,b], Mark E. Rupp, MD[b,*]

KEYWORDS

- Coagulase-negative Staphylococci
- Staphylococcus epidermidis
- Intravascular catheter-associated bloodstream infection
- Biofilm • Prosthetic device infection
- *Staphylococcus haemolyticus*
- *Staphylococcus saprophyticus*

Coagulase-negative staphylococci (CNS) are differentiated from the closely related but more virulent *Staphylococcus aureus* by their inability to produce free coagulase. First identified in microbiological cultures in 1880 by Pasteur and Ogston when it was called *Staphylococcus albus*,[1] *Staphylococcus epidermidis* is the most commonly isolated CNS.[2] Currently, there are more than 40 recognized species of CNS. These organisms typically reside on healthy human skin and mucus membranes, rarely cause disease, and are most frequently encountered by clinicians as contaminants of microbiological cultures.[3,4] However, CNS have been increasingly recognized to cause clinically significant infections.[5–7] The conversion of the CNS from symbiont to human pathogen has been a direct reflection of the use of indwelling medical devices.[6,7] This review deals with the clinical syndromes, epidemiology, prevention, and management of infections caused by this unique group of organisms. Emphasis will be placed on *S. epidermidis*, with brief sections on *Staphylococcus lugdunensis, Staphylococcus saprophyticus,* and *Staphylococcus haemolyticus;* each an important member of the group capable of causing distinct infections.[8] The other members of the genus, most of which are only occasionally implicated in human disease, are generally indistinguishable from or less virulent than the infections caused by *S epidermidis*.[8]

[a] Department of Pathology and Microbiology, University of Nebraska Medical Center, 986280 Nebraska Medical Center, Omaha, NE 68198-6280, USA
[b] Department of Internal Medicine, University of Nebraska Medical Center, Nebraska Medical Center, Omaha, NE 68198-4031, USA
* Corresponding author.
E-mail address: merupp@unmc.edu (M.E. Rupp).

Infect Dis Clin N Am 23 (2009) 73–98
doi:10.1016/j.idc.2008.10.001 **id.theclinics.com**
0891-5520/08/$ – see front matter

CLINICAL SYNDROMES AND EPIDEMIOLOGY

The CNS, especially *S epidermidis*, are rarely implicated as the cause of infections of natural tissue.[9] They are found ubiquitously residing on human skin with healthy adults harboring 10 to 24 different strains of *S epidermidis*.[10] The number of CNS on human skin varies from 10 to 10^5 colony-forming units (CFU)/cm^2 on healthy adults in the community.[11] Their pathogenic potential lies in their ability to colonize and proliferate on biomaterials.[12] Every type of implanted biomaterial approved for use in humans has become prey to CNS infection.[13,14] These infections are often indolent and unresponsive to antimicrobials,[15,16] and frequently result in removal of the adulterated device.

INTRAVASCULAR CATHETER INFECTIONS

CNS are the most common cause of nosocomial bloodstream infection, responsible for 30% to 40% of these infections.[17] Most CNS bloodstream infections are the result of infections of intravascular catheters. Approximately 180 million peripheral intravascular catheters and 7 million central venous catheters (CVC) are used in the United States yearly.[18] Because of their transient nature (<72 hours usage) and placement sites (generally forearm or hand veins), peripheral intravascular catheters are not as commonly infected as CVCs. However, because of their ubiquitous usage, appreciable morbidity as a result of these infections does occur annually.[19]

A detailed description of the pathogenesis of these infections is beyond the scope of this monograph. Briefly, for peripheral intravenous catheters and short-term, nontunneled CVCs, infection most commonly results from CNS stemming from the patient's skin, migrating via the cutaneous surface of the catheter to gain access to the bloodstream.[20] However, for longer-term catheters and tunneled catheters, hub colonization (either from the patient's skin flora or from the health care environment) and migration of organisms via the luminal surface becomes increasingly important. Infrequently, catheter colonization occurs via hematogenous seeding or via infusate contamination.[19,21] As related later in this article, CNS have a number of adhesins that allow them to interact and adhere to the catheter surface and other factors that promote persistence.

It is estimated that approximately 250,000 cases of intravascular catheter-associated bloodstream infections occur yearly in the United States. The attributable mortality ranges widely in the literature from 1% to 2% to greater than 25% with an average additional cost per episode of $25,000 and excess hospital stay of 7 days or more.[19,22] It is estimated that many, if not most, of these infections are preventable, a topic addressed further in this article.[23,24]

Prompt and definitive diagnosis of these infections is necessary to decrease both morbidity and mortality, and to enable a decision to be made whether removal of the device is necessary or salvage is possible. Diagnosis of CNS intravascular device-related bloodstream infection is sometimes difficult because of the propensity for these organisms to cause blood culture contamination.[4,18,25,26] When diagnosing a bloodstream infection caused by CNS, it is imperative that at least two separate blood cultures be obtained, and if the patient has an indwelling CVC, that one of the blood cultures be collected through the catheter.[27] An incubation time to positivity of less than 25 hours has been considered consistent with true bacteremia.[28,29] In addition, the ''differential time to positivity'' test can be used to determine whether a vascular catheter is the source of bacteremia.[30] Blood drawn from the suspect catheter should have a higher inoculum, and turn positive more quickly, than blood obtained from the peripheral bloodstream. A 2-hour or more differential time has been demonstrated to be a sensitive and specific marker of catheter-associated bacteremia.[30,31]