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Staphylococcal Infections: A Historical Perspective 1  
Henry R. Shinefield and Naomi L. Ruff

Staphylococcus aureus is an unusually successful and adaptive human pathogen that can cause epidemics of invasive disease despite its frequent carriage as a commensal. Over the past 100 years and more, S aureus has caused cycles of outbreaks in hospitals and the community and has developed resistance to every antibiotic used against it, yet the exact mechanisms leading to epidemics of virulent disease are not fully understood. Approaches such as bacterial interference have been effective in interrupting outbreaks, but to better prevent staphylococcal disease, we will need to be vigilant about environmental factors that facilitate its spread. Even more importantly, we need to understand more about the mechanisms that lead to its virulence and transmission. With such information, it may be possible to develop a vaccine that will prevent both endemic and epidemic staphylococcal disease.

Host Defense and Pathogenesis in Staphylococcus aureus Infections 17  
Frank R. DeLeo, Binh An Diep, and Michael Otto

Staphylococcus aureus is the most abundant cause of bacterial infections in the United States. As such, the pathogen has devised means to circumvent destruction by the innate immune system. Neutrophils are a critical component of innate immunity and the primary cellular defense against S aureus infections. This article reviews human neutrophil function in the context of S aureus virulence mechanisms and provides an overview of community-associated methicillin-resistant S aureus pathogenicity.

Staphylococcus aureus: A Community Pathogen 35  
Loren G. Miller and Sheldon L. Kaplan

Staphylococcus aureus is a common human pathogen. S aureus infections most commonly clinically manifest as skin infections. There has been much interest in S aureus infections in the community over the past decade because of the rise of community-associated methicillin-resistant S aureus (CA-MRSA) infections, which have emerged globally over a relatively short period of time. In contrast to health care-associated methicillin resistant S aureus (HA-MRSA), circulating strains of CA-MRSA have
characteristic pathogenesis, strain characteristics, epidemiology, and clinical manifestations that are distinct from HA-MRSA. In fact, CA-MRSA probably behaves more like community-associated methicillin-sensitive \textit{S aureus} (MSSA). This article reviews current knowledge of the epidemiology and clinical manifestations of community-associated \textit{S aureus} and CA-MRSA infections.

**Staphylococcal Surgical Site Infections**

Deverick J. Anderson and Keith S. Kaye

\textit{Staphylococcus aureus} is the leading cause of surgical site infections (SSI) in the United States. In particular, SSI caused by methicillin-resistant \textit{Staphylococcus aureus} (MRSA) has emerged as a devastating complication, leading to increased mortality rates, increased length of hospitalization, and increased costs. Proven strategies for prevention of SSI caused by \textit{S aureus} include addressing modifiable risk factors and correct choice and timing of antimicrobial prophylaxis. Other strategies, including decolonization and the use of vancomycin, remain controversial.

**Coagulase-Negative Staphylococcal Infections**

Kathie L. Rogers, Paul D. Fey, and Mark E. Rupp

Coagulase-negative staphylococci (CNS) are differentiated from the closely related but more virulent \textit{Staphylococcus aureus} by their inability to produce free coagulase. Currently, there are over 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. However, CNS have been increasingly recognized to cause clinically significant infections. The conversion of the CNS from symbiont to human pathogen has been a direct reflection of the use of indwelling medical devices. This article deals with the clinical syndromes, epidemiology, prevention, and management of infections caused by this unique group of organisms.

**Antistaphylococcal Agents**

Howad S. Gold and Satish K. Pillai

These are interesting times in the treatment of infections caused by \textit{Staphylococcus aureus}, with shifting epidemiology of antibiotic resistance; changing prevalence of clinical syndromes (probably reflecting changes in virulence of circulating strains); and the recent availability of a variety of new agents with activity against multidrug-resistant gram-positive cocci. The abundance of riches in new drugs for the multidrug-resistant gram-positive space is timely, and these agents show great potential, but as yet have incompletely tested durability and comparative efficacy. This article reviews the advantages and disadvantages of a variety of antistaphylococcal agents by providing basic information including mechanism of action; mechanisms of resistance; clinical use (including dosing for and data supporting common indications); drug toxicities; and major drug interactions.
Decolonization may be defined as treatment to eradicate Staphylococcus aureus or methicillin-resistant S aureus (MRSA) carriage. Potential benefits of decolonization include decreased risk of subsequent staphylococcal infection and prevention of staphylococcal transmission to reduce endemic rates of infection or manage outbreaks. This article reviews available data regarding various proposed treatment regimens for eradicating staphylococcal carriage and the effectiveness of decolonization for infection prevention and as an infection control measure.

Staphylococcal Vaccines and Immunotherapies

Adam C. Schaffer and Jean C. Lee

Staphylococcus aureus is an important pathogen in the hospital and in the community, and it is increasingly resistant to multiple antibiotics. A non-antimicrobial approach to controlling S aureus is needed. The most extensively tested vaccine against S aureus, which is a capsular polysaccharide-based vaccine known as StaphVAX, showed promise in an initial phase 3 trial, but was found to be ineffective in a confirmatory trial, leading to its development being halted. Likewise, a human IgG preparation known as INH-A21 (Veronate) with elevated levels of antibodies to the staphylococcal surface adhesins ClfA and SdrG made it into phase 3 testing, where it failed to show a clinical benefit. Several novel antigens are being tested for potential inclusion in a staphylococcal vaccine, including cell wall-anchored adhesin proteins and exotoxins. Given the multiple and sometimes redundant virulence factors of S aureus that enable it to be such a crafty pathogen, if a vaccine is to prove effective, it will have to be multicomponent, incorporating several surface proteins, toxoids, and surface polysaccharides.