Introduction

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INDEX TERMS: MRSA, methicillin-resistance, *Staphylococcus aureus*

Clin Lab Sci 2009;22(2); 109

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***Wanda Reygaert PhD** is the **Focus: Methicillin-Resistant Staphylococcus aureus** guest editor.*

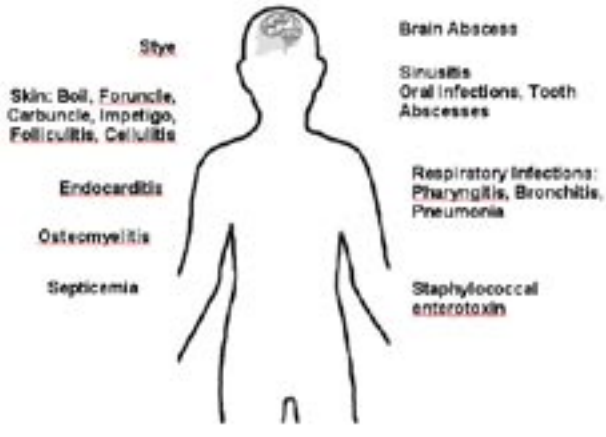
Staphylococcus aureus is a non-motile, gram-positive cocci that colonizes in clusters. It is found world wide and is a leading cause of disease. It can normally only transiently colonize the outside and entry portals of the human body (skin, ears, eye, nasal passages, etc.), but it is estimated that 20% of humans are carriers (asymptomatic permanent colonization)[1]. However, even transient colonization can lead to infection if the conditions are right; such as a breach in the protective layer of epithelial cells, or a compromised immune system. The ability to cause disease is via two mechanisms: 1) toxin production, and/or 2) proliferation of the organism, which causes tissue destruction.

Most infections remain localized at entry portals and are usually self-limiting and non-life threatening. Much less frequently, more serious infections may occur when the organism is able to invade deeper into the body (osteomyelitis, septicemia, pneumonia, etc.) (Fig. 1). These deeper infections may be extremely serious and even fatal. Because infections of *S. aureus* occur at a higher rate than that of many bacteria, the costs that are incurred for hospitalization and treatment can be tremendous. In just one year, 1995, in New York City, it was estimated that there were at least 13,550 cases of *S. aureus* infections resulting in an estimated cost of about $435.5 million[2].

In a study that was published in 2007 with data from the year 2003, it was found that nearly 390,000 people in the U.S. were hospitalized with *S. aureus* infections, with the average hospital stay for this type of infection costing $37,251. The total cost of *S. aureus* infections in the U.S. for 2003 was $14.5 billion[3].

Before the advent of antibiotics the mortality rate from *S. aureus* infections was near 80%. When penicillin therapy was introduced in the 1940s, it seemed that *S. aureus* (along with many other bacteria) infections could now be easily treated. However, within a short amount of time penicillin-resistant *S. aureus* had appeared, with approximately 80% of S. aureus now being penicillin resistant[4]. This led to the discovery and use of other antimicrobials such as methicillin in the 1960s.

Figure 1. Infections caused by *Staphylococcus aureus*



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Once again, the organism seemed to be under control. It wasn't long however, before methicillin-resistant *S. aureus* (MRSA) appeared, and strains that were sensitive to methicillin became known as MSSA (methicillin-susceptible *S. aureus*)[5]. Then clinicians turned to the use of Vancomycin for serious MRSA infections, and recently we have seen that MRSA strains are evolving that are able to overcome Vancomycin. A few Vancomycin-Intermediate Resistant *S. aureus* (VISA) have been isolated (Fig. 2)[6]. It seems that it's only a matter of time before we will be faced with full-blown Vancomycin-Resistant *S. aureus* (VRSA). At that point what will we be able to use to fight it?

MRSA is now a significant cause of infections worldwide. It has been estimated that in the U.S. over 126,000 hospitalized people become infected with MRSA each year. Over 5,000 patients die from these infections which cost the U.S. over $2.5 billion per year, and result in an average of $20,000 in excess cost per case of MRSA infection[7]. There has also been a dramatic increase in the prevalence of community-acquired MRSA, which is now thought to be responsible for up to 74% of skin and soft tissue infections acquired outside of the hospital[8].

Since methicillin was found to have limited therapeutic value and sometimes had serious side effects, usage in the U.S. was discontinued, and it is now unavailable for resistance testing. A closely related antimicrobial, oxacillin, has replaced methicillin in actual resistance testing, so MRSA may also be referred to as oxacillin-resistant *Staphylococcus aureus* (ORSA) in some sources, especially in articles not written in the U.S.[9, 10].

This series of articles is designed to provide a general well-rounded knowledge of MRSA. The second article in the series will delve into the prevalence and epidemiology of MRSA, showing how serious a problem it has become since the advent of antibiotics. The third article will cover the pathogenesis and virulence of the organism as well as the molecular basis of some antimicrobial resistance issues. The last article will explain how MRSA is identified, by manual and automated methods, including traditional and more modern methods, and will discuss what antimicrobial therapy options may now be available.

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Figure 2. Timeline of the Development of Antibiotic Resistance in *Staphylococcus aureus*