Editorial

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Innocent Neonate, Resistant Staph, and Embarrassed Staff

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The neonatal period is the time when a human being is most vulnerable to bacterial infections such as *Staphylococcus aureus*, which is a major pathogen causing neonatal morbidity and mortality. Staphylococci, aerobic or facultative anaerobic gram-positive bacteria, are able to survive in usual hospital environments, such as on fomites, in dust, on the surfaces of various materials. *S. aureus* can asymptomatically colonize the anterior nares, pharynx, skin, nails, axillae, perineum, and vagina. *S. aureus* is a major pathogen in early- and late-onset neonatal infection, and especially in nosocomial infections.

The spread of *S. aureus* from a mother can cause fetal infection and consequent premature delivery, intrauterine growth restriction, or persistent infection in the newborn. Colonization of *S. aureus* in the maternal genital tract can result in infection of the fetus *in utero* or of the neonate intrapartum,or may simply lead to colonization of the infant. Thereafter, colonized *S. aureus* in a newborn may cause localized infections and/or bacteremia. Premature infants are more vulnerable to staphylococcal infection due to undeveloped host defense mechanisms, the presence of catheters, skin-interrupting procedures, prolonged total parenteral nutrition, and steroid treatments [1].

After strains of *S. aureus* resistant to methicillin (MRSA) were first identified [2], those strains emerged as an important nosocomial pathogen. MRSA isolates are resistant to the penicillinase-resistant penicillin class of antibiotics, such as methicillin, nafcillin, oxacillin, cloxacillin, and dicloxacillin, due to their production of a penicillin-binding protein (PBP), PBP2a, which has a low affinity for ß-lactams [3]. However, the spectrum of clinical diseases is similar between methicillin-susceptible *S. aureus* (MSSA) and MRSA, with the exception of bone or joint infections, which have been reported to be less likely to be caused by MRSA [4].

Colonization rates of *S. aureus* have been observed to be higher in people with skin diseases, drug abusers, those with indwelling intravenous catheters, and healthcare workers. Many of outbreaks of *S. aureus* in neonates have been associated with medical personnel who are colonized [5]. Recently, whole-genome sequencing has begun to be used to track and define transmission pathways to elucidate neonatal MRSA outbreaks [6]. Additionally, environmental antibiotic pressure may increase the prevalence of MRSA in nurseries. In one

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study, Kim et al. reported that 45% of *S. aureus* isolates from 28 neonates in a nursery were MRSA [7].

A meta-analysis reported by Park et al. in this issue of *Infection and Chemotherapy* compared mortality rates for MSSA and MRSA bacteremia in pediatric patients. Their study concluded that the methicillin resistance of *S. aureus* was considered to be associated with an increased mortality rate in neonates. However, due to its nature, the meta-analysis study could not investigate detailed host factors such as prematurity and low birth weight, type of neonatal sepsis, length of hospital stay, catheter placement, and proper antibiotic usage.

From the bedside clinicians' perspective, it is more of interest how to manage the MRSA infection and how to prevent its spread. Only a few antibiotics are available to treat MRSA infection in neonates. ß-lactams and ß-lactam/ß-lactamase inhibitor combinations are not effective. Clindamycin is not effective against most hospital-associated MRSA (HA-MRSA) infections, while it may be useful for treating community-associated MRSA (CA-MRSA) infections. Linezolid and tetracyclines are bacteriostatic agents and are not recommended for the treatment of endocarditis or other intravascular *S. aureus* infections. Daptomycin can be used for the treatment of complicated skin and soft tissue infections, but it is not yet recommended for the treatment of meningitis, endovascular infections, or osteoarticular infections caused by MRSA due to the lack of sufficient clinical data regarding its use in children. Rifampin is not recommended as monotherapy because resistance emerges rapidly. However, it is effective as combination therapy with vancomycin in treating serious MRSA infections. Aminoglycosides are also believed to be effective in treating MRSA infection only when used in combination with vancomycin. Tigecycline is a newer antimicrobial agent against polymicrobial infections including MRSA, but there are not yet sufficient clinical data in children for it to be recommended as a first-line treatment for serious pediatric MRSA infections [8].

At present, the therapeutic agent of choice for HA-MRSA is vancomycin. Vancomycin should be considered the initial therapy of choice in nurseries with a high prevalence of MRSA infection. However, the usefulness of vancomycin is threatened by the emergence of vancomycin-intermediate *S. aureus* (VISA) and vancomycin-resistant *S. aureus* (VRSA) [9]. These strains are usually intermediately susceptible or resistant to teicoplanin, a glycopeptide alternative to vancomycin. The resistant strain has been proven to have the *vanA* gene transferred from enterococci. While *S. aureus* rapidly acquires various tools and tactics to survive the effects of therapeutic antimicrobials, the development of new antibiotics has been dramatically protracted in the last quarter century. This will result, in the near future,in a substantial problem in practicing the advanced medical treatment which is considered usual these days, including newborn care [10].

In addition to strategies to strengthen infection control interventions and antimicrobial stewardship practices, extensive efforts to develop new, effective antibiotics and biological substances, such as vaccines and specific immunoglobulin, have been undertaken by scientists, physicians, organizations, industry, and even policy makers [10]. However, newborns are expected to be the last beneficiaries of the newly developed drugs for various reasons, including but not limited to the difficulty in proving the effectiveness and safety of the drugs. Especially when treating neonates, we should always consider how to reduce the number of resistant staphylococcal infections, how to decrease transmission of the pathogen, and how not to be a source of it.

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