COMMUNITY ACQUIRED METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS IN ADOLESCENTS AND YOUNG ADULTS

By

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IN ADOLESCENTS AND YOUNG ADULTS

Abstract

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Of all the challenges that patients bring to the office of a family nurse practitioner (FNP), infectious diseases in adolescents and young adults can be some of the most challenging disease processes, especially in light of the constantly changing face of bacterial infections which develop resistance to the arsenal of antimicrobials in the practitioner’s formulary. Infections with community associated methicillin resistant *Staphylococcus aureus* are some of the most common and potentially dangerous infections to young people and these infections may be seen on an almost daily basis in a busy practice. Current evidence shows this pathogen to be steadily increasing in frequency and virulence. There is a huge knowledge pool now available due to a wealth of research recently conducted that makes it very difficult to stay abreast of this pathogen. The purpose of this article is to update the nurse practitioner on the latest developments in this area, with evidence-based advice on how to keep young people as safe as possible.
Community Associated Methicillin Resistant *Staphylococcus aureus* in Adolescents and Young Adults

**Introduction**

Bacterial infections of many kinds are frequently seen and treated by the nurse practitioner in family practice. One of the most commonly treated sources of infection is *Staphylococcus aureus*. At one time almost all *S. aureus* were susceptible to penicillin, but by 1944, the first resistant strains were being noted, and today, virtually all *Staphylococcus aureus* are resistant to the natural penicillins, aminopenicillins, and antipseudomonal penicillins available (Rice, 2006). Methicillin (and other penicillinase-resistant penicillins) were developed and marketed in the United States (US) in 1961 to treat infections caused by such resistant organisms. By 1968, the first methicillin resistant strains began to be detected (Huang, et al, 2006). However, it was not until the 1980s that these resistance issues became a big problem to health care in terms of nosocomial infections, and microbiologists began to differentiate isolates as “methicillin sensitive *Staphylococcus aureus*” (MSSA) and “methicillin resistant *Staphylococcus aureus*” (MRSA), based upon antimicrobial susceptibility patterns observed (Rice, 2006), and then later as “community associated MRSA” (CA-MRSA) and “hospital acquired MRSA” (HA-MRSA).

The professional journals have been rich with published research on MRSA since 2000. MRSA is an area of huge interest for nursing, medicine, infectious diseases, microbiology, pharmacy, industrial research and development, and athletic agencies. The difficult task for the FNP is staying abreast of the most recent knowledge and theories. Several publications considered to be landmark studies have just recently been made available. The October, 2007
Journal of the American Medical Association, “Invasive Methicillin-Resistant Staphylococcus aureus Infections in the United States” is one of the largest, regionally diverse studies examining the MRSA problem in the United States. Data from almost 9,000 infections were collected and reported to the Active Bacterial Core Surveillance system (ABCS)/Emerging Infectious Program of the Centers for Disease Control and Prevention (CDC) from July 2004 to December 2005 in nine regions across the country. A second landmark study was published by Moran, et al, in 2006. CA-MRSA infections identified in eleven university affiliated emergency departments across the country were evaluated. These two large studies helped us all understand that the increasing prevalence of CA-MRSA is a nationally recognized phenomenon, although regional, cultural, ethnic and age differences are reflected (Moran, et al, 2006). A full literature review reveals that literally thousands of studies and articles have been dedicated to the topic of MRSA, and hundreds of those have focused on CA-MRSA. Several of the studies which focused on this problem in young people are cited here.

Background

The prevalence of MRSA has been steadily increasing in the past decade, and currently the CDC estimate that 59-64% of S. aureus cultures across the country are resistant to beta lactams and methicillin, e.g. “MRSA” (CDC, 2007). In 1981, a new sub species of MRSA was isolated. The emergence of MRSA was initially associated with inappropriate use of antibiotics by health care facilities and hospitals. However, strains of MRSA were noted that came from individuals with no association with or recent exposure to hospitals, health care, or recent antibiotic use. This new strain was labeled as “community associated methicillin resistant Staphylococcus aureus” or CA-MRSA (Huang, 2006). This was at first a novel incidence, but with the passage of time, more and more isolates of CA-MRSA have been identified. Healthcare
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acquired MRSA (HA-MRSA) is noted to be more resistant to the currently available armamentarium of antibiotics than the more sensitive CA-MRSA, which is typically only resistant to methicillin, oxacillin, other beta lactams and cephalosporin's (Gorwitz, 2006, p. 3).

Upon closer examination and genetic sub-typing these two types of MRSA have shown themselves to have evolved into epidemiologically distinct populations (Klevens, et al, 2007, p 1764). Utilizing such sophisticated techniques as pulsed field gel electrophoresis (PFGE), polymerase chain reaction (PCR), and gene sequencing, strains of CA-MRSA are found to be typically one of several types: USA300 accounts for anywhere from 67-97% of the CA-MRSA isolated, while USA 400 or USA100 typically are found in the remaining 23-3%(Klevens, et al 2007,Moran et al, 2007). The incidence varies depending upon what study, what region, and what year the data are from, with a recently increasing incidence in USA300 over the last ten years (Gorwitz, 2006; Moran, 2007; Klevens, 2007). In a landmark study published in the New England Journal of Medicine, Moran et al (2006) described a study conducted in eleven emergency departments across the country (including sites in Portland, Albuquerque, Atlanta, Los Angeles, Minneapolis, New Orleans, New York, Philadelphia, Phoenix, Kansas City, and Charlotte). The cause and outcome of skin and soft tissue infections (SSTI) were retrospectively studied. It was found that 59% of the hundreds of SSTI they examined were caused by CA-MRSA and USA300 accounted for 97% of these infections across all ages (Moran, et al, 2006).

Awareness of the different subspecies and genetic types of MRSA may seem to be only of academic interest to the FNP. However, it is important to recognize that the different genotypes also differ in the possession of virulence factors. Possession of the panton valentine leukocidin exotoxin (PVL), while rarely identified in HA-MRSA, is present in 90-98% of all CA-MRSA (Grayson, 2006). Although the in vivo activity of PVL toxin continues to be
Better pediatric data are being yielded in states which have made CA-MRSA a reportable condition. In 2004, Tennessee did so, and that year reported an incidence of 33.4 cases/100,000 people, where it is the third most commonly reportable condition, trumped only by Chlamydia and gonorrhea (Jernigan, 2006). Los Angeles county has made CA-MRSA a pediatric reportable condition, finding that the rate of hospitalization for children less than 18 years of age (10.3/100,000) is much higher for CA-MRSA than for other reportable diseases (Jernigan, 2006).

Multiple cluster outbreaks of CA-MRSA have emerged and been reported in the literature. In 2000, the CDC was consulted to investigate an outbreak of MRSA among ten members of a Pennsylvania football team, seven of which required hospitalization (CDC MMWR, 2003). In 2003, ten players on a college football team in Connecticut developed SSTI due to a genetically identical MRSA strain of USA300. Incidence was linked to frequent skin to skin contact during scrimmage and the use of whirlpools (Begier, 2004). Nguyen, et al, reported on a similar case in 2005 in which eleven players from a southern California college football team had a similar outbreak with a clonally identical strain of MRSA USA300. The authors identified multiple behaviors all too common to adolescents and young adults that contributed to the outbreak: shared bars of soap; pre-existing cuts, abrasions and skin breaks due to practice/game trauma; shared towels; shared whirlpools, cosmetic shaving; chapped skin; recent use of antimicrobials; living in dormitories/frats (Nguyen, 2005).

Lindenmayer et al reported on a Vermont high school wrestling team from which seven of thirty-two teammates became infected during a season (Lindenmayer, 1998). The literature describe multiple similar outbreaks on athletic teams of various other kinds—not just football and wrestling, but also soccer, cheerleading, rugby, fencing, softball, canoeing, and fencing.
elucidated, in vitro PVL acts to inactivate and lyse leukocytes, and is largely thought to be responsible for the large pus filled fluctuant soft tissue abscesses most frequently associated with CA-MRSA (Gorwitz, et al, 2006). Clinically, if a CA-MRSA infection remains walled off in a pocket of pus, it is reasonably easy to treat. However, if left untreated, or if it gains access to systemic circulation, it may result in life threatening or fatal infections due to cardiopulmonary failure and necrotizing pneumonia. Castaldo et al (2007) reported retrospectively on eight young patients less than 19 years of age who yielded CA-MRSA positive blood cultures between 2004-2006. Only four of these adolescent/teenage patients survived neurologically intact, and four expired. Similarly, Gonzalez et al reported in 2004 about twelve adolescents with severe CA-MRSA admitted to the pediatric intensive care unit at Texas Children’s Hospital in Houston. The ages of the children were 10-15 years, and all had previously been healthy and without risk factors. Most of the children experienced pulmonary or vascular complications and three of the children expired. All isolates were of the USA300 genotype typical of the Houston area. Clearly, this is an organism that must be respected when it presents in primary care, and is certainly an infection that must be treated effectively and aggressively.

Risk factors for Adolescents and Youth

CA-MRSA infections are seen across all ages from neonatals to geriatrics, and in all lifestyles, but adolescents, teens, and young adults tend to participate in or own a variety of risk factors which make them in some ways more susceptible. Although risk factors for CA-MRSA are not clearly elucidated and sometimes infections occur with no clearly identified risk, some of the currently recognized risk factors include: (1) having diabetes mellitus; (2) participating in recreational intravenous drug use; (3) living in a community of high MRSA prevalence (e.g. the
incidence of CA-MRSA in Maryland in the Klevens' study was 29.7 per 100,000, but in Portland was only 4.7 per 100,000 (Klevens, et al 2007); (4) being a member of a population of high prevalence (African-Americans, Pacific Islanders, Alaska Native, Native Americans) (Gorwitz, et al, 2006; Klevens, et al, 2007); (5) having recent or current antibiotic use; (6) living in close contact with others infected or colonized with MRSA; (7) having recurrent or chronic skin disease (acne, eczema); (8) living in crowded living conditions (dormitories, homeless shelters, prisons); (9) participating in any sport which is characterized by a) skin-to-skin contact, b) propensity for skin damage, or c) shared clothing or equipment; and 10) being a man who has sex with men (MSM) (Dellit, et al 2004).

Incidence in Adolescents and Young Adults

Incidence of CA-MRSA varies with both age and race, with higher incidence in black peoples, and in the very young and the old (70+). While the reported incidence of invasive infections in the adolescent and young adult age group is lower than for other ages (approximately 4 cases per 100,000), data on the prevalence of SSTI are a little more difficult to find and evaluate. However the infection is relatively common in primary care. Moran et al estimated that 59% of all SSTI are caused by MRSA, with 97% of those infections caused by USA300, or CA-MRSA. Many pediatric and primary care infections are not reported or documented with culture and sensitivity, but are treated empirically, and a good number of infections in the adolescent/young adult age group have been reported as cluster infection outbreaks (e.g. among cohorts from an athletic team, within families, or in dormitories, etc.). In another CDC published study, it was found that the prevalence of MRSA among military recruits age 17-25 fluctuated from 2-11 cases per 1000 recruits in 2002 (Zinderman, 2004).
Clearly the naivety and lack of life experience of young people coupled with the propensity of young people to share belongings, activities, and close physical contact with their peers put them at great risk for developing CA-MRSA infections. Hormonal influences on developing bodies that result in acne and skin breaks; participating full tilt as only children and youngsters can in contact sports; as well as a high incidence of intravenous drug use; and an increased tendency to tattoo, pierce, and shave body parts all increase their susceptibility.

**Diagnosis of CA-MRSA SSTI**

Diagnosis of CA-MRSA is usually relatively simple. Roughly 80% of CA-MRSA infections present as very characteristic boils, furuncles, larger abscesses, “spider bites”, or more superficial impetigo like lesions (Marsden-Haug, et al, 2008). Across the nation, roughly 40-60% of all lesions presenting as such will, if cultured, grow out MRSA (Grayson2006, Epitrends, 2008). It is very important with this infection to document and verify it with a culture and sensitivity (Gorwitz, 2006). While most clinical labs lack the sophistication to do PFGE or PCR testing, and will simply identify the organism as MSSA or MRSA, they will be able to confirm the diagnosis and validate the practitioner’s choice of antimicrobial therapy. It is prudent to treat the infection as if it were MRSA until proven otherwise.

Of the other 20% of CA-MRSA infections, 13% will appear as respiratory infections, and 4% as septic patients, either of which will probably be much more ill appearing and will either present to the emergency room, or may be admitted or referred to the hospital by the FNP if they appear in family practice (Davis, 2007). According to the findings of the landmark *Journal of the American Medical Association*, non invasive CA-MRSA infections by far outnumber invasive infections, with only seven percent of CA-MRSA producing systemic symptoms (Klevens, 2007). Because invasive MRSA disease can be very devastating, immediate
hospitalization with appropriate drug therapy (currently intravenous vancomycin) is clearly indicated if the patient presents with systemic symptoms. Dellit, et al (2004), presented an excellent algorithm for treatment of CA-MRSA in the outpatient setting based upon Eron classes determined by severity of presentation. These guidelines prove useful in determining which patients should be hospitalized, and which can safely be treated in the clinic (Dellit, 2004).

Treatment of CA-MRSA

The roughly 80% of MRSA presenting as SSTI in adolescents and young adults may often safely and effectively be treated in the office, although large abscesses, or abscesses with near access to joint or systemic circulation may need to be incised and debrided in the hospital. Once an MRSA suspected SSTI is recognized, the best tactic is to initiate the "Treatment Triangle for Staphylococcal Infections", as described by M. Lindsay Grayson (Grayson, 2006), which consists of (1) surgical incision and debridement (I and D), (2) wound culture and sensitivity, and (3) appropriate antibiotic therapy, if deemed necessary. Thoroughly understanding the magnitude of CA-MRSA in family practice is hampered by the fact that fluctuant abscess and cellulitis resembling spider bites are commonly incised and debrided (as they should be) and prescribed empiric antibiotics (as they sometimes need to be; MSSA and some CA-MRSA infections typically do very well with only I/D) in primary care without the benefit of culture and sensitivity. Although it may save the patient some money to avoid this practice, primary care can not accurately evaluate the prevalence of such infections in its respective region, nor will the antibiogram of the clinical laboratory used by the practitioner benefit by the inclusion of the organisms being treated. Worse yet, if the patient returns later with a worsening cellulitis or enlarged abscess, the practitioner has little susceptibility information for guidance, and there of course exists a statistical chance that the infection may be
due to a less commonly seen organism other than Staphylococcus, such as Streptococcus. While hospitals are performing routine surveillance cultures of incoming patients with increasing frequency to determine colonization levels in their patient populations, current CDC recommendations encourage culturing all such wounds, including infections presenting in all outpatient facilities (Dellit, 2007). Some states have gone so far as to make MRSA a mandatory reportable infection. In the state of Washington, hospital acquired MRSA infections are reportable, but Governor Gregoire just recently assembled an expert panel to meet and debate the need to require mandatory reporting of CA-MRSA (Aleccia, 2007). This panel decided against mandatory reporting, leaving reporting up to facilities on a voluntary basis for now, but the issue may be revisited if this pathogen becomes more problematic. Schools, day care facilities, athletic associations, health care facilities, etc. are all encouraged to solicit help from their state or county department of health if outbreaks are encountered (Gorwitz, 2006).

The three legs of the treatment triangle are not equivalent in importance when it comes to treating SSTI due to MRSA, but rather are "weighted in favor of surgical drainage as the priority intervention" (Grayson, 2006, p. 725). Moran (Moran, et al, 2006) studied 320 S.aureus isolates obtained from SSTI in eleven emergency departments across the country. Fifty-nine percent of these infections were caused by CA-MRSA, 97% of which were genotype USA300. Of these isolates, susceptibility rates were as follows: trimethoprim sulfamethoxazole and rifampin (100%), clindamycin (95%), tetracycline (92%), fluoroquinolones (60%) and only 6% of strains were sensitive to erythromycin. (This high level of erythromycin resistance is of concern because erythromycin resistant strains show a high level of inducible resistance to clindamycin, which is otherwise usually a good treatment choice). In this study, antibiotics elected to treat these SSTI were inappropriately chosen in 100 of 175 patients based upon culture and sensitivity
information obtained later. However, when patients were contacted two to three weeks after treatment, this inappropriate prescribing did not affect long term outcomes, as 85% of the patients who had undergone incision and drainage had successfully recovered. Johnson, et al obtained similar findings in 2005 when they studied 125 pediatric patients eighteen and younger with CA-MRSA infections. Half of these patients received inappropriate treatment with beta lactams or clindamycin. “In patients receiving inappropriate antibiotic therapy, treatment success was attributable to concomitant surgical incision and debridement”(Johnson, et al, 2007).

Although I/D is clearly the most important intervention, it is not appropriate or indicated in all SSTI. When CA-MRSA is suspected, a culture should always be obtained prior to initiating any empirical antibiotic therapy. If empiric therapy is to be started prior to obtaining susceptibility data, it would be prudent to be guided by the practitioner’s local antibiograms, which are regularly published by local clinical microbiology labs. Recommended therapy would probably consist of TMP-SXT, tetracycline (not indicated for pregnant patients in last half of pregnancy or children younger than eight years due to bone development retardation and dental staining), clindamycin, and doxycycline (Nursing 2008, 2008.). Superficial skin infections such as impetigo do not always yield positive cultures. Topical mupirocin, bactroban and altabax ointments are good treatment options to treat more superficial infections. Empirical antibiotic therapy should always be re-evaluated once culture and susceptibility data are obtained with appropriate patient follow up.

To decrease the development of more antibiotic resistance, individuals who are colonized or in a carrier state are typically not treated. The colonization rate of young people has been assessed in several studies and has been found to be relatively high. Pan, et al, cultured 308 young people characterized as homeless or runaways, and found a 27.6% carrier rate of S. aureus
with a 6.2% MRSA carrier rate (Pan, 2005). Other studies have suggested that carrier states may be transient, with the organism cleared spontaneously, or may be persistent, either following a treated infection, or with no known infection or exposure whatsoever. When outbreaks do occur, mupirocin ointment applied to the nares, and chlorhexidine skin scrubs or bleach baths may be recommended to a population to decrease incidence (Oregon DHS, 2008).

Further Practice Implications

Coupled with the preceding “treatment triangle” the prudent nurse practitioner will devote appropriate attention to patient education to ensure that the infection is treated successfully and does not return or become shared with others who come in contact with the young patient at hand. Topics to be discussed include but are not limited to: (1) Does the patient indulge in risk factors that are putting them at greater risk (IVDA, sharing personal items such as towel, soaps, razors, cosmetics, etc)? (2) Are other family members, classmates, team members, dorm acquaintances similarly infected? (3) Are there pets (dogs, cats, horses, pigs) in the household? (4) Is there current other antibiotic use that may be affecting patients natural flora defenses? Instructions to the patient to finish antibiotics, return without delay if symptoms worsen, keep wounds covered utilizing frequent hand washing both before and after dressing changes should be given. While the young person does not need to stay home from school or avoid team or group activities, he must protect others from drainage from wounds by first getting them treated, and then keeping them covered while they heal. If this can’t be done, the child may need to be isolated from his peers, schoolmates, or team mates until the wound is no longer draining. There may be a need to disinfect common surfaces at home, school, the gym; to wear disposable gloves for dressing changes; and to use impeccable hand hygiene. Booklets such as “Living with MRSA”, a pamphlet available from the Washington State Department of Health,
review all these recommendations and are available from local health departments. Pamphlets from the local health department may be kept on file in the practitioner’s office to be given as a take home to reinforce the practitioner’s advice.

Conclusion

CA-MRSA infections have increased dramatically since 2000, and are frequently diagnosed in adolescents and teenagers. Whether these infections will continue to increase in frequency or will level off soon remains to be seen. A huge amount of time, revenue, and energy are currently being devoted to the study of this pathogen and the infections it causes. While rare disastrous and fatal infections have been associated with CA-MRSA, these incidents are very uncommon. The organism is a challenging one to treat in primary care, but armed with knowledge and respect for this pathogen, the vast majority of CA-MRSA infections in young people can be effectively cared for in the family nurse practitioner’s office, with the simple and routine tools currently available. Patient education is an imperative to decrease the spread of this pathogen.
References


