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Risk Factors For Pediatric Community Acquired Methicillin Resistant *Staphylococcus aureus*

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Risk Factors For Pediatric Community Acquired Methicillin Resistant

Staphylococcus aureus

by

Melissa Gail Kessler

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science in Public Health
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DEDICATION

To my loving husband, Scott for all your help with SAS and LaTeX and for your patience, support, and comforting words, and drying my tears. To my parents for all their support and helping me to "not screw up" and "keep my focus." To my brother, Eric thanks for listening to my trials and tribulations and providing me some much needed comic relief. To Kelly & Will, thanks for all the endless hours of proofreading and rehearsal for defense. To Andreas, thanks for all your support and kind words. To Foundations, thanks for listening ears and many prayers. To my Coworkers, thanks for listening, support, kind words, and sacrificing so I could go to class. To my committee members, thank you for your help and direction.

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Risk Factors for Pediatric Community-Acquired Methicillin-Resistant
Staphylococcus aureus

Melissa Gail Kessler

ABSTRACT

Methicillin-Resistant *Staphylococcus aureus* (MRSA) began as a nosocomial infection due to overuse of antibiotics. Several previous studies have reported an increase in this infection in adult patients who have not been hospitalized. It has also been reported that there is an increase in MRSA in children. Some of these children became infected even though they were not at high risk for the infection. After approval from the All Children's Hospital Institutional Review Board (IRB), a cross sectional study was conducted with pediatric admissions and pediatric emergency room visits to determine the characteristics of Methicillin-Sensitive *Staphylococcus aureus* and MRSA. During this study, a review of 672 medical charts was conducted. The study participants ranged in age from newborns to 18 years of age. In order to be enrolled in the study, the subjects' cultures were collected either as outpatients or within 72 hours of admission. The data that was collected from each chart included age, race/ethnicity, gender, type of infection, preexisting medical conditions, and risk factors for infection. The potential risk factors include antibiotic use, previous surgery or outpatient procedure, previous MRSA infection, immunotherapy, community worn device, and residence in a facility. Statistical analysis was conducted using Epi Info and SAS software packages. In regards to demographic characteristics, black children are 2.98 times more likely to have an MRSA infection than white children. Gender and age were not risk factors for the development of the infection. The risk factors that were significant in whites were home health care (OR= 6.12, CI= 5.16, 7.08),

community worn device (OR= 2.28, CI= 1.67, 2.89), previous hospitalization (OR= 2.43, CI= 1.95, 2.91), previous MRSA infection (OR= 3.69, CI= 2.90, 4.48), and previous surgery (OR= 2.02, CI= 1.51, 2.53). In blacks, females were more likely to have MRSA (OR= 2.57, CI= 1.73, 3.41). This finding may be due to the small sample size of black children in the study. Of the analyzed risk factors, home health care (OR= 2.95, CI= 1.11, 4.79), community worn device (OR= 2.85, CI= 1.71, 4.01), previous hospitalization (OR= 1.98, CI= 1.13, 2.83), previous surgery (OR= 2.79, CI= 1.79, 3.79), and previous antibiotic (OR= 5.60, CI= 4.66, 6.54) use were all significant risk factors in blacks. Effect modification was tested between race and all risk factors. Race was an effect modifier only for the risk factor of previous antibiotic use (pvalue =.02). Adjustment of confounding was performed for each race due to the presence of effect modification. After the adjustment for confounding in whites, only home health care (OR=4.37 CI= 1.55, 12.32), previous MRSA infection (OR= 2.86 CI= 1.16, 7.05), and previous hospitalization (OR= 2.00 CI= 1.14, 3.50) remained statistically significant. In blacks, after adjustment of confounding, only previous antibiotic use (OR= 5.13 CI= 1.75, 15.08) remained significant. Adjustment for confounding was also performed on the total risk factors model. A dose response relationship was present with increasing risk factors present.

CHAPTER 1

INTRODUCTION

In the past twenty years, there has been an increasing number of cases of Community-Acquired Methicillin-Resistant *Staphylococcus aureus* (CA-MRSA). Many studies have been conducted on the adult population but very little attention has been paid to the pediatric population. Of the studies that have been conducted, many found a startling increase in CA-MRSA in children. Herold et al conducted a study comparing the prevalence of pediatric CA-MRSA in August 1988-July 1990 to August 1993-July 1995 at The University of Chicago Children's Hospital. [1] The study concluded that the prevalence had risen from 10 per 100,000 in 1988-1990 to 259 per 100,000 in 1993-1995. [1] The predisposing risk factors for CA-MRSA noted in this study were prolonged hospitalization, invasive or surgical procedures, indwelling catheters, endotracheal tubes, and prolonged or recurrent exposure to antibiotics. [1] Sattler et al also conducted a comparison of risk factors and clinical characteristics of CA-MRSA in children and found that hospitalization of household contacts increased the risk of MRSA infection. [2] Another risk factor that has been reported in the literature is the association between parents and household contacts working in the health care field and these infections. [2] It has also been noted that CA-MRSA infections are more likely to be superficial skin infections than nosocomial MRSA infections. [1, 2, 3] CA-MRSA can also be more easily treated because of their lack of resistance to non-beta-lactam antibiotics when compared to nosocomially acquired isolates. [1]

1.1 Purpose of the Study

This study was initiated as a result of the concerns expressed by the staff at All Children's Hospital to Roger Sanderson, Regional Epidemiologist for the Florida Department of Health, about a possible increase in CA-MRSA at their institution. The purpose of this study is to examine the cases of MRSA over a period of one and a half years, 2002-2003 to perform epidemiologic analysis of children with *Staphylococcus aureus* infections. The risk factors for infection will also be collected in order to determine type of patient most likely to become infected. The information from this study will be utilized to better assess patients upon entry to the hospital as to their risk of harboring MRSA. This will also help the hospital prevent the spread of MRSA to other patients.

1.2 Research Questions

1. Determine if the risk factors for MRSA in the adult population, identified in previous studies, also apply to the pediatric population.
2. Determine which risk factors are more likely to predispose children to Methicillin-Resistant *Staphylococcus aureus* infection.
3. Compare the demographic characteristics of children with MRSA to children with Methicillin-Sensitive *Staphylococcus aureus* .

CHAPTER 2

HISTORY

Infection from *Staphylococcus aureus* was a serious cause of mortality before the advent of penicillin. It was recorded in the *Iliad* by Homer that 75% of wounded soldiers died following their injuries and the most likely cause was infection. [4] It was also recorded that 90-100% of amputations from 1870-1871 resulted in death during the Franco-Prussian war. [4] During the Surgical Congress, in Berlin on April 9, 1880, Alexander Ogston delivered a lecture on abscesses in which *Staphylococcus aureus* was first described and illustrated. [4] He named them Staphylococcus because their appearance in clusters looked like a bunch of grapes. [4] Staphyle means bunch of grapes in Greek. *Staphylococcus aureus* is a gram positive cocci in the Micrococci family and measures 0.5-1.5 microns in diameter. [5] In Ogston's lecture he stated that he recovered these cocci from nearly 100% of samples from acute abscesses from varying parts of the body. [4]

After the introduction of penicillin, mortality due to *Staphylococcus aureus* infections dramatically decreased. [4] However, resistance to penicillin soon began to develop. [4] Methicillin was then introduced to treat infections caused by penicillin resistant strains. [4] Then, in 1961, the first reports in Britain of methicillin resistant strains began to surface and soon after, several countries were reporting similar findings. [4, 6] In 1980 only 20% of *Staphylococcus aureus* strains were susceptible to penicillin. Now Methicillin-Resistant *Staphylococcus aureus* (MRSA) is a global problem in hospitals. [4]

2.1 Transmission

MRSA infections may be acquired in several different ways. The most common way is to be colonized by these strains. [7] Health-care workers are the most frequent source of exposure for patients. [7] The health-care workers' hands frequently become transiently colonized with the bacteria from their own sources or through other infected patients. [7] Patients may also become colonized or infected through other various sources such as stethoscopes, bedding, bed rails, bedside tables, and other environmental sources. [8]

2.2 Epidemiology

2.2.1 Seasonality

The rate of *Staphylococcus aureus* infections is constant throughout the year, therefore *Staphylococcus aureus* does not show any seasonal trend. [4]

2.2.2 Age

Those most susceptible to infections caused by *Staphylococcus aureus* are those with weaker immune systems. [5] With regard to age, the two populations with the weakest immune systems are the very young and the elderly. [5] Neonatal infection usually occur in the first several weeks after birth. [5] In the elderly, the infections are associated with increased exposure to various health-care settings including long-term nursing home facilities. [5]

2.2.3 Geographic Distribution

Staphylococcus aureus infections are found worldwide. [4] Incidence of infection is higher in areas associated with poverty where overcrowding is common and running

water is scarce. [4] Clusters of infections have been documented in aboriginals in Canada, New Zealand, and Australia. [4] A study was conducted between January 1997 and December 1999 where bloodstream isolates were recorded in various areas of the world including the US, Canada, Latin America, Europe, and the Western Pacific. [9] This study found that *Staphylococcus aureus* was found to be the most prevalent cause of infection in all geographic regions. [9] The rates of MRSA in both community and nosocomial isolates are steadily increasing. [9] In the US between 30-40% of *Staphylococcus aureus* isolates were MRSA and the rate of MRSA in European countries is about 25%. [9] The highest rates were found in the Asia-Pacific region which included Taiwan, Singapore, Japan, and Hong Kong. [9] The rate of MRSA in this region was greater than 60%. [9]

2.3 Underlying Medical Conditions

Several underlying medical conditions increase a person's likelihood of becoming infected with MRSA. The most important risk factor for becoming infected with MRSA is to be colonized. [10] Of healthy adults, 30-50% are colonized, with 10-20% persistently colonized. [7] Patients with type I diabetes, patients undergoing hemodialysis, surgical patients, burn patients, and patients with HIV/AIDS are all at increased risk for infection. [10] Patients with qualitative or quantitative defects in white blood cells such as cancer and leukemia patients and transplant patients are also at risk. [7] Patients with chronic skin conditions and intravenous drug users are also at an increased risk. [7, 11] This was first described in a Community-Acquired Methicillin-Resistant *Staphylococcus aureus* (CA-MRSA) outbreak in a Detroit hospital. [11] It is hypothesized that the increased risk is due to the use of communal needles and sharing of

other drug paraphernalia. [11] Intravenous drug users also tend to have poor hygiene which increases their likelihood to be colonized by the bacteria. [11]

2.4 Clinical Features

Infections caused by *Staphylococcus aureus* can either be localized or systemic. This depends on the degree of invasion and toxin production of the bacteria. Localized infections are commonly known as abscesses. Systemic infections may include but are not limited to bacteremia, endocarditis, osteomyelitis, and pneumonia. There are also two toxigenic staphylococcal diseases: toxic shock syndrome and Staphylococcal scalded skin syndrome.

2.4.1 Abscesses

Staphylococcus may invade the skin in several ways including wounds, follicles, or skin glands. [5] The most common type of infection is folliculitis and hidradenitis. [5] These infections are a mild, superficial inflammation of hair follicles or glands. [5] These infections are usually self limiting but may progress to subcutaneous tissue infections. [5] Furuncles or boils are a progression of folliculitis or hidradenitis to a large red tender pustule. [5] These often occur in clusters, in friction bearing areas of the body such as buttocks, breasts, axillae, and back of the neck. [5] Carbuncles are an aggregation of a cluster of furuncles. [5] These infections are much larger and more painful. [5] They usually appear on areas of thicker skin such as the back of the neck. [5] This infection may progress to systemic disease. [5] Another type of staphylococcal skin infection is impetigo. [5] This infection is characterized by bubble-like epidermal swellings and may break and peel away. [5]

2.4.2 Bacteremia

Bacteremia is defined as the presence of viable bacteria in the bloodstream. [7] The bacteria gain entry to the bloodstream from any type of Staphylococcal infection in which the body's immune system cannot contain. [7] The mortality of Staphylococcal bacteremia has remained between 11-43% over the past 15 years. [7] Factors associated with increased mortality due to bacteremia are over 50 years of age, non-removable foci of infection, and serious underlying cardiac, neurologic, or respiratory disease. [7] Complications from bacteremia frequently occurs and the rate may be anywhere from 11-53 %. [7] Bacteremia caused by MRSA does not have an increase in mortality when compared with Methicillin-Sensitive *Staphylococcus aureus* . [7]

2.4.3 Endocarditis

Endocarditis is the inflammation of the valves and lining of the heart. [7] The incidence of endocarditis caused by *Staphylococcus aureus* has increased from 1981 to 1988 and may account for 25-35% of all endocarditis cases. [7] Some risk factors for Staphylococcal endocarditis are being an intravenous drug user, elderly patients, patients with prosthetic valves, and hospitalized patients. [7] *Staphylococcus aureus* endocarditis differs in presentation from other endocarditis by its rapid onset, high fever, and frequent involvement of normal cardiac valves. [7] In intravenous drug users who develop endocarditis, the disease is most often found on the right side of the heart. [7] The patients also tend to be younger and have a lower mortality rate if not also infected with HIV. [7] In endocarditis, not related to drug use, the disease is more often found in the left side of the heart and has a high mortality rate. [7] The disease usually involves previously damaged valves. [7] *Staphylococcus aureus* is one of the most common pathogens in nosocomial and prosthetic valve endocardi-

tis. [7] Intravenous catheters are the most frequent source of bacterial inoculation. [7] The mortality rate for nosocomial endocarditis regardless of pathogen is 40-56%. [7] The rate may be even higher when the only pathogen taken into consideration is *Staphylococcus aureus*. [7]

2.4.4 Osteomyelitis

Osteomyelitis is an infection of the vascular metaphysis of bones. [5] The bones that are most commonly involved are the femur, tibia, ankle, or wrist. [5] Necrosis of bony tissue and abscess formation lead to an elevated and tender lump. Osteomyelitis occurs in two forms, primary and secondary. [5] Primary osteomyelitis is typically seen in growing children, adolescents, and intravenous drug users. [5] Secondary or traumatic osteomyelitis typically develops after a compound fracture or surgery in cancer or diabetes patients. [5]

2.4.5 Pneumonia

Staphylococcus aureus can be aspirated into the lungs and cause pneumonia because the bacteria frequently colonizing the nasopharynx. [5] The fatality rate is 50% even though *Staphylococcus aureus* accounts for only a very small proportion of pneumonia cases. [5]

2.4.6 Toxic Shock Syndrome

Toxic Shock Syndrome came into prominence in 1980-1981, when numerous cases were associated with introduction of super absorbent tampons. [7] The disease had a fulminant onset and was often seen in previously healthy females. [7] Toxic Shock Syndrome does not develop from a site of colonization and is not always associated with menstruation. [7] In fact, a third of all cases are non-menstrual. [7] The

non-menstrual cases are associated with localized infections from surgery or insect bites. [7] Toxic Shock Syndrome toxin I is present in 90% of Toxic Shock Syndrome menstrual cases, however other Toxic Shock Syndrome toxins have been associated with nonmenstrual cases. [7] Patient with nonmenstrual Toxic Shock Syndrome have a higher mortality rate than those associated with menstruation. [7]

2.4.7 Staphylococcal Scalded Skin Syndrome

Staphylococcal Scalded Skin Syndrome is commonly seen in children with infections of the umbilical stump or eyes. [5] These infections lead to toxemia and when the toxin reaches the skin it induces a painful bright red flush over the entire body. [5] The skin then blisters followed by desquamation of the epidermis. [5] The majority of cases have been described in infants and children under age four. [5] Exfoliative toxin is the toxin that is responsible for this infection. [5] This toxin also causes Staphylococcal impetigo which can affect all ages. [5]

2.5 Microbiology

Staphylococci can be isolated from pus, tissue exudates, sputum, urine, and blood. [5] These specimens are then inoculated onto sheep or rabbit blood agar. [5] The colonies that grow if *Staphylococcus aureus* is present in the specimen are large, round, and opaque. [5] The bacteria grows best at 37 degrees Celsius and is a facultative anaerobe. [5] This means the bacteria's growth is enhanced in the presence of oxygen and carbon dioxide. [5] The bacteria can withstand high salt contents, extremes in pH, and high temperatures. [5] It can also remain viable after months of air drying in addition to being resistant to many disinfectants. [5] These characteristics have allowed

the organism to continue to plague the health-care system despite improvement in both public health and health-care.

When a gram stain is performed on *Staphylococcus aureus* colonies it stains gram positive and may be observed in irregular clusters. [5] Gram stain alone is not enough to confirm the presence of *Staphylococcus aureus*. [5] The bacteria will be tested for the presence of catalase which differentiates it from Streptococci which lack the enzyme. [5] Staphylococci are differentiated from Micrococci by their ability to grow anaerobically and to ferment sugars. [5] After the genus Staphylococcus has been confirmed, a coagulase test is performed. [5] *Staphylococcus aureus* is the only species of Staphylococci to produce coagulase, therefore, the presence of the enzyme confirms a positive culture for *Staphylococcus aureus*. [5]

2.6 Antibiotic Resistance

Shortly after the introduction of penicillin, resistant strains to the antibiotic were noted. Despite the presence of the antibiotic, the bacteria continued to grow. The bacteria had adapted to its new treatment by producing β lactamase or penicillinase. This enzyme inactivates the penicillin by hydrolyzing the β -lactam ring in its structure. [7] This enzyme is inducible and is often coded for in plasmids. [7] Today, less than 5% of *Staphylococcus aureus* isolates are sensitive to penicillin. [7]

Other antibiotics, such as methicillin, were created to overcome the presence of β -lactamase. [7] After the introduction of methicillin and other similar antibiotics, resistance was also noted. Resistance to methicillin confers resistance to all penicillinase-resistant penicillins and cephalosporins. [7] This resistance requires the *mec* gene which encodes for penicillin-binding protein 2a. [7] Penicillin-binding proteins are membrane bound enzymes that become altered with the presence of the *mec*

gene. [7] The penicillin-binding proteins are the targets of the β -lactam antibiotics. [7] Without the *mec* gene these antibiotics have a high affinity for the penicillin-binding proteins. [7] With the introduction of the *mec* gene the bacteria produces modified penicillin-binding proteins which have a lower affinity for the antibiotic. [7]

2.7 Pathogenic Mechanisms

Staphylococcus aureus is a common organism that can be found as part of a person's normal flora. [7] It can colonize various areas of the body including the nares, axillae, vagina, pharynx, and damaged skin. [7] *Staphylococcus aureus* can remain colonized on a person indefinitely without causing any problems. [7] Only when the organism is introduced into surrounding tissues or the bloodstream through a break in the skin or mucous membrane, may a problem arise. [7] The infection may remain contained in one area or disseminate depending on the individual's defense mechanisms. [7] The presence of intravenous devices and urinary catheters increases the risk of infection. [7]

The pathogenicity of *Staphylococcus aureus* is caused by several enzymes and toxins. The principle enzymes that are documented are catalase, coagulase, hyaluronidase, and β -lactamase. The principle toxins are hemolysins, exotoxins, and exfoliative toxin.

2.7.1 Enzymes

Catalase: All Staphylococci species produce catalase. [5] This enzyme breaks down hydrogen peroxide into water and oxygen. [5] Hydrogen peroxide is used by neutrophils during phagocytosis. [5] The neutrophils use hydrogen peroxide to form toxic oxygen radicals. [5] The presence of catalase counteracts this mechanism. [5]

Coagulase: Only *Staphylococcus aureus* species produce coagulase. [5] This enzyme coagulates plasma and blood and causes fibrin to surround the bacteria and protect it from the host defenses. [5] The enzyme also promotes adherence to tissues. [5]

Hyaluronidase: This enzyme is also known as the spreading factor. [5] It digests the intracellular glue or hyaluronic acid that binds the connective tissue in the host. [5]

β -Lactamase: This extracellular enzyme opens the β -lactam ring of penicillin based antibiotics. [5]

2.7.2 Toxins

Hemolysins: This group of toxins causes the lysis of red blood cells. [5] There are four different types of this toxin α , β , γ , and δ . [5] α -toxin is the strongest hemolysin. [5] As well as lysing red blood cells it also damages leukocytes, and skeletal muscle, and heart and renal tissue. [5] β -toxin degrades sphingomyelin and effects red blood cells, leukocytes, and fibroblasts. [5] γ -toxin lyses red blood cells but the mechanism is unknown. δ -toxin acts as a detergent disrupting biologic membranes. [5]

Exotoxins: The two most important exotoxins are leukocidin and enterotoxin. [5] Leukocidin damages the cell membrane of macrophages and neutrophils and is another way to inhibit the phagocytic host defense. [5] Enterotoxins act on the gastrointestinal tract of humans to produce diarrhea. [5]

Exfoliative Toxin: This toxin separates the epidermal layer of the skin from the dermis causing it to peel away. [5] It is responsible for Staphylococcal Scalded Skin Syndrome, in which the skin appears burned. [5]

2.8 Immunologic Response

Staphylococcus aureus invades the host by a break in the skin or mucous membrane. [7] Once invasion takes place the host responds by activating the neutrophils and macrophages. [7] The complement system also plays a role in the host defenses. [7] There are several components in the cell wall of *Staphylococcus aureus* that activate the complement system. [7] One of these components is peptidoglycan which activates the alternative complement pathway which results in the release of C3a and C5a, as well as activation of neutrophils, macrophages, and natural killer cells. [7] After the bacteria is coated with complement, the macrophages attaches. [7] During phagocytosis, the bacteria is exposed to oxygen radicals. [7] This leads to a decrease in pH and then the lysosomal enzymes become effective. [7] This, along with lactoferrin, are another means of the intracellular mechanism. [7] Humoral and cell mediated responses are launched in addition to intracellular killing. [7]

2.9 Treatment

Abscesses must be surgically perforated and cleared of pus and foreign bodies. [7] Severe systemic infections respond slowly and require intensive and lengthy oral or injected therapy. [7] Penicillin is still the drug of choice if the isolate is sensitive. [7] Semi-synthetic penicillins are preferred if β -lactamase production is demonstrated. [7] If the patient has an allergy to penicillin, cephalosporins are used. [7] If MRSA is recovered vancomycin, fluoroquinolones, trimethoprim-sulphamethoxazole, clindomycin, or minocycline may be utilized. [7] There are several other antimicrobial combinations that may be utilized to increase bacteriocidal activity or prevent the development of resistance. [7] Therapy for invasive, life threatening infections is four

weeks or longer. [7] If the infection is originating from an indwelling device, removal is suggested when possible. [7]

2.10 Prevention

It is impossible to prevent all colonizations and infections as long as humans are the bacteria's primary reservoir. The best way to prevent the spread of any bacteria is handwashing. [12] Healthcare workers and family members need to be educated on the proper handwashing techniques. [12] APIC guidelines specify that hands should be washed for at least 10 seconds before leaving a patient's room regardless if gloves are worn or not. [13] SHEA guidelines also indicate that when there is no visible contamination of gloves with blood or body fluids that alcohol based hand rubs with emollient may be used. [14]

Contact precautions should be practiced on all cases of MRSA . [12] Patients on contact precautions should have a private room. [12] Contact precaution guidelines specify that you should wear gloves and gowns upon each entry to the patient's room for all direct patient care. [12] SHEA guidelines suggest however, that gloves and gowns should be worn even if there will only be contact with the environmental surfaces of an infected patients room. [14] The gowns should be removed before leaving the patients room in order to prevent the spread of MRSA to other patients. [12] Patient care equipment should be dedicated to a single patient to prevent the spread of the bacteria as well. [12] All hospital personnel should have annual continuing education on patient care and basic infection control practices. [12] Patients should not share food or drinks and all personal items should be thoroughly disinfected before sharing with other patients or family members. [12]

CHAPTER 3

LITERATURE REVIEW

Methicillin-Resistant *Staphylococcus aureus* (MRSA) was first isolated in 1961 in the United Kingdom. [15] This was one year after methicillin was introduced as a treatment for *Staphylococcus aureus*. [15] Then MRSA slowly disseminated until it began causing serious hospital infections in the 1970's. [15] MRSA has become increasingly prevalent in nursing homes, rehabilitation facilities, and now even in the community. [15]

Methicillin resistance is conferred by the SCC *mec* gene. [15] There are four genetic classes of the *mec* gene. [15] It is hypothesized that type I SCC *mec* was present in the first strains of MRSA that were isolated in the 1960's. [15] Type I SCC *mec* does not contain any other antibiotic resistance genes. [15] Type II and type III SCC *mec* contain multiple resistance genes. [15] These types became prominent in the 1980's in nosocomial isolates. Type IV SCC *mec* is commonly isolated from community acquired cases. [15] This type only encodes for methicillin resistance. [15] It is susceptible to many other non- β -lactam antibiotics. [15] Type IV SCC *mec* has been isolated from many countries including Japan, France, and Australia which demonstrates the international dissemination of type IV SCC *mec*. [15]

The majority of literature discusses risk factors for the acquisition of MRSA. Some of the most common risk factors are previous hospitalization, especially in intensive care units or burn units, preceding antimicrobial therapy, and surgical procedures. [16, 17, 18, 19, 1, 3, 20, 21] Some studies have also noted intravenous drug use and nursing

home residence as risk factors. [16, 17, 18, 19] In the pediatric population, day care attendance and having a family member hospitalized within the past six months are noted as potential risk factors. [2, 22, 19, 1, 3, 20]

3.1 Previous Studies

There have been several outbreaks of Community-Acquired Methicillin-Resistant *Staphylococcus aureus* (CA-MRSA) noted in the United States. The first of these was reported by Rathore and Kline in 1989. [23] There were two cases of serious MRSA infections in children who lacked any prior history of serious medical or surgical illness, antibiotic therapy, or hospitalization. [23] The first case was an eight year old boy with osteomyelitis of the left calcaneus. [23] The second case was a ten month old girl with bacteremia. [23] Both children had parents that were healthy and denied intravenous drug use or contact with of any family member with health-care workers or health-care facilities. [23]

The Centers for Disease Control and Prevention has also released several reports of CA-MRSA . There were four pediatric deaths in Minnesota and North Dakota. [24] The first case was a seven year old girl with an infected right hip joint. MRSA was isolated from the blood, hip joint, and sputum. [24] The girl had no recent hospitalizations and no family members with any contact with nursing homes or health-care settings. [24] The second case was a sixteen month old girl with a prior otitis media infection. [24] The organism was isolated from her blood and spinal fluid. [24] She also had no predisposing risk factors. [24] The third case was a thirteen year old girl with no predisposing risk. [24] MRSA was isolated from her blood, sputum, and pleural fluid. [24] The last case was a twelve month old boy whose sister was treated for an MRSA abscess. The organism was recovered from the boy's pleural fluid and post

mortem blood. [24] The isolates of the brother and sister were identical. [24] All of the MRSA isolates in these four cases susceptible to all antimicrobial agents except β -lactams. [24]

There were also three community outbreaks of skin infections associated with MRSA in Los Angeles County in 2002. [25] The first outbreak was from two athletes on the same wrestling team. [25] The second outbreak was reported by two large infectious disease clinical practices who had an increase in MRSA in homosexual men. [25] The last outbreak was reported by the Los Angeles County jail. [25] Each of these outbreaks had similar antimicrobial susceptibility patterns and were all the same predominant strain. [25]

The last reported outbreak of MRSA in the community was food-borne. [26] This outbreak was linked to a food handler, food specimens, and three ill patrons. [26] This was the first report of an outbreak of gastrointestinal illness caused by CA-MRSA . [26]

There have been two prevalence studies conducted on adults concerning community colonization by MRSA . Both of these studies were performed in the United Kingdom. The first was conducted by Abudu et al using a random sample of adults residing in Birmingham, UK in 1998. [27] The sample was randomly selected from the survey practices list on the Health Authority population register using random number sequences. [27] The participants had to be over the age of sixteen and nursing home residents were excluded. [27] Swabs of the anterior nares were taken. [27] Common culture and antimicrobial susceptibility testing practices were utilized. [27] The participants also completed a questionnaire which assessed information about risk factors for the acquisition of the organism. [27]

The response rate was 58%. [27] Females comprised 60% of the sample and minority ethnic groups made up 8% of the sample. [27] *Staphylococcus aureus* was obtained

from 63 isolates, which is a prevalence of 23%. [27] MRSA was isolated from 4 of the 63 isolates which is a prevalence of 1.5%. [27] No significant difference was found between any of the participants from which *Staphylococcus aureus* was isolated. [27] All of the MRSA isolates that were recovered were consistent with the prevalent strain in Birmingham hospitals. [27] This suggests that these isolates were more likely to be associated with carriage of hospital-acquired strains in the community rather than transmission within the community. [27] This study had several limitations resulting from sampling bias. [27] This was due to a poor response rate, small sample size, and a higher proportion of subjects over sixty five than in the general population. [27]

The second prevalence study that was performed in the United Kingdom was by Grundmann et al who investigated the prevalence of nasal carriage of MRSA in a sample of people aged sixty five and over. [28] These participants all resided in their own homes in the greater Nottingham Health District. [28] The sample size was 962. [28] Samples were taken from the anterior nares and demographic characteristics and risk factor data was also collected from the participants. [28] *Staphylococcus aureus* was isolated from 257 participants, eight were MRSA. [28] The population prevalence was eight per thousand. [28] MRSA was associated with hospital admission in the past six months and diabetes. [28] The presence of chronic skin ulcers was a strongly associated confounder with MRSA and previous hospital admissions. [28] All MRSA isolates were indistinguishable from the clone of MRSA was prevalent in English hospitals. [28]

There were several medical chart reviews that were performed in various hospitals on adult CA-MRSA patients. The first chart review was performed by Morin and Hadler. They did a retrospective review of all persons admitted with *Staphylococcus aureus* bacteremia in 1998, in four Connecticut metropolitan areas. [29] The purpose of this study was to analyze the magnitude and epidemiology of community-onset

Staphylococcus aureus and MRSA . [29] The four metropolitan areas comprised forty-one towns with a total population of over one million and included nine acute-care hospitals. [29] The medical charts of patients with *Staphylococcus aureus* bloodstream infections during 1998 were analyzed. [29] The information extracted from the charts was the town of residence, age, sex, race/ethnicity, date of admission and discharge, date of culture, outcome infection, antibiotic susceptibility, hospitalization history, iatrogenic risk factors for bacteremia, and underlying illnesses. [29] The study population was one hundred ninety two patients with community-onset bacteremia. [29] The overall incidence of infection was 17/100,000. [29] The highest incidence of infection were among males, adults over sixty five, blacks, and residents of urban areas. [29] MRSA was found in 15% of infections which made the overall incidence of community-onset MRSA bacteremia 2.5/100,000. [29] Healthcare associated infections accounted for the majority of bacteremia. [29] Of all community-onset *Staphylococcus aureus*, only 6% had community-onset with no underlying medical conditions. [29] The overall case-fatality rate for MRSA was 14%. [29] The main limitation of the study was that the only infection under consideration was bacteremia. [29] There was also no information on outpatient antibiotic use and no molecular method was used to compare nosocomial to community strains. [29]

Salmenlinna et al conducted a study to estimate the proportion of CA-MRSA. [30] The analysis was conducted on previous hospitalizations for all MRSA positive persons in Finland from 1997-1999. [30] A comparison of MRSA isolates in persons with and without hospital contact in terms of strain type, antibiotic resistance, and *mec* determinant profile. [30] Data was obtained from the National Hospital Discharge Register. [30] The records contained the date, the specimen source, patient date of birth, sex, and place of treatment. [30] Phage typing, pulse field gel electrophoresis, and antimicrobial drug susceptibility were also recorded. [30] There were five hundred

and twenty MRSA isolates in Finland during that period. [30] The annual incidence ranged from 2.3/100,000-4.1/100,000 and the proportion of CA-MRSA isolates was 21%. [30] Three strain types were identified that were associated with community acquisition and none of these strains were multi-resistant. [30] Children were found to be more likely to have CA-MRSA . [30] The limitations of the study were that some MRSA could have been isolated from nursing home residents. [30] These cases should have been classified as health-care-associated. [30] Also, local sample policy differences may have affected the number and type of CA-MRSA identified. [30] Sampling and screening policies in the community setting are not specified in the national guidelines for MRSA prevention in Finland. [30] These guidelines are primarily directed for use in a hospital setting with nosocomial infections as their focus. [30] Thirdly, no clinical and risk factor data was collected besides previous hospitalization. [30]

The last chart review of adults was conducted by Johnson et al. [17] They conducted a review of CA-MRSA cases of bacteremia and evaluated the risk factors and epidemiology. [17] This was a case control study comparing MRSA to Methicillin-Sensitive *Staphylococcus aureus* bacteremia at a 600 bed urban academic medical center. [17] The charts of the participants were reviewed to collect data regarding underlying conditions, sources of bacteremia, microbiology, patient outcomes, previous hospitalizations, and antibiotic susceptibility. [17] The cases and controls were similar in all aspects except that the patients with MRSA bacteremia was more likely to have presented from a long-term care facility and to have multiple admissions within the preceding year. [17] This study concluded that the majority of CA-MRSA bacteremia was health-care-associated and occurred in patients with underlying medical conditions. [17]

Tambyah et al conducted a study assessing the frequency of CA-MRSA infections at a teaching hospital in Singapore. [18] The study was prospective in nature, collect-

ing data for MRSA isolates from January to December 1998. [18] The prevalence of Community-Acquired Methicillin-Resistant *Staphylococcus aureus* was 43%. [18] The majority of infections were of the skin and soft tissue. [18] Of all of the Community-Acquired infections, all but one case had been exposed to outpatient centers, visiting nurses, or community hospitals. [18] The antibiotic resistance patterns in CA-MRSA were similar when compared with nosocomial isolates. [18] This study demonstrated that many presumed CA-MRSA infections are truly health-care associated due to the increase in health-care in outpatient settings. [18]

Some studies have been conducted on the pediatric population. Among these are several chart reviews. The most well documented of these was conducted by Herold et al. The purpose of this study was to determine whether CA-MRSA infections in children with no predisposing risk factors was increasing. [1] The study also defined the spectrum of disease associated with MRSA isolation when compared to Methicillin-Sensitive *Staphylococcus aureus* infections. [1] The study described the epidemiology of CA-MRSA among hospitalized children in four ways. [1] A comparison of the prevalence of CA-MRSA with identified risk in two time periods 1988-1990 and 1993-1995. [1] A comparison of the proportions of infecting versus colonizing isolates was conducted for the two time periods. [1] A third comparison of the clinical spectrum of disease for infecting isolates in 1993-1995. [1] The infecting isolates were split into five categories: CA-MRSA with identified risk, CA-MRSA without identified risk, nosocomial MRSA, Community-Acquired Methicillin-Sensitive *Staphylococcus aureus*, and nosocomial Methicillin-Sensitive *Staphylococcus aureus*. [1] A fourth comparison of the three MRSA groups susceptibilities to other antibiotics was also conducted. [1] The prevalence of of CA-MRSA without identified risk factors increased from 10/100,000 admissions in 1988-1990 to 250/100,000 admissions in 1993-1995. [1] Clinical disease was associated with 43% of Community-Acquired isolates from children with iden-

tified risk and 37.5% of nosocomial isolates were associated with clinical disease in 1988-1990. [1] In contrast, in 1993-1995, 80% of Community-Acquired isolates from children with identified risk and 88% of Community-Acquired isolates from children without identified risk, and 71% of nosocomial isolates were associated with clinical disease. [1] In addition, comparing the clinical spectrum of disease, the distribution of clinical syndromes associated with CA-MRSA in children with identified risk was similar to that of children with nosocomial acquired disease. [1] The clinical spectrum of disease for CA-MRSA without identified risk was very different. [1] Bacteremia was associated with nosocomial and CA-MRSA with identified risk. [1] Abscesses are more commonly seen in CA-MRSA without identified risk. [1] The disease association rate for Community-Acquired Methicillin-Sensitive *Staphylococcus aureus* is similar to CA-MRSA as well as the distribution of clinical syndromes. [1] With regards to antibiotic susceptibility, isolates from children with CA-MRSA and no identified risk were more likely to be susceptible to other antibiotics when compared to CA-MRSA with identified risk and nosocomial isolates. [1]

Another pediatric chart review study was performed by Gorak, Yamada, and Brown. This study was conducted from 1992-1996 using patients hospitalized with CA-MRSA infections in Honolulu. [3] The purpose was to assess the patients risk factors. [3] All the medical records of patients admitted with CA-MRSA were analyzed. [3] Patients were excluded if they had a previous hospitalization within the past six months, transferred from other hospitals, or were residents of nursing homes or other long-term care facilities. [3] The records were reviewed for residency status, travel history, admitting service, history of alcohol, tobacco, and intravenous drug use, family member or close contact with pyoderma, previous antimicrobial therapy, surgical intervention, site of culture, antimicrobial susceptibilities, and underlying medical conditions. Of clinically infected patients, 93 % had skin and soft tissue

infections. [3] Community acquired isolates were susceptible to a greater number of antibiotics. [3] This study was unique because the patient population in these hospitals were primarily young and healthy military men. [3]

Fergie and Pucell conducted a retrospective study to report the frequency of CA-MRSA isolates, describe the spectrum of disease of children infected with CA-MRSA and compare the antibiotic susceptibility patterns of Community-Acquired and nosocomial MRSA infections. [20] All cases of *Staphylococcus aureus* were identified from October to December 2000. [20] The medical records were reviewed for all children with CA-MRSA and the following information was recorded from the charts: diagnosis, site of culture, antibiotic susceptibility, and presence of any known risk factors. [20] These risk factors were underlying chronic disease, residence in a long-term care facility, day care attendance, household contact with identified risk factors, recent hospitalization or surgery, presence of an indwelling catheter, intravenous drug use, and previous antibiotic use. [20] The prevalence of CA-MRSA was 47% with 88% of these cases having no identified risk. Soft tissue infections accounted for 91% of these cases. [20] CA-MRSA accounted for 12% of the MRSA isolated from 1990-1996 and 59% from 1997-2000 peaking at 80% in 2000. [20] The annual rate of MRSA isolation increased from 2.9% of all *Staphylococcus aureus* isolates in 1990 to 19.0% in 2000. [20] CA-MRSA isolates from children without identified risk were more likely to be susceptible to trimethoprim-sulphamethoxazole and clindomycin. [20] Nosocomial isolates were more susceptible to tetracycline. [20] This study has demonstrated a dramatic increase in CA-MRSA in children with no known predisposing risk factors. [20]

A retrospective cohort study was conducted by Campbell et al to describe the relative contribution of risk factors for both Community-Acquired and nosocomial MRSA infections. [21] The participants were all children with MRSA infections, at

a tertiary care children's hospital between October 1999 and September 2001. [21] Medical records were used to collect data on demographics, date and site of culture, diagnosis, initial and final antibiotic and surgical therapy, and previous medical, microbiological, surgical, and device history. [21] The sample size was 62. [21] Patients with CA-MRSA tended to be older with a median age of 5.5 years versus 1.5 years. [21] Significant risk factors for CA-MRSA were previous surgery and antibiotics at presentation. [21] Exposure to endotracheal tubes, central vascular catheters, and chest tubes were less common in CA-MRSA patients and resistance patterns were similar between Community-Acquired and nosocomial isolates. [21] Only 8% of patients with CA-MRSA had no health-care risk. [21] These researchers concluded that the majority of Community-Acquired cases were in reality nosocomial cases due to similar resistance patterns and the presence of risk factors including contact with the health-care environment. [21] This risk factor alone could have led to colonization which later progressed to infection. [21] This obscured the likelihood of nosocomial transmission and delayed the investigation of poor adherence with infection control practices. [21]

There have been two studies conducted with children at daycare centers following the diagnosis of a child with Methicillin-Resistant *Staphylococcus aureus*. Shahin et al conducted a study of the prevalence of MRSA and Methicillin-Sensitive *Staphylococcus aureus* colonization in a child care center in Toronto. [31] The index case of CA-MRSA was a two and a half year old child. [31] Consenting parents completed a questionnaire and permitted screening of their children from throat, nose, and perianal sites and nasal and perianal swabs were obtained from the child center staff. [31] There was a response rate of 81.8% for children and 100% for staff. [31] Positive *Staphylococcus aureus* cultures were recovered from 24.4 % of children. [31] Only one classmate and the sibling of the index case had positive Methicillin-Resistant *Staphylococcus aureus*

cultures. [31] The classmate had a diagnosis of dermatitis that preceded the index case for this by three months which raises the possibility that the index case in this study may actually be a secondary case. [31] All three children's isolates had similar pulse field gel electrophoresis profiles. [31] No risk factors were found to be significantly associated with positive *Staphylococcus aureus* isolates. [31]

A second study was conducted by Adcock et al of the prevalence of MRSA colonization at two child care centers. [32] These two centers had a child hospitalized for MRSA infections. [32] A culture of the anterior nares and axilla was taken from each child and child care provider. [32] Parents and child care providers completed a questionnaire about factors associated with MRSA infections. [32] At day care center one, the colonization rate of MRSA was 24% and day care center two had a rate of 3%. [32] At day care center one two strains of MRSA were isolated and were associated with two different classrooms. [32] At day center two, one strain was isolated from the index case and a colonized child. [32] Of all children, 60% had contact with a health-care facility or had a household member who had contact with a health-care facility within two years prior to the study. [32] However, this result was not significant because the P-value is too large. [32]

Two community colonization prevalence studies were performed. The first was conducted by Hussain, Boyle-Vavia, and Duam. The purpose of their study was to ascertain whether healthy children attending an outpatient clinic were colonized with MRSA. [19] The study was performed at a primary outpatient facility at University of Chicago from January to August 1999. [19] Children sixteen years and younger attending the clinic for well child visits were eligible for the study. [19] Those eligible had specimens obtained from the nares and perineum. Of the 500 children tested, 24.4% were colonized with *Staphylococcus aureus* and of those colonized, three isolates had MRSA. [19] Two of the MRSA colonized children had a predisposing risk factor. [19]

The generalizability of the study is in question due to the fact that this clinic was in the inner city in which the majority of patients were African American. [19]

The second community colonization study was performed by Nakamura et al. The study was conducted to ascertain the prevalence of nasal carriage of MRSA in Nashville, TN. [22] Children receiving well child visits at either a university pediatric clinic or private pediatric office were eligible for enrollment regardless of chronic medical conditions. [22] Nasal swabs were collected and a questionnaire was administered to collect demographic data and risk factors. [22] Of the 500 enrolled patients, 29% were colonized with *Staphylococcus aureus* and of those colonized patients, four were colonized with MRSA. [22] None of the patients had risk factors, but all had household contacts with risk factors. [22] The risk factors of the household contacts that were analyzed are chronic illness, hospitalization, employment in the healthcare in a hospital or long term care facility, and community worn device. [22] Of these risk factors, only employment in a hospital or long term care facility was significant. [22] The MRSA isolates were susceptible to many antibiotics except erythromycin. [22]

Sattler, Mason, and Kaplan conducted a prospective observational study to compare the presence of risk factors for methicillin resistance between CA-MRSA and Community-Acquired Methicillin-Sensitive *Staphylococcus aureus* patients and household contacts, as well as the demographic and clinical characteristics between patients. [2] The study was conducted in Houston, Texas at Texas Children's Hospital from February 2, 2000 to November 14, 2000 excluding two one month periods in May and September. [2] Inpatients and outpatients were eligible if the isolate was community-acquired. [2] Patients were excluded if they had any underlying illness predisposing them to frequent hospitalizations, hospitalization in the prior six months, infants less than six months old who had been hospitalized during the neonatal period greater than 72 hours, or outpatient surgery within the past six months. [2] Risk

factors were assessed by interview and included antibiotic exposure, prior hospitalizations, health-care visits, daycare attendance, health-care worker or nursing home resident contact, and presence of underlying illness. [2] None of these risk factors were found to be statistically significant. [2] Of the 144 enrolled, 44% were MRSA. This organism was more frequently recovered from African Americans. [2] Methicillin-Sensitive *Staphylococcus aureus* infections tended to be deep-seated when compared to MRSA infections. [2] Recall bias of the presence of risk factors was decreased by excluding patients if the investigator or patient's guardian were aware of the antibiotic susceptibility test results. [2]

CHAPTER 4

METHODS

4.1 Study Design

This is a cross-sectional study of children 18 years or younger, who have a positive *Staphylococcus aureus* culture as an outpatient or within 72 hours of becoming an inpatient at All Children's Hospital in St. Petersburg, Florida.

4.2 Institutional Review Board

This study received approval by the Institutional Review Board at All Children's Hospital (ACH #03-0747) on July 29, 2003. The study was also submitted to the Institutional Review Board at University of South Florida, who deferred approval of the study to the All Children's Hospital Institutional Review Board. This study was performed under the supervision of Roger Sanderson, the regional epidemiologist for the Florida Department of Health. The principle investigator became an official Department of Health Volunteer and was therefore given access to the medical records. Patient confidentiality was assured by not removing the medical charts from All Children's Hospital grounds. Limited private health information was entered into the database in order to ensure that the patients in the study population could not be identified. A unique number was assigned by the database, and therefore, subjects names and dates of birth were not abstracted from the charts. The only unique patient information that was abstracted from the medical charts was date of admission

to the hospital, date of culture, and date of discharge from the hospital. Courses of Health Insurance Portability and Accountability Act (HIPAA) guidelines and the National Institute of Health Protection of Human Subjects were also taken by the Principle Investigator.

4.3 Study Population

All patients admitted to All Children's Hospital or seen as an outpatient in the Emergency room at All Children's Hospital St. Petersburg, Florida from January 1, 2002 to August 20th, 2003 were eligible for entry into the study. Records after August 20 were unavailable because the hospital infection control department had not yet updated their files. In order to be enrolled into the study, the patients also must have a positive culture for *Staphylococcus aureus*. Positive cultures from inpatients had to be collected within 72 hours of being admitted to the hospital. Patients who were admitted multiple times during the study period were only enrolled once using the first admission with a positive culture result.

4.4 Inclusion Criteria

Patients were enrolled if they were under 18 years of age at admission and had a positive *Staphylococcus aureus* culture within the first 72 hours of admission or had a positive culture as an outpatient.

4.5 Exclusion Criteria

Subjects were excluded if their charts were unavailable for review. Charts were unavailable if the patient was currently hospitalized or if the patients visited an outpatient clinic associated with the hospital.

4.6 Sources of Data

All of the data, for this study, was obtained from a chart review at All Children's Hospital in St. Petersburg, Florida. The hospital provided a computer generated list of all positive *Staphylococcus aureus* cultures for the study period of January 1, 2002 to August 20, 2003. The medical charts of all patients who met the study criteria were reviewed.

4.7 Data Collection

Data was collected by performing a chart review of 672 patients. All reviews were performed at All Children's Hospital. A standardized form was made using Microsoft Access and was utilized on all charts. The principle investigator performed all chart reviews.

Patient confidentiality was maintained by ensuring that no private health information was utilized in the study. No names or date of births were abstracted from the medical charts in order to assure patient confidentiality. All of the data collection took place at All Children's Hospital and the charts were promptly returned to medical records after data entry was completed.

Some of the information needed to assess the patients risk for getting a *Staphylococcus aureus* infection was missing. The missing information was marked as "not noted" for the particular question in the database. Seventeen subjects out of 672 had some missing data from their charts. The percentage of charts reviewed with missing data was 2.5%.

4.8 Definitions and Classification of Variables

The following variables were collected for this study and are defined below.

Age: The age of a patient was determined as the subjects age at date of culture.

Race/Ethnicity: This variable was collected as indicated on the subjects medical chart. White, Black, Asian, American Indian, or other were defined as races. Ethnicity was defined as either Hispanic or non-Hispanic. Note: All Children's Hospital defined Hispanic as a race in medical records.

Outcome/Transfer: This variable identified where the patient was going after being discharged from the hospital. The possible categories were home, long-term care facility, rehabilitation hospital, other hospital, or dead.

Previous Antibiotic Use: Previous antibiotic use was defined as any use of antibiotics within the previous 12 months as noted on the medical chart.

Previous Surgery: The variable is noted as a patient having any surgery within the past 12 months prior to the date of culture.

Outpatient Surgery: Outpatient surgery within the previous 12 months prior to the culture.

Patient Receiving Home Health Care: The variable was defined as a patient receiving home health care within the previous 12 months prior to the date of culture.

Previous MRSA Infection: This variable was identified as a patient having a previous infection with Methicillin-Resistant *Staphylococcus aureus* as noted on the medical chart.

Resident of a Facility within 12 Months of Admission: A patient that lived in a long-term care facility or rehabilitation hospital 12 months prior to the culture date.

Community Worn Device at the Time of Admission: These devices were defined as dialysis-related, urinary/ foley catheter, PIC line, Central line, and other lines (PEG, J tube, shunts) in place at the time of admission. Endotracheal tubes were also included in the "other" category.

Cardiovascular Disease: A patient with any history of arteriovenous malformations, congenital heart defects, pulmonary atresia, or Scimitar syndrome as noted on the medical chart.

Liver Disease: A patient with any history of acute hepatitis, or any congenital abnormalities of the liver as noted on the medical chart.

Pulmonary Disease: A history of asthma, cystic fibrosis, or broncho-pulmonary dysplasia as noted on the patient's medical chart .

Neurologic Disease: A patient with a history of any encephaly, skull or spinal deformities, cerebral palsy, Down's syndrome, or demyelinating disease as noted on the medical chart.

Immuno Therapy: A patient who was undergoing treatment with corticosteroids or chemotherapy/radiation therapy within the previous 12 months as noted on the medical chart.

Chronic Dermatological Condition: A patient with any history of eczema, psoriasis, dermatitis, or decubitus ulcers as noted on the medical chart.

4.9 Statistical Analysis

Data for the study was analyzed with the Epi Info software package from the Centers of Disease Control and Statistical Analysis Software (SAS). The data was analyzed both descriptively and analytically. The frequencies for the demographic characteristics as well as the risk factors were obtained. Univariate Analysis was conducted for each risk factor and a crude odds ratio and a 95% confidence interval were obtained from Epi Info. Race specific analysis was then conducted which suggested that effect modification may be present. Analysis was conducted utilizing the logistic regression function, proc logistic in SAS to assess if race was an effect modifier for any of the

risk factors. This analysis confirmed that race was an effect modifier for the variable previous antibiotic use. The logistic regression function was also used to adjust the risk factors for the presence of confounding.

A variable was created to reflect multiple exposures to healthcare to determine if risk increased as the numbers of potential exposures increased. The total number of risk factors for each subject was tabulated and analysis was performed looking for a dose response relationship. The subjects were broken into four categories: those with no risk factors, 1 risk factor, 2 risk factors, and greater than 2 risk factors. Each group was compared with the the no risk factor group. The same procedure was utilized to adjust for confounding and assess if effect modification was present as was outlined above.

CHAPTER 5

RESULTS

5.1 Demographic Characteristics

Demographic characteristics of the study participants are indicated in Table 1. In this study a total of 672 charts were reviewed and there were 126 cases of MRSA infection. The results are shown as the total study population and then broken into those with MSSA and MRSA.

Age: Subjects were enrolled in the study if they were 18 years old or younger at the time of admission. For analysis, age was broken into 5 categories: less than 1 year old, 1-4 years old, 5-9 years old, 10-14 years old, and 15-18 years old. The 1-4 year old group was the largest in the study and the 15-18 year old group was the smallest. These age categories were chosen in order to maintain consistency with CDC and Florida Department of Health age reporting standards. Table 1 shows the distribution of age as a whole group as well as a comparison of the MRSA and MSSA groups.

Race: All races and ethnicities were eligible for the study. The majority of subjects were non-Hispanic whites, followed by black, then Hispanic whites. Table 1 shows the break down of the study population by race. When compared with the total population by race in Pinellas county, 7.7% of of the county population is black and 2.4% are Hispanic in the total population as compared with the study population where 15.2% are black and 9.1% are Hispanic. The race breakdown in the study

	Total		MRSA		MSSA	
	Number	%	Number	%	Number	%
Age						
less than 1 yr	84	12.5	12	14.3	72	85.7
1 - 4 yr	243	36.2	58	23.9	185	76.1
5 - 9 yr	199	29.6	26	13.1	173	86.9
10 - 14 yr	104	15.5	20	19.2	84	80.8
15 - 18 yr	42	6.2	10	23.8	32	76.2
Race						
White	482	71.7	74	15.4	408	84.6
Black	102	15.2	36	35.3	66	64.7
Asian	11	1.6	1	9.1	10	90.1
Hispanic	61	9.1	10	16.4	51	83.6
Other	16	2.4	5	31.3	11	68.7
Gender						
Male	424	63.1	71	16.7	353	83.3
Female	248	36.9	55	22.2	193	77.8
Risk Factors						
Community Worn Device	81	12.1	28	34.6	53	65.4
Previous Antibiotic Use	210	31.3	53	25.2	157	74.8
Home Health Care	23	3.4	12	52.2	11	47.8
Previous Hospitalization	190	28.3	56	29.5	134	70.5
Previous MRSA Infection	36	5.4	16	44.4	20	55.5
Previous Surgery	141	26.9	41	29.1	100	70.9
Previous Outpatient Procedure	56	8.3	14	25.0	42	75.0
Immunotherapy	17	2.5	2	11.8	15	88.2
Residence in a Facility	17	2.5	6	35.3	11	64.7
Medical Conditions						
Cancer	13	1.9	2	15.4	11	84.6
Cardiovascular Disease	22	3.3	8	36.4	14	63.6
Chronic Dermatological Conditions	45	6.7	10	22.2	35	77.8
Diabetes	6	0.9	1	16.7	5	83.3
Liver Disease	9	1.3	4	44.4	5	55.6
Neurologic Disease	72	10.7	19	26.4	53	73.6
Pulmonary Disease	181	26.9	37	20.4	144	79.6

Table 1. Characteristics of study participants age 18 or younger seen at All Children's Hospital 1/1/02 - 8/20/03 in total and by methicillin status.

	Odds Ratio	95% Confidence Interval
Risk factors		
Community Worn Device	2.65	1.60, 4.41
Previous Antibiotic Use	1.79	1.40, 2.20
Home Health Care	5.12	4.28, 5.96
Previous Hospitalization	2.46	2.06, 2.86
Previous MRSA infection	3.83	1.92, 7.62
Previous Surgery	2.15	1.72, 2.58
Black	2.98	2.51, 3.45
Female	1.42	0.95, 2.10
Medical Conditions		
Cardiovascular Disease	2.58	1.74, 3.47
Chronic Dermatological Conditions	1.26	0.53, 1.99
Neurologic Disease	1.65	1.09, 2.22
Pulmonary Disease	1.16	0.32, 2.00
Total Risk Factors		
0 Risk Factors Present	1.00	-
1 Risk Factor Present	1.30	0.79, 1.81
2 Risk Factors Present	2.45	1.83, 3.07
greater than 2 Risk Factors Present	5.82	5.26, 6.38

Table 2. Odds Ratios and Confidence Intervals for Risk Factors for MRSA infections in children age 0 - 18 years at All Children's Hospital 1/1/02 - 8/20/03.

population is comparable with Florida and United States, with 14.6% black in Florida and 12.3% black in the United States. Hispanics make up 16.8% of the population in Florida and 12.5% in the United States.

Gender: The breakdown of the study population by gender is shown in Table 1. In this study 36.9% of the subjects were female. This is significantly lower than in Pinellas county (53.3%), Florida (51.2%), and the US (50.9%).

5.2 Risk Factors for Methicillin-Resistant *Staphylococcus aureus*

Data for eight risk factors were collected from each subjects medical chart. The risk factors were community worn device, previous antibiotic use, home health care, previous hospitalization, previous surgery, previous MRSA infection, immunotherapy,

and residence in a facility. Table 1 shows the breakdown on the distribution of the risk factors by total population and a breakdown by methicillin resistance status. The variable residence in a facility and immunotherapy were not analyzed due to the small number of subjects with these risk factors. Table 2 shows the crude odds ratios and the 95% confidence intervals for each of the risk factors. Gender was found not to be associated with MRSA infections (OR=1.42, CI= 0.95, 2.10)(Table 2). Blacks were found to be at a greater risk to be diagnosed with an MRSA infection than whites (OR= 2.98, CI= 2.51, 3.45). (Table 2) Community worn device (OR= 2.65, CI= 1.60, 4.41), previous antibiotic use (OR= 1.79, CI= 1.40, 2.20), home health care (OR= 5.12, CI= 4.28, 5.96), previous hospitalization (OR= 2.46, CI= 2.06, 2.86), previous MRSA infection (OR= 3.83, CI= 1.92, 7.62), and previous surgery (OR= 2.15, CI= 1.72, 2.58) were all found to be statistically significant risk factors for MRSA infection.

5.3 Medical Conditions

It was hypothesized that certain medical conditions may predispose subjects to an MRSA infection. These medical conditions were cancer, cardiovascular disease, chronic dermatological conditions, diabetes, liver disease, neurological disease, and pulmonary disease. Table 1 shows the breakdown of medical conditions in the total study population and by methicillin status. Cancer, liver disease, and diabetes were not analyzed due to the small number of subjects that demonstrated these disorders. Table 2 demonstrated the crude odds ratios and 95% confidence intervals for each of the medical conditions that were analyzed. Of these, only cardiovascular disease (OR= 2.58, CI= 1.74, 3.47) and neurologic diseases (OR= 1.65, CI= 1.09, 2.22) were shown to be associated with MRSA infection (Table 2). The reason that these medical con-

ditions are associated with MRSA infection is that they often require more frequent contact with healthcare providers in order to monitor and treat their illness.

5.4 Total Risk Factors

As many of the risk factors of interest reflect opportunities to acquire hospital based infections, a variable was created to reflect multiple exposures to care to determine if risk increased as the numbers of potential exposures increased. The total number of risk factors for each subject was tabulated and analysis was preformed looking for a dose response relationship. The subjects were broken into four categories: those with no risk factors, 1 risk factor, 2 risk factors, and greater than 2 risk factors. Each group was compared with the the no risk factor group. The more risk factors that a subject possessed, the greater their risk for MRSA infection (Table 2). There were only 35 out of 126 MRSA patients that had no risk factors for MRSA infection documented in their chart. This is a prevalence of 28%. This finding demonstrates that the majority of MRSA infections in this study were associated with some kind of previous exposure to the healthcare setting and were not truly community acquired infections.

5.5 Effect Modification

Testing for effect modification was performed in SAS because univariate analysis suggested that race may be an effect modifier for the risk factors. Effect modification was tested between race and all risk factors. Race was an effect modifier only for the risk factor of previous antibiotic use (pvalue =.02). This finding suggests that race plays a role in a subjects access to antibiotics. This finding may be explained by the fact that whites traditionally have more access to healthcare than blacks. This would give

	Total		MRSA		MSSA	
	Number	%	Number	%	Number	%
Age						
less than 1 yr	17	16.7	5	29.4	12	70.6
1 - 4 yr	34	33.3	14	41.2	20	58.8
5 - 9 yr	20	19.6	7	35.0	13	65.0
10 - 14 yr	25	24.5	8	32.0	17	68.0
15 - 18 yr	6	5.9	2	33.3	4	66.7
Gender						
Female	39	38.2	19	48.7	20	51.3
Risk Factors						
Community Worn Device	14	13.7	8	57.1	6	42.9
Previous Antibiotic Use	28	27.5	18	64.3	10	35.7
Home Health Care	5	4.9	3	60.0	2	40.0
Previous Hospitalization	35	34.3	16	45.7	19	54.3
Previous MRSA Infection	4	3.9	2	50.0	2	50.0
Previous Surgery	20	19.6	11	55.0	9	45.0
Total Risk Factors						
0 Risk Factors	49	48.0	12	24.5	37	75.5
1 Risk Factors	28	27.5	8	28.6	20	30.3
2 Risk Factors	9	8.8	6	16.7	3	71.4
greater than 2 Risk Factors	16	15.7	10	62.5	6	37.5

Table 3. Characteristics of black study participants age 18 or younger seen at All Children's Hospital 1/1/02 - 8/20/03 in total and by methicillin status.

white children more exposure to healthcare as a total population. It may be hypothesized that only the sickest of black children are exposed to healthcare and as a result more susceptible to MRSA infection Table 3 and Table 4 illustrates the breakdown of each of the risk factors within their respective race as a total population and by methicillin status. As a result of effect modification of race being present, subjects were categorized according to race and then odds ratios and confidence intervals were computed. This analysis was performed on blacks and whites. Hispanics were included with the white population. All other races and ethnicities were present in too small numbers to permit analysis. The risk factors that were significant in whites were home health care (OR= 6.12, CI= 5.16, 7.08), community worn device (OR= 2.28,

	Total		MRSA		MSSA	
	Number	%	Number	%	Number	%
Age						
less than 1 yr	60	11.1	5	8.3	55	91.7
1 - 4 yr	199	36.7	42	21.1	157	78.9
5 - 9 yr	172	31.7	18	10.4	154	89.6
10 - 14 yr	78	14.4	12	15.4	66	84.6
15 - 18 yr	34	6.3	7	20.6	27	79.4
Gender						
Female	198	36.5	34	17.2	164	82.8
Risk Factors						
Community Worn Device	63	11.6	17	27.0	46	73.0
Previous Antibiotic Use	173	31.9	31	17.9	142	82.1
Home Health Care	18	3.3	9	50.0	9	50.0
Previous Hospitalization	144	26.5	36	25.0	108	75.0
Previous MRSA Infection	29	5.3	11	37.9	18	62.1
Previous Surgery	119	21.9	28	23.5	91	76.5
Total Risk Factors						
0 Risk Factors	221	40.7	22	10.0	199	90.0
1 Risk Factors	193	35.5	27	14.1	166	85.9
2 Risk Factors	65	12.0	11	16.9	54	83.1
greater than 2 Risk Factors	63	11.6	24	38.1	39	61.9

Table 4. Characteristics of white study participants age 18 or younger seen at All Children's Hospital 1/1/02 - 8/20/03 in total and by methicillin status.

	White		Black	
	Odds Ratio	CI	Odds Ratio	CI
Female	1.22	0.74, 1.70	2.57	1.73, 3.41
Risk Factors				
Home Health Care	6.12	5.16, 7.08	2.95	1.11, 4.79
Community Worn Device	2.28	1.67, 2.89	2.85	1.71, 4.01
Previous Hospitalization	2.43	1.95, 2.91	1.98	1.13, 2.83
Previous MRSA Infection	3.69	2.90, 4.48	1.88	-0.12, 3.89
Previous Surgery	2.02	1.51, 2.53	2.79	1.79, 3.79
Previous Antibiotic Use	1.31	0.81, 1.79	5.60	4.66, 6.54
Total Risk Factors				
0	1.00		1.00	
1	1.23	0.63, 1.83	1.23	0.18, 2.28
2	1.84	1.06, 2.62	6.17	4.03, 7.70
greater than 2	5.57	4.90, 6.24	5.14	3.94, 6.34

Table 5. Odds Ratios and 95% Confidence Intervals for Subgroup Analysis of Black and White of Children ages 0 - 18 years from All Children's Hospital 1/1/02 - 8/20/03

CI= 1.67, 2.89), previous hospitalization (OR= 2.43, CI= 1.95, 2.91), previous MRSA infection (OR= 3.69, CI= 2.90, 4.48), and previous surgery (OR= 2.02, CI= 1.51, 2.53) (Table 5). All of these risk factors increased the subjects contact with health-care and therefore increased the likelihood of acquiring MRSA infection. In blacks, pediatric females were more likely to have MRSA (OR= 2.57, CI= 1.73, 3.41). This finding may be due to the small sample size of black children in the study. Of the analyzed risk factors, home health care (OR= 2.95, CI= 1.11, 4.79), community worn device (OR= 2.85, CI= 1.71, 4.01), previous hospitalization (OR= 1.98, CI= 1.13, 2.83), previous surgery (OR= 2.79, CI= 1.79, 3.79), and previous antibiotic (OR= 5.60, CI= 4.66, 6.54) use were all significant risk factors in blacks (Table 5). With these risk factors contact with the healthcare environment and healthcare workers is increased and therefore increases the possibility of acquiring an MRSA infection.

	White		Black	
	Odds Ratio	95% CI	Odds Ratio	95% CI
Age	0.98	0.93, 1.03	1.00	0.92, 1.10
Female	1.19	0.72, 1.95	1.88	0.72, 4.90
Previous Antibiotic Use	1.10	0.65, 1.86	5.13	1.75, 15.08
Community Worn Device	0.98	0.46, 2.09	0.93	0.18, 4.88
Home Health Care	4.37	1.55, 12.32	1.96	0.19, 20.84
Previous MRSA Infection	2.86	1.16, 7.05	0.65	0.06, 6.98
Previous Hospitalization	2.00	1.14, 3.50	0.77	0.25, 2.41
Previous Surgery	1.25	0.68, 2.29	1.94	0.50, 9.56
1 Total Risk Factor	1.47	0.80, 2.67	1.30	0.45, 3.76
2 Total Risk Factors	1.85	0.84, 4.05	5.50	1.16, 26.16
greater than 2 Total Risk Factors	5.36	2.74, 10.49	4.19	1.20, 14.61

Table 6. Adjustment of Confounding for Black and White of Children ages 0 - 18 years from All Children's Hospital 1/1/02 - 8/20/03

5.6 Confounding

Logistic regression was used to adjust for confounding. Adjustment of confounding was performed for each race due to the presence of effect modification. After the adjustment for confounding in whites, only home health care (OR=4.37 CI= 1.55, 12.32), previous MRSA infection (OR= 2.86 CI= 1.16, 7.05), and previous hospitalization (OR= 2.00 CI= 1.14, 3.50) remained statistically significant (Table 6). In blacks, after adjustment of confounding, only previous antibiotic use (OR= 5.13 CI= 1.75, 15.08) remained significant. Adjustment for confounding was also performed on the total risk factors model. A dose response relationship was present with increasing risk factors present (Table 6).

CHAPTER 6

DISCUSSION

6.1 Findings

The results of this study indicate several factors in the population of pediatric patients that lead to MRSA infection. In regards to demographic characteristics, black children are 2.98 times more likely to have an MRSA infection than white children. Gender and age were not risk factors for the development of the infection. The risk factors that were significant in whites were home health care (OR= 6.12, CI= 5.16, 7.08), community worn device (OR= 2.28, CI= 1.67, 2.89), previous hospitalization (OR= 2.43, CI= 1.95, 2.91), previous MRSA infection (OR= 3.69, CI= 2.90, 4.48), and previous surgery (OR= 2.02, CI= 1.51, 2.53). In blacks, females were more likely to have MRSA (OR= 2.57, CI= 1.73, 3.41). This finding may be due to the small sample size of black children in the study. Of the analyzed risk factors, home health care (OR= 2.95, CI= 1.11, 4.79), community worn device (OR= 2.85, CI= 1.71, 4.01), previous hospitalization (OR= 1.98, CI= 1.13, 2.83), previous surgery (OR= 2.79, CI= 1.79, 3.79), and previous antibiotic (OR= 5.60, CI= 4.66, 6.54) use were all significant risk factors in blacks. Effect modification was tested between race and all risk factors. Race was an effect modifier only for the risk factor of previous antibiotic use (pvalue =.02). Race may be an affect modifier due to the fact that blacks may be more likely to utilize emergency rooms and urgent care centers to have their child treated for an illness. Whites are traditionally known to have better and

more access to healthcare and may therefore be more likely to take their child to a doctor's office than take their child to the emergency room to have an illness treated. Adjustment of confounding was performed for each race due to the presence of effect modification. After the adjustment for confounding in whites, only home health care (OR=4.37 CI= 1.55, 12.32), previous MRSA infection (OR= 2.86 CI= 1.16, 7.05), and previous hospitalization (OR= 2.00 CI= 1.14, 3.50) remained statistically significant. In blacks, after adjustment of confounding, only previous antibiotic use (OR= 5.13 CI= 1.75, 15.08) remained significant. Adjustment for confounding was also performed on the total risk factors model. A dose response relationship was present with increasing risk factors present.

As compared to this study, the results of other MRSA studies on adults had some discrepancies and some similarities. Abudu et al conducted a study comparing MRSA and MSSA with regard to previous hospitalization, recent antibiotic use, and any contact with a healthcare facility. [27] None of those risk factors were found to be statistically significant. [27] This is contradictory to the current study which demonstrated many risk factors that were significant to the development of MRSA infections. The inconsistency may be explained by a poor response rate of 58% which suggests a strong likelihood of the presence of selection bias. [27] A study conducted by Morin and Hadler found an increase of the incidence of MRSA in males and blacks. [29] Gender was not found to be a risk factor for MRSA infection in the current study. The discrepancy with regard to gender may be explained by the type of study that was conducted which only included patients with bacteremia and excluded all patients with other types infections. [29] However, both the current study and the Morin and Hadler study found race to be a risk factor for MRSA infection. [29] A study conducted by Johnson et al reported an increase risk with previous hospitalization and residence in a facility. [17] These results are consistent with this study except

for the fact that there were not enough patients who resided in a facility to permit statistical analysis. Grundmann et al reported an increase risk of MRSA infection with previous hospitalization and patients with diabetes. [28] There were not enough patients with diabetes in this study to permit statistical analysis but it was found that previous hospitalization was statistically significant.

As compared to the current study, the results of other studies of MRSA on children showed some similarities as well as some discrepancies. The study by Sattler et al found that blacks were more likely to have MRSA than whites or Hispanics, which is consistent with the results of this study. [2] The study by Sattler et al did also report that there was no significant differences in the exposure to risk factors between the MRSA and the MSSA group. [2] This finding is inconsistent with the current study which found significant risk associated with MRSA for those with many of the risk factors as well as race. This discrepancy may be due to the small sample size of 144 subjects of the Sattler et al study. [2] Herold et al found an association between age and MRSA, 89% of the MRSA isolates were from children ages three to 36 months which was hypothesized to be a result of the childrens' exposure to a day care setting. [1] This is not consistent to the results in this study in which age was not found to be a risk factor for MRSA. This discrepancy may be due to the small sample size of 88 subjects as well as the specialization of the hospital where the study was conducted. [1] The study was conducted at University of Chicago Children's Hospital which is a tertiary care pediatric hospital in the inner city of Chicago. [1] Herold et al also reported an increase of MRSA infection in blacks which is consistent with the findings of this study. [1] The study conducted by Campbell et al found that males were twice as likely to have CA-MRSA. [21] Campbell et al also found the CA-MRSA patients were more likely to be older and to have received antibiotics prior to admission. [21] Age and gender were not found to be risk factors in the current

study but previous antibiotic use and community worn device were found to be a risk factor. The discrepancy between the studies with regard to gender and age may be explained by the small sample size of 62 subjects by the Campbell et al study. [21]

6.2 Strengths & Weaknesses of the Study

The strengths of this study are the large sample size which increases the power of the study. The 20 month length of the study period is also a strength. The cross-sectional design used in this study allowed for the evaluation of multiple risk factors. A cross sectional study enables the resulting data from the study to be utilized to calculate prevalence estimates of exposure and disease.

A weakness of the study is that it was only performed at one hospital. The results must be generalized with caution. The population may not closely mirror the pediatric population of Pinellas county or the state of Florida due to the high amount of transfers to All Children's Hospital from many of the adjacent counties. This may result in the hospital having an overall sicker population than other pediatric populations seen in other hospitals. The main weakness of the cross sectional study design is that temporal sequence between exposure and disease can be difficult to establish. This was not an issue in this study because the risk factors that were collected were specifically defined as having taken place in the previous 12 months prior to the positive culture. There is also a question of accuracy of the medical charts to reflect the presence of the subjects risk factors. Several patients were not listed as having previous antibiotic use when their history and diagnosis would suggest otherwise. This may have lead to misclassification of those patients with regards to exposure status.

There are two main types of bias that may have played a role in this study. The first is selection bias which occurs when those enrolled in the study cause an association to be present or absent when in reality the opposite is true. This could have occurred as a result of the charts that were unavailable for review. The charts that were unavailable were those of patients currently hospitalized and those of patients only seen in the outpatient clinics associated with All Children's Hospital. Out of 827 charts that were requested 155 of them were unavailable for review. The most common reason was that the child was seen in the outpatient clinic. This is approximately an 82% response rate. This could have introduced some selection bias into the study. The other type of bias that may have played a role in this study was information bias which occurs when the information about the subjects enrolled in the study is incorrect or missing. This may cause a subject to be classified incorrectly in regards to either exposure or outcome causing misclassification bias. In this study there may have been inadequate documentation of the presence of risk factors for MRSA. Information bias can also occur when information on other possible confounding factors is not available because of the limited amount of data collected in the chart. This could be the case with some of the risk factors that were listed in other studies. For example, child's attendance in daycare and family member's exposure to healthcare are risk factors that could have created bias. Information bias can also be caused by a misclassification according to disease status. This could result in a patient with MRSA not being identified as such. Information bias could happen if there was an instrument malfunction or if the medical technologist entering the results made a typographical error.

Some other types of bias that may be present are recall bias and interviewer bias. Recall bias occurs when there is inaccurate recall of past exposure. This could be a common problem when a parent is more worried about the immediate welfare of

their child than the questions that are being asked by the doctor or nurse filling out the paperwork. It is possible that the amount of recall bias could differ by whether the child had MRSA or MSSA. This may be a result of the child with the resistant infection having more contact with healthcare and therefore the parent would be more likely to recall the presence of risk factors in their child. Interviewer bias is a type of information bias in which the means for obtaining the information about the study subject leads to incorrect assessment of exposure or disease status. This type of bias could have occurred in this study as a result of each subject not having the same nurse or doctor interview them. Each healthcare professional has a different way of completing the necessary forms. This alone is enough to introduce interviewer bias.

6.3 Future Directions

Many of the previous studies mentioned that the susceptibility patterns were similar in CA-MRSA and nosocomial MRSA isolates. [30, 17, 33, 27, 18, 28, 22, 19, 34, 2, 1] This suggests that the infections were really the result of the same strain of MRSA. MRSA that is nosocomially acquired typically is resistant to multiple antibiotics where CA-MRSA is only typically resistant to penicillin and methicillin. [30, 17, 33, 27, 18, 28, 22, 19, 34, 2, 1] Therefore it is important to assess the patient previous healthcare exposure in order to distinguish between CA-MRSA and nosocomial MRSA. Assessing this exposure has been made more difficult with the increase in outpatient procedures and the decrease in overall hospital stays for many surgeries. This decrease or absent hospital stay may lead to poor patient recall as well as an increase in the patients exposure to home healthcare or frequent doctor's office visits for follow-up further increasing the patient exposure to healthcare. There is also an increase in the use of broad spectrum antibiotics. [15, 35] This increases the selec-

tive pressure of *Staphylococcus aureus* and other bacteria and leads to increases in antimicrobial resistance. [15, 35]

Currently, the medical definition of CA-MRSA is any outpatient isolate or an inpatient isolate that is cultured within 48 to 72 hours of admission to a hospital. This definition needs to be modified to take into account many of the predisposing risk factors so a more accurate prevalence of true CA-MRSA can be assessed. This can be done by altering the definition of nosocomial MRSA to include patients with these risk factors. A term of healthcare associated MRSA could be utilized instead of nosocomial. [18] This would result in the term CA-MRSA being utilized only for patients with MRSA and no predisposing risk factors.

There was also an article recently published on the BBC News website that suggested that MRSA may be carried by pets. [36] There was no suggestion as to how the animals acquired the infection. [36] Cats, dogs, and rabbits all tested positive for colonization of MRSA. [36] This article is another reason why there is a need for more studies on MRSA and the risk factors associated with its transmission. [36]

There should also be more intensive studies focused in the areas of daycare centers and the possible spread of CA-MRSA and the role of household contacts in the spread of CA-MRSA. Some studies have suggested a link between CA-MRSA and daycare centers. [32, 31] These studies found nothing statistically significant to suggest that daycare played a role in the spread of the infection. [32, 31] There were no studies that solely focused on the role of household contacts and CA-MRSA in children. Another aspect that merits further study is the relationship between parents' or caregivers' occupation and MRSA infection. It has been hypothesized that parents who work in the healthcare industry are likely to be colonized with MRSA and as a result colonize their children. [2, 22] This would increase the likelihood of the children to develop an MRSA infection. If these studies are carried out we may find a better way to predict

patients that may have MRSA and therefore start adequate treatment more quickly and prevent children from dying.

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