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An In-Depth Study of Staphylooccus aureus Infections and Cases of Colonization in the Inpatient Population at a University Teaching Hospital

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An In-depth Study of *Staphylococcus aureus* Infections and Cases of Colonization in the Inpatient Population at a University Teaching Hospital

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An In-depth Study of *Staphylococcus aureus* Infections and Cases of Colonization in the Inpatient Population at a University Teaching Hospital

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ABSTRACT

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a pathogen that has historically been identified in hospital-acquired infections since the mid 1900's. Epidemiologically significant trends have occurred which have identified the increasing prevalence of MRSA in the community setting.
Methods: An investigation of all isolates positive for *Staphylococcus aureus* of the inpatient population was conducted over a nine year time period in a university teaching hospital. Additionally, a unit specific case/control study was conducted during an outbreak of MRSA in a neonatal intensive care unit.
Results: From January of 1997 through December of 2005, the number of isolates identified as positive for S. *aureus* had increased. Additionally, the proportion of MRSA to Methicillin-sensitive *Staphylococcus aureus* (MSSA) had increased from 40 to 60%. A chi-square test was conducted comparing the number of isolates positive for MRSA in 1997 versus 2005 which was found to be statistically significant with a P value < 0. 001.

Additionally, from January 1997 through December 31, 2001, the first greatest change in proportion of MRSA to MSSA was noted. The increase in isolates identified as positive for MRSA was found to be approximately three times as great. The comparison of isolates identified as MRSA in 1997 versus 2001 was statistically significant with a P value <0.001.

A hospital-acquired case is defined as one in which the specimen positive for MSSA or MRSA was obtained 48 hours after admission to the hospital. Conversely, a community-acquired case is defined as having a culture positive for MSSA or MRSA obtained within 48 hours of admission. Using a chi-square test we found no statistically significant difference in identification of the acquisition of MSSA or MRSA as to whether the patients were admitted from home or another health care institution. The number of community-acquired cases identified as positive for MRSA was higher than those that were hospital-acquired.

Lastly, through a case/control study of infants leading to NICU employee screening for identification of employees for positive colonization status with MRSA, we identified the common source who served as a reservoir for transmission of this pathogen.

Conclusion: Methicillin-resistant *Staphylococcus aureus* has emerged as a significant public health burden and serves as a warning requiring the attention of key stakeholders to implement rigorous actions to control the spread and reduce the development of multi-drug resistant organisms.

I. INTRODUCTION

Background of Problem

During the time period of January 01, 1997 through December 31, 2005, the Department of Epidemiology observed what was suspected to be an increasing endemic rate of infections positive for methicillin-resistant *Staphylococcus aureus* (MRSA) at Hospital A.

An investigation was conducted to determine if we were actually seeing a significant increase in the number of infections positive for Staphylococcal *aureus* (S. *aureus*), in which 2001 appeared to be the pivotal year during which the numbers increased at a greater rate. Additionally, it would be important to determine if the proportion of MRSA to methicillin-sensitive *S. aureus* (MSSA) remained stable or if we were observing an increase in prevalence of one of the two organism subtypes. Lastly, of significant importance was to determine whether or not Hospital A was experiencing a change in the epidemiology of S. *aureus.* This would include identifying whether or not these cases that were positive for infections or colonization with S. *aureus* were determined to be community or hospital-acquired.

During the time period of January 1, 2001 through December 31, 2001, we noted that there was a significant increase in the number of isolates which were determined by the microbiology laboratory to be positive for MRSA. Because of the increasing number of this clinically important, antibiotic-resistant pathogen, we conducted an investigation to determine the epidemiologic characteristics of patients infected with MSSA and MRSA in Hospital A over a one-year period. It

was our goal to determine if the proportion of MRSA isolates had increased in relation to MSSA, or if we were beginning to see an increase in the prevalence of both organisms. Additionally, we were interested to determine if patients with specific characteristics such as age or gender were predisposed to acquire an infection positive for S. *aureus* identified as methicillin resistant or methicillin sensitive.

Lastly, to illustrate the potential magnitude of harm to patients and impact on the health system caused by infections with this pathogen, we also conducted an in-depth description of a hospital-based inpatient investigation. The study was an investigation of a cluster of cases positive for MRSA which were identified during routine surveillance in the neonatal population.

For the purpose of this thesis, I applied to the University of Connecticut Health Center's Institutional Review Board and was granted approval to conduct certain aspects of surveillance and investigation for this project (IRB Protocol number 05-019).

This overview will identify three goals of the S. *aureus* investigations that were conducted:

- To identify if there had been an increase in the prevalence of patients identified as having a culture positive for S. *aureus.*
- To determine any changes in the proportion of cultures positive for MSSA versus MRSA of the total number of cultures identified as positive for S. *aureus*.

- To identify of the inpatient population admitted to Hospital A during this time period, any epidemiologically significant change in trend between the relationship of the number of community-acquired versus hospital-acquired infections positive for S. *aureus*.

Definitions of *Staphylococcus aureus:* Physical Status

In discussing the physical status of a person who has acquired an organism, one must first determine the level of activity the potential pathogen is exhibiting in the person's body. This activity, caused by mere existence or proliferation of the organism, may impact one's health, causing serious illness and, in extreme circumstances, death.

Determining the level of activity of the organism may also help us understand the infection control practices of importance that will prevent the active or passive transmission of this organism from one person to another.

A person may have one of four levels of physical response after a potential or actual exposure to an organism. The first level is a negative response in which the person may or may not have had a significant exposure to an organism but, because of many different potential actions or non-actions, there were no consequences. For example, the person may have touched something contaminated with the organism, but did not touch his or her mouth, nose or eyes and adhered to good hand hygiene, therefore eliminating the risk of exposure.

The second level of status is colonization. The person has had a significant exposure to an organism, may or may not have attempted to conduct

adequate preventative measures and was unable to prevent the acquisition of the organism. The person may have presence of this organism externally or in non-sterile sites (i.e., their nares [inside the nose] or in tissue), but it remains indolent (i.e., not multiplying). The person does not exhibit signs or symptoms of illness and is generally not infectious, although there has been evidence that the organism potentially can be transmitted to another person by exposure to body substance material from the colonized person (e.g., the colonized person wipes his or her nose or sneezes into the hands and does not wash the hands). The colonized person has contaminated his or her hands and proceeds to make contact with the non-colonized person by engaging in shaking hands. The non-colonized person potentially has now contaminated his or her own hand with this organism and could become inoculated by introducing it into his/her own body by touching the mouth or nose. As discussed by Siegel, Rhinehart, Jackson, Chiarello, and the Healthcare Infection Control Practices Advisory Committee (2007), there are basic activities that could prevent transmission and self-inoculation, such as covering your mouth and nose by coughing or sneezing into your sleeve and following good hand hygiene practices.

The third level of physical status related to exposure to an organism is clinical infection. If this organism was introduced into a sterile body site or an opening in the skin such as blood or a wound, the chances of developing a more severe infection increases and the person would exhibit signs and symptoms of illness. The person has been exposed to an organism which has been introduced into the body in one of several routes. These may include

introduction through the mucous membrane; through the impaired integrity in the integumentary system, such as the skin; or through a breach in a sterile body site. Introduction into a sterile body site may occur as an unintended consequence of an invasive procedure. Regardless of the specific route, once the organism is allowed to enter the body it proliferates, causing the development of a localized infection, soft tissue abscess, or a more serious systemic infection. The person would exhibit any or all symptoms of illness such as fever, pain and swelling, and the condition would require medical intervention.

The fourth level of exposure is of a person who had been infected with the organism and received treatment resulting in either eradication of the organism (negative status) or a stable, colonized status. See Table 1 below.

Table 1. Definitions of levels of physical status when exposed to S. *aureus*

Physical Condition	**Status of S. *aureus* Inoculum site**		**Infectious**
	Non-sterile	Sterile	
Negative	No	No	No
Colonized	Yes	No	Unlikely through casual contact
Infected	Yes	Yes	Yes
Infected and treated and negative status achieved	No	No	No
Infected and treated and patient remains colonized	Yes	No	Unlikely through casual contact

Methods of Determining Patient's Physical Status of *Staphylococcus aureus*

The methods used to determine the patient's status in the studies presented include surveillance data from many sources within the hospital. Among these sources, the most frequently accessed are described in the following paragraphs.

It is not routine practice at this time to conduct bacterial surveillance cultures on all patients admitted to the hospital or standard practice to screen all patients for MSSA or MRSA. Specimens collected on inpatients are sent to the laboratory if ordered by the physician to aid in determining medical diagnosis. The studies explained in the context of this paper only include those patients who had microbiology laboratory tests ordered by their physician which were obtained and processed and which concluded in the positive identification of S. *aureus*. If culture results were negative for S. *aureus* the patient was not included in the study.

Microbiology laboratory reports of isolates positive for S. *aureus* were investigated from January 1, 1997 to December 31, 2005 in order to analyze trends in incidence, prevalence and emerging patterns of antimicrobial resistance to antibiotics. The documented minutes from the Infection Control Committee which are generated monthly from this time period and the line listing of cases positive for MRSA which were compiled over the previous nine years were reviewed. The cases that were included were those determined to have clinical infections with MRSA that were identified as either hospital-acquired or community-acquired.

In addition to the nine-year review, an in depth epidemiologic analysis was conducted on all isolates identified as positive for S. *aureus* in the Hospital A Clinical Microbiology Laboratory from a single year: January 1, 2001 to December 31, 2001. This analysis was conducted in order to identify the association with MSSA and MRSA positive isolates and to better characterize the risk factors of patients potentially predisposed to developing these infections. This was accomplished by review of the patients' medical records to determine the physical status of the patient regarding colonization or infection.

Finally, an epidemiologic investigation was undertaken involving a cluster of cases positive for MRSA colonization and infection that were identified during the course of conducting routine field surveillance during the time period of 2000-2001.

The specific methodology unique to each project is described in the sections that review the overall investigations that were conducted.

Pathogen

Staphyloccocus aureus (S. *aureus*) is an organism that has historically been identified as a pathogen responsible for causing a wide variety of infections in hospitals, primarily involving the urinary tract, abdominal wounds, pneumonia and blood stream infections. In the 1940's and 1950's, virtually all infections involving S. *aureus* were susceptible to all β – lactam drugs, including penicillin and cephalosporins. However, naturally occurring resistance to β – lactam

drugs, such as penicillin, began to increase in the 1960's and is widespread today (Stapleton & Taylor, 2002).

Microbial resistance to antibiotics occurs in bacteria and other organisms in different ways. The development of resistance can occur with gene mutations i.e., from antibiotic pressure as a natural development of the bacteria or random changes in DNA (Wikipedia, 2010). Antibiotic resistant DNA may either be transferred to, or acquired by staphylococci from other bacteria in the species via usual bacterial horizontal transference. The transfer or acquisition of mutated DNA occurs more frequently than individual bacterium developing DNA mutation on their own. Once mutated DNA is acquired, resistance is caused by the DNA in several potential ways. One method of resistance occurs when the bacteria acquires mutations that enable it to evade the activity of the antibiotics by secreting an enzyme that inactivates the antibiotic. Another method is the development of the ability to either pump the antibiotic out of the cell or prevent the antibiotic from binding to the cell wall through the action of penicillin–binding proteins (National Institutes of Health, 2006; Ito, Katayama, & Hiramatsu, 1999; W. Hryniewicz, 1999). Because of their proliferative nature, bacteria, which are single cell organisms, have the capability of increasing the enormity of the problem of antimicrobial resistance at an alarming rate.

Increasing prevalence of antibiotic resistance began to emerge in isolates from hospitals during the 1950's and 1960's. The occurrence of resistance emerged soon after the development and widespread use of β – lactam antibiotics, such as penicillin, to treat infections during the wake of World War II.

The initial response toward the resolution of this significant public health issue was to develop new; semi-synthetic antibiotics similar in structure and action to penicillin to treat infections demonstrating resistance to penicillin. In turn, wide-spread use of these new drugs, such as oxacillin and methicillin, resulted in increasing resistance to the semi-synthetic antibiotics (Sack, 2007). The pattern of the development of resistance was observed by Klein, Smith, & Laxminarayan (2007). They described the process of resistance to newer, synthetic antibiotics as mimicking the "wave-like" development of resistance that was seen with penicillin. This wave-like pattern refers to the initial identification of a low incidence of infections with organisms that had developed resistance and the subsequent recurring rise or prevalence in numbers of infections identified in which many patients were affected.

During the 1960's and over the next three decades, resistant infections continued to be limited to hospitals where MRSA was identified primarily as infecting very ill inpatients with complicated medical and surgical histories. Infections with MRSA were attributed to the hospital setting because it was believed that the development of resistance was a product of antibiotic pressure. Antibiotic pressure is defined by the Alliance for the Prudent Use of Antibiotics (2010), as the natural selection of some bacterium to survive and multiply in the presence of certain potential barriers such as antibiotics.

These infections were usually serious blood stream infections, pneumonia, surgical site infections, abdominal wounds and heart valve infections. They were

associated with high morbidity and mortality and were responsible for increasing length of hospital stay and costs of care.

During the early 1990's, MRSA, for the most part, remained confined to the institutional setting. However, as we entered into the late 1990's and early 2000's there was a dramatic shift in the epidemiology of this pathogen. During this time, the first wave of community-acquired cases of MRSA were identified in patients who were not previously hospitalized and did not have a history of living in an extended care facility or short term rehabilitation center.

The significance of the increased incidence of infections positive for community-acquired MRSA was demonstrated in a study by Kuehnert, Hill, Kupronis, Tokars, Solomon, & Jernigan (2005). The study looked at discharges from United States hospitals during the time period of 1999 through 2000. The investigators used the International Statistical Classification of Diseases and Related Health Problems ("ICD 9") codes to determine that almost 130,000 patients over this time period were hospitalized from the community with infections caused by MRSA. These observations illustrated that community-acquired MRSA had emerged as a significant public health burden. In another study by Kuehnert, et al (2006), the prevalence of nasal colonization rates of MSSA in the general population was studied. The investigators tested the nares of 9,622 people as part of the National Health and Nutrition Examination Survey and found that 3,079 (32%) of the total number tested were colonized with MSSA and 77 (0.8%) were colonized with MRSA. They concluded that while the overall rate of colonization with MRSA in 2001-2002 appears low in comparison with

MSSA, the rate might vary depending upon demographics, specific virulence factors with this organism and host risk factors, including prior exposure to antibiotics. The influence of these factors could indicate that those people living in a different demographic area or specific living environment such as physically close living arrangements may be predisposed to the development of colonization with MRSA at a higher rate compared to MSSA.

The emergence of community-acquired MRSA infections had rapidly become a significant public health threat over the past decade. Infections diagnosed in the community typically differ in comparison to those that are considered hospital-acquired. Community-acquired infections are usually identified as occurring in different anatomical sites and also differ in what antibiotics are most effective for treatment. These infections typically involve skin and soft tissue with the development of abscesses and pustules and are most successfully treated with clindamycin or bactrim. The majority of these infections can be treated in the outpatient setting. However, some are serious and may even be life threatening and require admission to an acute care facility for treatment with intravenous antibiotics and in extreme cases life support.

Fridkin, et al. (2005) studied the prevalence of MRSA infections in three communities and identified the most frequently infected physical site. The group identified 1,647 patients with isolates positive for MRSA from the three communities during the time period of 2001 through 2002. Of these isolates positive for MRSA, they determined that between 8 and 20 percent of all laboratory isolates tested from patients in these communities were positive for

MRSA and were identified as community-acquired. Of the total number of community-acquired infections positive for MRSA, the majority, or 1,270 (77%), involved skin and soft tissue. One fourth of these infections progressively developed into infections requiring admission to a hospital for treatment.

One issue influencing the impact of infections positive for community-acquired MRSA on public health is the lack of familiarity with the emergence of these community-acquired infections. The lack of knowledge of the Licensed Independent Practitioners in the community and private offices inhibits the timely diagnosis and swift initiation of appropriate antibiotic treatment. To facilitate appropriate treatment these practitioners need education on the characteristics of the infections, typical progression of the infection process and appropriate antibiotic treatment. This knowledge deficit in the outpatient setting has led to cases being largely misdiagnosed and, therefore, ineffectively treated. For instance, as has been observed by Tom Frank, Pharm. D., B.C.P.S., an associate professor of pharmacy practice and assistant professor of family and community medicine (Peck, 2004) and Dr. Tamara Dominguez (2004), some infections positive for MRSA were treated as spider bites. These infections involving soft tissue, resembling spider bites, were treated as such even when occurring in geographical areas not commonly known to be inhabited by spiders. Consequently, these infections progressed to deep, intrusive, multi-layered abscesses which were serious and difficult to treat. If mistreated, community-acquired MRSA infections can be very aggressive, involving multiple organ systems and even death. An example of this lack of awareness was reported in

a news article by Manning (2006). The article described the case of a 14-month-old male who had been brought to the pediatrician's office for assessment and was diagnosed with a common cold. Over the following week the child's condition continued to progressively worsen. Eventually his health status plummeted and he was diagnosed with necrotizing (death of tissue) pneumonia caused by MRSA. The child recovered after a complicated 55-day hospitalization including intensive care and support by mechanical ventilation.

The review of literature has demonstrated an increasing prevalence of antibiotic resistant infections positive for S. *aureus* over time. The changing epidemiology of MRSA from being primarily a hospital-acquired pathogen to community-acquired has been well documented over the past decade. The impact and significance of these infections on public health, both real and perceived, have changed the usual and customary way hospitals and communities have responded to infections. A thorough investigation and analysis of S. *aureus* isolates and cases of infection in Hospital A has proven to reflect accurately on the changing trends in epidemiology as documented in the literature. This report will validate the similarities of these study findings and demonstrate the tremendous impact that these infections have on the health-care system at this university teaching hospital.

It has become paramount and essential that we, as responsible healthcare providers and public health agents, understand the changing epidemiology of these pathogens and continue to develop effective strategies to treat our patients

therapeutically and appropriately in a timely manner and prevent further transmission of this life-threatening pathogen.

II Methods

The following describes the methods used in both Section I and II. The Microbiology lab responds to the identification of *Staphylococcus* species in all clinical samples. They do this by the technique described in the following paragraph.

Inpatient specimens are processed through the hospital's microbiology laboratory. All specimens sent to the laboratory for bacteriological culture are inoculated onto various kinds of solid plated media. Specimens resulting in a positive culture undergo a gram stain process for further identification. Once a bacterial colony is identified as gram positive cocci (in clusters or groups), the sample then undergoes a latex agglutination test called Staphaurex. If the organism is identified as being coagulase positive, that is, causing clumping of the Staphaurex latex reagent, it is *Staphylococcus aureus*. Further testing for the minimum inhibitory concentration (MIC) is determined by inoculating an MIC panel of different antibiotic concentrations with the organism. The lowest concentration of antibiotic that inhibits the organism from growing is the MIC. Additionally, in the case of oxacillin resistant Staphylococcus, such as MRSA, the organism may also be plated onto an oxacillin screening agar to confirm oxacillin resistance. To identify those patients who had isolates which were positive for

MSSA or MRSA, a retrospective review of all cultures positive for S. *aureus* was conducted for the specified time period of each investigation. The patients who were included in the study were identified through a microbiology laboratory query. They included those who had a culture from any body source positive for MSSA and/or MRSA.

Only the first positive MSSA or MRSA isolate obtained from the patient was used for the working diagnosis. The nature of these investigations involved the use of medical records and laboratory results of the inpatient population at Hospital A.

Upon identifying the patients with cultures positive for MSSA or MRSA during the stated time period, a chart review was conducted to access medical information including patient history through the Health Information Systems Department. The purpose of the chart review was to determine if the patient was infected or colonized with the identified organism. The criterion to determine the physical status of a patient who had acquired S. *aureus* colonization or infection includes: i) an isolate positive for S. *aureus*, and ii) physician documentation of diagnosis of infection. The diagnosis may or may not have been supported by additional criteria such as: identification of symptoms, antibiotic treatment or illness indicative of infection such as fever, pneumonia or bacteremia.

Once a patient is identified as having an infection positive for *S. aureus*; we defined the acquisition date of the samples that grew the *S. aureus* isolate as the start of the infection. In order to investigate whether or not there was a true

increase in MRSA infections, only the first positive *S. aureus* isolate from each person was considered.

Upon determination of infection or colonization with staphylococci, we analyzed the cases to categorize them into one of two groups: hospital-acquired or community-acquired. Further breakdown of the two groups separated them into patients who were either infected or colonized. Cases were defined as hospital-acquired if the sample that was positive was collected 48 hours after the patient's admission date. Conversely, cases were defined as community-acquired if the positive culture had been obtained within 48 hours of admission. For consistency, these are accepted definitions used by the infection control community which take into account the general incubation periods of common bacterium.

The analysis of the medical records was conducted with the guidance of a surveillance sheet or check list which included the demographics described in the following paragraph. The data collected on these sheets were eventually used to compile the working case line listing. Data regarding unit and room location of admission, age, gender, past medical history and whether the patient came from home or an alternate residence such as an extended care facility was compiled.

III Project I: A chronological report of the recovery of S. *aureus* isolates as reported by the microbiology laboratory over a nine-year period from January 01, 1997 through December 31, 2005.

A. Background

For the last decade, because of growing awareness of the impact of antibiotic resistant strain of organisms, it is important that health-care facilities are aware of the prevalence of infections with these organisms among their inpatient population. An in-depth review of these positive cases, commonly referred to as "surveillance," is routinely conducted by the Infection Control Department. Because of the necessity of timeliness and efficiency, and the meaningfulness of such data, surveillance has undergone a change over the past decade from hospital-wide to targeted (Hoffman 2000). Targeted surveillance is restricted to specific concerns (types of infections or organisms causing those infections) or risk determined priorities as identified by the Infection Control Plan specific to each institution. At Hospital A, one aspect of the targeted surveillance program is of epidemiologically significant organisms such as MRSA. The characteristics and epidemiology of all MRSA infections are reviewed and the infections are defined as hospital-acquired or community-acquired. The results of this surveillance are reported to the Infection Control Committee on a monthly basis to identify any occurring trends in terms of person, place and time and determine required action for the prevention and control of these infections.

The following is a chronological report of the recovery of S. *aureus* isolates as reported by the microbiology laboratory over a nine-year period from January 01, 1997 through December 31, 2005. Also included is a specific focus

on the time period January 2001 through December 2001, which has resulted in the identification of significant shifts in the epidemiologic trends of these organisms in the inpatient population at Hospital A.

During the time period of 1997 through 2000, we identified increasing numbers of this clinically important, antibiotic–resistant organism. Additionally, during the time period of January 2001 through December 2001, it appeared that the number of isolates identified as positive for MRSA increased significantly. We were interested to see if there was a proportional increase of MRSA isolates to MSSA isolates and if there was a point in time that indicated a spike in the total number of MRSA isolates. Further, we were interested to see if there was a trend that showed an increase in MRSA isolates in relation to colonization or infection and the identification of factors predisposing these patients to acquisition of this organism.

B. Specific Methods

In addition to the methods described in the overview are the following methods of research specific to the investigations reviewed in this section. In order to account for the proportion of MSSA isolates to MRSA isolates identified by the Hospital A Microbiology Laboratory from 1997 through 2005, we conducted a review of the isolates positive for S. *aureus* retrieved from the Microbiology Laboratory computer system.

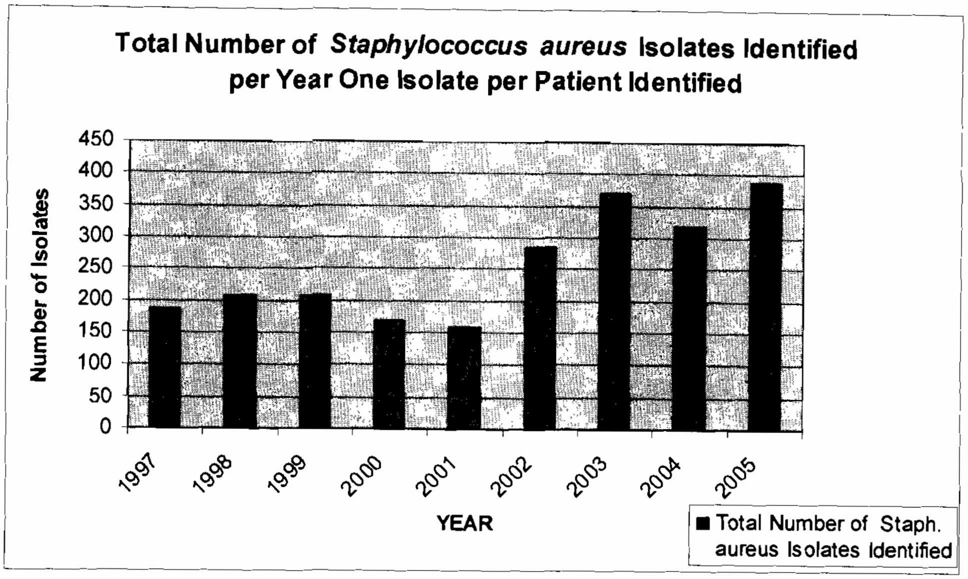
Additionally, a review of the monthly Infection Control Committee minutes and a line listing of patients with isolates positive for MSSA and MRSA have

been reviewed in order to define clinical impact and to determine the prevalence of infection and risk factors predisposing patients to acquiring infections positive for MRSA over a one-year time period.

C. Results

Review of the data showed that most patients who had samples sent to the laboratory which tested positive for S. *aureus* had more than one culture sent during their hospital admission. Therefore the total number of isolates positive for S. *aureus* was approximately two times greater than the number of patients who had cultures positive for S. *aureus*. However, when using the criterion of counting only the first culture identified as positive, we demonstrated support of our hypothesis of an increase in the number of isolates positive for S. *aureus*. The total number of S. *aureus* isolates identified by the laboratory per study criteria for inclusion is illustrated in Figure 1.

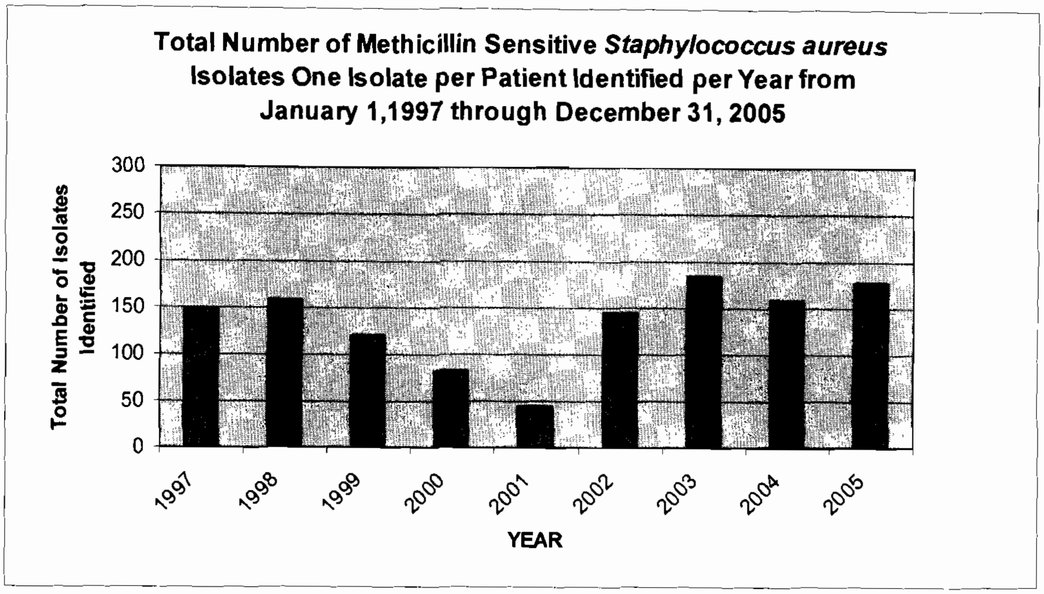
Figure 1



Additionally, when the number of isolates positive for S. *aureus* was compared to the annual inpatient census, we found that the number of isolates positive for S. *aureus*, one per patient, had continued to increase overall during this time period.

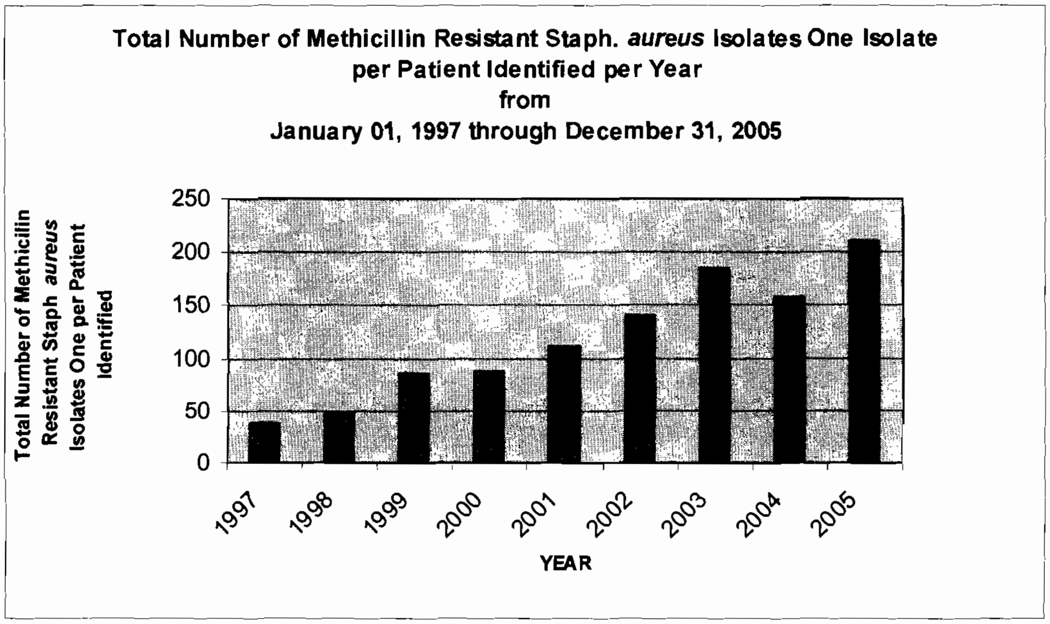
In order to identify any change in the proportion of MSSA to MRSA isolates the total number of S. *aureus* isolates was reviewed. The number of isolates positive for methicillin-sensitive S. *aureus* is depicted in Figure 2; and, the total number of isolates positive for S. *aureus* paralleled this pattern (Fig.1).

Figure 2



The analysis of the number of isolates positive for MRSA over the nine year period depicted in Figure 3 shows a trend of overall increasing numbers of isolates.

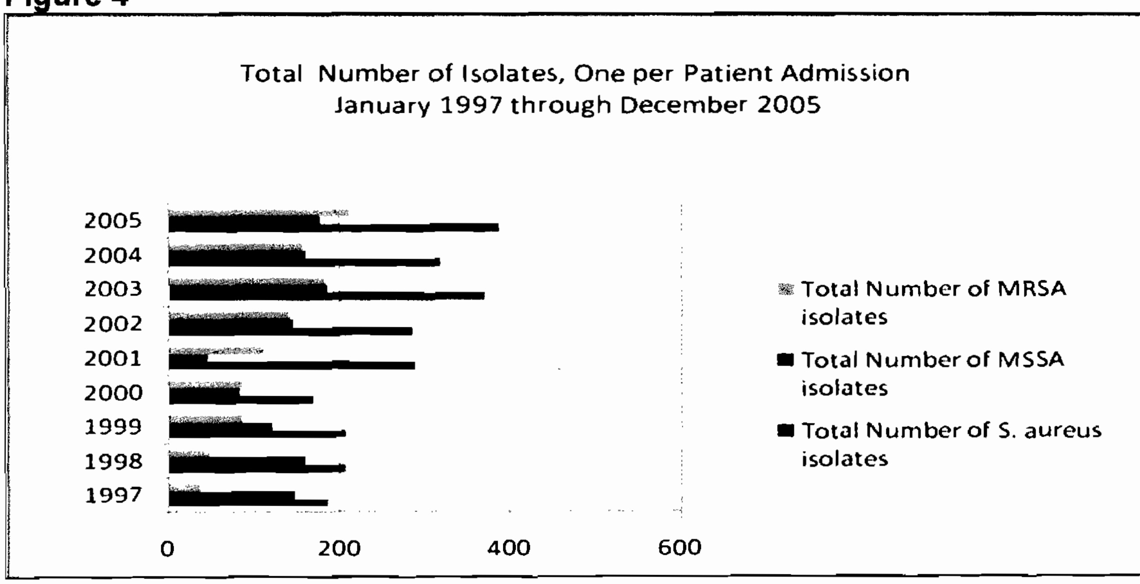
Figure 3



Next, a chi square test for independence was conducted to determine whether the increasing trend of isolates positive for MRSA was statistically significant. The increase in the number of patients with cultures positive for MRSA in 1997 versus 2005 was found to be statistically significant with a P value < 0.001.

The numbers of isolates positive for MSSA in comparison to MRSA in relation to the total number of isolates positive for S. *aureus* are depicted in Figure 4. The figure illustrates the gradual increase in proportion of MRSA to MSSA. As of 2005, MRSA comprised the majority of the identified strain for all S. *aureus* isolates.

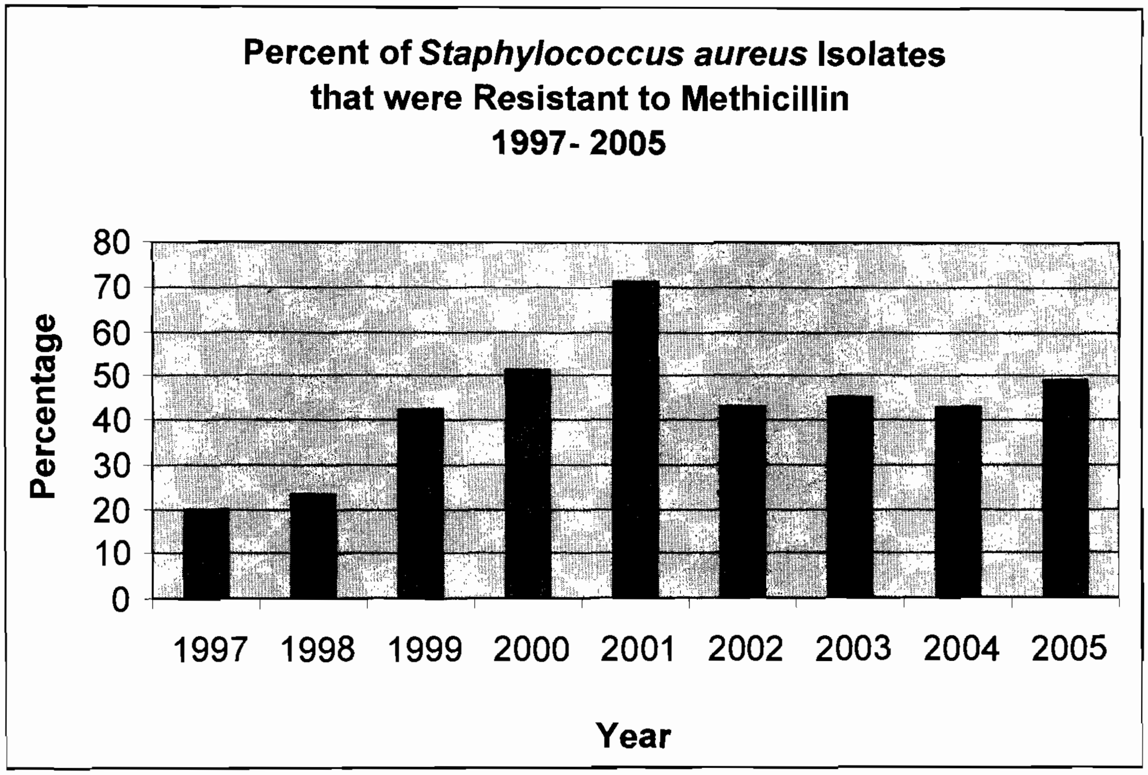
Figure 4



The data illustrated in Figure 5 more specifically demonstrates the relationship of isolates identified as MRSA in comparison to the overall numbers of isolates identified as positive for S. *aureus*. The data shows that in the year

2001, of all isolates positive for S. *aureus,* 70% were identified as MRSA compared to 30% MSSA. Additionally, over the entire time period studied, approximately 50% of all isolates identified as S. *aureus* were methicillin resistant.

Figure 5



The proportion of MRSA to MSSA in relation to overall number of isolates positive for S. *aureus* has increased in recent years. While there had been some increase in the total number of isolates positive for S. *aureus*, the most startling result was that the number of isolates positive for MRSA was increasing until

2001. From 2002 through 2005 the percentage of MRSA remained consistent. MRSA was replacing MSSA as the largest portion of S. *aureus* isolates identified. This is shown in Figure 6 as the rate of positive isolates of S. *aureus*, MSSA and MRSA, per 1000 patient admissions.

Figure 6

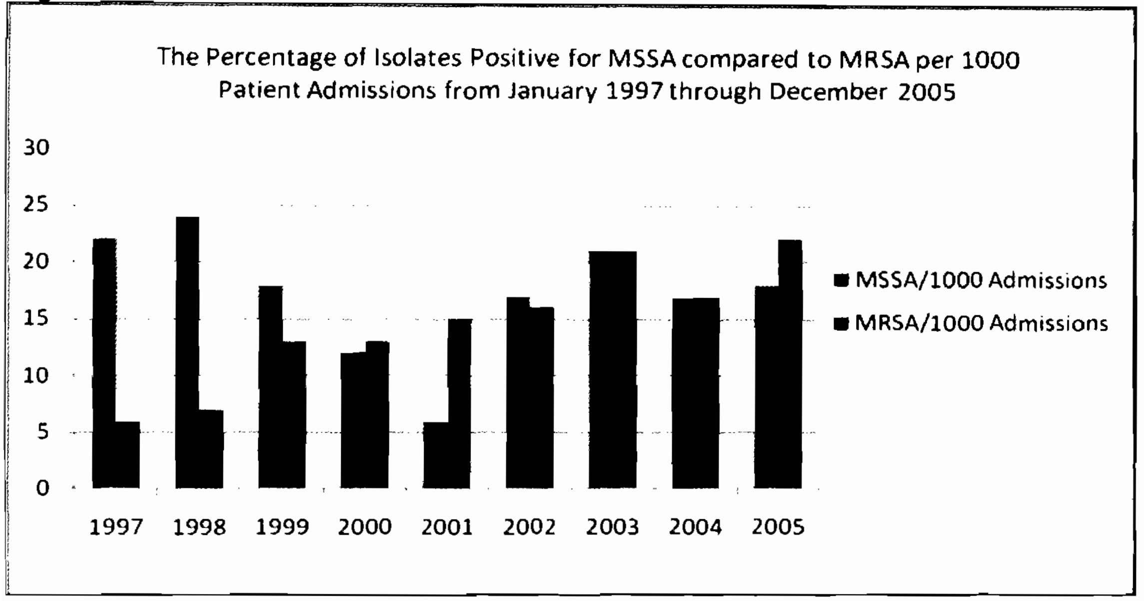
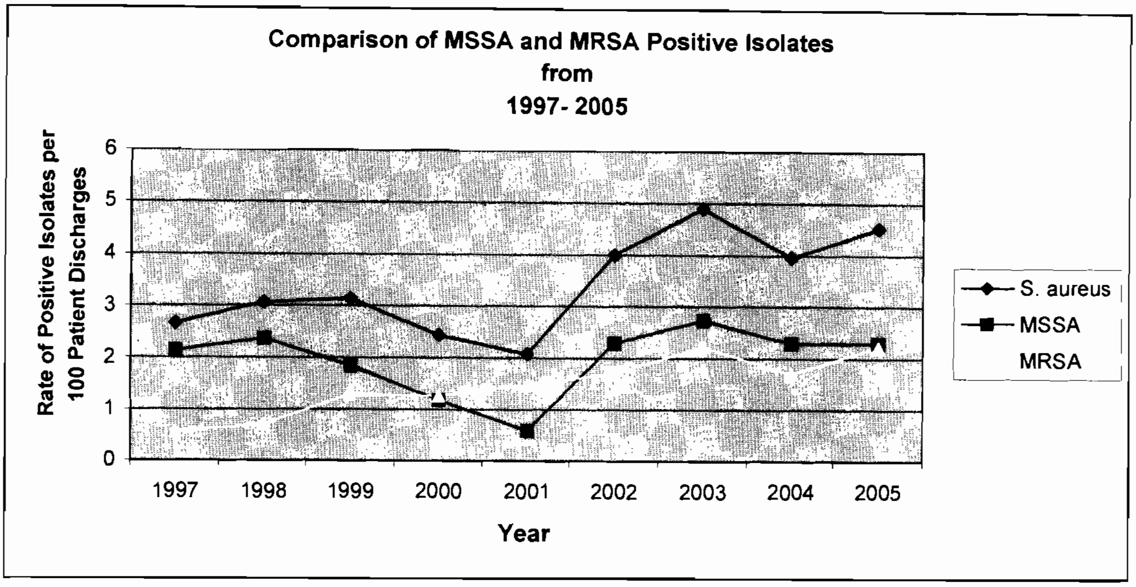


Figure 7 illustrates the trend of these organisms over time. It depicts the number of isolates per 100 discharges in relation to the total number of isolates positive for S. *aureus*, one per patient from January 1997 through December 2005.

Figure 7



We determined that the apparent increased trend in isolates positive for MRSA, one per patient, was statistically significant using the chi square test. We noted that the increase in isolates identified as positive for MRSA from 1997 versus 2001 was approximately three times as great and was statistically significant with a P value < 0.001.

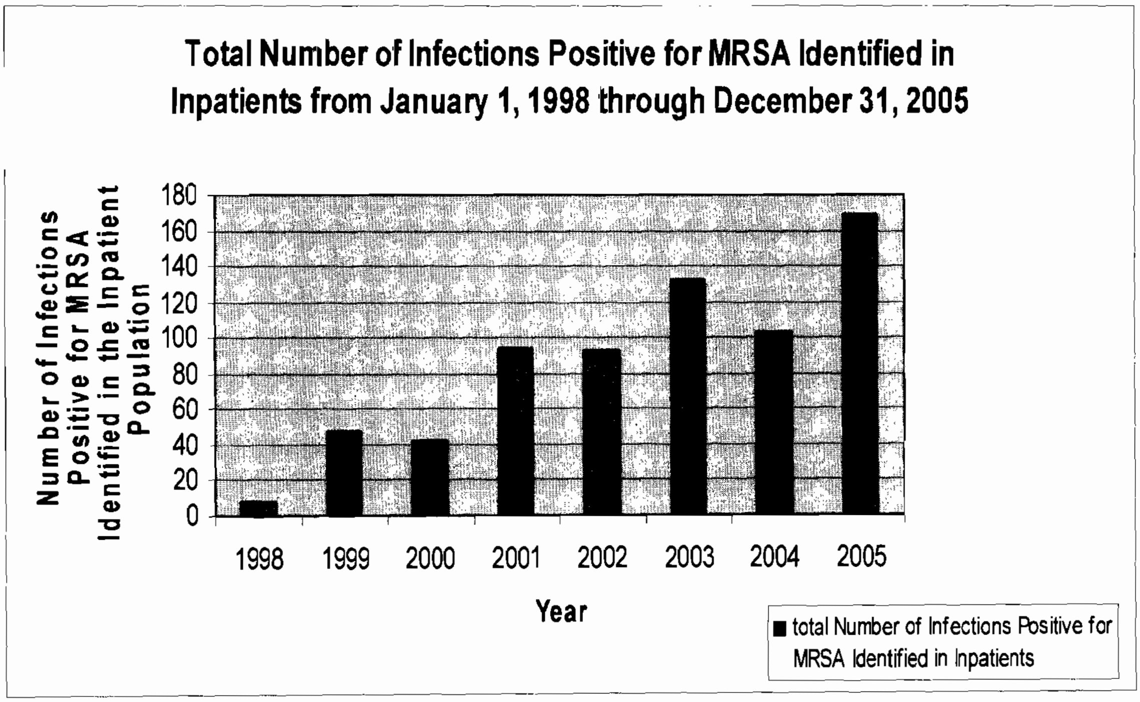
Furthermore, an increase in the proportion of isolates positive for MRSA in 1997 versus 2005 showed that patients were noted to be four times as likely to be positive for MRSA in 2005 when compared to 1997. The data reflecting this analysis is shown in Table 2.

Table 2. The Percentage of Patients identified with Isolates Positive for MRSA for the Time Periods of 1997/2001 and 1997/2005

	MRSA	No MRSA	Total Admissions	Percentage MRSA of Total Admissions
1997	38	6742	6780	0.5605%
2001	119	7399	7518	1.5829%
2005	211	9625	9836	2.1452%

A further analysis of the data was completed to identify cases of clinical interest consistent with our definition of infection and identified as positive for methicillin-resistant S. *aureus.* The data demonstrated an increasing prevalence of infections positive for MRSA were being identified in our hospital, as seen in Figure 8.

Figure 8



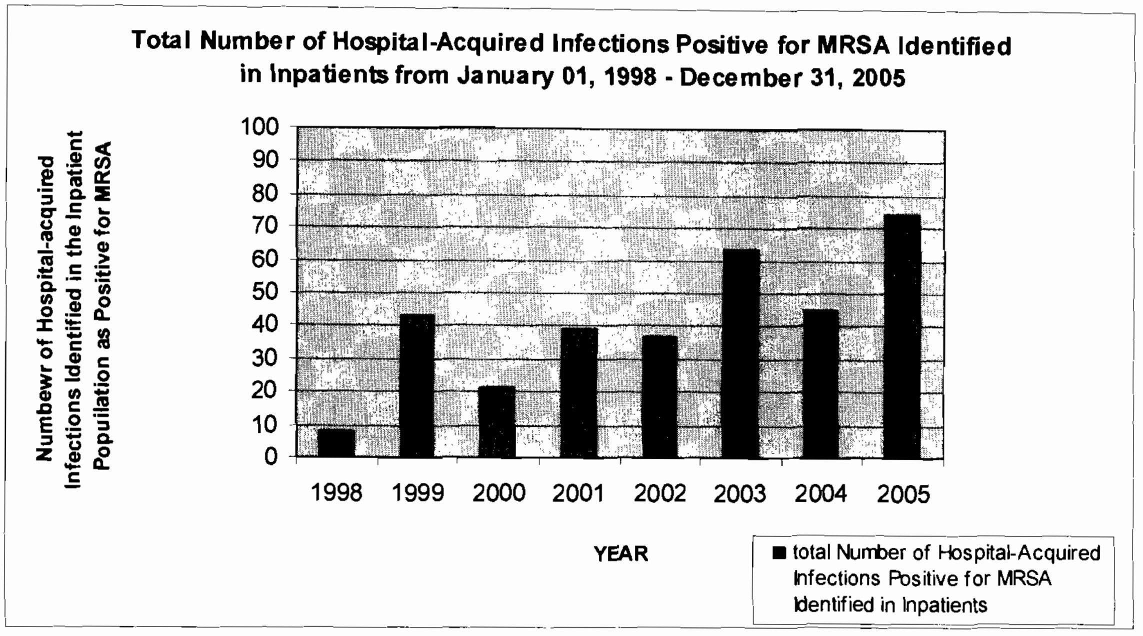
A chart review to determine characteristics of the clinical status of patients positive for MRSA infection was conducted in an effort to identify potential elements predisposing patients to developing these infections. Analyzing the data obtained from the clinically significant cases, we found that the mean age of the patients with infections positive for S. *aureus* was 61, with a slightly higher number of males than females. The majority of these patients had been residing at home, with the second highest patient population admitted from an extended care facility. Also included were patients who had been born in the hospital and directly admitted to the Neonatal Intensive Care Units.

Of these patients with infections, the majority were noted to have been admitted to the Adult Intensive Care, Medicine and Surgery units. Most cases of these infections were related to blood and pneumonia. Urinary tract infections, wounds and abscesses were identified more frequently on the medical and surgical units. A particular concentration or prevalence of infections involving abscesses was noted on the Department of Corrections unit. Also noted was a higher incidence of infections which were identified in the neonatal population over a one year period and primarily manifested as eye, trachial and blood infections.

Of significant interest to an infection control program is the number of infections positive for MRSA designated as community-acquired in comparison to hospital-acquired. The implication of cases identified as hospital-acquired is of potential transmission of the organism to the patient in relation to appropriate infection control practice adhered to by the health-care providers. The number of

hospital-acquired infections positive for MRSA increased consistently through this time period, as illustrated in Figure 9.

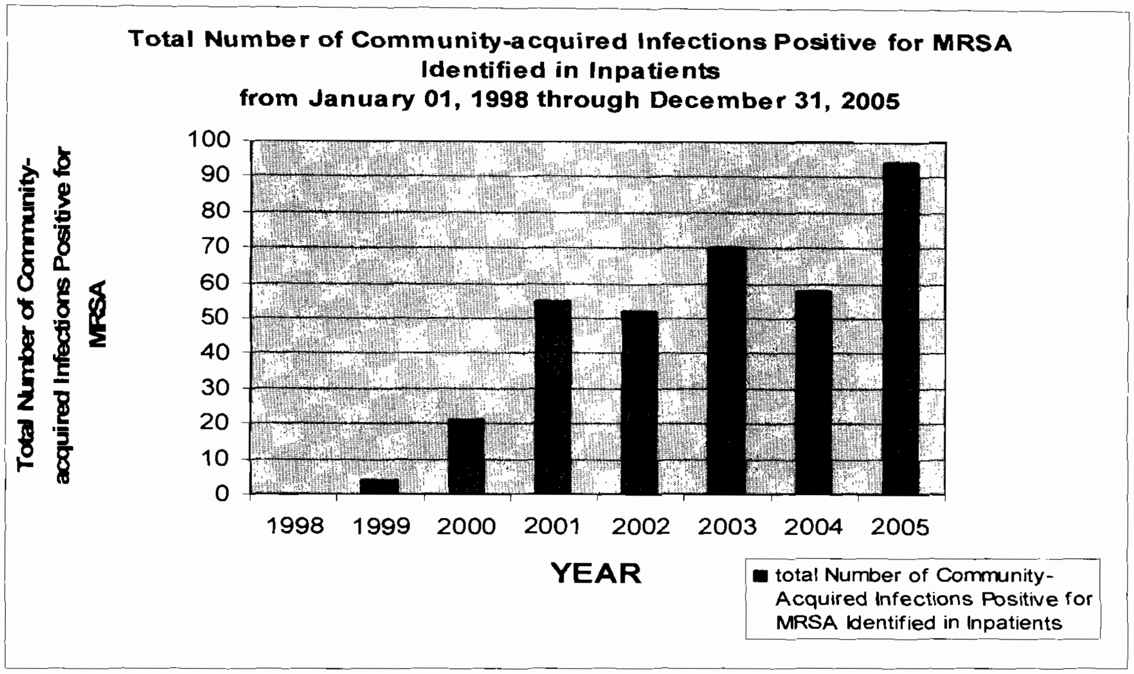
Figure 9



Specifically, we identified that during January 1, 1999 through December 31, 1999 and January 1, 2001 through December 31, 2001, there was a large increase in the number of infections that were positive for MRSA. The increase in the number of infections during the year 2001 was 50% greater than the previous year. We were interested in identifying any changes in epidemiology which may have been responsible for the persistent increase in infections positive for MRSA from this time period forth.

A remarkable discovery from this investigation was the consistent increase in the number of infections positive for MRSA which were determined to be community-acquired, as illustrated in Figure 10.

Figure 10



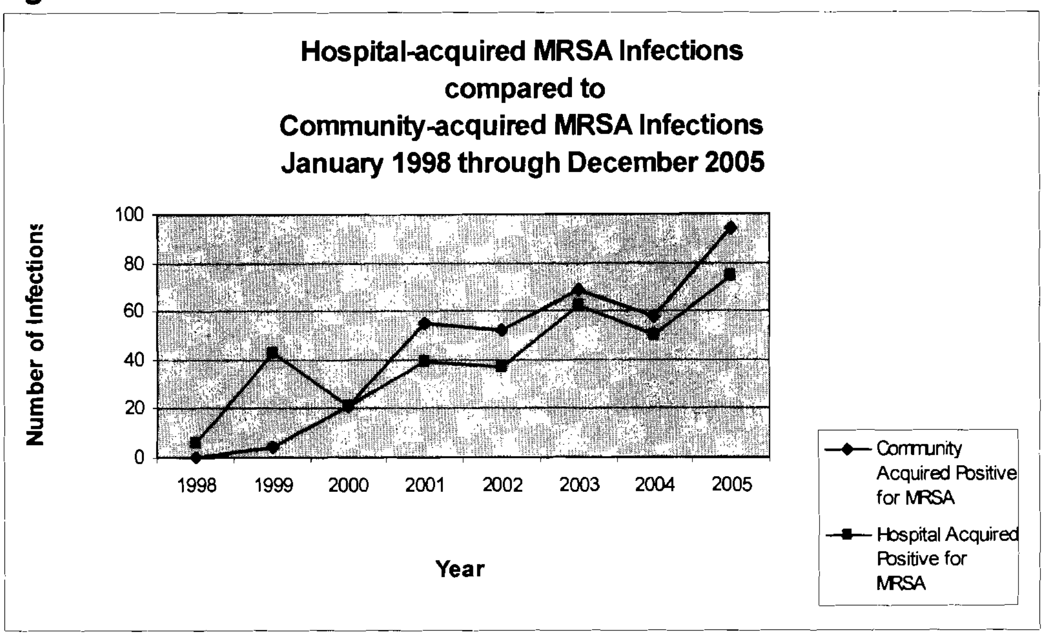
During the time period of January 1, 1998 through December 31, 1998, all infections identified in the inpatient population as positive for MRSA were considered hospital-acquired. However, over the next seven years a remarkable trend in the epidemiology of this pathogen was identified in our hospital, as noted in Table 3 below.

Table 3. The percentage of hospital-acquired MRSA infections compared to the number of community-acquired infections identified at Hospital A per year from 1998 through 2005.

Year	Percent of Hospital-Acquired Infections	Percent of Community-Acquired Infections
1998	100%	0%
1999	92%	8%
2000	50%	50%
2001	42%	58%
2002	41%	59%
2003	47%	53%
2004	40%	60%
2005	44%	56%

The relationship between infections positive for hospital-acquired MRSA as compared to community-acquired infections is illustrated in Figure 11. It is clearly depicted that in 2001 the number of infections positive for MRSA identified as community-acquired surpassed the number identified as hospital-acquired.

Figure 11



Further analysis of what appeared to be a pivotal year was conducted with a retrospective study of the time period of January 2001 through December

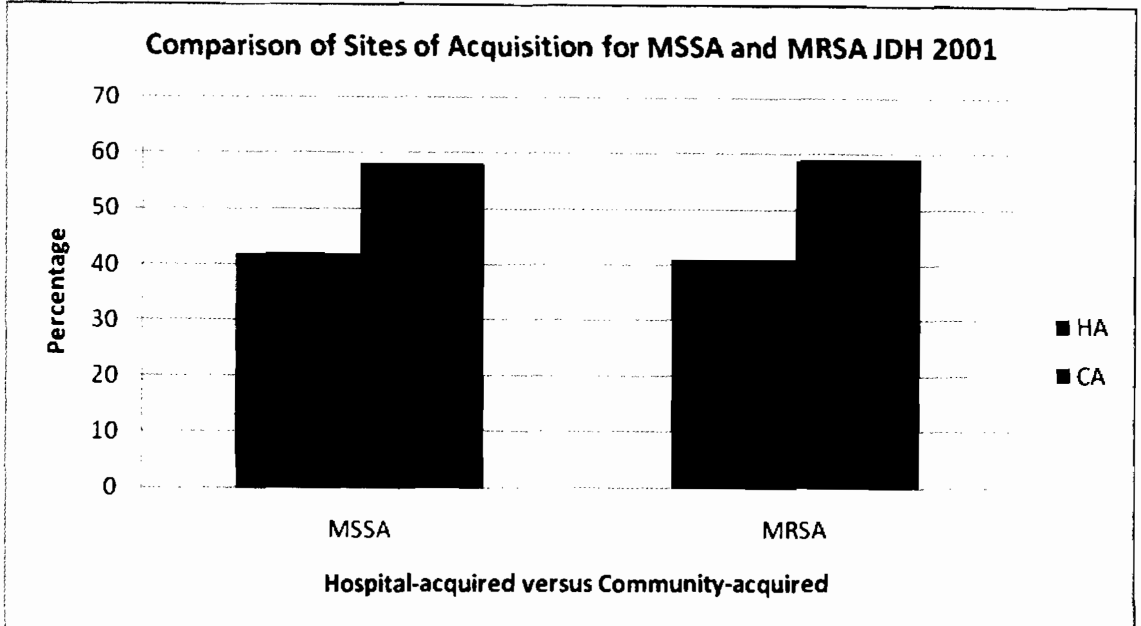
2001. We found that during this time period the microbiology laboratory identified 601 isolates of *S. aureus* from 291 patients (approximately 2.06 isolates per patient). Of the 291 isolates positive for S. a*ureus*, 241 patients were infected and 50 were determined to be colonized. Therefore, 241 patients fulfilled the criteria for inclusion in the study. Table 4 illustrates the specific pathogen (MSSA or MRSA) and whether or not they were hospital-acquired or community-acquired cases for these 241 patients.

Table 4.

241 Infections Positive for S. *aureus* January 01, 2001 – December 31, 2001		
Pathogen	**Hospital-acquired**	**Community-acquired**
MSSA 147 (60%)	62 (42%)	85 (58%)
MRSA 94 (40%)	39 (42%)	55 (58%)

This comparison between MSSA and MRSA and hospital-acquired versus community-acquired is depicted in Figure 12.

Figure 12



To further analyze the characteristics of these four groups designated as MSSA or MRSA and hospital-acquired or community-acquired, a summary of the analysis of the data are documented in the following two tables. Table 5 reflects the demographics of the patients with infections positive for MSSA which were identified as hospital-acquired or community-acquired as compared to the characteristics of patients identified with infections positive for hospital-acquired and community-acquired MRSA infection noted in Table 6.

Table 5. Characteristics of 147 patients identified as positive for an infection positive for MSSA; hospital- acquired and community-acquired

	Hospital-acquired MSSA Infections 62 (42%)		Community-acquired MSSA Infections 85 (58%)	
Gender	Male 36 (58%)	Female 26 (42%)	Male 53 (62%)	Female 32 (38%)
Age, mean	53		55	
Admission Source				
ECF	17		*34	
Home	37		15	
Hospital	**8		0	
Mean Number of Days from Admission until First Positive Isolate	***20.32		Unknown	

*We attributed the relatively young age of patients in the extended care facility group as being a reflection of the inclusion of the Department of Corrections patients and patients admitted from sub-acute rehabilitation facilities.

**Neonates born in this hospital were considered to have an admission source categorized as hospital and were automatically considered hospital-acquired cases.

***Date of admission counted as day one.

Table 6. Characteristics of 94 patients identified as positive for an infection positive for MRSA; hospital-acquired and community-acquired

	Hospital-acquired MRSA Infections 39 (41%)		Community-acquired MRSA Infections 55 (59%)	
Gender	Male 25 (47%)	Female 14 (34%)	Male 28(53%)	Female 27 (66%)
Age, mean	69		67	
Admission Source				
ECF	13		22	
Home	25		33	
Hospital	1		0	
Mean Number of Days from Admission until First Positive Isolate	10		Unknown	

Of the patients with community-acquired MRSA who were admitted from home, slightly more were females than males (19 females and 14 males). A similar proportion of females to males (8 females and 14 males) were found in cases admitted from Extended Care Facilities; which includes the cases admitted from prison. Because the numbers of patients in these sub-categories are small we found no significant relationship between gender and infection with MRSA.

An important consideration is to identify inpatient populations who may have characteristics that predispose them to a higher risk of acquiring an infection with MSSA or MRSA. We analyzed the number of positive infections related to physical sites of infection and which hospital units had the highest rates of infections with these body sites. The percentages of infections and locations of occurrence are described in the following paragraphs.

In order to identify specific patient populations at greatest risk for acquisition of these pathogens, we determined the patient care areas with the highest rates of infection with these organisms, as illustrated in Table 7.

Table 7. Identification of Infections positive for hospital-acquired and community-acquired MSSA and MRSA by hospital location

Hospital Unit	HA MSSA Infection	CA MSSA Infection	HA MRSA Infection	CA MRSA Infection	Totals
NICU	9	0	1	0	10 (4.1%)
OB/GYN	0	6	0	0	6 (2.5%)
PSYCH 1	1	0	0	0	1 (0.4%)
ICU	15	10	13	13	51(21%)
CSDU	1	1	3	3	8(3.3%)
PSYCH 3	2	0	2	0	4(1.7%)
MED 4	12	33	9	23	77(32%)
MED/SURG 5	6	10	0	3	19 (7.9%)
ONC 6	3	6	2	1	12(4.9%)
SURG 7	13	19	9	12	53(22%)
Totals	62	85	39	55	241

As illustrated in Table 8, the greatest percentages of hospital-acquired infections positive for MSSA were found in the Adult ICU, Surgery 7 and Medicine 4, in descending order of magnitude. The greatest percentage of hospital-acquired infections positive for MRSA was identified in the Adult ICU, followed by Surgery 7 and Medicine 4 with equal percentages.

Table 8. Identification of Infections positive for hospital-acquired MSSA and MRSA with percent of total MSSA/MRSA infection by hospital location

Hospital Unit	HA MSSA Infection	HA MRSA Infection	Totals
NICU	9 (15%)	1 (3%)	10
OB/GYN	0 (0%)	0 (0%)	0
PSYCH 1	1 (1.6%)	0 (0%)	1
ICU	15 (24%)	13 (33%)	28
CSDU	1(1.6%)	3 (7.7%)	4
PSYCH 3	2 (3.2%)	2 (5.1%)	4
MED 4	12 (19%)	9 (23%)	21
MED/SURG 5	6 (9.7%)	0 (0%)	6
ONC 6	3 (4.8%)	2 (5.1%)	5
SURG 7	13 (21%)	9 (23%)	22
Totals	62	39	101

We determined that the most frequent sites of infection identified as positive for MSSA or MRSA and either community-acquired or hospital-acquired were blood, sputum, and wounds, as illustrated in Table 9.

Table 9. Hospital-acquired and Community-acquired cases of MSSA and MRSA according to physical site of culture acquisition.

Sites of Infection	HA-MSSA	CA-MSSA	HA-MRSA	CA-MRSA
Blood	11	20	5	10
Sputum	13	21	19	15
Urine	2	9	1	4
Catheter	5	0	2	0
Wound	22	25	8	24
Trachial Aspirate	4	0	1	0
Bronchial Lavage	0	2	1	0
Fluid	2	3	0	1
*Other	3	5	0	1

*Other body sites include samples taken from: stool, cervix, peri-anal, eye and nasopharyngeal

Table 10 illustrates the specific sites of infection, the pathogen and the unit with the highest rate of those infections.

Table 10. Three most prevalent sites of infection percentage HA-MSSA as compared to HA-MRSA per unit with highest incidence

Unit with highest incidence	Site of Infections	HA-MSSA	HA-MRSA
Adult ICU	*Sputum	8 (62%)	10 (53%)
Surgery 7	**Wound	9 (41%)	7 (88%)
Med 4 /Adult ICU	Blood	5 (46%) / 3(27%)	2 (40%each unit)

*We observed that patients admitted to the Intensive Care unit were much more likely to develop respiratory infections with MRSA/MSSA than any other unit in the hospital. Additionally, of the patients who developed a Staph *aureus* respiratory infection while in the ICU, there was a 56% chance that a patient would develop an infection positive for MRSA as opposed to a 44% chance of developing an MSSA respiratory infection.

**The majority of wound infections identified as positive for MRSA were community-acquired. Wound infections positive for MRSA which were identified as hospital-acquired accounted for approximately ¼ of all wound infections positive for MRSA. Wound infections identified as positive for MSSA were similar in proportion. Additionally, of the 16 patients on Surgery 7 who developed hospital-acquired wound infections with S. *aureus*, there was a 56% chance it would be MSSA as opposed to MRSA.

Of the 241 patients identified with having an infection positive for S. *aureus,* 79 (33%) involved wound infections. Twenty-two (28%) of the total 79 wound infections positive for Staph were found on the Surgery 7 unit.

When we looked only at those patients who had hospital-acquired infections, 30 (30%) involved wound infections. Over half (16) were identified on the Surgery 7 unit. Of these 16 wound infections, 9 (56%) were identified as hospital-acquired MSSA and 7 (44%) were hospital-acquired MRSA.

A total of 46 blood stream infections were identified from the inpatient population as positive for either MSSA or MRSA. Of the total 39 hospital-acquired MRSA infections, 5 (13%) were isolated from blood in comparison to

the 10 (18%) community-acquired MRSA infections. Additionally, of the 62 hospital-acquired MSSA infections, 11 (18%) were isolated from blood and 20 (24%) were attributed to community-acquired cases of bacteremia. It appears that a patient is 50% more likely to be admitted with a blood stream infection positive for either of these pathogens compared to developing a hospital-acquired bacteremia.

During the time period of January 1, 2001 through December 31, 2001, Hospital A experienced a significant shift in the epidemiology of isolates identified as MRSA compared to isolates positive for MSSA. While the number of isolates positive for S. *aureus* may have increased slightly, it became apparent that MRSA was increasing in prevalence and in proportion to MSSA. Even more remarkable was the discovery that there was a significant increase in the number of community-acquired MRSA infections identified in the inpatient population.

Of the patient population studied during this time period, it appeared that those patients admitted to the Adult ICU, Medicine 4 and Surgery 7 were much more likely to develop infections identified as positive for S. *aureus* and that these infections were more likely to involve sputum, wounds or blood.

Hospital census data from 2001 shows an average length of stay for all inpatients was 6.85 days per admission. Of the patients with community and hospital-acquired MRSA, the average length of stay was 17.5 days per admission with a median of 11 days per admission.

D. Discussion

During the investigation of routine surveillance of epidemiologically significant organisms, the identification of a significant increase in isolates positive for S. *aureus* in 2001 prompted an in-depth study of all isolates of S. *aureus* over a nine-year period. We were interested to better understand the changing epidemiology of S. *aureus* identified as infections in our inpatient population. The report of isolates identified as positive for MSSA and MRSA by the lab indicated that in the year 2001 there was a significant increase in the number of isolates positive for MRSA in the inpatient population. Nosocomial transmission of this pathogen resulting in increased nurnber of infections was a concern of the infection control program. The largest increase in isolates positive for MRSA appeared to occur first in 2001. The null hypothesis was that the expected incidence of MRSA in the inpatient population would be equal to the 1997 rate. A chi square statistical test for independence was used. The increasing number of isolates positive for MRSA comparing 1997 versus 2001 was shown to be statistically significant, indicating that this increase in incidence had an impact on patients and hospital-systems in the early part of the decade. Using the chi square statistical test to compare the incidence of MRSA positive isolates in 1997 and 2005 resulted in a value indicating strong support for rejecting the null hypothesis. The significant increase in incidence of MRSA in 1997 versus 2005 based on statistical analysis was unlikely to occur by chance alone.

Hospital-acquired infections are a serious problem affecting large numbers of patients in all venues of healthcare and institutions despite consistent, routine efforts to inhibit transmission of pathogens. Infection control policies and procedures such as the use of Standard Precautions for all patients to protect the health-care provider and patient from exposure to potentially infected blood and body fluids require the use of gloves and other additional protective barriers. Another important component of Standard Precautions is hand hygiene, which has been identified by the CDC as the primary mode to prevent the transmission of infection. Hand hygiene with alcohol-based waterless hand sanitizer or antimicrobial soap and water must be performed by health-care providers in a thorough and consistent manner.

In addition to Standard Precautions, Contact Precautions are implemented for patients who have an infection positive for epidemiologically significant organisms such as MRSA. Contact precautions require the heath-care provider to use protective gear such as gloves, gowns, and masks and goggles to protect mucous membranes and eyes from droplets. Infective droplets could be generated if procedures are conducted creating aerosols such as suctioning a patient.

Hospital-acquired infections are adverse patient events that affect approximately two million persons annually according to Cosgrove, et al., (2005). Nosocomial infections, also referred to as hospital-acquired infections, are potentially caused by many factors such as break in infection control practice, significant exposure to environmental contamination, lack of appropriate use of

personal protective equipment such as gowns and gloves and exposure of the patient to multiple, highly invasive procedures and devices. Some examples of infections that are device related are ventilator-associated pneumonias, central venous catheter related blood stream infections and postoperative surgical wound site infections. These infections occur throughout hospital populations and, consistent with the results of our investigation, are more prevalent in areas such as intensive care units that are characterized by frequent use of invasive devices. This equipment is commonly used in patient care for ventilator support, hemodynamic monitoring and infusions.

Another possible rationale for the higher numbers of infections positive for MRSA in these areas was discussed by Cohen, et al., (2006). The frequent and expansive use of antibiotics with critically ill patients causes antibiotic pressure, which would increase the incidence of resistant organisms. Because of the prevalence of these organisms, transmission of multi-drug resistant pathogens would occur from patient to patient via the contaminated hands of direct patient care providers on a more frequent basis.

In an article published in the American Journal of Infection Control in 1996 describing the data reported from the National Nosocomial Infections Surveillance (NNIS) System between 1990 and 1996 (NNIS, 1996), it was determined that S. *aureus* was the most common cause of hospital-acquired infections. S. *aureus* was also identified to be the leading cause of nosocomial pneumonia and surgical site infections and the second leading cause of

nosocomial bloodstream infections, findings which are consistent with the data from our investigation of 2001.

Investigators have identified S. *aureus* as a leading cause of blood-stream infections among the hemodialysis patient population, with increasing prevalence of antimicrobial resistance and severity of illness. Reed, et al., (2006) discussed the outcomes among hemodialysis-dependent patients with MRSA compared to MSSA bacteremia. As one would expect, the patients with bacteremia positive for MRSA had higher mortality, length of hospital stay and cost of care.

In addition to the increased prevalence of infections positive for S. *aureus*, our study discussed the increased proportion of MRSA to MSSA isolates per total number of isolates positive for S. *aureus*. This discovery is supported by the conclusions from a cohort study in the United Kingdom by Wyllie, et al., (2006). These authors discussed the emergence of a significant increase in the number of patients identified with bacteremia which was positive for MRSA while the number of those positive for MSSA stayed the same.

It is well documented in the literature that infections with multi-drug resistant organisms contribute significantly to increased length of stay which increases cost. Pittet, et al., (1994) reviewed the impact of hospital-acquired S. *aureus* infections in New York City hospitals, showing the affect on length of stay for critically ill patients. These infections were found to increase length of stay in the intensive care unit by 8 days and their total hospital stay by 14 days. Brachman, et al., (1980) found that postoperative wound infections increased the patient's length of stay an average of 7.4 days. We found the average length of

stay for inpatients during 2001 to be 6.84 days per admission as compared to 17.5 for those patients who were identified with infections positive for MRSA, an average of 11 additional days. The increased length of stay burdens patients with hardship and risk such as additional antibiotic treatment; subsequent returns to the operating room for debridement of wounds, incision and drainage procedures and transfers to the Intensive Care Unit for monitoring and stabilization of the their physical status.

Increasing hospital and community-acquired infections positive for MSSA and MRSA have been documented to have a substantial negative impact on the patient population and health-care facilities, a finding supported by the data generated from our investigation at Hospital A. The magnitude of effect depends upon several factors, such as specific pathogen, resistance to individual antimicrobials, and even the pathogen's mechanism of resistance.

A concern of any Infection Control Program is the risk of transmission of these pathogens to patients. In order to protect the patients and health-care providers from acquiring these organisms, specific infection control practices are put into place. These interventions are nationally accepted standards issued by the CDC for isolation precautions developed by the Healthcare Infection Control Practices Advisory Committee (Siegel, et al., 2007a) and for the control of multi-drug resistant organisms (Siegel, et al., 2007b).

Hospital A requires contact and in some cases droplet isolation precautions once a patient is identified as positive for an infection with MRSA and other multi-drug resistant organisms (MDRO). This practice increases the

amount of time required for staff to prepare themselves to enter these patients' rooms prior to providing direct care. Facilitation of this intervention is also dependent on the involvement of other employees. Materials Management staff provide and replenish supplies necessary to maintain isolation and housekeeping staff dispose of the additional trash and adhere to policies specific to cleaning of these rooms. Hospitals incur considerable expense providing these services and the personal protective equipment to maintain precautions.

Ideally, once identified as having an infection positive for MRSA, the patient is placed in a private room, posing a significant issue for our institution because of the limited number of private rooms. If all these rooms are occupied, patients with infections positive for the same organism may be "cohorted" or placed in the same room. The least favorable scenario is that there are no other patients positive for MRSA and the unit has restricted bed availability, resulting in placement of the patient in a room with another patient who is the least susceptible to infection. Evaluation and decision making for the placement of these infected patients is instituted on a case-by-case basis and is time consuming. These discussions involve the infection control practitioner and generally the nurse caring for the patient, assistant nurse manager, nurse manager and nursing supervisor. If a room must be changed during a patient's hospital stay, he or she may find it confusing and disruptive. Communication with patients and families is essential for a successful hospital stay. A significant amount of additional time and emotional energy is expended in comforting and educating patients and families about the requirement for isolation precautions.

It has been our experience that they are fearful of the concept of having acquired an infection with a resistant organism and of changes in routine care such as the need to use personal protective equipment. In an attempt to address this issue, the Infection Control Department has developed Patient and Visitor Information Sheets on MRSA and other epidemiologically significant organisms (see Appendix A).

In addition to the need to prevent the spread of infection, another significant impact the increased prevalence of MRSA infections have had on our hospital relates to the initiation of empiric antibiotic treatment. The usual treatment initiated prior to obtaining the sensitivities of a specimen result identified as positive for S. *aureus* historically was a β- lactam antibiotic or semi-synthetic β- lactam antibiotic. Over the course of the past eight years, as the epidemiologic trend has shifted, hospital staff have been educated about increased identification of isolates positive for MRSA. As a result, physicians at our hospital are more inclined to order the administration of vancomycin for treatment of these infections in high-risk populations. Antibiotics that are effective in the treatment of these pathogens may be initiated but may be changed if the organism is identified as methicillin sensitive. According to other recent studies, this has become the recommended practice for populations identified as high-risk for infections positive for MRSA in geographical areas with high rates of endemic MRSA. A potential unintended and dangerous consequence of this change in treatment is that this methicillin-resistant S.

aureus will also develop a resistance to vancomycin with overuse, limiting effective choices of antibiotics even further.

Another method to control the spread of MRSA is eradication of colonization status of patients. Many studies related to the identification, control and eradication of MRSA colonization have been published. In one such study of Rhode Island hospitals conducted by Arnold, et al., (2002), a change in the pattern of susceptibility of MRSA to vancomycin was reported by one of the hospitals. This change supports the concern about the increasing limitation of antibiotics available to provide effective treatment of these resistant infections. A common recommendation for prescribers is to adhere to judicious use of antibiotics in both hospital and community settings. Its purpose is to reduce the evolution of multi-drug resistant organisms by avoiding the excessive and unnecessary use of antibiotics resulting in what is referred to as "antibiotic pressure." An important initiative by many facilities is the development of an antibiotic stewardship program. As discussed by Lesprit and Brun-Buisson (2008), these programs are developed with the intention of monitoring cost and effectiveness of antibiotics and putting practices into place to eliminate antibiotic overuse, thereby preventing antimicrobial resistance. These programs require dedicated and committed staff and demand additional funding from facilities for support.

In addition to health-care activity within an institution for the prevention and control of these infections, a major concern of public health is the education of the general public regarding these important health issues. Patients can be

discharged from their hospital admission to the community and may continue to be positive for MRSA colonization. These patients hopefully return to their activities of daily living including school and work. The media has paid a tremendous amount of attention to MRSA, presenting it to the general public as a new and unknown entity to be feared. Additionally, hospitals are shown to be filthy as described in newspaper articles and on television potentially inflaming the fear. The lay public has been led to believe that MRSA represents a "Superbug" epidemic rather than being an epidemiologically significant but treatable pathogen that has been around for half of a century. Special interest groups are demanding that specific actions be taken by hospitals to control the "spread "of these infections, without medically-based evidence of their efficacy i.e., global MRSA screening for all patients upon admission to the hospital. The general population lacks the ability to recognize the "unintentional" consequences which may occur. Universal "screening" of patients admitted to health-care facilities which have been proposed by some states and special interest groups could potentially cause a severe financial strain on the health system. Additionally, as discussed by Diekema, et al., (2001), active screening has yet to be proven effective. Little guidance is available to hospitals as how to handle appropriately the patients and health-care workers who are identified as positive for MRSA colonization. The current recommendation is to avoid decolonization of asymptomatic carriers for several reasons, such as inefficient sustained "decolonization" of some individuals in addition to potential development of resistance to treatment, which is typically mupirocin.

Additionally, a study by Harbarth, et al., (2008) discusses some of the obstacles of universal screening including cost of equipment, a greater than 20-hour turnaround time for results and number of private rooms available for isolation per facility.

The discordant relationship between a patient's beliefs and accurate knowledge can be large. A descriptive pilot study of 110 patients by Madeo, et al., (2008) was conducted in the United Kingdom on the perceptions and beliefs of inpatient populations regarding infections. They found that the majority of patients believed they had adequate knowledge of hospital-acquired infections. Upon admission to the hospital they were able to identify by name pathogens common to hospital-acquired infections such as MRSA. However, the patients expressed uncertainty about the modes of transmission. The majority of patients cited the news media as the major source for their education on hospital-acquired infections, but about 50% felt that the information delivered by the media was not always accurate. This study supports the need to provide appropriate education to hospitalized patients as well as the general population. It is important for the public to become appropriately educated and knowledgeable about steps hospitals are currently taking to prevent the transmission of MRSA, and the steps they, themselves, can take to prevent exposure to this organism. The burden of this education should fall squarely on public health agents and health-care providers to ensure that a clear, concise and medically accurate message is delivered.

As this investigation has demonstrated, MRSA is now found largely in the community setting and is no longer only considered a hospital-acquired pathogen. In addition to routine infection control precautions, we at Hospital A have routinely educated hospital personnel on the specific policies and procedures, consulted and collaborated with hospital staff to place patients in proper room assignments, educated patients and families, conducted targeted surveillance and managed potential outbreaks. Connecticut hospitals including Hospital A have taken further initiatives to address the issue of this significant pathogen. The Connecticut Hospital's Association (CHA) has organized an effort to create a "Pledge," which is a position statement to the general public and to the state legislature on an individual facility's plans to reduce infections positive for MDRO's. The pledge includes statements about continuing to enforce and monitor good infection control practices, assist in educating the public and others and screen for MRSA specific patient populations assessed as high risk by the Infection Control Department. Acute-care facilities have been developing a culture of patient safety which includes the prevention of hospital-acquired infections and have implemented numerous programs to aid in these initiatives. There is significant evidence that has been published suggesting positive patient outcomes with the development of patient empowerment and educational programs. One example of a successful patient empowerment initiative has been developed at Hospital A. The initiative evolved from the Hand Hygiene Committee, which has developed a program for monitoring, analyzing and improving hand hygiene compliance. A program entitled "JUST ASK" was

initiated as an empowerment strategy to encourage patients and families to ask their health-care providers if they have washed their hands before caring for them. Signs explaining the program are placed on the patient's doors and colorful badges illustrating the "JUST ASK" motto are given to the health-care provides to attach to their identification badges after they are educated on the meaning of the slogan We found that employees want a badge to "belong" to the group. McGuckin, et al., (2001) found a 50% increase in hand washing compliance when patients were empowered to ask their health-care providers if they had washed their hands. Interestingly, a little over half of the patients enrolled in the study felt comfortable asking their health-care providers this question. Of those who were comfortable asking, nearly 80% received favorable "yes" responses. All the patients who participated in the study were comfortable asking their nurses if they had washed their hands, while only a small portion, a little over a third of the participants, asked their physicians. At Hospital A we have seen an increase in hand hygiene compliance from 35% before implementation of the "JUST ASK" campaign and other interventions to 77–80% compliance.

A second action taken to prevent hospital-acquired infections at Hospital A was the establishment of a Central Venous Catheter-Related Blood Stream Infection subcommittee in December of 2005. Although the incidence of catheter-related blood stream infections positive for MRSA identified in the Adult Intensive Care Unit was less than that for other pathogens during our study period, the health consequences for a patient who acquires an illness caused by a multi-drug resistant organism can be serious. Salgado, et al., (2003) looked at

several studies to see if there was a difference in severity of illness caused by MRSA as compared to MSSA in the hospital setting. These studies found increased length of hospital stay (1 to 38 days), indicating increased severity of illness due to the acquisition of infection with this pathogen. The Hospital A subcommittee developed a program which adhered to CDC guidelines for the monitoring and assessment of central line infections. We found that our baseline rate for central venous catheter (CVC) related blood stream infections (BSI) in the adult ICU was 7.05 per 1,000 catheter days. After the implementation of a central line bundle that includes proven steps to reduce infection, we reduced our infection rate to 1.03 infections per 1,000 catheter days. With the cost of central line infections estimated at approximately 20,000 to 30,000 additional dollars per infection and up to 50,000 additional dollars for infections positive for MDRO's, in addition to the hardship one suffers, this becomes a significant infection issue to address on behalf of the patient and the health-care system.

An important component of many of these interventions is the attempt to change the "culture" of the institution, encouraging staff of all disciplines to become active team members and change agents of the process. One of the most important aspects of this process of change is education of employees. Coopersmith, et al., (2002) conducted a study at the Washington University School of Medicine attempting to lower the rate of CVC related BSI in the Adult Intensive Care Unit. One of the most significant efforts that effected change was education focused on the nursing staff. Through empowerment of nursing staff, they reduced the incidence of CVC related BSI by two-thirds over an 18-month

period, resulting in a cost savings in the range of $185,000 and $2.8 million dollars due to the decrease in infections.

E. Study Limitations

A potential flaw in this study is that all isolates for inclusion were identified on the basis of one per patient per hospital stay. While surveillance was conducted with the use of a data collection tool to ensure consistency and adherence to inclusion criteria, these isolates may mistakenly reflect inpatients who were colonized, not infected, with these organisms. Also worth noting is that even when a patient was identified as infected with an isolate positive for MSSA or MRSA, it is possible that another pathogen was causing the signs and symptoms of infection. In these cases the identification of colonization with MSSA or MRSA was a result of the in-depth targeted surveillance. We believe that these circumstances would be unusual and not typically counted because of the intense review of the medical record and microbiology laboratory results identifying the presence or not of other pathogens.

Limitations of the Laboratory Medicine computer system have also been identified. Many patients who are admitted to Hospital A have several co-morbidities which result in multiple admissions within short time periods. The number of isolates may reflect a duplicate count of individual patients who have had multiple admissions. MSSA or MRSA physical status may not have been successfully eradicated, therefore resulting in the identification of a patient with

isolates positive for these pathogens on more than one admission during this time period.

Additionally, because of the lack of data storage space, the lab is required to archive microbiology lab results. During the retrospective study of isolates from January 01, 2001 through December 31, 2001, some discrepancy was noted between the data that was collected in real time, for the nine year microbiology review and the retrospective one year review. Although some discrepancies in the number of positive isolates were identified, such as a lower number of isolates retrieved from archived data compared to surveillance data collected concurrently, overall trends remained consistent.

Finally, results inputted into the computer database for microbiology laboratory results are person dependent and therefore subject to human error. It was discovered during these investigations that lab technicians have the ability to “free text” and/or input data in variable ways. This latitude in data entry may have had a major impact on the consistency of the data. For instance, if I, as the Infection Prevention Specialist, have learned to retrieve results of isolates that were positive for MRSA by identifying these isolates using the code “MRSA,” but a subset of the lab technicians have entered these positive isolates as “oxacillin resistant,” the system may not render the total number of isolates positive for methicillin resistance. It has been noted that currently the laboratory is purchasing a new computer data system.

Surveillance of this pathogen is ongoing for the purposes of the Health Center’s infection control program and appears to reflect consistent trends for

this organism. It would be beneficial overall to conduct an investigation in the same manner as documented in this paper to determine if there has been consistent change or new trends in the epidemiology of MRSA identifying the incidence and prevalence or any significant changes in this patient population through the current time period.

It is well documented that the epidemiologic trends that evolved in the patient population of this university hospital over time are consistent with what has been identified nationally and in the United Kingdom. The responsibility now on healthcare and the general public is to strive for the control and prevention of these infections and implement medically evidenced-based practice to inhibit the increase in incidence, prevalence and progression of the development of these resistant pathogens.

IV Project II: An Epidemiologic Investigation of a MRSA Outbreak in a Neonatal Intensive Care Unit

The following is a report of a cluster of MRSA cases that occurred from October 2002 through October 2003 in the Neonatal Intensive Care Unit (NICU) at Hospital A while I was conducting normal field surveillance.

A. Background

The neonatal population at Hospital A has historically been born from high risk mothers whose infants are significantly premature and immunocompromised because of their underdeveloped immune systems. As a consequence, these infants are at great risk for developing serious illnesses after birth, including sepsis and severe respiratory distress. Up until a few years ago, the entire neonatal patient population consisted of severely compromised patients. More recently, Hospital A's OB/GYN Department has expanded its practice to include healthy mothers with uncomplicated pregnancies and non-compromised infants.

The NICU area is distinctly separated from other patient care units in the hospital. It is located on the ground floor and is protected by an alarm system. All personnel and visitors must be identified prior to entering this unit. Once inside the doors, all staff and visitors are confronted by a large scrub sink. All who enter the nurseries are required to complete a full three-minute scrub.

The two high-risk NICU nurseries and the Special Care Nursery consecutively follow each other to form the shape of a letter "C". Each unit has a framed windowed entrance as you move from one room to the next.

To enter into the "C", one must enter through an electronically operated glass door. The high risk nursery is divided into three rooms determined by the level of acuity of the infant's illnesses, from high risk intensive care to moderate and low risk called the Special Care Nursery (SCN). There are approximately seven enclosed bassinettes in each of the three subdivisions of the high-risk nursery, which is dependent upon patient census. Additionally, a well infant, or "normal" Newborn Nursery, is located outside the high-risk core. The "well infant" Newborn Nursery, while in close proximity to the other three rooms, is completely separate. This unit is surrounded by glass with another scrub sink positioned outside its entrance, and one must enter through a separate electronically operated door.

The infants in all the nurseries are cared for in individual isolettes and in incubators, both of which provide an isolated environment for each infant. One of the high-risk nursery units contains two isolation rooms that are enclosed by sliding glass doors and completely separated from the other isolettes in the room.

The Neonatal Unit has approximately 550 admissions per year and the average daily census in the high risk NICU nurseries is approximately 25 infants, 6 or 7 infants in the SCN and 6 in the "normal" newborn nursery. Typically the staff-to-infant ratio is as follows; 2:1 with few 1:1's in the NICU, 3:1 in the SCN and usually 4:1 in the Newborn Nursery. The census in the Newborn Nursery varies daily because of the general good health and early discharge of these infants.

During 2001 and 2002, there were several programs that were being conducted in this hospital to improve infection control performance; the Neonatal Department had been an integral part of these activities as described in the following paragraphs. These programs included an evaluation of gloves used for infection control purpose, hand washing "blitzes," in-service training and posters that promoted hand washing, and "give aways" such as free samples of lotion and waterless hand sanitizers used as a reward when someone was "caught" washing their hands. Numerous presentations and hospital publications on the value of hand washing were delivered. Additionally, waterless hand sanitizers containing a 62% alcohol base were strategically placed in convenient areas throughout all units to increase accessibility of the hand hygiene products. Specifically in the NICU, the waterless hand sanitizers were placed on the counter of each infant's designated area. Also, during this time, after a trial of several new soap products in high-use areas, an antimicrobial soap solution was chosen that contained 2% chlorhexidine gluconate. This component delivers four to six hours of persistent effectiveness for reducing resident and transient flora on hands of those who use the product. The use of this specific antiseptic is recommended by the Centers of Disease Control Hand Hygiene Task Force.

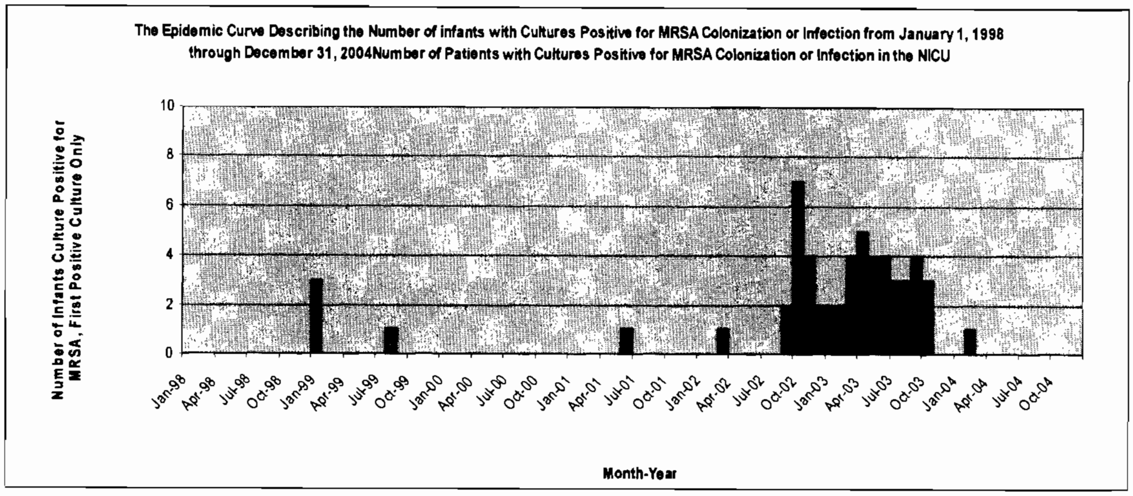
Prior to the year 2002, there were few isolates of MRSA from infants hospitalized in the Neonatal Intensive Care Unit. There were no infections with MRSA identified in the NICU in 1998, three infections in 1999, and none identified in 2000 and 2001. In 2001, there was a significant rise in the number of MRSA infections throughout the hospital population with the exception of the NICU. In March of 2002, an infant was born at Hospital A and admitted to the NICU who had MRSA isolated from an infection in his right eye on the 13th day of his hospitalization, and he received treatment with vancomycin eye drops. We were unable to determine whether or not this infant had acquired MRSA from a family member who had been colonized with this organism in the community or from hospital personnel. Because most of the infants in the NICU remain for long periods of time in the hospital after birth, virtually all cultures positive for MRSA in these highly susceptible patients are considered hospital-acquired.

Subsequent to this case, neonatologists in the NICU ordered surveillance cultures from infants to identify other potentially colonized patients.

In September 2002, one infant was found to be colonized from a trachial aspirate culture and one infant had an eye culture positive for MRSA. In October 2002, seven infants were identified as colonized with MRSA in cultures taken from axillae, nasopharynx, groin, trachea, sputum and broviac catheter wound site. Immunocompromised infants identified as colonized with MRSA in October were treated with antibiotics because of their health status. In November 2002, one infant was identified with MRSA bacteremia 15 days after being identified as

having a colonized broviac catheter insertion site; and 3 other infants were identified with MRSA colonization as depicted in Figure 13.

Figure13



By December 2002, we had implemented a number of interventions as a result of our surveillance, as we continued to identify new cases. The staff of the NICU was provided training on proper precautions, including contact isolation and conscientious hand washing practices, in order to reinforce the role of hand hygiene in preventing the transmission of MRSA among the infants.

Despite these interventions, cases continued to be identified over the next 12 months. In total, 58 infants were identified with either infections or colonization with MRSA. Of these, 29 were infected and 29 were colonized. The sites of infection or colonization are displayed in Table 11. The timeframe for these identified sites of infection or colonization of infants from whom MRSA was recovered was between January 1999 and December 2004. The one case identified in January 2004 was from an infant previously identified in 2003. This

case was not counted to be consistent with counting only the first culture positive for MRSA.

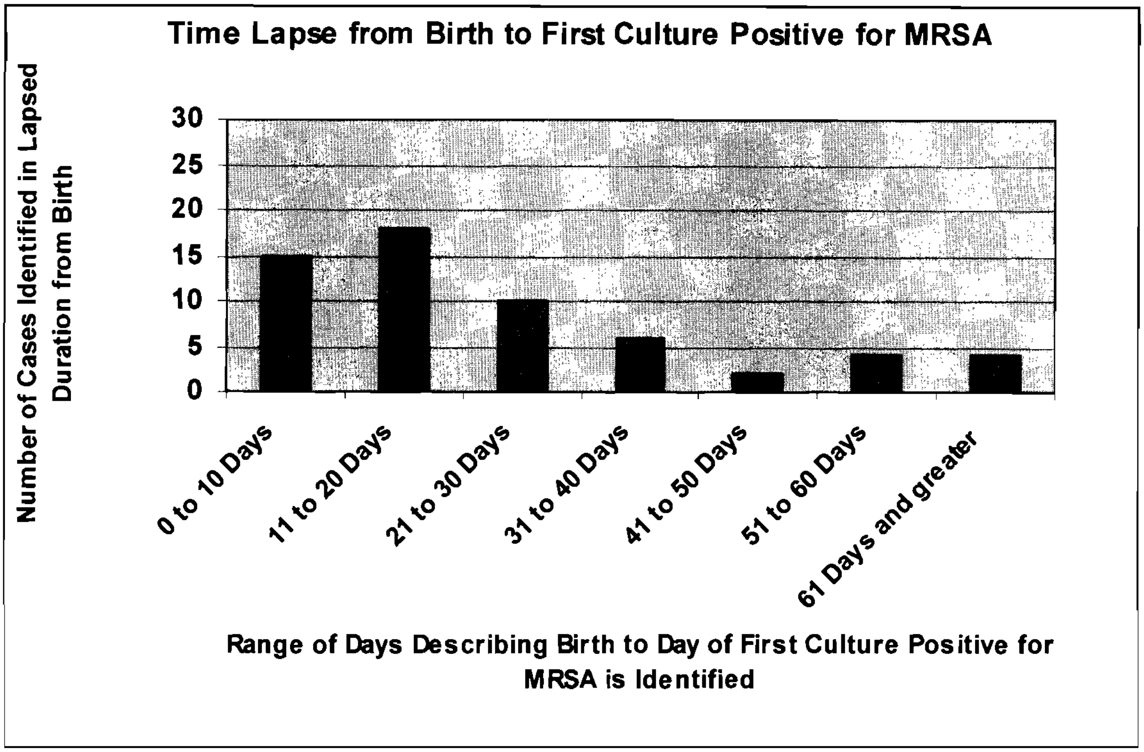
Table 11. Site of colonization or infection identified as positive for MRSA January 1999 through December 2004

Physical Site of Positive Culture	Infection	Colonization
Blood	6 (21%)	0 (0%)
Wound	3 (9.7%)	1 (3.5%)
Resp. Tract	6 (21%)	18 (62%)
Urine	2 (6.9%)	0 (0%)
Skin	2 (6.9%)	4 (14%)
Eye	10 (35%)	6 (21%)
Totals	29	29

Of the total 58 infants with cultures positive for MRSA, 42 had been admitted into room one of the two high-risk NICU areas. Of the remaining 16 infants, nine had been admitted to the SCN and seven into the Newborn Nursery.

The infants in the high-risk NICU and SCN are the most vulnerable and seriously ill infants with the longest admissions. The time from birth to the identification of first culture positive for MRSA ranged from 5 days to 132 days for our 58 cases. (Figure14)

Figure 14



Of the 42 high-risk neonates whose cultures were positive for MRSA, 24 (41%) received antibiotic treatment.

When their physical condition improves, infants from the NICU often "graduate" to the SCN, where they continue to be monitored by nursing staff, but are stable enough to be handled and cuddled on a routine basis. For infants in the SCN, the time from birth to identification of the first positive MRSA culture ranged from was 15 to 96 days, with six infants positive for colonization and one for a blood infection, also known as bacteremia. The infants admitted into the Newborn Nursery are "well" children. The time from birth to identification of first positive MRSA culture for this room ranged from 6 to 22 days.

It should be emphasized that the percent of infections versus colonization was higher for the immunocompromised infants than the healthy ones.

To validate that this outbreak of MRSA cases was related to a common source, seven clinically significant isolates from infants positive for MRSA infection and two isolates from patients identified as positive for MRSA infection outside the NICU were sent to the Associated Regional and University Pathologists, Inc. (ARUP) in Salt Lake City for Pulse-Field Gel Electrophoresis. The seven isolates were from blood samples from infants diagnosed with bacteremia; and two epidemiologically-unrelated isolates of MRSA from other units were also sent as a "control." All seven isolates from the NICU were indistinguishable in pattern from one another; the two controls were different from each other and different in sequence from the neonatal isolates.

B. Specific Methods

Methods utilized in this section included a case-control study comparing infants with infections positive for MRSA to infants with the same admission time frame who were free of infections positive for MRSA. An anonymous staff screening for MRSA was conducted on employees who had contact with cases and controls.

C. Outbreak Investigation

In August of 2003, we conducted an intense review of each infected or colonized infant's chart to generate a line listing. This assisted us in identifying common features that linked one infant with the other (Table 12). We identified common exposures, contacts with specific personnel and activity records for the infected and colonized infants for comparison with a control group consisting of 5 infants. The control group was comprised of infants who were the same age, were in the same NICU nursery room for the same length of time, and had similar illnesses or procedures, but who were not infected or colonized with MRSA. Once the chart review had been completed, members of our Infection Control team met to examine possible common links among the infants.

Table 12. Components of the line list generated from chart review of 16 infants identified as having an isolate positive for MRSA and 5 infants in the comparison group.

Infant's Name
Birth Date
Admit Date
Room Number
Isolette Number
Discharge Date
Gestational Age
Weight
Gender
Medical Record Number
Culture Date (If Positive)
Duration of Time from Admission to First Positive Culture
Site of Culture (If positive)
Treatment Administered for infection or Colonization with MRSA

Each infected and colonized infant had multiple common exposures, activities and procedures during this time period. A significant number of personnel regularly had direct patient contact with all infants on a day-to-day basis. The line list of individual patient contacts by personnel with cases and controls were tallied. (Table 13) We identified six caregivers, all physicians and nurse practitioners, who had higher numbers of contact with the cases than controls, including one nurse practitioner who appeared to have had the most encounters.

Table 13. Tally of the most frequent exposures of 129 persons employed in the neonatal unit to 16 cases of infants who were identified as having an isolate positive for MRSA as compared to 5 controls

Health-care worker	Exposure to cases (16 Cases)	Exposure to Controls (5 Controls)
*10	12	2
19	11	5
22	8	4
36	6	4
***47	11	4
53	7	4
***56	13	5
66	6	4
84	7	1
85	8	4
**87	12	4
89	10	4
98	7	3
117	6	3
121	8	4
122	12	4
128	8	4

* Healthcare Provider of Interest identified as Nurse X

** Preferred healthcare provider to be tested but was not

*** Nurse Y and Z with sterile (no growth) results

While it is not common practice to screen health-care workers for MRSA colonization routinely, in outbreak situations it may be necessary to identify a source of transmission. A surveillance culture survey for MRSA was initiated to identify a health-care provider who may have transmitted MRSA to infants identified as infected or colonized.

We conducted an anonymous screening of the selected health-care providers by culturing specimens obtained by nasal swab. The line list of employees was created in alphabetical order. The number assigned to the employee was where their name fell in consecutive order on the list. The lab slips were coded by number; names could not be connected to the sample number except by a separate confidential list that identified the sample number with a name.

We were able to culture four of the six employees within a one-week time period. Work schedules delayed screening of two remaining employees until the following week. From the six employees who were screened, four samples were positive for MSSA (Methicillin-Sensitive Staph. *aureus*) colonized from the nasal swabs and two samples (from nurses Y and Z) had no growth. It was discovered that Nurse X was re-cultured five days after initial screening which originally was positive for S. *aureus*. The result of the second culture showed no growth of any organism. Table 13 displays an abbreviated example of the table tallying the most frequent exposures of 129 persons employed in the neonatal unit to 16 cases of infants who were identified as having an isolate positive for MRSA as

compared to 5 controls. (See appendix for a listing of exposures for all 129 staff in the NICU.)

D. Infection Control Activities

In an effort to prevent transmission of MRSA to other infants, we adhered to the following protocol. Once infants with anterior nares swabs or other culture sites were identified as positive for MRSA colonization or infection, they were placed in a single room in the SCN and cared for consistently by the same caregivers. Intense contact isolation was implemented and caregivers were screened by nasal swab for MRSA colonization. .

Parents of the infants were given a letter explaining modifications in daily standard operating practices because of the outbreak of MRSA in the NICU. Another information sheet was created for neonatal staff on the modified standard practice and in-services were conducted. Information and education were free flowing among frontline staff, neonatal administration and infection control personnel.

To prevent further spread of MRSA in this unit, during the same time that the medical record investigation and screening was being conducted, we conducted a prevalence survey to identify all colonized infants. Anterior nares swabs were obtained from all 37 infants in the NICU room 1, SCN and the Newborn Nursery. The staff and MRSA positive infants were then cohorted and strict adherence to intense contact isolation was required. The infants who had results positive for MRSA from the screening procedures were treated with nasal mupirocin to decrease the risk of transmission to other infants. Anterior nares

cultures and cohorting were done on all infants with cultures previously identified as MRSA positive every Tuesday each week until there were four weeks without any cultures positive for MRSA.

Once a previously identified MRSA-positive infant was culture negative from the nares, the infant was re-cultured the next week from the anterior nares, trachea, axilla, any wound sites, and all intravenous sites. The rationale for obtaining cultures from multiple sites was to ensure that we were not changing practice based on a false negative result obtained from an anterior nares sample that had been treated with mupirocin. Culture-negative infants were moved into another area of the nursery.

Infants who had tested positive in the past and remained hospitalized in the NICU and newly colonized infants were continued on topical mupirocin to their nares for the duration of their hospitalizations.

In October 2003, five additional isolates from neonates with clinically significant MRSA infections identified in the previous month were sent to ARUP for Page Field Gel Electrophoresis. These five isolates were indistinguishable from each other and from the seven previously tested specimens. This indicated that the index case or source continued to transmit the MRSA to additional infants as late as September 30, 2003.

In a prevalence survey in late October 2003, 51 cultures were sent from 39 infants. One of the cultures returned positive from an infant who previously had positive cultures and two others from newly identified patients positive for MRSA. The three infants were cohorted in the same area of nursery room 1 and

a physical screen was placed dividing the room to maximize awareness of the contact isolation precautions. The infants were treated with a course of mupirocin to their nares.

Over the next three weeks, approximately 170 nasal swabs were cultured for MRSA from 110 infants. From these 110 infants, only one newly colonized patient was identified. Beginning in mid November of 2003, three weekly screenings of all hospitalized infants found no infants identified as positive for MRSA colonization. The neonatal units continued screening for an additional week to ensure that the screening cultures were negative for four consecutive weeks. Additional random screening continued as indicated by clinical circumstances. Because NICU infants are significantly immunocompromised due to their premature physical status, multiple cultures from many body sites, including nares, axilla, and insertion sites for tubes and catheters were cultured frequently.

No further cultures positive for MRSA were identified for two months after this cluster resolved. The one culture identified in January of 2004 was from an infant who had a culture positive for MRSA in 2003.

E. Discussion

During the outbreak investigation in Hospital A, enhanced infection control practices were implemented and conscientious infection control practice i.e., hand hygiene were enforced. Despite these efforts, cases of colonization and infection continued to be identified. However, upon completion of the anonymous employee screening, cases of colonization and infection ceased to occur.

Several outbreaks of neonates colonized or infected with MRSA from different institutions have been described by Anderson, et al., (2002), and Regev-Yochay, et al. (2005). Importantly, an outbreak investigation has been described by Bertin, et al. (2006). The outbreak occurred in a level III NICU in a tertiary care center. The investigation identified a health care worker who served as a reservoir for MRSA. The outbreak included nine of 12 infants who were either colonized or infected with MRSA, for an attack rate of 75%. Of the nine infants, three had MRSA blood stream infections and six were colonized with MRSA. A multidisciplinary task force was convened to develop a plan. Subsequently, a seven point plan was implemented. The plan included the following interventions: employees were retrained in cleaning and disinfection procedures, infected and colonized infants were cohorted, staff who delivered direct patient care to the infants were cohorted, infants who tested positive for MRSA received treatment with mupirocin, hand hygiene practices were reviewed and enforced, surveillance cultures were conducted on infants three times a week, and contact precautions were implemented. Also, the hands of health care workers were

visually inspected to assure they were free of lesions and that no one had artificial nails.

These measures appeared to be successful for a two-month period during which no further cases of infection or colonization were identified. Subsequently, two additional infants were identified as colonized and a month later a third infant developed a MRSA blood stream infection. At this time a health care worker voluntarily came forth disclosing a history of a previous ear infection which left the health-care worker with a residual external dermatitis. Polymerase chain reactions were performed on specimens from all infected and colonized neonates and the implicated health care worker. The isolates were more than 90% similar, suggesting that the health care worker may have been the index case transmitting this organism to infants via the hands. The health care worker received treatment with mupirocin and was screened as negative initially, but became recolonized with MRSA. This individual was reassigned to an adult unit and retreated with nasal mupirocin and a topical ear solution. Routine surveillance cultures were implemented for infants in the NICU. Once the health care worker was removed from the unit, identification of infants positive for MRSA ceased.

The investigation and interventions conducted in our NICU had many similar components to this facility's seven point plan, with a couple of significant differences. The page field gel electrophoresis conducted on samples in our investigation included infants positive for MRSA colonization or infection and a control group of patient samples from other units. This methodology

demonstrated that the samples from the infants were similar to each other and that our epidemic strain was unique to the NICU. While the samples in the Bertin investigation were 90% similar, the samples identified in our NICU were considered indistinguishable from each other.

In the Bertin investigation, a health care worker voluntarily offered the history of ear infection and subsequent dermatitis. This health care worker had nasal colonization with MRSA and a PCR which showed 90% similarity with the outbreak strain from infected or colonized infants. In our study none of the involved health care workers volunteered a history of infection; therefore, we needed to initiate a comprehensive epidemiologic investigation to identify the individual having the greatest number of contacts with cases. This investigation revealed a single nurse practitioner who had contact with 75% of the infants infected or colonized with MRSA, and only 40% of MRSA negative controls. When a nasal screening survey was conducted on our employees, only two initially yielded specimens which showed no organisms present, suggesting that these health care workers may have received treatment with mupirocin to eliminate colonization of MRSA. However, we had no direct knowledge that such treatment had been received. More significant was the suspect index case, who initially had a screening culture with results positive for MSSA and a subsequent culture which showed no growth. This added support to the concept that she may have self treated. During the time period immediately following our employee screening investigation, identification of new isolates positive for MRSA from infants ceased. Potential flaws in the screening process were

noted. In a review of the line list of employees after screening had been completed, it was noted that an employee was chosen to be screened who had less contact with cases positive for MRSA compared to the employee listed above his or her name. Reader error was responsible for identification of the wrong employee to be screened. Secondly, an employee on the list of most frequent contacts was not chosen even though she had the same number of contacts with cases as an employee who was screened. These identified flaws in the process could have caused us to miss the identification of the source of transmission. Another significant finding was that Nurse X was screened twice and that the second culture result was negative, suggesting that she was the index case who self-treated. However, it may not be accurate to assume that she was the index case because all employees with results positive for S. *aureus* were not re-cultured. They also may have self-treated, but because they were not tested again, the other three employees were the ones implicated as possibly being the index case.

Another study by Ben-David, Mermel & Parentau (2008) supports active screening of health care workers. This study acknowledges the importance of active screening of patients and strict infection control precautions. However, despite these control measures, they continued to experience an outbreak of MRSA infection and colonization in a burn patient population. Active screening of the anterior nares and hands of health care workers in the unit identified three employees positive for colonization with MRSA strains identical to those of the patients infected or colonized. The employees were treated and MRSA was

eradicated during this screening period. No further cases of patients with MRSA were identified. This study suggests that, despite active screening of patients and adherence to strict infection control methods, MRSA cases continued to be identified. When MRSA was eradicated in the staff of the burn unit, the transmission of MRSA from employees to patients stopped and the outbreak ceased.

It has been suggested that standard infection control practices routinely followed by hospital personnel are not sufficient to prevent the transmission of MRSA in the neonatal population. It is believed by many health officials and expert groups, such as the Society for Healthcare Epidemiology of America (SHEA), that additional measures, such as active surveillance of patients and staff, treatment with mupirocin of infected and colonized infants and staff and strict cohorting of infants and direct patient care staff, must be implemented in addition to conventional infection control practices when MRSA is identified, specifically in a NICU setting.

In response to the absence of accepted guidelines of routine infection control measures to contain and control MRSA in neonatal intensive care units, the Chicago Department of Public Health convened a working group to provide a consensus statement. The statement acknowledged that the neonatal population is particularly vulnerable to infections and colonization with MRSA. A survey of seven Chicago hospitals was conducted to identify the incidence of clusters of infants with MRSA infection or colonization in neonatal intensive care units. From June 2001 through September 2002, 13 clusters were identified.

Successful eradication of clusters of MRSA included interventions such as the cohorting of infants positive for MRSA and direct patient care staff, obtaining surveillance cultures of staff, and in five of the 13 clusters, both infants and health care workers were treated with mupirocin.

We identified and controlled a common source outbreak of MRSA infection/colonization that involved 58 cases in 2002. The source of this outbreak appeared to be a single health care worker who was involved in the care of a majority of cases. When this health care worker was "treated" for MRSA nasal colonization and subsequently identified as negative for Staph colonization, and infection control recommendations were implemented, the outbreak was brought under control.

Prior to this outbreak investigation, we believed that NICU infants were "naturally" isolated because their environment was limited to isolettes. It was astounding for us to document the number of encounters by different employees that these infants had on a daily basis. We calculated approximately 75 encounters per infant per day. It was not uncommon for nurses to "cover" for each other, perhaps when one is taking a break or retrieving medications to administer. Whenever a nurse is working with a single infant in the NICU and an event such as apnea occurs with another infant, there is no time for the nurse to complete her task, wash her hands and then tend to the distressed infant. During this type of emergency situation, the nurse proceeds directly to the other infant and conducts necessary actions. This type of activity usually requires direct patient contact and may increase the likelihood of transmitting organisms from one infant

to another. While this situation may not be ideal, it is doubtful that anyone would criticize the nursing staff for emergently attending to the distressed infant. The use of physical "screens" established to separate MRSA positive infants and the staff caring for them from the rest of the patient population may truly have limited the progression of transmission of this pathogen. By cohorting staff specifically with the cases positive for MRSA, episodes of emergency interventions by "contaminated staff" were eliminated, therefore preventing transmission of MRSA on unwashed hands.

It is not uncommon for employees involved in this situation to question standard activities that are carried out routinely. This type of scenario creates an atmosphere of stress and fear and adds to employee exhaustion. During the outbreak, the staff had grown exhausted and extremely concerned about their patients.

A positive outcome from our investigation and control of this outbreak was a greater cohesiveness among the NICU staff and a greater awareness of the need for consistent infection control practices.

While review of infection control precautions implemented in caring for patients with epidemiologically significant organisms continues on an ongoing basis, policies and protocols have been developed as a result of this outbreak to aid in the effective and timely management of infants and mothers who are positive for MRSA. Some of these newly implemented interventions are as follows:

- Infants transported to the NICU from other facilities or admitted from home are to have cultures of the nares and tracheal aspirate (if applicable) done upon admission.

- "Rooming In" is encouraged if physically possible for all mothers and infants who are culture positive for MRSA.

- Mothers of infants with MRSA were allowed to perform "Kangaroo care" (breast feeding). In the case of twins, the non-colonized infant should be Kangarooed first. The mothers were asked to wash the chest area with a wash cloth and Basis soap after Kangaroo.

- Housekeepers should wear gowns and gloves when handling laundry and trash.

- It is acceptable for families of colonized infants to remove bottles for breast milk storage and their infant's laundry for cleaning at home. These should be placed in plastic bags for transport.

- Families and visitors will be reminded about the importance of hand washing after leaving the infant's bedside and before leaving the hospital.

- The bedsides of all infants (counters, pumps, other surfaces) will be wiped down at the beginning of each shift with hospital-approved disinfectant.

- Dietary Technicians are to wipe down the counter surface before and after making formula.

- If colonized infants leave the unit for transport to X-Ray or the OR, personnel of those areas are to be informed that infants are on SOAP isolation. This is a standardized infection control designation throughout the hospital.

After the implementation of the above measures, the NICU experienced the identification of few infants with cultures positive for MRSA and no further clusters or outbreaks of cases positive for MRSA. Routinely, standard measure of infection control practice is sufficient to prevent transmission of epidemiologically significant organisms. These include appropriate isolation precautions, effective hand hygiene and cohorting of patients and staff. It appears that especially during an outbreak situation, a successful measure to control transmission may be surveillance screening of patients and staff and judicious treatment of colonized individuals.

V. Conclusion:

As demonstrated through these investigations and the review of literature, MRSA and all multi-drug resistant organisms have evolved into a significant public health issue. The serious nature of the infections has been identified for many years. Hospitals have placed a great deal of resources in attempt to control the transmission of these pathogens including infection control interventions. Over the past decade there has been a significant increase in the prevalence of community-acquired cases of MRSA infections and colonization. The changing trends in the epidemiology of this pathogen have posed a monumental challenge to health care facilities and public health institutions. It has become paramount to continue to control the transmission of this organism by increasing awareness of health care providers and the general population of good infection prevention and control practice. In addition to the control of transmission of this pathogen, there is increasing awareness that prevention of antibiotic resistance is equally important. The development of antibiotic stewardship programs recommend judicious use of antibiotics and medically evidenced based accurate education. This public health problem has expanded beyond the confines of the hospitals, geographical borders and now has challenged public health entities globally. Prevention and control of this significant issue requires the collaborative effort of government, both local and federal, healthcare, public health, and the general population.

APPENDIX A

Glossary

ARUP- A medical reference laboratory located in Salt Lake City, Utah that provides services for specialized laboratory testing. The Department of Laboratory Medicine at Hospital A utilizes this laboratory for tests that are currently not performed in the hospital laboratory.

β- lactam antibiotics - Antibiotics that share a common structure known as the beta - lactam ring which is a structure composed of three carbon and one nitrogen molecules. This ring inhibits the synthesis of the bacterial cell wall, thus destroying the further formation of susceptible bacteria. Penicillins and cephalosporin antibiotics have β- lactam rings.

Colonization- Bacteria residing and multiplying in the GI tract, upper respiratory tract, skin, etc. without causing signs or symptoms of infection. These organisms may become resistant to commonly prescribed antibiotics and may subsequently cause infections in the patient or be transferred to other patients, usually via the hands of health care providers.

Community-acquired- Infection or colonization is defined as "community-acquired" if a causative organism/pathogen is cultured from that site within 48 hours of admission to a hospital. The rationale for this time frame is that the incubation period of the majority of bacterial infections is 12 to 48 hours.

Extended Care Facility- A facility in which there is a population of patients or clients maintained in general living conditions with separate or shared rooms. These include, but are not limited to, skilled nursing homes, assisted living facilities, rehabilitation facilities, veteran affair facilities and prisons.

Hospital A- is a 234-bed acute-care teaching hospital in the Farmington Valley with approximately 10,000 discharges in 2005. It offers a full spectrum of clinical services in addition to specialty centers and a full set of diagnostic and therapeutic services such as invasive cardiac procedures. There are the following inpatient units: Neonatal Intensive Care unit, Labor and Delivery, Obstetric and Gynecological Unit, Emergency Department, Adult Intensive Care Unit, Cardiac Step-Down Unit, Psychiatric Unit, Geriatric Psychiatric Unit, Medicine Unit, Medical Department of Corrections Unit, Medical Oncology Unit, and a Surgical Unit that offers specialty care in Orthopedics, Urology, Neurosurgery, and Cardiovascular services.

Hospital-acquired- Infections and/or colonization involving any body site identified in a patient who has been hospitalized more than 48 hours
that was not present on admission. Infection- The diagnosis of infection implies a clinically significant event. The criteria for infection with any staphylococcal isolate includes the physician's documentation of the diagnosis of infection and may or may not have the additional criteria such as; classic signs of inflammation (redness, induration, warmth, swelling, pus, pain), antibiotic treatment, or the documentation of symptoms indicative of infection e.g., fever.

International Classification of Diseases (ICD) 9 codes- these are numbers applied to conditions of morbidity and mortality issued by the World Health Organization to create a system for international comparability of illnesses. These codes can be used for statistical data and also for reimbursement purposes in the clinical setting.

Isolate- reflects the recovery of bacteria from clinical specimens by the microbiology laboratory at Hospital A. The laboratory uses standard techniques to identify organisms, characterize them according to species, and identify their sensitivity and/or resistance to specific antibiotics.

Line listing – A tool used in Epidemiology to assist the practitioner in analyzing compiled patient-specific data in terms of person, place and time.

Methicillin-resistant *Staphylococcal aureus* – (MRSA) A *Staphylococcal aureus* organism that is not sensitive to β-lactam antibiotics. These bacteria can continue to multiply in the presence of penicillin and cephalosporin and can either colonize or cause infection in susceptible hosts.

Methicillin-sensitive *Staphylococcal aureus* – (MSSA) An organism identified as *Staphylococcal aureus* that is sensitive to β-lactam antibiotics and can either colonize or infect patients. The growth of these bacteria is inhibited in the presence of virtually all penicillins and cephalosporins.

Minimum Inhibitory Concentration – (MIC) is the least concentration of antibiotic that prevents an organism from growing in that environment. This result indicates the relative sensitivity or resistance of that isolate to a specific antibiotic.

Pulse-Field Gel Electrophoresis – A technique used in the laboratory to separate long strands of DNA of a specimen in order to identify a fingerprint or a pattern of a specific organism in order to compare it with the fingerprint of other epidemiology-related organisms.

Sites of Infection- The most common body locations of infections are the urinary tract (related to use of indwelling urinary catheters), surgical sites (wounds), skin, lungs (pneumonias, often ventilator associated pneumonias in patients hospitalized in the ICU) and blood stream (in particular central line intravenous catheter - associated infections).

Staphylococcus aureus- A ubiquitous organism that can colonize or infect patients. It is commonly cultured as a colonizer of the anterior nares. This organism is a common cause of skin and wound infections and can sometimes cause fatal cases of pneumonia or blood stream infections in very sick patients. It is also responsible for hospital-acquired infections, including pneumonias, serious wound infections and blood stream infections.

Appendix B

List of Abbreviations

ARUP	Associated Regional and University Pathologists, Inc.
CSDU	Cardiac Step-Down Unit
DOC	Department of Corrections unit
ECF	Extended Care Facility
ED	Emergency Department
ICU	Adult Intensive Care Unit
MIC	Minimum Inhibitory Concentration
Med-4	Medicine-4 Unit
Med/Surg 5	DOC Prison Unit
MRSA	Methicillin-resistant *Staphylococcus aureus*
MSSA	Methicillin-sensitive *Staphylococcus aureus*
NICU	Neonatal Intensive Care Unit
OB/GYN	Obstetrical and Gynecological Unit
Onc-6	Oncology-6 Unit
Psych 1	Psychiatry Nursing Unit
Psych 3	Geriatric Psychiatric Unit
S. *aureus*	*Staphylococcus aureus*
Surg-7	Surgery-7 Unit

Appendix C

MRSA Information for Patients and Families

MRSA Information for Patients and Families

What is Staphylococcus aureus (S. aureus)?
S. *aureus*, often simply called "staph," is a germ, often found on the skin of healthy people.
Sometimes, staph can get into the body and cause an infection.
This infection can be minor (such as pimples or boils) or serious (such as blood infection or pneumonia).

What is MRSA?
MRSA (Methicillin Resistant S. *aureus*) is a kind of S. *aureus* germ that can not be treated by some antibiotics often used to treat staph infections.

What is the difference between MRSA colonization and infection?
Colonization means that MRSA is living on or in the body without causing illness
Infection means that MRSA is making the person sick.

Who gets MRSA?
Anyone can get MRSA but especially people who have been in the hospital or a nursing home for a long time, have an open wound, have a tube (such as a urine drainage tube, or feeding tube) going into the body, are sick with a long term illness, or have taken many antibiotics are more likely to get MRSA. Also, people in the community can get MRSA usually those with close contact to those with MRSA

Healthy people rarely get MRSA infections (but they may).

How does the doctor know that someone has MRSA?
A doctor or nurse may take a culture to see if MRSA is present.
The culture is taken by rubbing a cotton swab or sending a sample of urine, sputum, wound drainage, or blood
The test results are ready in two or three days.

Can MRSA be treated?
Yes
Different antibiotics can still cure MRSA infections.
Patients who are only colonized with MRSA often do not need treatment.

Can MRSA spread?
Yes, MRSA is almost always **spread by touching**, often by hands contaminated with MRSA, and NOT through the air. John Dempsey Hospital takes special steps to prevent the spread of MRSA from patient to patient by practicing frequent hand washing and to separate, or isolate, patients with MRSA infections from other patients when appropriate.

What happens for all patients in John Dempsey Hospital?
- Health care workers will put on gloves and a gown (and sometimes a mask) before going into the patient's room.
- Health care workers must remove the gloves before leaving the room
- Health care workers must wash their hands with soap and water or waterless hand cleaner, before leaving the room. A squirt is all you need to cleanse your hands

What happens when a patient with MRSA is isolated? In addition to above precautions.....
- The patient is placed in a room with a patient with a similar diagnosis and treated with strict contact precautions.
- Health care workers will put on gloves and sometimes a gown and mask before providing direct patient contact.
- Health care workers must remove the gloves, and gowns (and masks) before leaving the room
- Health care workers must wash their hands with soap and water or waterless hand cleaner before leaving the room. A squirt is all you need to cleanse your hands.

What about visitors?
- Visitors should wash hands frequently with soap and water or waterless hand cleaner (as long as hands are not visibly soiled).
- If Families or Visitors are involved in direct patient care they should wear gloves and gowns and remove them before leaving the room. Remember to always wash your hands thoroughly after taking off gloves and gowns!!
    - Most families should not bring children or infants into the room of a MRSA patient, because it is hard for children to follow hospital isolation rules.

Should the person with MRSA be isolated at home?
If a person is colonized with MRSA, isolation is rarely needed
Most people can return to their daily routine. Good hand washing is most important.

If you have further questions
Please speak with the patient's nurse or physician or ask to speak Nancy Dupont, the Infection Control Specialist

Appendix D

Outbreak Investigation in a Neonatal Unit: Employee Contact with MRSA Cases and Non-Cases

Health-care worker ID	MRSA Cases Seen	Non-MRSA Cases Seen	% of MRSA cases seen	% of Non-MRSA cases seen
	16	5		
	total cases	total cases	(b) / 16	(c) / 5
(a)	*(b)*	*(c)*	*(d)*	*(e)*
56	13	5	81%	100%
10	12	2	75%	40%
87	12	4	75%	80%
122	12	4	75%	80%
19	11	5	69%	100%
47	11	4	69%	80%
89	10	4	63%	80%
22	8	4	50%	80%
85	8	4	50%	80%
121	8	4	50%	80%
128	8	4	50%	80%
53	7	4	44%	80%
84	7	1	44%	20%
98	7	3	44%	60%
8	6	3	38%	60%
36	6	4	38%	80%
57	6	2	38%	40%
58	6	4	38%	80%
66	6	4	38%	80%
117	6	3	38%	60%
33	5	4	31%	80%
42	5	1	31%	20%
60	5	2	31%	40%
80	5	0	31%	0%
82	5	2	31%	40%
113	5	2	31%	40%
44	4	3	25%	60%
45	4	1	25%	20%
62	4	0	25%	0%
64	4	1	25%	20%
71	4	3	25%	60%
75	4	0	25%	0%
81	4	4	25%	80%
83	4	3	25%	60%
90	4	2	25%	40%
115	4	1	25%	20%
116	4	0	25%	0%

Appendix D(Continued)

Health-care worker ID	MRSA Cases Seen	Non-MRSA Cases Seen	% of MRSA cases seen	% of Non-MRSA cases seen
	16	5		
	total cases	total cases	(b) / 16	(c) / 5
(a)	*(b)*	*(c)*	*(d)*	*(e)*
1	3	1	19%	20%
9	3	1	19%	20%
21	3	2	19%	40%
24	3	3	19%	60%
25	3	3	19%	60%
29	3	1	19%	20%
32	3	0	19%	0%
39	3	1	19%	20%
49	3	0	19%	0%
50	3	0	19%	0%
51	3	0	19%	0%
52	3	0	19%	0%
54	3	0	19%	0%
55	3	3	19%	60%
99	3	1	19%	20%
104	3	1	19%	20%
108	3	0	19%	0%
109	3	0	19%	0%
118	3	0	19%	0%
119	3	1	19%	20%
123	3	1	19%	20%
124	3	2	19%	40%
129	3	3	19%	60%
2	2	0	13%	0%
11	2	0	13%	0%
12	2	2	13%	40%
14	2	0	13%	0%
18	2	0	13%	0%
23	2	0	13%	0%
30	2	1	13%	20%
31	2	1	13%	20%
40	2	0	13%	0%
43	2	0	13%	0%
48	2	0	13%	0%
61	2	1	13%	20%
69	2	1	13%	20%
74	2	2	13%	40%
76	2	0	13%	0%

Appendix D(Continued)

Health-care worker ID	MRSA Cases Seen	Non-MRSA Cases Seen	% of MRSA cases seen	% of Non-MRSA cases seen
	16	5		
	total cases	total cases	(b) / 16	(c) / 5
(a)	*(b)*	*(c)*	*(d)*	*(e)*
77	2	0	13%	0%
88	2	1	13%	20%
92	2	0	13%	0%
94	2	3	13%	60%
95	2	2	13%	40%
107	2	0	13%	0%
112	2	1	13%	20%
125	2	3	13%	60%
3	1	0	6%	0%
4	1	0	6%	0%
5	1	0	6%	0%
6	1	0	6%	0%
7	1	0	6%	0%
13	1	2	6%	40%
15	1	0	6%	0%
16	1	1	6%	20%
17	1	0	6%	0%
20	1	2	6%	40%
26	1	3	6%	60%
27	1	2	6%	40%
28	1	0	6%	0%
34	1	0	6%	0%
35	1	0	6%	0%
37	1	3	6%	60%
38	1	3	6%	60%
41	1	0	6%	0%
46	1	0	6%	0%
59	1	0	6%	0%
63	1	0	6%	0%
65	1	0	6%	0%
67	1	0	6%	0%
68	1	0	6%	0%
70	1	0	6%	0%
72	1	2	6%	40%
73	1	0	6%	0%
78	1	2	6%	40%
79	1	0	6%	0%
86	1	1	6%	20%

Appendix D(Continued)

Health-care worker ID	MRSA Cases Seen	Non-MRSA Cases Seen	% of MRSA cases seen	% of Non-MRSA cases seen
	16	5		
	total cases	total cases	(b) / 16	(c) / 5
(a)	*(b)*	*(c)*	*(d)*	*(e)*
91	1	1	6%	20%
93	1	0	6%	0%
96	1	0	6%	0%
97	1	3	6%	60%
101	1	0	6%	0%
102	1	0	6%	0%
103	1	0	6%	0%
105	1	0	6%	0%
106	1	0	6%	0%
110	1	0	6%	0%
111	1	0	6%	0%
114	1	0	6%	0%
120	1	1	6%	20%
126	1	1	6%	20%
127	1	0	6%	0%
100	0	0	0%	0%

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