Fall 2012

An analysis of the incidence of Antibiotic Resistant Infections in the state of New Hampshire

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Abstract

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The organism Methicillin Resistant *Staphylococcus aureus* (MRSA) was selected as the focus of study because of abundant current research and regulated monitoring of this organism in healthcare organizations. Data about the incidence rates of MRSA in theUnited States was collected from reports disseminated by the Center for Disease Control (CDC). Information about the number of healthcare-associated infections in the state of New Hampshire was provided by the State Department of Health, and two hospitals contacted offered information on the number of MRSA isolates recorded.

The national data revealed that the overall trend is a significant decrease in the number of cases of MRSA. Statewide data collection also showed reduced numbers of healthcare-associated infections. The data from individual hospitals reveal steady, very low grade infection rates.

The major conclusion of this research endeavor is that current infection control plans and procedures, including standard and specialized precautions and innovative and sometimes aggressive treatment plans, have a positive effect on infection rates. Though MRSA and other antibiotic-resistant infections remain an ever-looming threat, human innovation and effort can still bring one of the most major medical concerns of this era under control.

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Introduction

In any healthcare setting, a significant amount of time, energy and money is spent on infection control studies and procedures. There is much talk of healthcare-acquired infections, categorization of them, and stringent procedures and regulations regarding their control. One of the primary concerns of infection control departments is the rise of antibiotic-resistant bacterial infections; they have become a ubiquitous problem both in the healthcare setting and in the general population. Their causes emerge from natural selection and mutation and are strengthened by human misunderstanding of the purpose and function of antibiotics. Hope for control of this situation lies in public health campaigns, standardized infection control precautions, and research and development of new methods of prevention and treatment.

One of the most well-known antibiotic resistant infections is Methicillin Resistant *Staphylococcus aureus*, commonly referred to as MRSA. Hospitals around the country routinely screen for the presence of this bacterium and characterize its many strains. The purpose of this research endeavor is to explore the history and mechanisms of antibiotic resistance, to collect and process national and local records of cases of MRSA, and to study and evaluate methods of control and response to this threat.

The research was performed in two parts: part one scrutinized the scientific literature to discover the origin of antibiotic resistance, mechanisms of resistance, and the species of most concern. Inquiry into current response and methods of control was also performed.

As MRSA is an organism of highest interest, the second part involved data collection on national, state, and individual hospital levels regarding number of cases of MRSA and

its significance in terms of healthcare-associated infection rates. National data on rates of MRSA infection were collected and analyzed to provide a frame of reference and to emphasize the significance of this topic and its relation to all people. Data from the state of New Hampshire's Division of Health and Human Services was recorded to form a platform of comparison to the national data. Individual seacoast area hospitals were contacted as a function of geographic interest to further explore the climate of antibiotic resistance in the immediate area. Six Southern New Hampshire hospitals were contacted and records of infection rates were requested; any available data offered was accepted and names of contributing hospitals were removed from analysis to prevent any implication of bias. Two hospitals agreed to participate under these conditions, and the rest declined, citing restrictions on the release of data collected for internal surveillance. All information provided was analyzed in the context of discovering the true prevalence of MRSA in our healthcare environment.

III. Background Research

1. Defining Antibiotic Resistance

In the 1940's, a brand new drug was introduced that held high promise for a disease-free world. Antibiotics, originally discovered by Alexander Fleming in 1928, were the cure to common infections that in those days killed (Hani.) Their widespread use caught on quickly, and by the 1950's, an unsettling trend developed. Certain bacteria which had been effectively treated by penicillin were no longer susceptible to the drug. This trend was described as antibiotic resistance, the loss of sensitivity of a microorganism to an antimicrobial drug ("Antimicrobial Resistance",WHO). Bacteria reproduce quickly and therefore, have the ability to change rapidly and to reduce the effectiveness of the drugs designed to stop or slow their growth. They then pass on those genes to future generations, propagating the resistance ("About Antimicrobial Resistance", CDC.)

Antibiotic resistance is now a worldwide concern that has arisen from long-term and widespread use of antibiotics. The World Health Organization has outlined some of the major causes of antimicrobial resistance. On a global level, the rise in antibiotic-resistant microorganisms is due to a lack of commitment to comprehensive response to disease, poor accountability within communities about antibiotic use, negligible surveillance, inadequate quality assurance for all areas of the world, inappropriate use of medicines, poor infection control, and insufficient research and development of new drugs ("Antimicrobial Resistance", WHO). In the United States, the largest contributors to antimicrobial resistance are inappropriate use of antibiotics, such as taking them when they are not needed (for prevention of infection or to treat viral illness) or failing to complete a course of antibiotics as prescribed, which selects for resistant organisms. In

addition, antibiotic use is heavier in hospitals, as doctors may prescribe antibiotics before a diagnosis is made to prevent an infection from reaching crisis level in a patient before cultures can be completed ("Antimicrobial (Drug) Resistance: Causes"). This creates a centralized environment in which resistance can arise and proliferate.

This increasing trend is problematic because infection with resistant organisms results in longer hospital stays, more expensive treatments and higher risk of death. Second- or third-line antibiotics are frequently used, which may have more side effects and higher toxicity ("About Antimicrobial Resistance", CDC.) Worldwide, antibiotic resistance reduces the control of infectious diseases, meaning that resistant bacteria may be spread more easily. With reduced disease control, major progress that has been made in medical technology is jeopardized. For example, surgery, organ transplantation, and cancer treatments are riskier procedures because it leaves people more susceptible to infection ("Antimicrobial Resistance", WHO.) In fact, the emergence of bacteria that is resistant to all available antibiotics, sometimes referred to as "superbugs", threatens all technology in the treatment of infections ("Antimicrobial Resistance", WHO.)

2.   Mechanisms

In order to understand how bacteria evade the influence of antibiotic drugs, it is important to know how antibiotics work. Antibiotics work to either kill bacteria outright or to hamper growth to the point where the human immune system can eliminate what is left. To kill bacteria, an antibiotic must damage the cell wall or vital organelles. To inhibit growth, an antibiotic must interfere with protein production, DNA replication, or cellular metabolism (Goering 479.)

Many classes of antibiotics are defined by the way in which they attack bacterial cells. Penicillins and other β-lactams such as penicillin derivatives and cephalosporins, kill bacteria by binding to penicillin-binding proteins and inhibiting an enzyme involved in the cross-linking of peptidoglycan in Gram-positive organisms, creating gaps in the cell wall (Goering 485.) Vancomycin and other glycopeptide antibiotics also attack peptidoglycan, but instead it binds to D-alanine-D-alanine chains of growing peptidoglycan to prevent cross-linking (Goering 489, Gilroy, "Discovery".)

The cytoplasmic membrane of bacterial cells is also a target for antimicrobial drugs. Polymyxins, though only used as oral antibiotics in rare occasions, break down the phospholipid bilayer structure of bacterial membranes (Goering 502.) Also, Lipopeptides such as Daptomycin depolarize the membrane, preventing the synthesis of ATP and absorption of nutrients in the cell. It is currently used against resistant organisms such as Methicillin-resistant *Staphylococci* and Vancomycin-resistant *Enterococci*, and shows little evidence that organism are developing resistance to it (Goering 502.)

Other mechanisms of bacterial inhibition include binding to the 30s ribosomes,
blocking formylmethionyl-transfer RNA or aminoacyl transfer RNA from approaching
the ribosome and beginning translation of RNA into protein. This is the mode of
operation of Aminoglycosides such as gentamicin or streptomycin and Tetracyclines
(Goering 491-492.) Translation can also be stopped at the 50s ribosomal subunit by the
Macrolide antibiotics such as azithromycin and erythromycin, lincosamides such as
clindamycin, streptogramins, and oxazolidinones. The drugs bind to the 23s ribosomal
RNA, preventing transfer RNA from being released from the ribosome (Goering 496.)

Nucleic acid can also be a target for antimicrobial treatment, and it can be attacked in
different ways. Replication is targeted by Fluoroquinolones (ciprofloxacin, levofloxacin,
etc.) by preventing DNA gyrase from regulating the supercoiling of DNA at the site of
the replication fork (Goering 498). Rifamycins such as Rifampin also attack nucleic acid
by binding RNA polymerase to block transcription (Goering 499.) Another old class of
drugs making a resurgence in infection treatment are the Sulfonamides, which prevent the
synthesis of nucleic acids by interfering with the synthesis of tetrahydrofolic acid, a
critical part of the nucleic acid bases. The drugs provide competitive inhibition in the
folate synthesis pathway's enzyme dihydropteroate synthetase (DHPS) (Goering 500.)
Trimethoprim is a drug commonly used with the sulfonamides to combat resistance, as it
also inhibits folate synthesis but stops dihydrofolate reductase closer to the end of the
pathway (Goering 501.)

A revolutionary new study performed by MIT and Boston University in 2007 resulted
in a major breakthrough in the way that antibiotic function is viewed. James Collins, BU
biomedical engineering professor and Graham Walker, MIT biology professor, proved

that β-lactams, amioglycosides, and quinolones all produce hydroxyl radicals that are the origin of their antibiotic activity. Hydroxyl radicals are extremely reactive molecules that will oxidize proteins, lipids, and DNA upon contact. In particular, the radicals damage guanine in DNA, activating a repair enzyme called DinB, which incorporates the altered guanine and base-pairs it with both cytosine and adenine in new DNA strands. As pairing guanine with adenine is incorrect, this produces defective DNA that cannot encode the proteins to make a successful living cell. If the oxidized guanine actually makes it into mRNA, as can happen with aminoglycoside antibiotics, the proteins produced work incorrectly and make more hydroxyl radicals to do more damage. In addition, more repair enzymes called MutY and MutM excise DNA for removal of oxidized guanine and repair. With high incorporation of defective guanine, there may be so many cuts in the DNA that both strands break, providing another means to destroy the bacteria's DNA (Trafton.)

The frequency with which reports of antibiotic-resistant infections in hospitals and increasingly within our own communities are heard on the news begs the question of how this could happen. The production of enzymes that inactivate antimicrobial drugs, alteration of binding sites that results in reduced reactivity with drugs, changes in pathways to the target sites to prevent drugs from accessing their targets, and the evolution of efflux pumps to drive antimicrobials out of cells ("Antimicrobial (Drug) Resistance: Gonorrheae") are the basic mechanisms which all strains of bacteria have utilized (Goering 486-502.) Their development may be shared or the result of random mutation, and specific mechanisms may vary from organism to organism, or even strain to strain.

Essentially since the first use of antibiotics, bacteria have been adapting to enhance their survival. The first mechanism of resistance to β-lactams was the insertion of a gene known as *mecA*, which codes for an extra penicillin-binding protein that does not actually bind penicillin and therefore, will continue to synthesize functional peptidoglycan. Bacteria have also begun to produce enzymes called Beta-lactamases, which break down the beta-lactam ring and prevent the antibiotic from having any effect. Gram-negative cells have even developed resistance mechanisms, despite the fact that they are not the primary target of beta-lactams. Because Gram-negative cells lack the thick peptidoglycan layer of Gram-positive cells, the drug must filter through porins in the cell membrane to access the penicillin-binding proteins. Mutations that decrease the permeability of the porins prevent the drug from filtering through, and may disable non-beta-lactams that use the same mechanism as well (Goering 486.)

The latter of the last three mechanisms may account for Gram-negative bacteria's widespread resistance to the glycopeptides antibiotics. They may also have polypeptides ending in D-alanine-D-lactate or D-alanine-D-serine instead of the D-alanine-D-alanine that is required for glycopeptide binding. The genes responsible for this mutation have been found in studies of Vancomycin-resistant Enterococci. The genes are titled *vanA, vanB,* and *vanD* and encode for the abovementioned D-alanine-D-lactate. The *VanA* and *vanB* genes have been tracked to transposons and are of particular interest because of the easily communicable nature of transposon DNA. The *vanA* gene has already been found on plasmids that have inferred vancomycin resistance to strains of *Staphylococcus aureus* (Goering 489-490.)

Transposons are also responsible for rising resistance to aminoglycosides and tetracyclines. In aminoglycosides, mutation changes the 30s ribosome to prevent the antibiotic from binding. More significantly, transposons carry genes that encode enzymes which react with the drug, changing it to an inert form. For tetracyclines, transposons transfer genes for an efflux pump; when tetracycline is present in a cell, different membrane proteins are produced which pump the drug out of cells (Goering 494-495.)

Plasmids are easily transmissible pieces of DNA and are, therefore, a large factor in resistance. In macrolide-resistant cells, plasmids contain genes for an efflux pump similar to the one seen in tetracycline-resistant bacteria. They may also transmit the *erm* gene for a methylase enzyme which methylates two adenines in the 23S rRNA of the 50S ribosomal subunit and discourages its binding to macrolides. Bacteria also feature plasmid-encoded resistance to the sulfa drugs. The plasmid leads to the production of altered enzymes which decreases the cell's affinity for the drug (Goering 496-501.)

 In some cases, neither plasmid nor transposon-mediated resistance is documented, and traditional chromosomal resistance is documented. As chromosomal resistance can only be transferred generationally, it is not an ideal mechanism, but it has proven very effective against many antibiotics. Chromosomal resistance is the main mechanism of widespread resistance to the quinolone antibiotics. This is achieved through mutations that result in altered target enzymes or less permeable cell walls, which may display decreased drug uptake or an efflux pump. This same resistance pattern is seen in the polymyxins and rifampicins but can be present in any resistant bacteria (Goering 492-503.)

The mechanisms for antibiotic resistance must proliferate throughout the bacterial population (and therefore, the patient population) in order for a resistant organism to be detected on a clinical level. Many types of bacteria have short generation times, which favor the communication of resistance genes. Resistance genes usually develop as the result of a chance mutation in the transcription or translation of the cell's DNA during replication ("Antimicrobial (Drug) Resistance: Causes".) If the mutation leads to production of a protein that enacts some form of resistance, the gene that carries the new mutation will propagate, as microbes without the resistance will be eliminated by antibiotics and only the resistant survivors will reproduce. A series of mutations may alter a group of proteins and work synergistically in resistance and may be passed on in a set of genes known as an integron (Goering 481-483.) This can occur by transcription and translation of the new gene, transposons infiltrating DNA, or by horizontal gene transfer by plasmids, small pieces of extrachromosomal DNA that are passed on by contact ("Antimicrobial (Drug) Resistance: Causes".)

3. Specific Organisms

The variety and versatility of antibiotic-resistant organisms seen by national and global surveillance today is a major concern in both public health and health management forums. One of the earliest recorded resistant organisms was *Staphylococcus aureus*, which became resistant to penicillin in the early 1950's. By the 1960's it was resistant to methicillin, and MRSA was first seen in the United States in 1968. It is now resistant to all β-lactams, and is beginning to show resistance to vancomycin ("Antimicrobial (Drug) Resistance: MRSA".) It is hypothesized that vancomycin resistance may have been passed to other bacteria via vancomycin-resistant Enterococci, first reported in the 1980's. VRE alone constitutes approximately one-third of intensive care unit infections, and its ability to transmit resistance genes magnifies its threat ("Antimicrobial (Drug) Resistance: VRE".)

In community-acquired antibiotic resistant infections, a major concern is multi-drug resistant *Neisseria gonorrheae*. *N. gonorrheae* is now resistant to all classes of antibiotics except for the cephalosporins, and it is only a matter of time before its resistance increases. In addition, other species of *Neisseria* can easily become resistant as well; characteristically, *Neisseria* adsorbs DNA and plasmids from other species of bacteria particularly well. Its widespread nature in sexually active populations is cause for concern; combined with resistance to almost all available treatments, presents a recipe for disaster ("Antimicrobial (Drug) Resistance: Gonorrheae".)

On a global scale, there is much concern about the rise of drug-resistant Tuberculosis. Tuberculosis is the leading infectious killer in the world, accounting for approximately 2 million deaths. Tuberculosis is now commonly resistant to two of the first-line

treatments, rifampin and isoniazid, and may be known as MDR TB. In addition, XTB is

resistant to those two antibiotics and most of the second-line treatment options. Both are

extremely difficult to treat and can require months or years of combined antibiotic

therapy ("Tuberculosis".)

Within hospitals, *Klebsiella* species and *Pseudomonas aeruginosa* are on the rise as

serious nosocomial infections ("Antimicrobial (Drug) Resistance: Examples".) No

medical center is exempt from the threat of takeover by resistant bacteria. In fact, in June

of 2011, at Washington D.C.'s NIH Medical Center, a large medical facility associated

with the National Institutes of Health, a strange outbreak pattern associated with

carbapenemase-producing *Klebsiella pneumonia*e surfaced. Carbapenemase is a beta-

lactamaze enzyme produced by the bacteria that inactivates carbapenems, penicillins and

cephalosporins (Queenan.) The outbreak began with the transfer of one woman who was

known to carry the resistant *Klebsiella* to NIH Medical Center's Intensive Care Unit.

The woman was accommodated in standard contact isolation precautions, and all patients

in the ICU were regularly tested with nasal and groin swabs to monitor any potential

spread; none was noted. In about a month, the woman recovered and was discharged,

with no trace of the bacteria in hospital equipment or patients. Three weeks after the

former patient was discharged, another patient was discovered to have an infection with

the same bacteria, and another woman came down with it another week later. Soon, 17

more patients fell ill, and genetic sequencing revealed that all patients were infected with

the same strain (Neergaard.)

   After this revelation, the hospital adopted more stringent isolation precautions,

including building an additional wall to further separate the ICU from the rest of the

hospital and not allowing any person who did any kind of work in the ICU to work in any other area of the hospital. All patients regularly underwent more invasive swab testing to check for infection. Hospital workers were tested and never found to be carriers. Despite these additional precautions, at least one patient per week continued to succumb to the infection. Automated disinfection methods that dispensed disinfectant into even the smallest crevices of patient rooms were employed, and still the outbreak escaped the ICU to infect patients in completely unrelated areas of the hospital. This prompted the construction of a new isolation room and regular testing of all hospital inpatients, and still, the outbreak continued until December of 2011. All seven of the survivors of this deadly and concerning outbreak are still carriers of the resistant *Klebsiella pneumonia*e (Neergaard.)

   This outbreak is particularly alarming because the exact mode of transmission was never pinpointed. Resistance to decontamination methods or infection of the ventilation systems are possible mechanisms of spread. Although the organism was never cultured from swabs of healthcare workers' hands, it is possible that they were carrying it from patient to patient on their clothing. It is also possible that a combination of infection mechanisms were implicated, making it almost impossible to control the spread of infection. This outbreak was extremely difficult to contain, and the infection was never completely extinguished in the survivors. These facts pose a very threatening picture of the future of antibiotic resistance; this outrageous instance may very soon become a normal pattern for resistant outbreaks if new and effective infection control measures are not implemented (Neergaard.)

4. Response and Control

The World Health Organization has developed a plan in response to the rise of antibiotic resistant microorganisms. The WHO's plan emphasizes the importance of a concerted effort from policy-makers, medical practitioners, pharmacists, the pharmaceutical industry, patients, and the general public to create and uphold policies and practices in infection control and responsible use of antibiotics. The WHO recognizes that surveillance, guidance in the making of policies, generation of partnerships, and disease prevention and control programs are vital to the success of this plan. In addition, maintenance of quality, reliable supply, appropriate use of antibiotics and laboratory testing excellence is a major part of the response to resistance. Consistent use of universal precautions, personal protective equipment, and isolation precautions in the healthcare environment are also critical to prevent the spread of infection ("Antimicrobial Resistance", WHO.)

New research holds much promise for the development of new antibiotics that will be effective against resistant organisms, and is desperately needed in order to regain control of the current health situation. In one Notre Dame study, for example, testing of three new cephalosporin-type antibiotics has shown that they interact with penicillin-binding protein in MRSA, which is inactivated in cases of resistance, to restore its normal function and to allow normal antibiotic action (Gilroy, "NewAntibiotics".)

In reference to the previously-mentioned article concerning oxidized guanine as the basis of antibiotic action, additional research in that field revealed potential targets for new antibiotics. When the action of the aminoglycosides was studied, it was found that

this class of drugs induces the incorporation of oxidized guanine into mRNA, which results in non-functional proteins that produce more of the hydroxyl radicals, leading to greater levels of oxidized guanine in the cell. The outcome invariably is progressively faster cell dysfunction and death (Trafton.)

Inquisition into the tactics used by the cell to repair the damage of oxidized guanine, such as DNA excision and repair, showed that DNA-destroying double-strand breaks are common due to the extent of infiltration of oxidized guanine in the cell. The cell undergoes homologous recombination in an attempt to repair the double-strand breaks, providing a new opportunity for antimicrobial action: inhibition of homologous recombination. Blocking a cell's repair mechanism will make recovery from the damage of oxidized guanine impossible and will, therefore, increase antibiotic effectiveness (Trafton.)

The CDC also has an action plan in response to antimicrobial resistance with updated focus on surveillance, research, prevention and control, and new product development. The 2012 Update on "A Public Health Action Plan to Combat Antimicrobial Resistance" outlines the goals of improving characterization of drug-resistant infections and measuring the impact of antimicrobial drug use, continuing the development and implementation of strategies to prevent propagation of resistant infections and misuse of antibiotics, increasing research and studies of the emergence of resistant infections and the creation of new antimicrobial drugs, and developing new rapid diagnostic tests and vaccines. Within the report, action plans to implement all of these goals are outlined in detail and delegated to task forces within the CDC or to other organizations such as the FDA. The development and implementation of such action plans on a worldwide basis is

a major factor in a successful response to the newest plague of our world ("Public Health

Action Plan").

IV. Research Findings

1. CDC

A national surveillance effort by the Center for Disease Control and Prevention has amassed data representative of trends and patterns seen in MRSA on a countrywide scale. Each year a population sample consisting of 14,000 to 20,000 individuals from California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, and Tennessee was selected and monitored with standardized case reports to provide nationally representative data.

In 2005, the surveillance population consisted of 16,489,254 people from the above-mentioned states. Of the total, 1,601 cases were found to be healthcare-associated, hospital-onset, meaning that MRSA was cultured on or after the fourth day of hospitalization. From this representation, the national estimate of cases of MRSA with hospital-onset was 29,311, accounting for 2.64% of the overall estimated 111,345 healthcare-associated and community-associated cases. The incidence rate was 9.89 cases per 100,000 population.

In 2006, the population consisted of 14,954,451 individuals from the same states, and the number of hospital-onset cases was 1,353. The national estimate based on this distribution was 27,309 (2.50% of 108,345 overall cases) with an incidence of 9.03 cases per 100,000 population. In 2007, the population was 16,968,233 and 1,402 hospital-onset cases were reported. This was adjusted to 25,356 (2.47% of 102,672 overall cases) with an incidence of 8.41 cases of MRSA per 100,000 population.

In 2008, the population was 18,300,643 persons, with 1,298 hospital-onset cases. The adjusted estimate was 21,840 (2.28% of 95,872 overall cases) with incidence of 7.18

per 100,000 population. In 2009, the population was 19,311,576, and 1,198 hospital-onset cases were reported. The national estimate was 19,235 (2.14% of 89,867 cases) with an incidence of 6.27 cases per 100,000 population. In 2010, the population was 19,154,389 people with 970 cases of hospital-onset MRSA. The nationally adjusted estimate was 15,744 (1.92% of 82,042 cases) with an incidence of 5.10 cases per 100,000 population.

The data from the years 2005-2010 was graphed and linear regression was performed to visualize the significant decline in number of cases of MRSA over those years. The mean number of cases over this time period is 1304, and the standard deviation is 211. The graph is consistent with an overall steady decrease in the number of cases of MRSA from 1601 to 970.

Hospital-Onset Cases per Year (2005-2010)

$y = -1.06E+02x + 2.15E+05$
$R^2 = 8.88E-01$
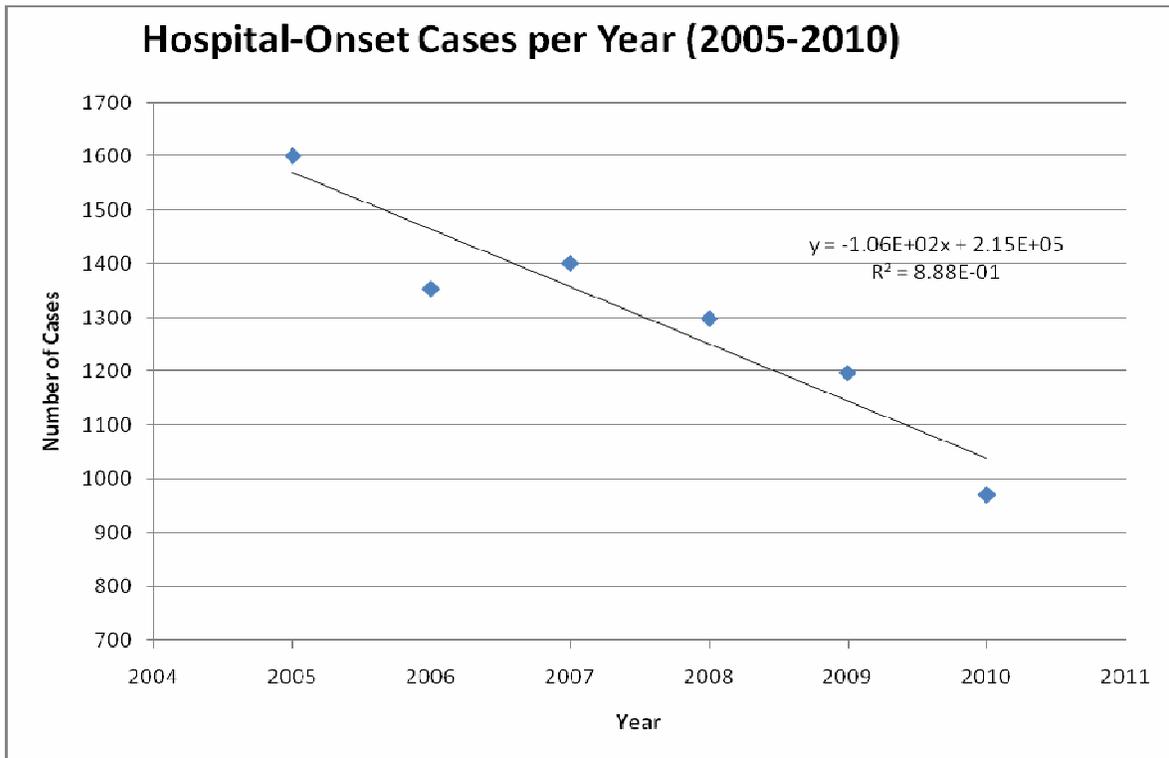
When this was translated to numbers representing actual estimates for the entire nation, the following linear correlation was found. The mean number of cases is 23,088 and the standard deviation is 5095. Over the five years studied, the number of cases decreased from 29,311 to 15, 744.

Estimated National Cases Per Year (2005-2010)

$y = -2.71E+03x + 5.46E+06$

$R^2 = 9.88E-01$
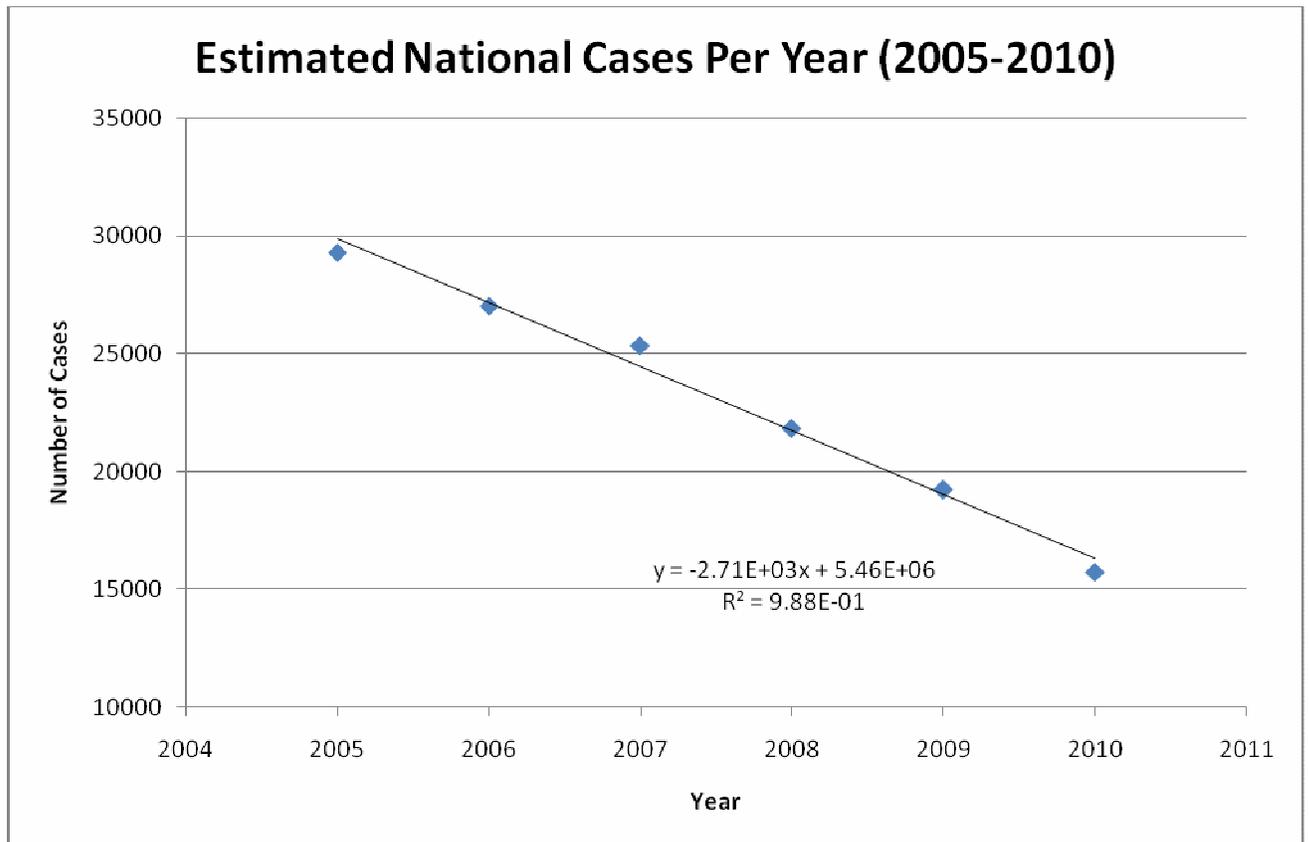
2. NH Department of Health and Human Services

The State of New Hampshire's Department of Health and Human Services provided its

2009 Report of NH Healthcare-associated Infections, which gives case data on all

healthcare-associated infections that occurred at all hospitals in New Hampshire. Darlene

Morse, RN, a member of the Bureau of Infectious Disease Control, stated that this is the

most comprehensive data about infection rates available at the state level, and that rates

of specific infections are not reportable to the State Health Department in the State of

New Hampshire. Reporting of healthcare-associated infection rates will connect the

broad national data to reports from individual seacoast area hospitals and serve as a frame

of reference with respect to hospital size and infection rate.

Throughout 2009, in all 26 New Hampshire acute care hospitals, only 134 healthcare

associated infections (as defined above by the CDC) were reported, 26% fewer infections

than the expected 180 defined by national rates. Of those 134 infections, 110 were

surgical-site infections, and 24 were associated with central lines (NH Healthcare

Infections Report.) Data gathered from voluntarily participating hospitals selected from

those mentioned in the report show that much less than 10% of these infections were due

to MRSA.

Within the state's report, data is represented as the actual numbers of cases recorded

and a Standardized Infection Ratio, which represents the comparison of the number of

cases occurred to the expected number of cases. Thus, an SIR of one means that the

number of actual and expected cases are equal, and an SIR of less than one means that

less cases than expected were recorded, and an SIR greater than one means that more cases than expected occurred (NH Healthcare Infections Report.)

Of the 26 hospitals recorded, six reported significantly lower numbers of infections than expected, and the rest were consistent with the predicted number of infections. The data table and graphical representation of results is included below. This information is important to understand before reviewing the findings of this study because it provides a context for the following analysis and a significant consideration in the analysis of rates of antibiotic-resistant infection.

The national data represent healthcare-associated cases of MRSA, meaning that the bacteria were acquired during hospitalization, and the state's data represent healthcare-acquired infections as well. Data acquired from participating hospitals represents all isolates, though not all isolates cause disease. It can, therefore, be surmised that the data from hospitals provides a more detailed analysis of the incidence of MRSA in the general population. National data is representative of the widespread incidence, the State of New Hampshire's data is evidence of the effects of this antibiotic-resistant bacteria, and the hospital reports present literal numbers of isolates found within their respective healthcare communities.

3. Local Hospital #1

Data from a small, local 100-bed hospital originates from yearly case reports collected by the infection control department and compiled based on culture isolates from the hospital only, and thus, represents an inpatient population. In 2006, 60 cases of MRSA were reported. In that year, 805 isolates of various species were screened for resistance to various antibiotics with varying levels of resistance resulting. In this hospital, MRSA represented 7.45% of these cases. In 2007, 91 cases of MRSA were isolated, 9.3 percent of 979 various isolates. In 2008, 133 cases of MRSA were found among 1089 isolates, representing 12.21% of isolates. In 2009, 121 cases of MRSA were reported from 1086 isolates, 11.14%. In 2010, 82 MRSA isolates were cultured from 1089 total isolates, 7.53%. In 2011 78 MRSA isolates were found among 1185 total isolates, 6.58%.

The graphical representation of these data shows a wide distribution of cases with a mean of 94 cases per year and a standard deviation of 28. Linear regression shows a very mild slope representing no significant increase or decrease in number of cases of MRSA due to the wide distribution of data points. The actual number of cases increased from 60 in 2006 to 78 in 2011, with very little significant change. The percentage of isolates that were found to be MRSA actually decreased from 7.45% to 6.58%, meaning that although slightly more cases were recorded, they represent less of all bacterial isolates from that hospital.

100-Bed Hospital Cases per Year

$y = 1.46E+00x - 2.83E+03$
$R^2 = 9.74E-03$
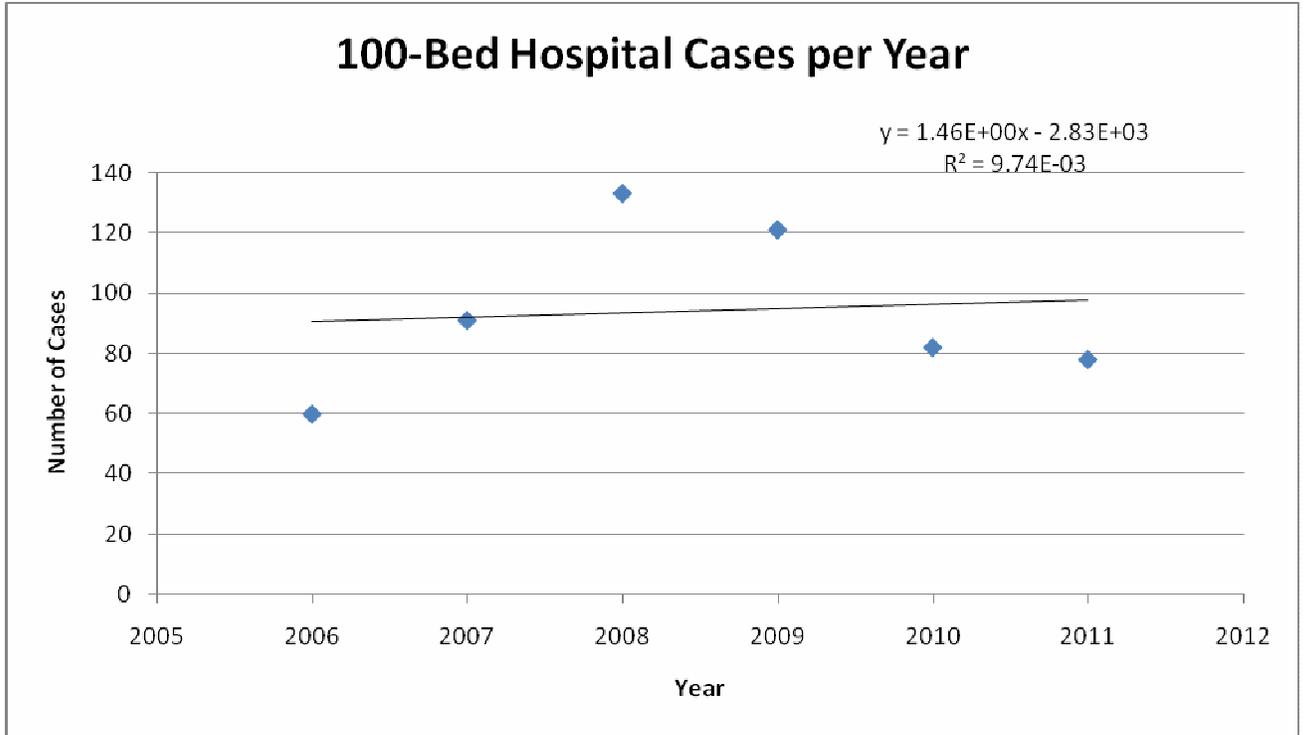
4. Local Hospital #2

A larger (330-bed) local hospital also submitted infection control and epidemiology

data in the same format as the 100-bed hospital. At this hospital in 2011, 5891 isolates of

various organisms were screened for resistance to varying antibiotics. Of the 5891

isolates, 507 tested positive for *Staphylococcus aureus*, and 235 of those also tested

positive for MRSA, 3.99% of all isolates. Although 46% of all *S. aureus* isolates were

MRSA, MRSA still represented only 3.99% of all isolates tested.

The following graphical representations show that although MRSA represented a very

small percentage of bacterial isolates, it represented almost half of all *Staphylococcus*

aureus infections. This statistic is of concern because it suggests that more and more

cases of *S. aureus* in hospitals are becoming antibiotic-resistant.
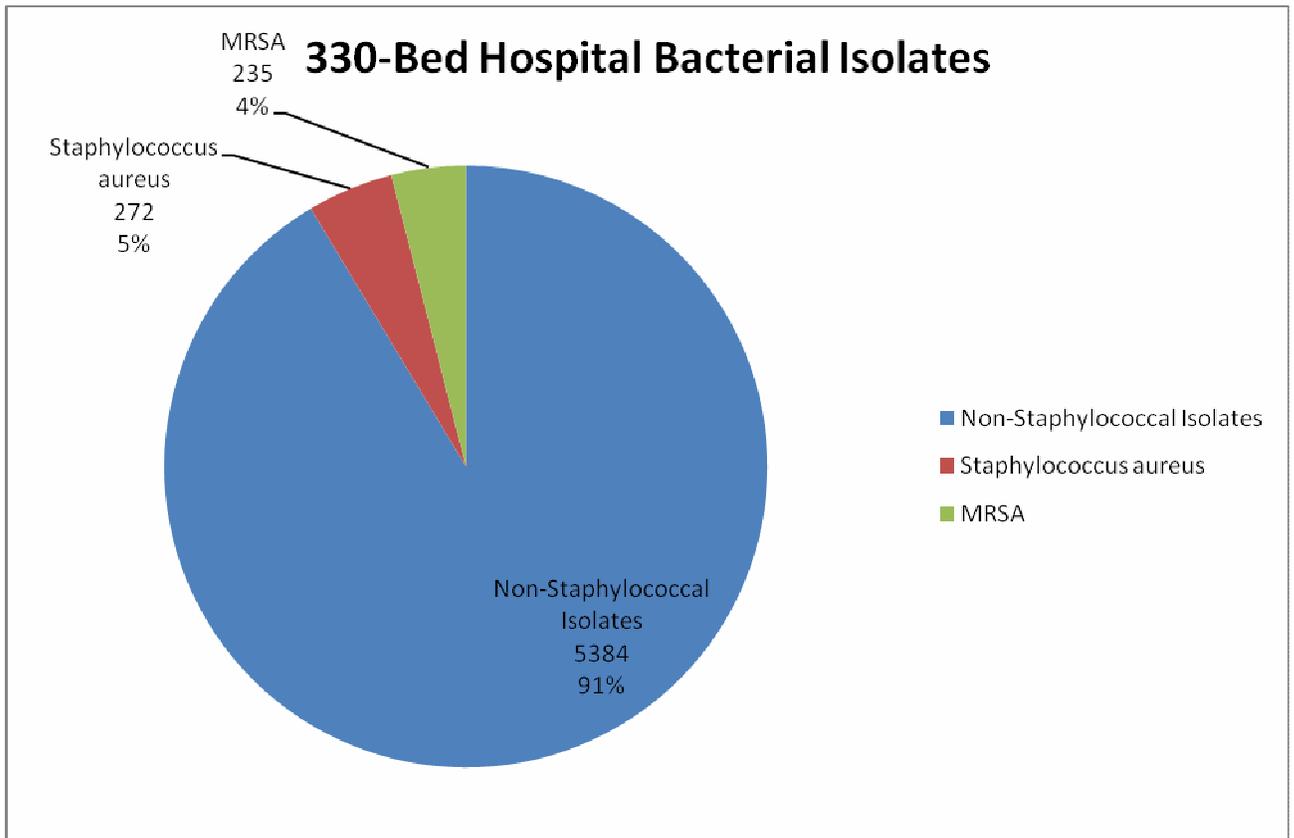
Staph Isolates (330-Bed Hospital)

MRSA
235
46%

Staphylococcus
aureus
272
54%

- Staphylococcus aureus
- MRSA
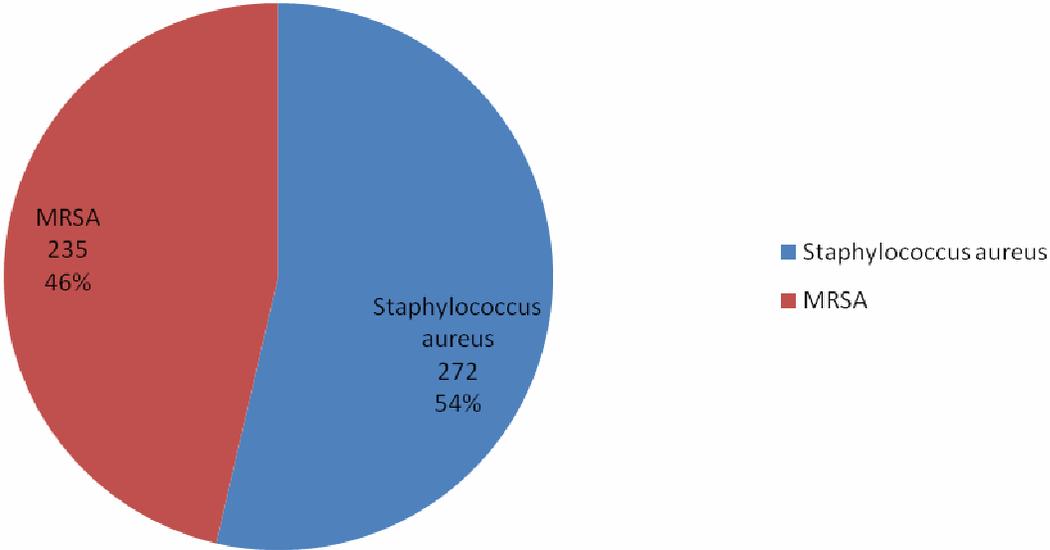
V. Conclusion

The threat of antibiotic resistance for the modern healthcare industry is a prominent and menacing reality. It is true that current medical technology is struggling to keep up with the many ways in which bacteria evade the strongest developed drugs and chemicals; they thrive in hidden corners of our bodies, environments, and even medically sterile locations. No place, person, race, sex, belief system, or amount of money can protect us; bacteria do not discriminate or spare anyone in their path. The only truly effective weapons we possess are our innate immune systems and the power of knowledge.

The research performed on national, state, and individual hospital levels has shown that our knowledge and organization of infection control protocols and measures has been effective in fighting one of the most prominent organisms, methicillin resistant *Staphylococcus aureus*. Though national rates of infection are still in the tens of thousands, there is a definite quantifiable decrease in the numbers of infections recorded over five years. State records reveal that 23% of hospitals had significantly lower infection rates than expected, and none significantly exceeded the expectation. Individual hospitals report steady low numbers of MRSA isolates over the past few years, although more cases of *S. aureus* infections are becoming resistant. The information from all sources is essentially in agreement.

Though antibiotic resistance is easily perpetuated across species of bacteria and absolute resistance is a reality in XTB and Vancomycin resistant *Enterococci* and *Staph aureus*, we gain an advantage by following standard precautions of infection prevention and improving education and compliance with antibiotic therapy. It will remain a tight

race as bacterial and human species coevolve, but the promise of new mechanisms to

fight infection keep hope of regaining control alive.