

**MRSA**  
**A GLOBAL THREAT**

THESIS

BY

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MRSA – A GLOBAL THREAT

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## ABSTRACT

Methicillin-resistant *Staphylococcus aureus* (MRSA) is the cause to some of the most common infections in the world. Its molecular distribution does not show the dissemination of one global strain. Studies show that, although community-acquired MRSA is more common in the United States, hospital-acquired MRSA still continues to be the most common pathogen around the world. Antibiotic resistance rates confirm that antibiotic availability is what continues to fuel the presence of MRSA. My experience abroad was a firsthand example of how the lack of resources in lower developed countries has affected the medical practice of physicians in those countries.

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I would especially like to thank Dr. Mihalic and Dr. Batteux for their tremendous support. They are the pillars on which this program has grown. My year would have been impossible without their guidance.

Finally, thank you to my family and friends for all their patience and love.

## DEDICATION

Para mi mami y mi cokes.

Son mi Corazon.

Los quiero mucho.

Gracias por siempre apoyarme y quererme tanto.

## INTRODUCTION

Whether you practice medicine in the western world or a lesser-developed country, your reality becomes the world you live in. The medications and options used to treat diseases and pathogens are a result of the population you are treating, the medications available, and the knowledge presented to the physicians in your region.

This fact became more apparent, last year, as I traveled through Europe, Africa, and Southeast Asia through the International Medicine Exchange Program at UT-Southwestern Medical School. I was fortunate enough to be one of two students chosen to study medicine abroad. The program consisted of six months of study in Paris, France and two three-month rotations in two lesser-developed countries. I completed Surgery and Dermatology rotations through Paris Descartes University at Cochin Hospital from July through December 2010. I participated in Emergency Medicine in Dakar, Senegal from January through March, and I finished with Infectious Diseases in Vientiane, Laos from April through June 2011. Once I was selected, I made a conscious decision to push myself academically and culturally. I wanted to experience the world. The contrasting cultures and environments of Senegal and Laos were instrumental in achieving my goal. Although I embarked upon my journey with an open mind, I could have not imagined how differently certain diseases were treated in different parts of the world.

In the United States, I do not believe one can practice medicine without being remarkably aware of methicillin-resistant *Staphylococcus aureus* (MRSA). Regardless of the specialty in question, this pathogen is a continuous nuisance and threat. Although it has been a common cause of infection in the hospital setting, it now accounts for more than 50% of staphylococcal infections in the community—making its existence more important than ever.<sup>1</sup> We have come to a point that if a patient is suspected of having a staphylococcal infection, most physicians automatically assume it to be MRSA. Defaulting to Vancomycin has become the



norm, with Daptomycin and Linezolid being used as common second-line treatments. Due to its prevalence in the U.S., I assumed it was a global hazard. The idea that it may not be global first surfaced in Senegal.

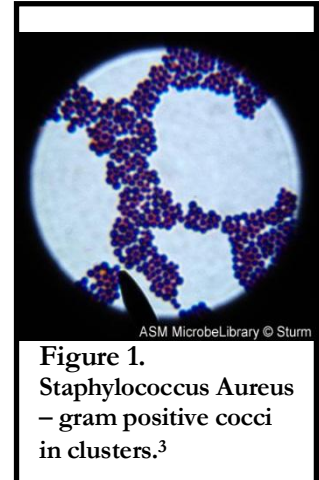
During a typical day in the Emergency Department at Hôpital Principal de Dakar, one patient, who had been dealing with a chronic lower-extremity wound infection, presented with symptoms concerning for septicemia. We started resuscitation procedures and drew blood for culture results. Typically, this patient would have been started on empiric antibacterial therapy, including Vancomycin for Gram positive coverage.<sup>2</sup> I asked the resident if their protocol included this antibiotic. I was told by the resident that they would be using Augmentin. This antibiotic was used on all gram-positive infections. Furthermore, MRSA was not a common pathogen in Senegal, so Vancomycin was not readily used or available. When I traveled to Southeast Asia for my last rotation, I was confronted with a similar scenario. My attending at Mahosot Hospital in Vientiane, Laos explained that the entire hospital would know if a patient presented with a MRSA infection. They did not have access to the antibiotics required to treat the pathogen.

How could a pathogen so prevalent in the United States, one of the most developed countries in the world with strict control over antibiotics, be almost irrelevant in countries where patients can buy any antibiotic at their leisure? It is not.

MRSA is prevalent throughout the world—due to a lack of education or resources, a larger threat.

## STAPHYLOCOCCUS AUREUS

*Staphylococcus aureus* (*S. aureus*) is the cause of the most common infections in the world; thus, it is an important pathogen in human diseases. It is the causative agent for skin, soft-tissue, muscular, respiratory, bone, joint, and endovascular diseases; in addition to life threatening conditions including bacteremia, necrotizing fasciitis, endocarditis, sepsis, and toxic shock syndrome.<sup>4-8</sup> The human body is a natural reservoir for this bacterium, and studies dating back as far as the 1950s have shown that the anterior nares are where it is routinely found. Carriers



can be divided into three groups: persistent, intermittent, and non-carriers. Persistent carriers usually carry only one strain and make up 20% of the population. About 60% of carriers harbor multiple strains of *S. aureus* for weeks at a time. They are characterized as intermittent carriers. The last group of individuals are categorized into persistent non-carriers and may yield negative cultures on repeat swabs over time.<sup>9</sup> If examined microscopically, *S. aureus* appears as a gram-positive cocci in clusters (Figure 1). It can be differentiated from other staphylococcal species by the gold pigmentation of colonies. Tests will be positive when examined for coagulase, mannitol-fermentation, and deoxyribonuclease activity.<sup>10</sup>

### RESISTANCE

Methicillin-resistant *S. aureus* (MRSA) was first discovered in London in 1961, two years after Methicillin was first introduced to the world.<sup>11-13</sup> By the 1980s, the first case in the U.S. was reported.<sup>14</sup>

The mechanism of action of antibiotics used for *S. aureus* infections is mainly focused on inhibiting its cell-wall synthesis. Peptidoglycan chains are the strongest structure in the cell wall and are transported extracellularly by lipid carriers present in the cytoplasmic membrane. Penicillin-binding protein (PBP) is the

enzyme responsible for linking newly formed peptidoglycan chains inside the cell. Beta-lactams covalently bind to PBP and inhibit cross-bridge formation of the peptidoglycan chains. Without a strong extracellular member, the cell ruptures, and *S. aureus* is no longer viable. Methicillin-resistant *S. aureus* produces a unique type of PBP, termed PBP2'. This protein has an extremely low affinity to beta-lactum antibiotics, allowing MRSA to continue cell-wall synthesis. It is known that MRSA acquired its resistance by acquisition of the *mecA* gene, which resides on Staphylococcal Cassette Chromosome *mec* (SCC*mec*), a mobile genetic element. The origin of this gene is still unknown. Nevertheless, it is partly through this element that most researchers characterize MRSA into phenotypes.<sup>15-22</sup>

#### HA-MRSA vs CA-MRSA

For many years, MRSA was an infection only associated to a hospital setting, invasive procedures such as urinary catheters, intra-arterial lines, or central venous lines, recent antibiotic use, or contact with health care workers. Hence, it became known as hospital-acquired MRSA or HA-MRSA.<sup>23</sup> Yet, in recent years, its prevalence has spread to the community. We no longer have to worry only about MRSA in hospital-related settings, we now have to deal with a widespread presence of community-acquired MRSA (CA-MRSA). First reported in the U.S. in the 1980s, CA-MRSA carries its own set of risk factors: participation in contact sports, close contact with athletic equipment, immunosuppression, crowded or low-hygiene living conditions.<sup>15,23,24</sup> Additionally, patients are considered to not have CA-MRSA unless they have a diagnosis of MRSA made in an outpatient setting or by a culture positive for MRSA within 48 hours after admission to the hospital, and do not have a medical history of MRSA infection or colonization, admission to a hospital or hospital-like facility, on dialysis, have undergone recent surgery, or have permanent medical devices.<sup>25</sup>

CA-MRSA is different from HA-MRSA in other ways. It is believed to be more virulent due to the exotoxin Pantone-Valentine leukocidin (PVL), allowing it to create pores in leukocytes. Although its relationship with PVL has been debated by some, this exotoxin is thought to be the reason why CA-MRSA is more often

associated with sepsis, necrotizing pneumonia, soft tissue, and skin infections.<sup>15,26</sup> It is actually estimated that 80-95% of CA-MRSA infections involve the skin and soft tissues; versus HA-MRSA, which is also linked to respiratory tract, urinary tract, and bloodstream infections.<sup>27-29</sup> Furthermore, studies show the majority of CA-MRSA strains contain the SCCmec IV and SCCmec V phenotypes. They are PVL positive; while HA-MRSA are more often comprised of SCCmec I-III.<sup>27,30,31</sup> In addition, when studied with pulsed-field gel electrophoresis, almost all CA-MRSA strains, in the United States, are from a single clone, USA 300 (ST8-IV).<sup>27,29,32,33</sup> Due to several molecular studies, as well as the fact that it is less resistant to antibiotics, experts believe that CA-MRSA is actually more like Methicillin-sensitive *S. aureus* and evolved simultaneously and independently of, HA-MRSA.<sup>34,35</sup>

However, CA-MRSA is becoming more and more common in the hospital setting, blurring the line between these two distinct causes of infection.<sup>29,36</sup>

## WORLD PREVALENCE

MRSA is not only present, it is growing throughout the world. Its prevalence ranges from 23.3% to 73%. Across the globe, it was found to be the most common cause of bacteremia, respiratory, and skin infections.<sup>37</sup> Its risk factors remain constant. In Malaysia, MRSA was most frequently isolated from orthopedic and surgical wards—evidence of its association with invasive procedures.<sup>38</sup> After extensive research, studies show that MRSA is not only present in disadvantaged regions, it is even more prevalent. In 1996, an international multicenter study showed that among the countries evaluated, S. Africa and Malaysia showed some of the highest rates of MRSA.<sup>41</sup>

## EUROPE

In Europe, the prevalence of MRSA is about 26%. The SENTRY program,

Variation in rates of methicillin resistance among <i>Staphylococcus aureus</i> isolates, by nation, at European SENTRY centers, 1997–1998.		
Nation <sup>a</sup>	No. of centers	No. of isolates (% resistant to methicillin)
Austria	1	117 (9.4)
Belgium	1	82 (25.6)
England	1	131 (27.5)
France	4	718 (21.4)
Germany	2	347 (4.9)
Greece	1	128 (34.4)
Italy	2	297 (50.5)
The Netherlands	1	147 (2.0)
Poland	2	159 (25.8)
Portugal	1	318 (54.4)
Spain	3	352 (19.3)
Switzerland	1	114 (1.8)
Turkey	1	104 (37.5)

<sup>a</sup> Only nations submitting  $\geq 50$  isolates are included.

Figure 2 - Prevalence of MRSA in Europe<sup>37</sup>

a study which collected 15,439 *S. aureus* isolates from all over the world from 1997-1999, showed that among the regions under investigation, Europe was the region with the most variation. Aside from demonstrating an increased rate from 12.8% in the early 1990s, this study also showed that MRSA rates were highest in countries from southern Europe (eg. Greece, Italy, Portugal, and Turkey), although Spain did not follow this trend (Figure 2).<sup>37,39</sup> In Finland, a country that was not included in the SENTRY program, the annual number of isolates

notified to their National Infectious Disease Register (NIDR) rose from 2.3 cases per 100 000 people in 1997 to 11.5 cases per 100 000 people in 2002. While this study did not calculate the prevalence of MRSA during that time, one can infer that

it most likely falls within the prevalence range of the northern European countries in the SENTRY program.<sup>40</sup> Yet, the focus of this paper was not set out to be that of the already known presence of MRSA in the developed world. This topic was chosen to evaluate the existence and prevalence of MRSA in lesser-developed countries, most notably those in Africa and Asia.

### AFRICA

One of the first cases reported in the continent was in S. Africa in 1978.<sup>42</sup> The same factors that aggravate the challenge of growing

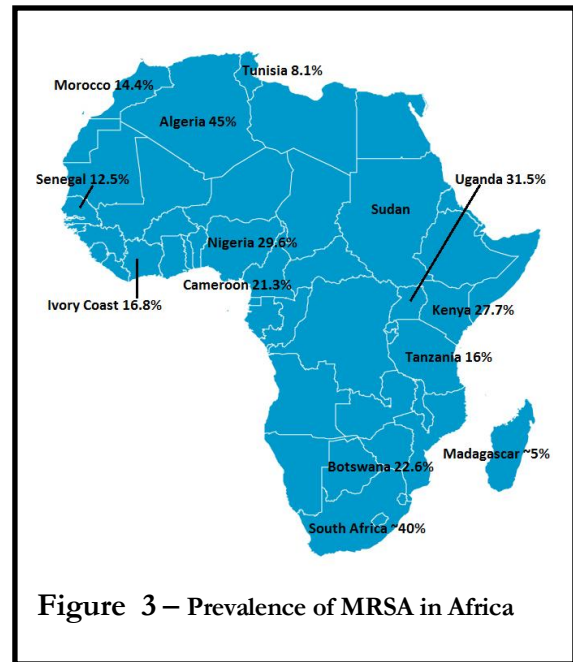


Figure 3 – Prevalence of MRSA in Africa

MRSA rates in the developed world, i.e. increasing antibiotic consumption, inadequate coverage, and inaccurate sensitivities are at work in Africa.<sup>43</sup> Figure 3 shows the prevalence rates found through the evaluation of articles for this scholarly work. The prevalence in Africa ranged from 5% to 45%.<sup>37,41,44-50</sup> In Sudan, MRSA was first reported in 1999;<sup>51</sup> the research there is so limited that

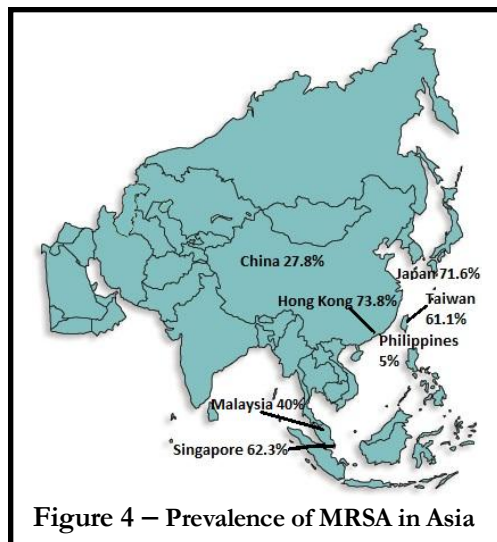


Figure 4 – Prevalence of MRSA in Asia

prevalence rates were not found. Madagascar did not report cases of MRSA until the 21st century; furthermore, an increase in rate has also been presented in this region.<sup>45,52,53</sup>

### ASIA

In the SENTRY program study discussed previously, the Asia-Pacific region that included Taiwan, Singapore, Japan, and Hong Kong showed the

highest rates at above 60%.<sup>37</sup> After analyzing 1,711 isolates the following year,

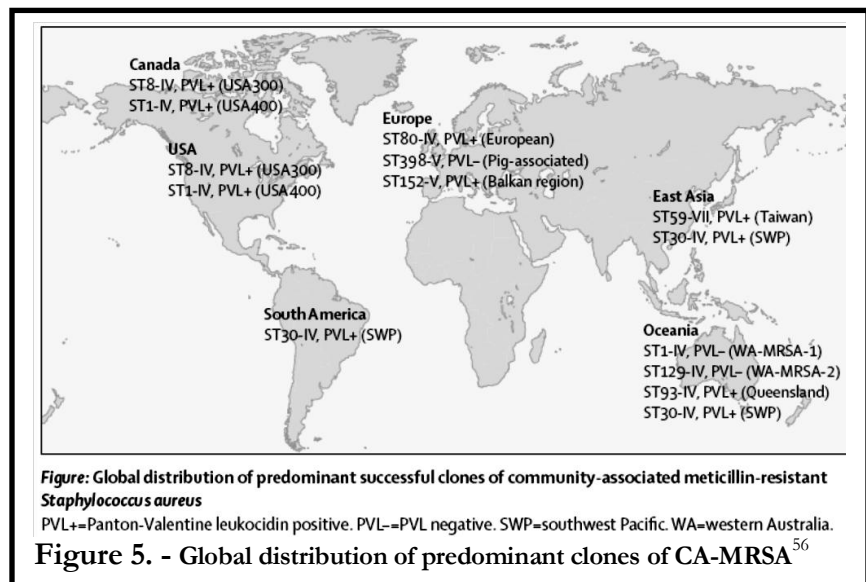
another SENTRY program that focused only on South East Asia and Africa showed a prevalence rate of 23.8%, 27.8%, and 5% from Australia, China, and the Philippines, respectively (Figure 4).<sup>54</sup> In Malaysia, the prevalence of MRSA grew from 17% in 1986 to 40% in 2000.<sup>55</sup>

It is no surprise there is limited data about the prevalence of MRSA in lesser-developed countries. The factors that play a role for this discrepancy will be explored in the Conclusion section of this paper.

### MOLECULAR DISTRIBUTION

Although it was interesting to see that MRSA has, in fact, spread throughout the world, the correlation of HA-MRSA and CA-MRSA to specific regions was also analyzed.

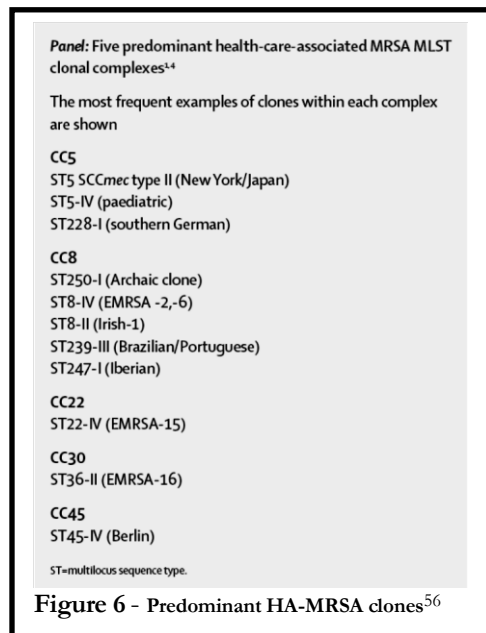
Multilocus sequence typing (MLST) is a technique in molecular biology used to characterize bacterial



species using DNA sequences of internal fragments of multiple housekeeping genes. Pulsed-field gel electrophoresis (PFGE) is considered the gold-standard; but this technique is often not used due to its time commitment and required experience. Although MLST is expensive and has a lesser discriminatory power than PFGE, its clear protocols and ability to be highly reproducible make it a favorite of researchers working on population genetics.<sup>57,58</sup> The majority of the studies under investigation for this paper used MLST and SCCmec phenotyping as parameters to identify MRSA clones, using the five major SCCmec phenotypes. SSCmec VI and VII have been recently discovered.<sup>59-63</sup>

USA300 was identified using PFGE, but can also be characterized by the MLST/SCCmec designation ST8-IV. In contrast to the U.S., where the majority of CA-MRSA is defined by the USA 300 and USA 400 (ST1-IV) strains, in Europe a greater amount of variability exists. ST80-IV, ST398-V, and ST152-V are the most common CA-MRSA strains, with ST80-IV being the most widespread. While the type IV SCCmec phenotype and PVL exotoxin are typically considered to be markers for CA-MRSA, there are exceptions.<sup>26</sup> ST398-V, for example, is PVL negative.<sup>56,64</sup> Throughout the world, ST8-IV (U.S.), ST80-IV (Europe), ST30-IV (Asia), and ST93-IV (Australia) are the most common CA-MRSA strains.<sup>31,64</sup> In Algeria, ST80-IV is considered to be the most prevalent clone in the country. It is responsible for 35.7% and 35.8% of community and hospital infections, respectively.<sup>47,65</sup> The same was true in Tunisia.<sup>66</sup> Figure 5 shows the global distribution of CA-MRSA. Countries in Africa were not included in the study from which the figure was acquired.

Despite the fact that ST80-IV seems to be the most dominant strain in Europe, hospital-acquired MRSA is still considered a greater burden than CA-MRSA.<sup>56</sup> This fact seems to be also true in South Africa, where five major clonal populations were identified, with only one being positive for PVL. ST612-IV was



the most widespread clone, but ST5-I, ST239-III, ST612-I, and ST36-II were also common. Although ST612 contained the type IV phenotype, it was still identified as being HA-MRSA, along with the other strains, which contained the typical HA-MRSA phenotypes, Type I-III.<sup>67</sup> MRSA strains in Malaysia were mostly SCCmec type III and PVL negative, but SCCmec type IV strains were also discovered. Of these, only two were PVL positive.<sup>35</sup> In an international study, which included 615



isolates from 11 Asian countries, it was observed that the majority of the strains belonged to ST239-III (in Saudi Arabia, India, Sri Lanka, Singapore, Indonesia, Thailand, Vietnam, Philippine, and China) and ST5-II (in Japan and Korea), both being known HA-MRSA clones.<sup>34,68</sup> Figure 6 demonstrates the five predominant clonal complexes of MRSA.<sup>56</sup>

As you may see, there is no clear worldwide distribution of MRSA. It has been demonstrated that CA-MRSA evolved independently of HA-MRSA, as described earlier, but molecular studies show that distinct clones of each also developed separately across the world. The diverse origins do not show a clear cut dissemination of one strain globally.<sup>31,64,69</sup> For now, it is postulated that each strain emerged spontaneously and locally.<sup>56</sup>

## RESISTANCE PATTERNS

In the United States, treatment options are directed by guidelines arranged using the best available data. In lesser-developed countries, the antibiotic available is what directs the type of treatment a patient receives.

CA-MRSA is the predominant type of MRSA in the U.S. Therefore, infections suspected of being caused by *S. aureus*, in an outpatient setting, are usually treated with the assumption that they are caused by this pathogen. Because the majority of CA-MRSA infections are resistant to beta lactams, fluoroquinolones, and macrolides, the Center for Disease Control (CDC) and Infectious Diseases Society of America (IDSA) recommend these infections be treated empirically with either oral Clindamycin, Doxycycline, or Bactrim. Oral Rifampin (used in combination therapy) and Linezolid are commonly recommended for invasive and complicated MRSA. In the hospital, bacteremia, endocarditis, osteomyelitis, pneumonia, meningitis, and brain abscesses are treated with IV Vancomycin, Daptomycin, Linezolid, and Clindamycin. In the United Kingdom, Teicoplanin is regularly used for patients who are intolerant of Vancomycin; but it is not available in the U.S. Furthermore, infections that fail treatment with the antibiotics mentioned above, are treated with combination therapy that includes intravenous Daptomycin with Rifampin, Linezolid, or Bactrim. Quinupristin/dalfopristin is commonly reserved as a last source of treatment for infections resistant to Vancomycin.<sup>2,25,70</sup>

Like most developed regions, Europe has treatment guidelines similar to the U.S.<sup>71</sup>, although small differences may exist. When the activity of selected antimicrobial agents was tested on *S. aureus* from European medical centers, Teicoplanin was found to be most active against *S. aureus*, with 100% susceptibility, compared to Linezolid (MIC 2mg/L), Vancomycin (MIC 1mg/L), and Daptomycin (MIC 0.5mg/L).<sup>71</sup>

When data was compared among antibiotics used to treat MRSA throughout the world, the U.S. and Europe demonstrated similar patterns. Figure 7 shows the

rate of resistance to selected antibiotics. The antibiotics included in Figure 7 were the ones most frequently used in resistance studies throughout the world.<sup>35,37,41,44,45,46,54,72,73,100</sup> Likewise, the rates of resistance were selected from the most current data available for each country and region.

Figure 7 - Worldwide antibiotic resistance patterns								
	Erythromycin	Gentamycin	Ciprofloxacin	Clindamycin	Bactrim	Chloramphenicol	Rifampin	Tetracycline
USA	92%	35%	88%	79%	26%	4.7%	7.7%	15.7%
Europe	87%	72%	90%	74%	23%	9.4%	44%	57%
Denmark	1%	0%	1%	0%			0%	3%
Norway	3%	0%	1%	1%			0%	3%
Sweden	3%	0%	4%	2%			0%	11%
Finland	4%	1%	8%	0%			1%	5%
Germany	13%	7%	9%	1%			1%	10%
Lithuania	22%	7%	8%	8%			0%	34%
France	24	4%	23%	6%			0%	11%
England	20%	11%	21%	10%			3%	10%
Spain	38%	26%	32%	30%			11%	19%
Belgium	42%	24%	30%	26%			5%	29%
Poland	29%	29%	26%	28%			17%	73%
Greece	70%	35%	64%	68%			25%	53%
Africa								
S. Africa	39%	35%	29%	39%			23%	34%
Botswana	+			+				+
Nigeria	69%	53%	79%		64%		78%	
Uganda	88%	58%	70%	82.4%	88%	88.2%		
Madagascar	33%	11%	14%		39%	23%	14%	75%
Asia	95%	74%	88%	79%	36%	96%	10%	82%
New Zealand	52%	2%	3%	1%			1%	1%
Australia	10%	0%	3%	0%			0%	2%
Malaysia	55-92%	48-76%	30-94%	2-18%	73%		12%	47-55%
Japan	+	+	+	+				+
Hong Kong	+	+	+	+				+
China	+	+	+	+				+
Thailand	94-96%			37-69%				

The countries in southern Europe showed the highest patterns of antibiotic resistance, confirming what was found in the SENTRY program in 2001. Africa and Asia showed antibiotic resistance patterns, on average, that were higher than in

the United States and Europe. This is most likely because in the majority of these countries, the antibiotics included in Figure 7 are the only ones available.

This hypothesis is supported by a study that analyzed the compliance to essential drug lists by countries from Europe, Latin America, Africa, and Asia. The World Health Organization's (WHO) Action Program on Essential Drugs provides a list of essential antibiotics needed for basic health care and infections. The WHO Action Program is "intended to aid decision-making on drug procurement and supply to serve the health care needs of the majority of the population." However, Fasehun shows there is only about 70% compliance to these lists. Yet, the antibiotics showing the highest resistance rates in Figure 7, like Erythromycin, Gentamycin, Tetracyclines, and Ciprofloxacin were the ones of which there was the most compliance. This demonstrates that they are the most widely available and used antibiotics in these regions, and the reason behind the high resistance rates. Cost, not surprisingly, was the most important factor behind non-compliance. Additionally, some of the antibiotics routinely used to treat frequently resistant bacteria, like MRSA, are restricted, for fear of widespread use, or need a specialty consult to be released, further perpetuating the cycle.<sup>74</sup>

Some of the rates, like the 79% resistance rate of Clindamycin may show a contraindication to the recommendations accepted in the U.S. and Europe for the treatment of MRSA. Then again, the guidelines mentioned previously were intended for the treatment of outpatient MRSA infections—CA-MRSA, which has been shown to have higher susceptibilities than HA-MRSA. The studies used to produce Figure 7 show rates of the resistance to antibiotics that were mostly calculated from MRSA isolates that were not differentiated at the molecular level. The majority of isolates were acquired from the hospital setting and from lesser-developed regions, both environments show a higher prevalence of HA-MRSA. Therefore, this discrepancy is most likely due to the Clindamycin resistance rate of HA-MRSA.

## VANCOMYCIN RESISTANCE

While the global presence and increased prevalence of MRSA may seem alarming, the main concern now is the dissemination of Vancomycin-resistant *S. aureus* (VRSA).

VRSA exerts its resistance by generating a thicker extracellular membrane and by producing a higher number of peptidoglycan monomers. Because glycopeptides, like Vancomycin and Teicoplanin, bind to these peptidoglycan monomers instead of the PBP enzyme beta lactams target, having a higher concentration of targets requires a higher concentration of antibiotic; hence a higher MIC.<sup>75</sup>

In May 1996, a four-month-old infant in Tokyo with a suspected MRSA infection failed treatment with Vancomycin. Subsequently, the patient received almost two months of combination treatment in order for the infection to subside. With a MIC > 8mg/L, this was the first case of Vancomycin intermediate *S. aureus* (VISA). Shortly after, this strain disseminated to hospitals across Japan.<sup>76,77</sup> In 1999, *S. aureus* resistance to Vancomycin was a reality.<sup>78</sup> By 2002, this nightmare reached the U.S. A swab was obtained from a catheter exit site from a Michigan resident that showed an infection caused by *S. aureus*. The minimum inhibitory concentration (MIC) for Vancomycin was greater than 32mg/L, which confirmed the presence of VRSA.<sup>79-81</sup> In the literature, there are also reports of a strain termed hetero-VRSA. Although not VRSA, it seems to generate VRSA cells at a high frequency within its cell population. It is thought to be the precursor stage of resistance to Vancomycin.<sup>75</sup>

First described in 1996, VISA, VRSA, and hetero-VRSA have subsequently been reported throughout the world. Cases have been described across Europe, Africa, and Asia.<sup>82-92</sup>

## CONCLUSION

My experience abroad provided insight into how the lack of education and resources has led to the continuous spread of MRSA. Still, the factors that have led to its dissemination throughout the world are distinct for different regions of the world.

One should be aware that the prevalence rates used were from articles that varied in number of isolates used for analysis, accuracy of results, and year of data collected. This discrepancy is due to the limited amount of data available for lesser-developed regions. Because resources are scarce in lesser-developed countries, funding for medical research becomes less of a priority. While there were multiple articles found analyzing the prevalence of MRSA in the U.S. and Europe, some of the prevalence rates reported in this paper were from one study for each country. One study reported results from a sample size of 12.

Europe's southern countries showed a higher prevalence of MRSA than its northern counterparts. In the lesser-developed regions examined in this paper, the frequency of MRSA was comparable between Europe and Africa. However, the rate of prevalence in some Asian countries surpassed both regions.

I believe the difference in prevalence rates are due to a variety of factors. In comparison to developed countries, where treatments of infection are based on sensibilities, or should be, antibiotics given in lesser-developed countries are mostly given based on empiric treatment and without sensibility testing or regulation. Regularly, antibiotics are given for generalized symptoms such as fever, nausea, myalgia, and headache. Of these, most are not adequately dosed or taken completely.<sup>93</sup> As in Dakar, laboratories are usually available in only the most urban of hospitals. However, at the district or rural level, the lack of resources and education sets that stage for substandard laboratories, with out-dated material in some of these areas, if they are existent at all. This is an important issue, well-structured and well-run laboratories are needed for proper diagnosis and surveillance.<sup>94</sup> Laboratories need to not only be in an appropriate space, they also

need the proper tools, supplies, and consumables required to run testing.<sup>95</sup> Resistance, at times, is only recognized when treatment for a suspected infection fails. Additionally, the drugs that are routinely used in the developed world for resistant pathogens are simply not available.<sup>96,97</sup>

On occasion, politics may present an obstacle to access of antibiotics that are recommended for treating MRSA and other infections. Even though organizations and developed countries try to provide aid, promotions by pharmaceuticals and an agenda based on monetary interests play the most important role in the type of antibiotics they provide.<sup>74,95</sup> Through my own experience and through research done in this field, it has become evident that cultural habits also impact the exponential growth of this problem. In Africa and Asia, antibiotics including ampicillin, penicillin, gentamycin, and cephalosporins are readily available, whether it be in make-shift “pharmacies”, at the corner store, or through “healers.” Although I was not confronted with this, a reflection paper in a well-known journal reported on the selling and administration of antibiotics by traveling “hawkers” in a town in Cameroon. They provided care for a fraction of the price demanded by the local hospital.<sup>93</sup> The culture in both regions also makes traditional healers a major part of daily life. Those not able to afford life in cities, the majority of the population, are usually restricted to the antibiotics provided by these important figures of their community.<sup>98</sup>

Control is more important in lesser-developed countries because increased resistance results in higher costs to treat infections. Those affected not only have to spend money, they do not have, but are not able to contribute to the productivity of their community, which ultimately can result in decreased productivity within that region.<sup>74</sup> In order to improve, the change needs to come from increased education, which would lead to better regulation and better laboratories.<sup>99</sup>

I believe these are some of the reasons why HA-MRSA is more common in Africa and Asia, whereas CA-MRSA is dominant in the U.S. The driving pressure that is antibiotic use, upon which HA-MRSA thrives, is present, and shows no sign

of dying down. Hopefully, a new antibiotic or breakthrough will emerge before VRSa becomes the next global challenge.



## *REFLECTION*

As I was boarding my final flight to Europe in July of 2010, I was hopeful, anxious, and scared. I was anxious that I was about to embark on one of the greatest journeys of my life. However, I was scared because I was jumping into the absolute unknown. I had prepared to the best of my abilities. Yet, in the end, all I had was I – and whatever wisdom I had attained in my 24 years of life. What if I failed miserably? Standing in line to handover my ticket, I had choice. I could turn around. I could go back to everything that was safe, to what was comfort. Or, I could just close my eyes, hold my breath, and jump.

That leap, will be what will define me from now until I take my last breathe. It has transformed me. It has turned me into who I have wanted to be my entire life, personally and academically.

I will remember my time abroad for the rest of my career. Going through medical school, you would always hear about the stories that had shaped the careers of countless physicians. You heard about the patients that affected them the most and the impact they had not only on their development as a physician, but on their life. Every time I heard one of those inspiring stories, I wondered which would be the patients that would shape my career. My curiosity would take me through different scenarios, which I thought would impact me the most. However, not even I could have envisioned the faces of my patients in Dakar and Vientiane.

No, it was not perfect. There were bad days; there were days that I felt petrified of what I was doing, days when I wondered whether I made the right decision in leaving what I knew behind. Although my time in Africa was the most challenging, it was my most treasured. It was daunting to arrive in Africa by myself and spend a week looking for a place to live, without knowing a soul. I had no choice but to adjust to the culture, almost instantly. I had no safety net there. French was the primary language, with English being the language of the very few. Furthermore, my time in the emergency department was emotionally grueling and brought tears to my eyes, at times. I had to watch a man, with his foot split in half,

wait for hours to simply receive medications for pain. I had to wrap a lifeless newborn baby in sheets because his mother lived too far away to receive any medical aid. I felt frustrated by the fact that I couldn't do more to help.

Yet, it was this same frustration that further inspired me to come back, finish residency, and be fully equipped to use my gift of medicine. I intend to use my fluency in Spanish and proficiency in French as an Emergency Medicine physician. My goal is to be able to use my clinical skills, ability to multitask, and international experience in an academic setting. Whether it is through research or clinical medicine, I will be back. I will be back and finally be able to use my abilities to fully aid those in need.

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