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Containing MRSA in the Age of Cannabinoid-Based Medicines

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Abstract

This disquisition mainly focuses on Methicillin-resistant *Staphylococcus Aureus* (MRSA) although the concepts discussed can be applied to nearly all strains of bacterial infections which have evolved defences to traditional approaches for treatment and containment. It begins with an overview of MRSA, including at-risk populations. Traditional approaches to preventing transmission of MRSA will be discussed, as well as why these approaches sometimes fail. A novel intervention protocol for treatment and containment of antibiotic-resistant infections will be proposed for both community and healthcare settings which is based on a multiple-faceted approach.

Keywords: Cannabinoid; Penicillin; Oxacillin; Methicillin

Introduction

It is not often a top federal health official for the US Centers for Disease Control and Prevention allows himself to be quoted using words like "nightmare" about an ailment, or utter the sentence, "*We have a very serious problem, and we need to sound an alarm*"[1]. However, this exactly what happened on March 5th of the year 2013. During a press conference, Dr. Thomas Frieden, Director of the US Centers for Disease Control and Prevention, announced that more than 70 strains of bacteria have become resistant to the "last-resort" family of antibiotics imipenem, meropenem, doripenem, and ertapenem, while sending a clear signal that the CDC is taking the drug-resistant bacteria problem seriously. As might be expected when discussing bacterial infections, national boundaries are not a deterrent. On the heels of that CDC announcement, the United Kingdom's Chief Medical Officer released a 152-page report in which she called antibacterial resistance a "catastrophic threat" that poses a national security risk as serious as terrorism, and that unless this resistance is curbed "*We will find ourselves in a health system not dissimilar to the early 19th century*" in which organ transplants, joint replacements, and even minor surgeries become life-threatening [2].

This disquisition will mainly focus on Methicillin-Resistant *Staphylococcus Aureus* (MRSA) although the concepts discussed can be applied to nearly all strains of bacterial infections which have evolved defenses to traditional approaches to treatment and containment. It will begin with an overview of MRSA, including at-risk populations. Traditional approaches to preventing transmission of MRSA will be discussed, as well as why these approaches sometimes fail. A novel intervention protocol for treatment and containment of antibiotic-resistant infections will be proposed for both community and healthcare settings which is based on a multiple-faceted approach.

Overview of Methicillin-resistant *Staphylococcus aureus* (MRSA)

MRSA is quite prevalent in hospitals and nursing homes, where people with weakened immune systems, open wounds and invasive medical devices like catheters tend to be at greater risk for infections of nosocomial origin. Hospitalized people and nursing home residents are often immunocompromised and therefore susceptible to bacterial infection of all kinds. It is not uncommon for surgical as well as nonsurgical wounds to become infected with MRSA and 49 to 65 percent of healthcare-associated *S. aureus* infections reported to National Healthcare Safety Network (NHSN) are caused by methicillin-resistant strains [3]. These result in a mortality rate between 28 percent to 38 percent [4].

MRSA is being contracted increasingly frequently outside of healthcare settings and has become quite common in community settings. Particularly common is what are termed community-acquired outbreaks which are frequently being reported in an increasing number of populations including children in daycare facilities, prison inmates, patrons of exercise facilities and locker rooms, and military recruits. Groups such as this do not possess the risk factors traditionally associated with MRSA infection. These include intravenous drug use and recent hospitalization or residence in a care facility, but share the common element of being crowded and confined, with poor hygiene practices proliferating. These elements put inhabitants at increased risk of contamination [5].

Traditional approaches to preventing transmission of MRSA

More than 39 million articles have been penned about techniques for preventing the spread of MRSA, and are somewhat neatly summarized in an article appropriately titled "*Prevent the Spread of MRSA." In this article, the following statement is made, "All the tools we need to prevent the spread of MRSA or any other multidrug-resistant organisms already exist*" [6]. After making this provocative and hopefully accurate assertion, the author then proceeds to claim that there is no need for special products or technology designed to combat the spread of multidrug-resistant organisms. The author justifies her stance against innovative approaches by citing a 2006 publication by the Centers for Disease Control and Prevention titled Guidelines for Management of Multidrug-Resistant Organisms in Healthcare Settings. As it was not included in the introduction part of this paper, the CDC has admitted that these traditional techniques are falling short in combatting the spread of MRSA as well as a plethora of

other multidrug-resistant organisms. An analysis of trends of antimicrobial resistance in twenty-three US hospitals between 1996 and 1999 found significant increases in the prevalence of resistant bacterial infections, including MRSA, oxacillin-resistant *Staphylococcus aureus*, ciprofloxacin-resistant *Pseudomonas aeruginosa*, and ciprofloxacin- or ofloxacin-resistant *Escherichia coli* [7].

The evidence indicates, and the CDC admits that traditional approaches are, if not failing, also not succeeding in getting the job done in combatting and containing the spread of these pesky multidrug-resistant pathogens. These bacterial infections are remarkably adaptable and enduring organisms. They appear to reinvent themselves, seemingly outwitting conventional antibiotics. *Staphylococcus*, especially in its methicillin-resistant form (MRSA), continues to pose to our healthcare facilities, public institutions, and communities an increasing burden of boils, abscesses of all sizes and locations, as well as potentially fatal sepsis, endocarditis, necrotizing fasciitis and pneumonia [8].

Why traditional approaches fail

Methicillin-resistant *Staphylococcus aureus* is genetically distinct from other strains of *Staphylococcus aureus* in that it is responsible for many difficult-to-treat infections in humans because through natural evolutionary mechanisms (horizontal gene transfer, natural selection, multiple drug resistance) it has become immune to beta-lactam which are the most widely used group of antibiotics. Typical examples of these antibiotics include Penicillin, oxacillin, and methicillin, in which the penams contain a β-lactam ring fused to a five-membered ring, where one of the atoms in the ring is sulfur, and the ring is fully saturated [9].

The time it takes to produce new medicines is not the only factor contributing to the human animal's difficulty in rising to this evolutionary challenge. Healthcare professionals now consider *Staphylococcus aureus* a threat not only in healthcare settings but to the community environment as well. Before the availability of antibiotics, invasive bacterial infections were often fatal, but the introduction of penicillin in the 1940s dramatically improved survival. Although penicillinase-producing strains soon emerged, methicillin and other penicillinase-stable β-lactam agents filled the breach. This success also resulted in a one molecule attack strategy for combatting bacterial infections. The development of new antibacterial medicines is a slow, arduous process and the paradigm the pharmaceutical industry has established inhibits success [10].

Subversion of the dominant paradigm

MRSA should no longer be considered an exclusively nosocomial originating pathogen but has become epidemic within communities. Harbor-UCLA Medical Center conducted a molecular analysis of five available strains of MRSA within a fifteen-month period which indicated community origins. Investigators from the CDC provide compelling evidence from studies conducted in Baltimore, Atlanta, and Minnesota that between eight percent and twenty percent of MRSA outbreaks originated in community settings [11].

Ironically, the emergence of the MRSA into community settings has the potential to lead to the pathogen's demise. Communities can employ CAM approaches to health issues that hospitals are bureaucratically forbidden to allow. Coupled with this, the paradigm established by the pharmaceutical companies restricts them to attacking the bacterium with an individual molecule. Hospitals have adopted the same paradigm because it is usually successful. Analogous to Newtonian physics which is usually successful, a paradigm shift was required when researchers began to apply it to subatomic particles. From an evolutionary perspective, societal transformations are now providing the elements necessary for a Kuhnian paradigm shift in pharmaceutical approaches. Traditionally, bacterial infections are attacked pharmacologically through utilization of a one molecule approach. Research has repeatedly demonstrated this attack strategy becomes ineffective over time because bacteria reproduce so rapidly they evolve genetic mutations capable of defending themselves against the molecule. The dual-pronged protocol being proposed represents a medicinal paradigm shift analogous to the shift from Newtonian physics to quantum mechanics because it entails an organic rather than synthetic approach to containing bacterial infections, even so-called "superbugs" such as *Staphylococcus aureus*. This change in paradigm is necessary because pharmacological approaches to containing the spread of drug-resistant bacteria have proved to be largely ineffective.

A community-based approach to MRSA eradication

It might be disconcerting for people to learn that bacterial infections are ubiquitous in society. One of every three people entering a fitness center carry staph, and two percent carry MRSA. No data showing the total number of people who contract MRSA skin infections in community settings exist [12], but the CDC has acknowledged, traditional methods of preventing transmission must be community-based, and that innovative approaches need to be developed within both healthcare organizations and communities. However, traditional methods should not be abandoned simply because the tide is beginning to turn against humanity. This turn is a natural process of evolution and bacteria have an evolutionary advantage because they reproduce so quickly and therefore develop successful genetic modifications at a faster rate than humans. Unfortunately, humanity must rely on its intellect for survival, and at times the intellect of humans collectively impedes the evolutionary competitions in which humanity is engaged. Our struggle against bacteria has both physiological and psychological components, and societal struggles are interfering with both. Many of the traditional methods for attacking bacterial infections have value and should not be abandoned but to fight this war more effectively some adjustments will have to be made to humanity's attack strategies.

Other than medications which are continuously being developed, most of the protocols for containing bacterial infections were developed in the mid-1900s while some date back to well before the 1840s. Analyzing each of these protocols individually, it is apparent that new attack strategies need to be developed to ensure humanity's survival in this continuous evolutionary process. The protocols humanity employs in the US have been established by the Center for Disease Control and Prevention, and while they acknowledge the shortcomings, there is an inherent and evidence-based value in each. CDC recommends contact precautions when the facility considers MRSA to be of special clinical and epidemiologic significance. In most federally funded hospitals, where MRSA is ubiquitous, mandated protocols include appropriate patient placement, gloving, gowning, patient transport, patient-care equipment and environmental measures [13]. Given that the CDC has now admitted that these protocols are falling short in their goal of preventing the spread of MRSA within hospitals as well as the surrounding community, these protocols should

be analyzed individually to determine if modifications or additions might prove more effective.

Patient placement: The CDC recommends single patient rooms be assigned to patients with known or suspected MRSA infections. When single rooms are not available, patients infected with the same strains of MRSA should be housed together.

Gloving: Gloves should be worn whenever touching the patient's skin or surfaces and articles near the patient (e.g., medical equipment, bed rails).

Gowning: Proper attire should be worn upon entry into a patient's room or cubicle. Care should be taken to ensure that clothing and skin do not contact potentially contaminated environmental surfaces which could result in the possible transfer of microorganism to other patients or environmental surfaces.

Patient transport restrict: Transport and movement of patients outside of the room only for medically-necessary purposes.

Patient-care equipment and instruments/devices: When possible, use disposable medical patient-care equipment. If common use of equipment for multiple patients is unavoidable, clean and disinfect such equipment before use on another patient.

Environmental measures: Care should be taken to ensure that rooms of infected patients are cleaned and disinfected at least daily, focusing on frequently-touched surfaces such as bed rails, overbed table, bedside commode, lavatory surfaces, doorknobs, and equipment in the immediate vicinity of the patient.

Pharmacological approaches: Bacterial infections are attacked pharmacologically through utilization of Penicillin, oxacillin, or methicillin, clindamycin, daptomycin, linezolid (Zyvox), minocycline, tetracycline, trimethoprim-sulfamethoxazole, or vancomycin.

As the CDC has acknowledged, somewhere these protocols are insufficient. If they were not, humanity would not be in the "*nightmare scenario*" they described. In a war against organisms such as this, the only weapon humanity has evolved to fight with is its intellect. I agree with Lovato (ibid) when she so eloquently states, "*All the tools we need to prevent the spread of MRSA or any other multidrug-resistant organisms already exist.*" However, it is my position that humanity has been bureaucratically mandated not to use the tools. The six protocol components the CDC provided are fine and brilliant as far as they go. However, it is now necessary for the sake of humanity's future for us to do something innovative. Creativity is the essence of science, and creativity and innovation are the tools necessary to defeat drug-resistant bacterial organisms.

Of the seven components of the MRSA containment protocol the CDC advises, three are open to creative innovation. The most obvious area to begin is the failure of the pharmaceutical industry has been having in combatting this, and other multidrug-resistant bacteria.

A multifaceted community-based approach to containing MRSA utilizing phytocannabinoids

Cannabinol, cannabigerol, cannabichromene, cannabidiol, and Δ9-tetrahydrocannabinol all demonstrate potent activity against all Methicillin-resistant *Staphylococcus aureus* (MRSA) strains of current clinical relevance. The molecular mechanism of this antibacterial activity is poorly understood because research on phytocannabinoids has been banned for nearly half-a-century. What is known is that these simple phenols demonstrate significant antimicrobial properties. From a molecular perspective, and to stay in compliance with the ban, we are forced to theorize that the resorcinol/benzenediol part of the phytocannabinoids serves as the antibacterial pharmacophore, with the alkyl, terpenoid, and carboxylic appendices modulating its activity. Given the abundance of *Cannabis sativa* strains in America which produce high concentrations of psychotropic phytocannabinoids, this plant represents a viable source of antibacterial agents to address the problem of multidrug resistance in MRSA and other pathogenic bacteria [14].

Rigorous trials on the use of cannabinoid molecules as systemic antibacterial agents are certainly warranted. However, these trials were forbidden in 1972. Trials cannot be conducted in the United States because all phytocannabinoid molecules were deemed schedule I drugs with no medicinal properties whatsoever. Thirty-two States have rejected this decree, and more states will surely join the rebellion, but most hospitals will not utilize the antibacterial properties inherent in phytocannabinoid molecules as doing so would jeopardize their federal funding. Major and minor research institutions are subject to the same constraints.

Many community organizations where MRSA proliferates do not receive federal funding and are therefore not subject to the onerous and unreasonable federal restrictions. The proposed protocol described is not designed to treat MRSA, although it will certainly be used to generate a cure when federal law allows. This protocol is merely designed as a two-pronged approach to keep MRSA from spreading within the community. It incorporates and adopts aspects of the protocol components set forth by the CDC while providing innovation in areas deemed insufficient. For example, a particularly compelling component of the CDC protocol entails ensuring that the community environment is cleaned and frequently disinfected, focusing on often-touched surfaces. The first component of the proposed protocol is comprised of an antibacterial liquid intended to be delivered in an aerosol form akin to Lysol but would likely be supplied in a pump bottle to be more environmentally friendly. Evidence suggests an organic ethyl acetate solution containing antibiotic phytocannabinoids and terpenes would act as a germicide and disinfect appropriate surfaces. Depending on the community setting, these include tabletops, floors, countertops, lavatory surfaces, doorknobs, and exercise equipment.

The second prong of this protocol can legally be used in federally funded healthcare organizations while still utilizing phytocannabinoids to attack MRSA and other drug-resistant pathogens from a variety of biomolecular fronts. Pathogens are spread by direct contact with the patient and by touching items that have been contaminated such as towels, hospital gowns, bed linens, and privacy curtains.

One of the most critical aspects of bacterial transfer is the ability of these infectious bacterial microorganisms to survive on these very common hospital surfaces. Cotton, polyethylene, and polyester and allow the pathogens to survive on these fabrics for months. Polyester is usually the material used in hospitals for privacy drapes. These are handled by both patients and staff when they are drawn around the patient's bed. *Staphylococcus aureus* survives for weeks to months on this fabric, indicating that such screens could serve as reservoirs for these bacteria, making these fabrics essentially vectors for the spread of *Enterococcal* or *Staphylococcal* organisms as a health care worker moves from one patient to another and their scrubs or lab coats contact different patients. Research has found that hemp fabrics kill bacteria, including pharmaceutical-resistant strains like MRSA.

In a study conducted on hemp-rayon fabric composites comprised of 60% hemp and 40% rayon, after the fabric was infected with staph, researchers found that the hemp material killed the staph bacteria at a rate that could only be described as incredible. The material was found to be 98.5% bacteria free upon measurement after 24 h. The same material was also infected with *Klebsiella pneumoniae* (pneumonia). At first measurement, the pneumonia-infected material was 65.1 percent bacteria free [15].

Summary

The entire dual-pronged approach for preventing the spread of MRSA and other drug-resistant pathogens cannot be implemented in institutions reliant on federal funding because the use of the antibacterial properties of phytocannabinoids was banned in 1972. However, many community organizations exist as privately-owned companies and reside in medical cannabis friendly states. Both prongs of this protocol can be implemented in these. For example, private gyms, golf courses, and exercise centers provide complimentary towels to the customers utilizing their locker-room facilities. As has already been discussed, 33 percent of the people entering these facilities carry the MRSA bacteria in with them. Providing hemp towels coupled with a phytocannabinoid-based disinfectant regimen provides a method of attacking pathogens within these community settings. Sports organizations like the International Boxing Federation which routinely lose fighters to staph could implement both prongs of this protocol, thereby protecting their fighters which make up a major portion of their financial expenditures.

Staph infections are common in athletes throughout the world. Locker rooms are a breeding ground for dangerous MRSA infections in the NFL, in the same season both Payton Manning and Tom Brady contracted staph infections. The list of NFL franchises that have battled MRSA infections is longer than of those which have not [16]. Theoretically, disinfecting locker rooms with antibacterial phytocannabinoids and terpenes in an ethyl alcohol base coupled with hemp uniforms and towels should lessen these outbreaks in states that are friendly to CBD products. At this time, the only NFL team that could not legally implement this germicide is the Kansas City Chiefs. Every organization could switch to hemp blend uniforms.

This is an area rife with research opportunities, but with rare exception, these opportunities are bureaucratically mandated to take place outside the United States. The protocol outlined is also economically infeasible because phytocannabinoid isolates are extremely expensive to produce. However, according to an analysis presented at the annual meeting of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), the annual nationwide cost to treat hospitalized patients with Methicillin-resistant *Staphylococcus aureus* (MRSA) infections was estimated in 2005 to be between 3.2 billion and 4.2 billion dollars annually [17-20].

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