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Antimicrobial Resistance in Vollum Anthrax: Current Status and Concerns

Eliana Martinez Sasson[1]

[1]London School of Hygiene and Tropical Medicine, University of London, London, ENG

INTRODUCTION

Antimicrobial resistance (AMR), when antimicrobial interventions no longer respond or are affected by antimicrobial therapies, occurs naturally over time through genetic mutations. The World Health Organization (WHO) estimates that bacterial AMR was responsible for 1.27 million deaths and implicated in 4.95 million deaths in 2019, particularly in lower-income countries that lack access to medication or alternative therapeutics, often linked to a lack of a sufficient healthcare system or difficulties in financing medical care.[1,2] This is seen even in higher-income countries, with infections of implanted valves and other interventions becoming riskier.[3] Although traditionally associated with nosocomial infections, there is increased community spread of AMR pathogens.[4] While the effects of AMR are seen globally, there is a higher disease burden shown in lower and middle-income countries.[5]

As such, the WHO has declared AMR a top global public health and development threat, with current action items including the prevention of infections that may result in unnecessary or overuse of antimicrobials, increasing global access to diagnostics and proper treatment of pathogens, and an increase in surveillance of AMR and the antimicrobial use in specific communities.[5] There is also a stated need for novel vaccines, diagnostics, and medicines.[5] Effective antimicrobial agents, novel and historical, will be tantamount to infection control and prevention. This is made difficult given the lack of research on AMR genes in specific pathogens of great concern, with some strains, such as Vollum Anthrax, having limited mutation screening studies or genetic analyses.

ANTHRAX

Despite the lack of person-to-person transmission, *Bacillus anthracis*, the bacterium responsible for anthrax infection, is not immune to AMR. Environmental spread still occurs, infecting at least 2,000 to 20,000 people per year and 20,000 to 100,000 animals, typically in endemic areas including sub-Saharan Africa and Asia.[6,7] An additional 1.8 billion people are considered at risk for anthrax infection, based on location or proximity to animal vectors.[6,7] Anthrax phages have been found in sewage, tanneries, and animal carcasses, even in non-endemic areas.[8,9] Strains of anthrax remain viable in the environment for over 200 years, causing certain locations to be associated with endemic infections.[10,11]

Anthrax infection can occur through four routes: cutaneous, ingestion, injection, and inhalation.[12] Cutaneous anthrax comprises the majority of cases; 95% of cases occurring in Africa are reported to be cutaneous.[13] Additionally, anthrax may spread person-to-person, though it is considered extremely rare and only through prolonged close contact, including breastfeeding, dressing wounds, or direct skin contact with infected blood.[12] Symptom onset is typically within 24 hours and two months post-exposure, with cutaneous anthrax presenting

Send correspondence to: ELIANASASSON@GMAIL.COM

with skin lesions that develop into a black ulcer at the site of infection.[12] Gastrointestinal anthrax, resulting from eating meat from an animal infected with anthrax, progresses with nausea, vomiting, abdominal pain, fever, and malaise, with severe disease characterized by hemorrhages, typically symptomatic as bloody diarrhea, intentional obstruction, and sepsis.[14] Inhalation anthrax occurs when aerosolized spores become deposited in the lungs.[15] Following a biphasic pattern, a shorter incubation period of up to six days is often observed, with the onset of myalgia, fatigue, non-productive cough, and fever occurring for approximately four days.[15] From then, symptoms may lessen before the second stage of infection begins, typically lasting 24 hours and resulting in death.[15]

Without treatment, the fatality rate for cutaneous infection is approximately 20%.[16] Gastrointestinal and inhalation anthrax are significantly more lethal, with fatality rates of over 50% and near total, respectively.[16-[1]] Treatment lowers the fatality rates of cutaneous anthrax to under 1%, and inhalation anthrax to approximately 45% with intensive and aggressive therapy.[17,18] However, regardless of modern intensive care, a 97% case-fatality rate was observed in patients who progressed to the fulminant phase.[19] Additionally, patients who developed meningoencephalitis had a fatality rate of 100%.[19] The high fatality rate and lack of person-to-person spread allow anthrax to be a potent bioterror weapon with the ability to target specific populations.

The main concern of anthrax is the potential for use in bioterrorism. The Centers for Disease Control and Prevention, National Institute of Allergy and Infectious Diseases, and Homeland Security categorize the pathogen as a Category A agent, along with smallpox (variola major), Tularemia, and the viral hemorrhagic fevers-filoviruses (Ebola, Marburg) and arenaviruses (Lassa, Machupo).[20] Unlike other diseases, person-to-person spread of anthrax is incredibly rare, with possible spread only through cutaneous infection.[12] However, anthrax occurs naturally, which can be easily modified or grown in a lab, and lasts for a significant period of time in the environment. Compared to other weapons, anthrax dissemination by a terror group would likely be a silent event, with the bacteria released inconspicuously into powders, sprays, food, or water.[18] Additionally, the spores may not be visible or have any odor or taste, increasing the possibility of undetected transmission.[12,16,21] Since there is minimal to no interpersonal transmission, anthrax can also be seen as a very effective "personalized" attack for a specific group without the risk of contagious or pathogenic vectors returning to the distributors, unlike a weaponized strain of influenza, which could have extensive impacts indiscriminately and transmit globally. Highly fatal without treatment, anthrax remains deadly even with treatment. More notably, anthrax has already been used as a bioweapon in the past and remains a likely agent of bioterrorism today.

ANTHRAX: VOLLUM STRAIN

Past experiments, such as in Gruinard Island, Scotland, have shown the persistence of anthrax spores. During World War II, Operation VEGETARIAN, an unused British biowarfare plan, was created to spread anthrax in Nazi Germany, led by Paul Fildes at Porton Down.[22,23] Through anthrax-infected linseed cakes spread in the German countryside, cattle and other animals would become infected with anthrax, leading to the mass death of cattle and humans who ate the meat or had environmental zoonotic infections.[23] Additionally, farms had to be abandoned during the massive food shortage, which caused further disruption and would impact the surviving German population.

Operation Overlord, also known as the Battle of Normandy, was deemed successful in June of 1944, shortly before preparations for Operation VEGETARIAN finished.[24] Scientists and military personnel were likely not overly concerned about the spread of AMR anthrax, arguing that germ warfare would allow for locations to be rendered uninhabitable for decades, and that the project and the militarization of anthrax were inexpensive compared to the atomic bomb.[23] For example, the linseed cakes were remarkably cheap, 12 to 15 shillings per thousand, with 5,273,400 cakes expected to be produced by April of 1943.[25] The operation would render the entirety of the German countryside uninhabitable for decades and risk the spread of anthrax-infected animals into British land. Nevertheless, the Chiefs of Staff asserted that biological weapons would be as devastating as the atomic bomb but "more humane," as the death of an entire population was not assured.[26] However, with the war ending, the Chiefs of Staff in the United Kingdom were of the opinion that biological warfare would need to be politically approved.

Despite not being pursued, decontamination was still an expensive and lengthy process for the Gruinard Island test site. Due to the testing, the island was quarantined for almost 50 years, until 1990.[21] Initially deemed too expensive and dangerous, the process involved over 280 tonnes of formaldehyde to be diluted by seawater to be spread over the 485 acres of testing ground, and soil was removed.[21,26] However, very shortly after, runoff containing formaldehyde and anthrax had a devastating effect on the local marine environment. Surveys from

2007 still report damage in intertidal organisms.[26]

The specific strain used in this bioweapon project is the 14578 Vollum strain (NCBI:txid261591; Bio ProSAMN02736982).[27,28] Beyond the United Kingdom, Vollum has also been used in the United States bioweapon programs at the US Army Biological Warfare Laboratory in Camp Detrick (now Fort Detrick, the current location of the United States Army Medical Research Institute of Infectious Diseases (USAMRIID)).[29] Beyond Europe and the United States, other actors also had biowarfare programs using the Vollum strain.

In the Gulf War, it was found that Iraq maintained stocks of Vollum strain for use in its bioweapons program, a direct violation of UN laws.[30] This was confirmed by UN biologists who tested waste samples from the facility, as well as the confession by Iraq, in 1995, that mass production of *B. anthracis* (as well as weaponized botulinum toxin and anthrax propellant) occurred.[30] Reports state that the focus was on deliberate procurement of the Vollum strain, and later weaponization through biological delivery systems, including missile warheads.[30] At the Al Muthanna site, it was determined that at least twenty-five warheads were filled with biological agents.[30] In the 1995 Iraqi Government Statements, it was stated that missile warheads and R-400 bombs were filled, with unmanned drone and spray-tank delivery systems in development.[31] It was confirmed that from December 1st to 23rd, 1990, 191 bombs and missile warheads were filled with 8,500 liters of concentrated *B. anthracis* at the Al Muthanna site.[30] Additionally, work with anthrax simulant *B. thuringiensis* was also evident at the Al Hakam test sites.[30] Due to the frequency and potential likelihood of future biowarfare efforts with Vollum, it is important to understand the specific AMR elements present in the genome, as well as preventative measures.

The Vollum strain is extremely virulent, and current vaccinations are often tested using the strain.[32] In 2016, a whole-genome Illumina sequence of 14578 Vollum was published by Los Alamos National Laboratory; the sample was received from USAMRIID. Recently, on April 6, 2024, the NCBI Prokaryotic Genome Annotation Pipeline computationally annotated the genome.

In-depth contig screening was conducted to determine the AMR status of the strain, using the Pathogen Detection Isolates Browser, developed by the NIH. For 14578 Vollum, nine resistant genes were found: bla2, bla, fosB2, satA, catA, fosB, lsa, mphL, and vat.[Table 1] Additionally, these results were confirmed using the NCBI Pathogen Detection Microbial Browser for Identification of Genetic and Genomic Elements (MicroBIGG-E) search.

TABLE 1. Summary of MicroBIGG-E and Pathogen Detection Isolates Browser Results, *Bacillus anthracis* str. Vollum, Isolate PDT000038063.2

Element	Element name	Class-Subclass	% Coverage	% Identity	Start	Stop	Strand
bla	class A beta-lactamase Bla1	BETA-LACTAM	100	100	1201337	1202275	+
bla2	BcII family subclass B1 metallo-beta-lactamase	BETA-LACTAM-CARBAPENEM	100	100	2090085	2090855	-
fosB	FosBx1 family fosfomycin resistance bacillithiol transferase	FOSFOMYCIN	100	89.13	789271	789687	+
fosB2	fosfomycin resistance bacillithiol transferase FosB2	FOSFOMYCIN	100	100	2651463	2651882	+
lsa	Lsa family ABC-F type ribosomal protection protein	LINCOSAMIDE/ STREPTOGRAMIN	100	82.52	1227858	1229336	-
mphL	macrolide 2'-phosphotransferase MphL	MACROLIDE	98.02	87.21	368022	368918	-
catA	type A chloramphenicol O-acetyltransferase	PHENICOL-CHLORAMPHENICOL	98.63	57.87	1119726	1120376	+

vat	Vat family streptogramin A O-acetyltransferase	STREPTOGRAMIN	98.1	66.67	1320690	1321322	+
satA	streptothricin N-acetyltransferase SatA	STREPTOTHRICIN	100	100	1806589	1807143	+

While not directly tested in the Vollum strain, the Ames Anthrax strain, used in the 2001 "Amerithrax" attacks, is also shown to have the same AMR genes bla and bla2.[33] In this strain, MIC testing and kinetic analyses found that bla1 is associated with penicillinase activity and bla2 with penicillinase, cephalosporins, and carbapenem-hydrolyzing ability.[33] As such, bla1 was found to effectively hydrolyze benzylpenicillin, ampicillin, amoxicillin, and piperacillin.[33] Additionally, there were measurable hydrolysis rates ($<0.2\ s^{-1}$) for cefepime, cefotaxime, cefoxitin, cefpodoxime, ceftazidime, ceftriaxone, and imipenem.[33] Further, bla1 demonstrated Km values of <70 μM for most of the tested penicillins, cephaloridine, and nitrocefin.[33] Due to the similarities in the strains, and the encoding of the same elements, it is hypothesized that Vollum may possess some level of penam resistance (bla) and penam, cephalosporin, and carbapenem resistance (bla2), all through antibiotic inactivation mechanisms, pending phenotypic confirmation.[Table 1; 33,34]

Fosfomycin resistance bacillithiol transferase, coded through elements FosB and FosB2, was also found in the Vollum sample, conferring resistance to the phosphonic acid antibiotic.[Table 1] Fosfomycin is a broad-spectrum antibiotic. While data is limited on the prevalence of FosB and FosB2 in *B. anthracis* strains, it is considered to be common among other gram-positive bacteria, including *Staphylococcus* and *Enterococcus* species, and *Bacillus subtilis*.[35] FosB and FosB2 protein homologs are found in *Bacillus anthracis, Bacillus cereus, and Bacillus thuringiensis*, at rates of 66.67%, 6.88%, and 9.25% in the NCBI whole genome shotgun library, respectively.[36] Recent evidence suggests that the adaptive conferment mechanism for environmental *B. anthracis* is likely due to phage-mediated mechanisms in the movement of the Fos gene in *B. anthracis*.[37]

Isa is a Lsa family ATP-binding cassette F (ABC-F type) ribosomal protection protein, often conferring lincosamide and streptogramin A resistance.[38, table 1] In methicillin-susceptible and methicillin-resistant Staphylococcus aureus, the Isa gene provides resistance to pleuromutilin antibiotics, as well as lincosamides and streptogramin A antibiotics.[39] Common examples of antibiotics that would not be effective include lincosamide clindamycin (common in veterinary medicine, as well), streptogramins A virginiamycin M_1, pristinamycin II_A, pristinamycin II_B, dalfopristin, pleuromutilins lefamulin, and retapamulin for human use, with valnemulin and tiamulin for animal use, particularly as poultry and swine medication.[39–41] The gene has 100% coverage of the one found in the Vollum strain, as well as over 80% identity, indicating that it is likely to display at least some of the resistance genes phenotypically.[Table 1]

Macrolide susceptibility is conferred through mphL, a macrolide 2'-phosphotransferase. As a chromosomally encoded macrolide phosphotransferase, common antibiotics are inactivated, including erythromycin, clarithromycin, and azithromycin, among other 14 and 15-membered macrolides.[42,43] Resistomes that show perfect matches are found in *Bacillus cereus* and *Bacillus thuringiensis* imperfect resistomes, such as with sequence variants, are found in *Bacillus anthracis* and in specific strains of *Bacillus cereus and Bacillus thuringiensis*.[42]

Present in the Vollum strain, catA functions by covalently attaching an acetyl group to chloramphenicol, from acetyl-CoA, preventing binding to ribosomes.[44] The histidine residue located in the C-terminal is largely responsible for the mechanism of action.[45] catA is considered common and is well characterized in *Salmonella typhi, Serratia marcescens, Shigella flexneri, Staphylococcus aureus, Staphylococcus haemolyticus, and Staphylococcus intermedius*, among many other bacteria.[46] Notably, the cat gene family, including catA, has not been well studied in *B. anthracis*.

The satA gene is also present in Vollum anthrax, conferring resistance to nucleoside antibiotics through antibiotic inactivation mechanisms, specifically the acylation of antibiotics. SatA, a streptothricin acetyltransferase, is present in *B. anthracis*, as well as in *Bacillus cereus* and *Bacillus thuringiensis*.[47,48] In the NCBI whole genome shotgun sequence library, 72.81% of *B. anthracis*, 3.39% of *Bacillus cereus,* and 1.22% of *Bacillus thuringiensis* samples show the gene or a protein homolog.[47]

Vat, Virginiamycin acetyltransferases, are present in the genome of Vollum (Figure 1). Inactivating virginiamycin-like antibiotics (such as) through enzymatically catalyzing a transferring acetyl group from acetyl-CoA to the

secondary alcohol on streptogramin A antibiotics, vatA confers resistance.[49] Commonly found in *Staphylococcus aureus*, and minorly in *Enterococcus faecalis* (0.04% of strains in the NCBI whole genome shotgun sequence library), there is no published research on the presence of this gene in *B. anthracis*.[49] However, resistance to streptogramin B antibiotics has been seen in a different strain, anthrax 590, conferred through ermJ.[50]

Further genomic screening was performed using the Comprehensive Antibiotic Resistance Database (CARD), created at McMaster University in Ontario, Canada, along with various other government agencies, including Canada's Institutes of Health Research, Natural Sciences, and Engineering Research Council, and the United Kingdom's Medical Research Council. The Resistance Gene Identifier function was used to screen the Vollum strain from USAMRIID and found many more resistance factors than the NCBI AMR search, which is likely due to do with the ability to include looser fits, rather than solely strict genome matches. Criteria were set to allow loose hits of e^{-10} or better, resulting in 2 perfect matches, 14 strict matches, and 375 loose matches when using the standardized algorithm settings. The high-fidelity, perfect and strict matches are described in the table below.

TABLE 2. Summary of Perfect and Strict Matches from CARD Resistance Gene Identifier

RGI criteria	Gene Family	Drug Class	Resistance Mechanism	% identity with Matching Region	% Length of Reference Sequence
Perfect	streptothricin acetyltransferase (SAT)	nucleoside antibiotic	antibiotic inactivation	100	100
Perfect	fosfomycin thiol transferase	phosphonic acid antibiotic	antibiotic inactivation	100	100
Strict	macrolide phosphotransferase (MPH)	macrolide antibiotic	antibiotic inactivation	87.21	98.35
Strict	fosfomycin thiol transferase	phosphonic acid antibiotic	antibiotic inactivation	89.13	100
Strict	vanY, glycopeptide resistance gene cluster	glycopeptide antibiotic	antibiotic target alteration	40	81.19
Strict	glycopeptide resistance gene cluster, vanT	glycopeptide antibiotic	antibiotic target alteration	34.38	57.3
Strict	class A Bacillus anthracis Bla beta-lactamase	penam	antibiotic inactivation	99.67	99.03
Strict	vanY, glycopeptide resistance gene cluster	glycopeptide antibiotic	antibiotic target alteration	35.14	104.29
Strict	tetracycline-resistant ribosomal protection protein	tetracycline antibiotic	antibiotic target protection	45.01	99.23
Strict	small multidrug resistance (SMR) antibiotic efflux pump	disinfecting agents and antiseptics	antibiotic efflux	39.25	112.15
Strict	subclass B1 Bacillus anthracis Bla beta-lactamase	carbapenem, cephalosporin, penam	antibiotic inactivation	99.61	100
Strict	vanW, glycopeptide resistance gene cluster	glycopeptide antibiotic	antibiotic target alteration	37.22	81.23
Strict	vanY, glycopeptide resistance gene cluster	glycopeptide antibiotic	antibiotic target alteration	34.87	96.64

Strict	vanY, glycopeptide resistance gene cluster	glycopeptide antibiotic	antibiotic target alteration	56.15	88.4
Strict	glycopeptide resistance gene cluster, vanT	glycopeptide antibiotic	antibiotic target alteration	30.6	54.63
Strict	vanW, glycopeptide resistance gene cluster	glycopeptide antibiotic	antibiotic target alteration	28.83	112.6

Furthermore, of the loose matches, the majority of the antibiotic resistance targets were found for fluoroquinolones (61), macrolides (60), peptides (58), glycopeptides (55), tetracyclines (51), aminoglycosides (38), phenicols (34), penams (26), cephalosporins (25), cephamycins (16), streptogramins (13), lincosamides (12), rifamycins (12), and aminocoumarin antibiotics (11), as well as disinfecting agents and antiseptics (31).
Interestingly, this search identified tetB (P), a tetracycline ribosomal protection protein that is located on the same operon as tetA(P), which gives resistance to tetracycline antibiotics through antibiotic target protection.[51] Specifically, this gene encodes for protection against tetracycline, doxycycline, minocycline, chlortetracycline, and oxytetracycline.[51] According to the NCBI whole genome shotgun database, tetB protein or homologs are present in *Paenibacillus mucilaginosus* (100% of strains), *Peptacetobacter hiranonis* (100% of strains), *Bacillus cereus* (84.25%), and *Bacillus thuringiensis* (88.48%), as well as in 77.63% of anthrax strains.[51] The tetB(P) finding is a Strict match with 45.01% identity, which is considered a strong, high-fidelity match, especially given the high 99.23% match with the reference sequence length.[Table 2] Considering the use of doxycycline as a first-line treatment and prophylaxis agent, the protein homolog present in a high percentage of anthrax strains is concerning.[52]

The wide variety of potential AMR genes in the Vollum strain is also concerning, particularly given the risks of further mutations and the potential for this strain to be utilized as a bioweapon. In the event of an anthrax outbreak, mass prophylaxis is typically indicated, with over 32,000 people undergoing prophylactic treatment for 60 days during the 2001 anthrax attacks.[53] Determining which medications are effective against the Vollum strain would prevent mistreatment of patients or ineffective prophylaxis among first responders and initial targets.

In all, it is clear that more testing is needed to confirm the resistance and susceptibility of the Vollum strain, rather than to fully rely on comparative genomics to describe the susceptibility of Vollum to common antimicrobial agents. Given the frequency and near-occurrences of bioweapon usage using Vollum, research would not only allow for better characterization of the *B. anthracis* genome, but also potentially elucidate more effective treatments in the event of a natural or intentional outbreak of the strain.

CLINICAL RESISTANCE CONSIDERATIONS

The first line of treatment and prophylaxis for anthrax exposures or illnesses is ciprofloxacin, in the fluoroquinolone drug class.[12] While the NCBI search did not identify any specific genes regarding fluoroquinolone resistance, the CARD search showed 61 individual elements that may confer resistance, including blt, a major facilitator superfamily (MFS) antibiotic efflux pump resistance mechanism, with 73.79% of the genome identity matching with 100.00% of the reference sequence length.[Table 2] Additionally, 10 of these genes have been proven to confer resistance to ciprofloxacin in *E. coli,* a common bacterium capable of horizontal gene transfer, prompting increased concern for wild derivatives of anthrax.[54, 62] Given the importance of ciprofloxacin in anthrax treatment, susceptibility testing should be conducted to ensure medications continue to work.

Since anthrax is extremely rare in humans, vaccination seems unnecessary except for select groups, such as laboratory personnel directly working with *B. anthracis*, certain military personnel, and some emergency or first responders.[12] Additionally, to reduce the need for routine vaccination, the anthrax vaccine is effective post-exposure.[55] The anthrax vaccine was historically successful in providing immunity to Vollum.[56] Recently, a novel anthrax vaccine underwent a lethal challenge using the Vollum strain in guinea pigs, with two doses providing a 100% survival rate.[57]

Given the risks of modified *B. anthracis*, vaccination stocks, such as in the Strategic National Stockpile, should continue to be renewed, as well as a variety of pharmaceutical agents if an antibiotic class is no longer effective. While the exact inventory is classified, it is stated that a vast assortment of antibiotics is present in the stockpile,

as well as over 28 million anthrax vaccines.[58,59]

FURTHER AMR POTENTIAL

Fortunately, gene editing and induction of mutations were not considered in most anthrax research until recently. With the development of bioengineering tools, such as CRISPR-Cas9, it would not be difficult to modify *B. anthracis* to be extensively drug-resistant, more than the Vollum strain already is.[60] High-level ciprofloxacin resistance has already been described in strains of anthrax.[61] While natural resistance to ciprofloxacin and doxycycline is currently understudied and subsequently under-documented, evidence has been provided to confirm conferment in vitro.

Currently, efflux-based ciprofloxacin resistance is characterized in anthrax strains and is further enhanced through mutations in the quinolone resistance-determining region (QRDR).[62] First-step mutants, with *gryA* QRDR mutations, resulted in a ciprofloxacin MIC of 0.5 µg/ml.[62] The majority (80%) of the identified first-step isolates showed a missense mutation of C254→T.[62] Two identified mutations conferred partial resistance to ciprofloxacin, both in the *gyrA* QRDR.[62] Further confirmation of increased resistance to ciprofloxacin was present in second-step mutants, with *parC* QRDR mutations, with MICs of 8 and 16 µg/ml.[62] Finally, third-step mutations were shown to be increasingly resistant with MICs of 32 and 64 µg/ml.[62] The MIC value of 64 was associated with mutations in the *gryA* QRDR or *gryB* QRDR.[62] Two additional mutations, compared with the first-step mutants, were seen in both *gryA* and *gryB*.[62] With the MIC cutoff of 0.25 µg/ml for ciprofloxacin susceptibility, all isolates confer some level of recognized susceptibility, often well over the required value, such as for third-step mutations.[63-1] As such, due to the extremely high MIC values reported, it can be assumed that a higher level of resistance to ciprofloxacin may be seen in these induced mutations.

Furthermore, resistance to tetracyclines has been observed in anthrax strains containing the pBC16 plasmid.[64,65] Tetracycline and doxycycline both had no therapeutic effects nor prophylactic ability against this strain.[65] Alternative therapeutics were used, with higher levels of minocycline shown to be somewhat effective. Interestingly, both doxycycline and minocycline are second-generation tetracyclines and display similar chemical structures, with minocycline containing differences at carbons 5 and 6, as well as an added dimethylamino group.[66] As such, minocycline has greater lipophilicity than other tetracyclines, possibly reducing the resistance seen in tetracycline-resistant strains.[67]

CONCLUSION

Given the resistance already present in the Vollum strain and the novel induction of resistance genes to first-line therapeutics like doxycycline, care must be taken to ensure proper pharmaceuticals and treatments are available. As anthrax is a likely agent for use in bioterrorism, further studies on the efficacy and susceptibility of common pharmaceutical products should be conducted to ensure protection from the growing threat of AMR.

1 The FDA has designated anthrax as an M45 organism, infrequently isolated or fastidious, concerning MIC value interpretation. Due to the lack of information, the susceptibility and resistance breakpoints are not well defined for anthrax, except for a few common antibiotics.

For doxycycline an MIC value less than or equal to 1µg/ml is sufficient to be categrized as susceptible. For fluoroquinolones ciprofloxacin and levofloxacin an MIC value less than or equal to 0.25 µg/ml can be considered susceptible. Finally, penicillin (including amoxicillin) values for susceptible and resistant are ≤0.12, and ≥0.25, respectively. The MIC required for susceptibility or resistance to any other medication is not defined for anthrax through the FDA.

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