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Project Proposal: Brucellosis-Syria

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-Brucellosis: Overview

Brucellosis spp. is the world's most widespread zoonosis and ranks as one of the seven most neglected diseases in the world according to the World Health Organization (WHO) ¹. Brucella has multiple subspecies, but the ones of most importance to human infections are associated with *B. abortus* (cattle), *B. melitensis* (sheep/goats), *B. suis* (swine), and *B. canis* (dogs). These four subspecies make up almost 90% of all human infections and are directly tied to the animals people work with ². Although brucellosis infections seem to have a relatively low overall global incidence of around 500,000 confirmed and reported cases per year, the actual numbers have been estimated to be closer to 5-12.5 million new cases per year ². This estimation is based on the symptoms of the disease likely being mistaken for the flu or a cold ². The infection generally affects humans that work in close association with animals, thus making it disproportionately associated with agriculture workers, those on lower economic standings, and ethnic minorities ³. Brucellosis affects these vulnerable populations the hardest, as the likelihood of them seeking medical care for apparently minor symptoms is relatively low. Vulnerable peoples are also disproportionately affected by the subsequent food insecurity as a consequence of the disease process in livestock.

Brucellosis is a gram negative, coccobacillus bacteria that is treatable in humans with 6-8 weeks of doxycycline with a 2% potential reoccurrence rate ⁴. The disease is considered a classical zoonosis, in which animals are the only source of infection. Transfer from person to person has only ever been demonstrated in laboratory settings, making

humans the true dead-end host for the bacteria ². Entry into the body for human infections occur through skin wounds, mucous membranes, inhalation, contact with animal birthing tissue, and from ingesting raw meat or unpasteurized dairy products. Clinical disease generally presents with flu-like symptoms such as fever, malaise, fatigue, headaches, and night sweats ⁵. The most important sequelae that occurs in 40% of the cases is osteoarticular symptoms resulting in lameness, painful joints (especially small bones), and inability to work or move properly for everyday functions ². The second most common sequelae affecting 4-8% of cases is orchitis & epididymitis in men and pelvic abscesses & salpingitis in women. These fertility impairments can perpetuate anywhere from 2-12 months, causing both chronic pain and infertility ². About 2% of clinical cases results in death, with 80% of these deaths attributed to Brucella associated endocarditis ².

How the disease affects animals is just as significant as direct human infections, especially to those living in impoverished or tumultuous regions of the world. In animals, brucellosis is a chronic disease and can perpetuate for years. From a production standpoint, livestock with active infections have low birth & growth rates, decreased milk production, high rates of abortion, increased feed to weight ratios, and occasional deaths from the disease. These problems can lead to loss of animals due to immediate slaughter, increased cost of production due to veterinary care & amount of feed, and loss of offspring leading to decrease in herd security. What this all equates to is a significant financial loss to the producer and a decrease in food security for the regional population. Brucellosis can survive in the soil for up to 100 days and is notorious for comingling with native ungulate populations. This situation can create continual reintroduction of the disease in a previously Brucella eradicated livestock herd. Cross infections and reintroduction patterns not only

affect the game within proximity to livestock, but the humans that are dependent upon the wildlife for food security as well ⁶.

-Brucellosis: Syria

Brucellosis has been an endemic disease within Syria for decades and accounts for the highest reported incidence worldwide with 200-350 tested positive cases a week ⁸. The incidence numbers have shown a steady decline since the start of the war in 2011 ⁸. This phenomena is not because of disease eradication protocols, but instead because of fewer reporting health facilities in war tattered regions of the country. When nationwide unrest and subsequent war broke out, the destabilization of the Syrian currency forced many people to revert back to traditional practices of using animals as a monetary and direct food source. Because of this occurrence, more of the population is currently in intimate contact with domesticated animals than ever before ⁸. Previous nationwide disease prevention practices and knowledge from the pre-war agriculture sector has gone by the wayside, as immediate survival for the people has become the most important aspect of everyday life. Low production of milk and meat in infected animals may subsequently force a hungry population to seek security elsewhere. People affected by the osteoarticular disease sequelae, are often unable to participate in rigorous labor. These vulnerable people become targeted by terrorist organizations through the offering of security of a stable food source, housing, protection, finances, and integration into a community (albeit a violent one) ⁹. Allowing the disease in the country to progress not only has a negative humanitarian effect, but also forces populations at risk into these extremist organizations, thus escalating the interregional and international conflict ⁹. Stabilization in animal health will positively influence the

population by helping to maintain a consistent and secure food source, prevent disease from directly infecting the people, prevent an increase in potential combatants and terrorists, and win over the hearts and minds of the people in conflict zones towards western intervention.

Brucellosis is known as an internationally reportable disease according to the World Health Organization for Animal Disease (OIE). The criteria to be classified for inclusion as a reportable disease is based on four factors; international spread is proven, reliable means of detection exists, natural transmission to humans is proven, and the most important factor is that at least one country has eradicated the disease within its borders ⁷. The importance of this criteria shows that with appropriate interventions, this disease has a potential to be eradicated from a region. This proposal will set forth a blueprint in an attempt to control or even eradicate the disease from the war-torn regions of the Syrian landscape with utilization of the proposed intervention.

-Targeted Intervention: Syria - Conflict Zones

The conflict in Syria is constantly shifting and plagued with multiple proxy wars across its landscapes. For this proposal to be successful it will not be implemented as a countryside campaign or in pro-western controlled territories since these regions are now supported by direct humanitarian aid. Instead, this proposal will be integrated into high tension areas, conflict borders, and accessible towns in pro-government controlled regions held by either ISIS, Assad, Russian, or Iranian forces. Those that will be integrated into this proposal may be subjected to conflict and the utmost care must be imposed for their safety. The proposal will be broken down into six phases, all with individual goals and timeframes for completion.

-Phase 1: Investigation

The first phase of the proposal is called the investigation step. This step will not involve investigators in the field, but instead utilize a conglomeration of information compiled from existing resources. The likelihood of classified and unclassified surveillance or reconnaissance data being freshly generated for this proposal is nil, so we must rely on what we can access. The information will be provided to us through the U.S. Department of Defense, contractors, and partner nations. The records provided will give coordinates on villages, communities, and family settlements in direct contact with animal agriculture that fit specific criteria in the pro-government controlled regions. The criteria for intervention in the regions will include; proximity to known extremist organizations or under control of extremists, have been directly impacted by attacks or bombardments, high levels of poverty & hunger, and unknown alliances. The regions or communities that fit the criteria will be then implemented into the next phase of the proposal. This stage of the program will be the shortest of all phases with the end point being the provision of a detailed map of locations fitting the aforementioned criteria with an estimated time to completion of less than one month.

-Phase 2: Examination

The examination phase is the step that immediately follows the investigatory period. As we don't want to waste resources on communities that are minimally affected by brucellosis, we must direct our attention towards the hardest hit and/or most impoverished people. In order to do so, we will create a reconnaissance for disease prevalence in the region based on the information generated from the investigation step. This will then

produce a map of brucellosis for integration into the program. Eight teams, consisting of one veterinarian accompanied by one security detail, one assistant, and one interpreter, will enter the pro-Assad regions via western-aligned borders in the north, west, and east. The southern region will be avoided due to the rebel held territory being likely integrated with ISIS forces ¹⁰. For this phase, and all subsequent phases; contractors, soldiers, assistants, NGOs, and whoever else is integrated in the program will be required to be discrete through use of regional attire and utilization of civilian transport. Once teams are within the proposed territory, they will be directed towards the villages and regions of concern. The examiners will enter the selected communities with caution, if any sense of hostility is perceived they will be ordered to withdraw and that particular community will not be included for implementation of the proposed intervention. Once the examiners successfully enter these communities, they will meet with either animal owners or, if applicable, community leaders to discuss animal sampling. Complete transparency will be utilized through all discussions. The stakeholders will be informed that the proposed future efforts to help eradicate the disease in both animals and humans in their village will be done through outside intervention integrated with local community efforts. Once given the green light by the stakeholders, the examiners will get to work on gathering animal test subjects for serum testing. In normal circumstances, a herd ring sample will occur to test for brucellosis, which involves an unbiased approach to testing of animals. In this circumstance however, we will seek out the sickest looking animals for testing. The samples will be tested on-site using IDEXX serum ELISA tests, with the assumption that the brucellosis vaccine has not been utilized in any of these herds that could potentially cross react. Although these tests have been released only for experimental purposes and are not authorized for regulatory analysis, they consistently produce results at

87% specificity and 93% sensitivity ¹¹. With these sens/spec parameters we can assume, with enough confidence, that a positive test will signify an infected animal. For even more confidence, a positive test will flag that animal for a confirmatory serum agglutination test, which is more time intensive and will only be utilized for absolute confirmation. For this proposal if we achieve a single positive brucellosis ELISA test w/ agglutination confirmation sample in the herd, the likelihood of widespread infection is plausible and the testing will cease. The herd and associated community will then be earmarked for intervention by the program. Enough ELISA tests will be provided to the investigators to sample 5-10% of animal herds (bovine or caprine/ovine). The examination step will conclude when all teams return with results or within three months, whichever comes sooner.

-Phase 3: Activation

The third and most complex phase of the proposal is the activation phase. This phase, as the name implies, is where teams are activated to implement intervention measures in the infected regions or communities. This phase will also have one sub-phase within it; the implementation phase. The number of teams deployed will be dependent upon the quantity of communities or individual herds affected, as determined through the examination phase. This number is predicted to be somewhere between 10-20 communities within the country. The teams will consist of one physician, one nurse, one veterinarian, one veterinary assistant, one community developer, one bilingual educator, six assistants, three interpreters, and a security detail (2-5 individuals). The logistics involved will include bringing in actors from various sectors (DOD personnel, NGO's, & international volunteers) as well as adequate supply management. The medical teams will be likely drawn from

Doctors without Borders, the veterinary teams will be drawn from Veterinarians without Borders, Educational and community building teams will be drawn from USAID or their partners, and the security detail will be provided by DOD or contractors. We will reach out directly to these various organizations from our points of contacts to enact a call for volunteers. From the pool of people available, we will select the most applicable candidates based on pre-selected criteria of resiliency and skill based knowledge. Supplies, herd replacement fees, and salaries for this endeavor will be budgeted and paid for by this proposed program. Once teams have been chosen and entered the selected sites of intervention, the implementation sub-phase will begin. The implementation phase will have three fronts; education, human medicine, and animal medicine.

The educational front begins at the very start of implementation sub-phase and carries over to the next main phase; the integration phase. Before the human or animal medicine aspects begin their duties, the educators will initiate the process by meeting with either local leaders or animal stakeholders to initiate a shared campaign on brucellosis eradication. It is vital that everyone involved with animal production in these territories know about the disease, its ill effects on both humans & animals, and the negative consequences of it infecting their community. The educators will collaborate with the animal and human medical team members and the community developer in order to relay appropriate and accurate information. They will then integrate themselves with local educators, if available, to provide simple, fact-based information for brucellosis disease, treatment, and prevention measures. Integrating the local educators will, hopefully, provide continuity in the knowledge passed down throughout the region. The collaborative educational touch points will include, but are not limited to, brucellosis disease transmission & preventions measures, how the

disease is contracted, construction of physical barriers to disease, the symptoms of brucellosis & sequelae effects, treatment of the disease, effects on animals & food production, and how to eradicate the disease from the herd. Syria has a relatively high literacy rate of 83% according to the World Bank in 2022 ¹². As such, we should be able to utilize a multi-modality approach of images, words, speech, and videos to enhance and solidify the education on Brucellosis. Multi-modality forms of learning have been shown to enhance both knowledge and retention on subjects and will help the communities retain the lasting effects of this intervention ¹³. The educational front will also include the community developer working with the local population to teach modalities for barriers from animals and reduction methods in direct sharing of resources with the livestock. The training will be conducted every other day using a train-the-trainer format in order to spread the message beyond our direct impact. The training will continue in a community forum or one-on-one format until ~25% of the local population has been introduced to the topics. Attendance will be monetarily incentivized.

The human medicine front will consist of local medical pop-up clinics that will commence after the educational front has been initiated. These teams will integrate with local medical staff (doctors, nurses, etc), if available, to not only establish a cohesive relationship with them but provide them a salary for their services as well. It is important to stress that the medical team should not be taking away potential income sources from those currently trying to make a living in an already tumultuous region. The pop-up clinics will be acting as general wellness clinics with the transparent underlying intent to treat brucellosis. Information on these clinics will be relayed through the interpreters to community leaders to disseminate, as well as through flyers and posters strategically placed around the region.

The medical team will take samples from the symptomatic citizens who allow it in order to test for potential brucellosis infections. If those seeking medical attention choose to not be tested, but are displaying symptoms associated with brucellosis they will be offered antibiotics to treat their symptoms regardless. Although it is not standard of practice for the medical community to empirically treat without positive results, it is important to do so in this situation due to potential distrust in outside intervention and blood sampling. Declination of antibiotic therapy, however, is out of our control and will not be pushed upon unwilling folk. Since these clinics will be acting as general wellness clinics as well, we will provide basic preventive care, basic procedures, and generalized treatments for minor ailments. This clinic will not act as an alternative for primary care or heavy intervention. Instead, we will work with the community to help the citizens seek the care they require if their needs outweigh the capacity of our clinics. Education on brucellosis will be provided to everyone seeking medical care by the providers. However, the overall burden of community education and integration will be left to the education team.

Arguably the most important part of this phase, from an upstream public health standpoint, is through the veterinary groups. The veterinary teams are entering regions of known brucellosis in the herds. Brucellosis infections in animals have been shown time and again to be untreatable ¹. Because of this problem, the veterinary teams will be subjected with two choices of approach; complete herd eradication or cull individual infected animals based on testing. These choices will be dependent upon the reception and decision of the animal owners or stakeholders of the community in question. Under normal circumstances, complete herd eradication is the only proven way to eradicate the disease from a herd and/or region ³. In war ravaged areas however, these animals are an absolute vital asset

that provides food, clothing, and finances. Therefore, herd eradication without immediate replacement or restitution is out of the question. This ultimately leaves us with choices from a proposal standpoint. These choices are in how we, as an outside entity, provide reimbursement or replacement for the herds either eradicated or individual animals culled in this process. One choice would be to provide a complete herd or individual animal replacement from a known negative brucellosis producer based on information from those previously tested during the examination phase. If complete cull and or an individual animal replacement is chosen, the producer will receive a small financial incentive for the hassle. Another choice would be to provide direct financial compensation for each animal at 15-25% above market value for either the entirety of the herd or of an individual animal culled and direct them towards finding negative animal replacements, if they choose to do so. These decisions should be ultimately left upon the stakeholder. However, it is important to stress that this proposal's success is vital on the animal owner to make at least one of these decisions. This means that positive and neutral reinforcement tactics may need to be implemented and financial incentives may need to be increased. Once a decision is made by the stakeholder, the veterinary team will set up a veterinary pop-up clinic much like the human medicine team has done. This clinic will also implement local veterinarians, if available, to be integrated in the plan and compensated for their time. Including local community members, especially veterinarians and animal workers in this process will help increase trust of the people throughout the operation. Once the clinic is operational, it will have two functions depending on the stakeholder's decision; eradication and health. If the stakeholder chose eradication and replacement, the clinical operation will focus first on humane euthanasia of the infected herd with proper disposal (burning or deep burial). The

clinic would then focus on incoming animal health and screening for brucellosis of the new herd, if the stakeholder chose replacement instead of complete reimbursement. If the animal owner chose the alternative method of individual testing and animal replacement based on positive tests, the clinic would initially be set up and focus on individual brucellosis ELISA testing with serum agglutination confirmation, euthanasia, and disposal of animals on an individual basis. After the brucellosis problem had been dealt with, routine vaccinations (to include *Brucella* vaccine), dewormings, and antibiotic treatments will be done for the entirety of the remaining herd or incoming herd. Although animal health clinics are above the scope of only dealing with brucellosis, by offering health services to these communities' animals, we increase production values, worth of the animal, food production, and appear to be of worth to the community. This creates an overall positive effect for not only the health of the people, but the stability of the region. This will also reduce reluctance by the community when we return during the evaluation phase to re-test. In its entirety, the activation phase and implementation sub-phase of the program will last until the veterinary side has completed the herd health program with an estimated time frame of three months.

-Phase 4: Integration

After completion of both the veterinary and medical team's respective aspects of the program, they will depart the country. Left behind will be the educator, community developer, assistants, and security detail to carry out the fourth phase of the program; the integration phase. This phase will be utilized to ensure proper integration and protection measures within the community are implemented and sustained. The educator will hold regular seminars with incentives for attending. The seminars will include discussing testing of new

introductions into the herd, vaccination strategies, seeking care for illnesses in both animals and humans, and hygiene and protection measures during/after animal care. The community developer will continue to work with the leaders and stakeholders that are willing to accept help on building and maintaining animal barriers from direct human contact as well as contact with wildlife. The community developer will work on creating segregated water sources for animal use only. This phase ends when certain parameters are met, which include greater than 25% of the regional population educated on brucellosis, segregated wells are established, or until supplies and incentives are exhausted. The estimated time frame to completion is three to six months.

-Phase 5: Evaluation

The evaluation phase is designed to assess our impact on the community on a bi-annual basis after the final pull out of the integrators. Every six months a team consisting of one veterinarian, one assistant, and security detail will re-enter communities previously impacted by the project, if able. This will be an immediate evaluation for each site assessed, lasting no more than a week per location. Teams may enter the country to assess one or multiple sites at a time, depending on how timelines overlap. During the evaluation phase, the veterinary team will perform surveillance testing of the animals in the herd of the farm or community. Since all animals should be vaccinated at this point, the rapid serum ELISA test will not be used due to the number of false positives it could generate. The serum agglutination tests will be utilized and can be aggregated from herds then returned to headquarters for further analysis. This will be done in order to save time in the field and create more confident results from accredited reference laboratories. A positive test will

indicate a sentinel animal, and be a sign that the herd has possibly been re-infected. If all parameters were followed initially in the activation phase, the likelihood of widespread infection in a vaccinated herd would be minimal.

-Phase 6: Readjustment

A sentinel animal exposed will immediately trigger the final phase of the program, the readjustment phase. This stage is designed to utilize similar methods of herd management performed in the activation phase. This phase will activate one veterinarian, one veterinary assistant, one interpreter, one bi-lingual educator, and a security detail to re-enter the country and re-assess the positive herd. This phase is meant to be an immediate readjustment period, and should last no longer than 3 weeks for each potentially infected herd. The educator will begin the process by gathering stakeholders and discussing the situation and previous positive results gathered during the evaluation phase. After the information has been disseminated by the educator, the veterinary team will set up a pop-up clinic and begin mass reassessment of the animals using on-site agglutination tests. Positive animals will be culled and either replaced or the producer will be compensated appropriately. Vaccination boosters will then be administered regardless of previous vaccine status to all negative tested animals. The animal health clinic will be performed to include dewormings and vitamin injections in order for producers to see the immediate positive effects of our presence in their community. The readjustment phase will be on an as-needed basis dependent upon the bi-annual evaluation results.

-Sustainability

This program has the intention to make a lasting difference. Education passed through the community leaders and stakeholders will disseminate not only through the community, but potentially throughout multiple regions in the country. The positive effects seen directly through healthier citizens and through improved, faster growing animals will hopefully assist in this dissemination of this knowledge. The program itself, however, is designed to last no longer than 5 years or until the cessation of the war in Syria. The period of the evaluation and readjustment phases will be the longest of the phases, but will require the least amount of manpower and funds to do so. Bi-annual evaluations with potential subsequent readjustment will consist of small teams and minimal supplies.

-Expected Outcome

Once this program has been activated we expect a significant reduction in not only animal disease in the region and its subsequent effects on humans, but in the overall burden of disease in man and the toll it takes on human health. This project will also give us important data on the effects of the disease, animal health, community health, and its direct correlation to falling victim to joining extremist organizations. Since we will likely have villages that choose not to participate in this program, we can use them to compare directly to those that participated. Population tracing done through the DOD can trace migration of peoples of at-risk populations to extremist organizations. Using this information we can determine if our overall intervention causes reduction in this migration, and if future iterations of this project are even worthwhile for this intended purpose. This type of data has never been ascertained before, and will be the first of its kind.

-Conclusion

Syria is a country suffering from multiple tribulations on several fronts. People are being neglected and forgotten by their own government and the rest of the world. Without sustainable intervention and outside involvement for agricultural practices, the people will continue to suffer and devolve into warring sects or integrate into extremist organizations. The purpose of this intervention is two-fold; improve the lives and stability of the populace and starve extremist groups from indoctrinating new people.

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