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Integrated tick management: Challenges and opportunities to mitigate tick-borne disease burden*

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Abstract

As the chief scientific in-house research agency of the USDA, the ARS finds solutions through research to agricultural problems that affect Americans every day from field to table. Animal production and protection programs of the ARS involve strategic research done at laboratories across the USA to prevent and control pests and animal diseases, including tick and tick-borne diseases (TTBD), that pose a threat to agriculture, public health, and the wellbeing of American citizens. TTBD burden the health of human, livestock, and wildlife populations around the world. Safer and more environmentally friendly technologies are required to manage TTBD. Hypothesis-driven research is advancing scientific knowledge, which can be translated to innovate TTBD control methods. Advancing tests to demonstrate the benefit of using different technologies together will help document that integrated tick management is a viable option to mitigate the burden of TTBD effectively. Here, we summarize recent collaborative research by the USDA-ARS on integrated tick control and eradication. Our research efforts in Puerto Rico on integrated control of cattle fever ticks (CFT) exemplify the benefits of adapting the management strategy to deal with invasive tick vectors and associated TBD such as bovine babesiosis and anaplasmosis as is the case with the CFT *Rhipicephalus microplus* and *R. annulatus*. We are adapting the concept of precision agriculture to interdisciplinary research conducted in partnership with wildlife biologists and others to understand aspects of the cattle-white-tailed deer and nilgai interface that are conducive to the spread of CFT across the landscape. This research offers the opportunity to further assess tick-host-landscape interactions and provides the means to assess the efficacy of integrated approaches that could be adopted by the Cattle Fever Tick Eradication Program of the USA to enhance efforts to keep the national cattle herd CFT-free. Research by the Veterinary Pest Genomics Center of the USDA-ARS is enabling exciting opportunities to translate scientific knowledge into safer and efficacious technologies, such as anti-tick vaccines, that can be integrated to manage TTBD effectively.

Introduction

As the chief scientific in-house research agency of the United States Department of Agriculture (USDA), the Agricultural Research Service (ARS) finds solutions through research to agricultural problems that affect Americans every day from field to table. The translation of research performed by USDA-ARS scientists can have global impact, and be adapted for applications beyond agriculture (Bassi *et al.,* 2015; Jin and Huffman, 2016). Animal production and protection programs of the ARS involve strategic research done at laboratories across the United States of America (USA) to prevent and control pests and animal diseases that pose a threat to agriculture, public health, and the wellbeing of American citizens (https://www.ars.usda.gov/animal-production-and-protection/).

The USDA-ARS Knipling-Bushland U.S. Livestock Insects Research Laboratory in Kerrville, Texas includes

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the Livestock Arthropod Pest Research Unit (LAPRU). The LAPRU's mission is to provide the Cattle Fever Tick Eradication Program (CFTEP) and the Screwworm Eradication Program of USDA-Animal and Plant Health Inspection Service (APHIS), the U.S. cattle industry, and the public, innovative systems benefiting from genomics science and remote sensing for the elimination or progressive control of invasive ticks, the New World Screwworm, and blood-feeding flies of veterinary and medical importance (https://www.ars.usda.gov/plains-area/kerrville-tx/knipling-bushland-us-livestock-insects-research-laboratory/). This mission is fulfilled through research efforts that center on the appropriated projects: Cattle Fever Tick Control and Eradication, Genomics of Livestock Pests, and Management of Flies Associated with Livestock (https://www.ars.usda.gov/research/programs-projects/?modeCode=30-94-05-00&show=projecttype). The highlights of research progress presented here relate to integrated tick management.

Challenges and opportunities

Ticks and tick-borne diseases (TTBD) burden the health of human, livestock, and wildlife populations around the world. As ectoparasites, ticks affect the health and productivity of livestock through their obligate blood-feeding habit, especially when heavy infestations occur (Brake and Pérez de León, 2012). The morbidity caused by microbes transmitted by ticks among livestock herds can be extensive, and mortality can be high with some tick-borne diseases (TBD). The TTBD can cause major problems for animal agriculture in tropical and subtropical regions of the world (Grisi *et al.,* 2014; Almazán *et al.,* 2017; Rodríguez-Vivas *et al.,* 2017a). Most TBD of public health importance are zoonotic (Esteve-Gassent *et al.,* 2014; Rodríguez-Vivas *et al.,* 2016). Several tick-borne pathogens cause syndromes in humans that are classified as emerging diseases.

Synthetic chemicals that kill ticks, known as acaricides, have been used widely to try to control ticks. By killing ticks infesting a susceptible host, the use of acaricides can also mitigate the risk for tick-borne pathogen transmission. However, the indiscriminate use of acaricides exerts a strong selection pressure for the evolution of biological processes in ticks, which results in populations that are resistant to these chemicals (Guerrero *et al.,* 2014a; Klafke *et al.,* 2017; Rodríguez-Vivas *et al.,* 2017b). The intense use of acaricides can also have undesirable side effects on the environment and public health (Lopez-Arias *et al.,* 2015; De Meneghi *et al.,* 2016).

Other aspects related to global change have unleashed the invasive potential of certain tick species (Benavidez-Ortiz *et al.,* 2016). Non-native ticks display a remarkable adaptability to parasitize species, other than their previously known hosts, in the invaded range (Goolsby *et al.,* 2016a). This situation can enable new vector-pathogen interactions with detrimental consequences for human and animal health (Biguezoton *et al.,* 2016; Yadav *et al.,* 2017).

Scientific advances are opening up exciting opportunities for TTBD control (Ferreira *et al.,* 2015; de Oliveira-Filho *et al.,* 2017; Krishnavajhala *et al.,* 2017; Renthal *et al.,* 2017). Systems biology provides the holistic approach that is allowing research to enhance our understanding of the complex organisms ticks are. In the context of the pathogens ticks transmit, interdisciplinary molecular investigations are also innovating new technologies for TBD prevention (Esteve-Gassent *et al.,* 2016). Advancing tests to demonstrate the benefit of using different technologies together will help document that integrated tick management is a viable option to mitigate the burden of TBD effectively (Pérez-de León *et al.,* 2014b). Examples of research to seize these opportunities are described next.

Integrated tick management: Research update

The spectrum of possibilities to deal with the problems posed by TTBD ranges from doing nothing, to control, and eradication as the ultimate management option. However, the eradication of ticks, whether they are native or invasive species in the area under consideration, is not risk-free (Pegram *et al.,* 2007; Walker, 2011). Our research efforts in Puerto Rico on integrated control of the Southern cattle fever tick (SCFT), *Rhipicephalus microplus*, exemplify the benefits of adapting the management strategy to deal with that invasive vector species and the associated TBD bovine babesiosis and anaplasmosis (Pérez-de León *et al.,* 2014a).

Puerto Rico remained infested with the SCFT, and bovine babesiosis and anaplasmosis continued to cause significant morbidity and mortality, particularly in the island's dairy herd, which consists primarily of pure European dairy cattle breeds despite previous eradication attempts. A research coalition was established with the support of livestock producer groups between federal and state agencies with the goal of generating science-based information that could be used to develop a program for progressive integrated control of the SCFT and associated TBD (for details see page 4 in https://www.caribvet.net/content/download/4325/32275/version/2/file/Newsletter+ResistT_2.pdf). The use of multiple technologies with different modes of action was combined with good acaricide management practices. This allowed us to address food safety and environmental health concerns with the ecological impact and residue levels of acaricides in dairy cattle products. Our protocol also incorporated the use of an experimental Bm86-based vaccine in dairy and beef cattle that resulted from a public-private partnership (Pérez de León *et al.,* 2017; https://www.youtube.com/watch?v=DkqS9dYLyys). Significant research outcomes included the absence of mortality among lactating dairy cows due to bovine babesiosis, reduction in morbidity due to SCFT-borne diseases, and low SCFT infestation levels. More information on the Research Project for Integrated Control of the Southern Cattle Fever Tick in Puerto Rico will be discussed during the presentation.

One of the reasons ranchers in the USA can realize the full productivity potential of their livestock is because the national cattle herd is free of bovine babesiosis. This was accomplished through efforts of the CFTEP when in 1943 the USA was declared free of the SCFT, and the closely associated CFT species *R. annulatus*, with the exception of a Permanent Quarantine Zone (PQZ) in south Texas along the Rio Grande on the border with Mexico. This PQZ provides a buffer for incursions by CFT and SCFT on infested stray livestock and wildlife moving from Mexico where the ticks remain endemic. The involvement of native and exotic wild ungulates, acaricide resistance, and other global change issues complicate efforts by the CFTEP to keep the USA SCFT, and CFT-free. An aspect requiring attention is the involvement of nilgai (*Boselaphus tragocamelus*) as a tick host, principally for SCFT (https://content.govdelivery.com/attachments/USDAAPHIS/2014/09/08/file_attachments/322328/Final%2BNilgai%2BEnviro%2BAssessment%2BSept2014.pdf). Nilgai is an exotic ungulate species native to the Indian subcontinent that was introduced to Texas at the beginning of the last century.

We are adapting the concept of precision agriculture to interdisciplinary research conducted in partnership with wildlife biologists and others to understand aspects of the cattle-white-tailed deer (WTD) and nilgai interface that are conducive to the spread of SCFT and CFT across the landscape (Goolsby *et al.,* 2016b; Singh *et al.,* 2017). Understanding the habitat, ecology, and behavior of hosts enables the development of treatment methods against ticks infesting wildlife. GPS collars were placed on nilgai inhabiting a ranch in south Texas to understand their movement patterns in the context of management practices by the CFTEP (Foley *et al.,* 2017). A portion of the resident population ventured beyond the ranch. Some nilgai moved away 30 miles from the ranch. Although females showed a higher likelihood of spreading ticks across the landscape than males, nilgai did not cross 1.25 m high cattle fences parallel to paved highways. The mobility of free-ranging nilgai make this bovid species a difficult target for tick treatment. It would be possible to treat nilgai if they are attracted to a station delivering the tick control technology. Cameras were setup around buckets containing substances that we hypothesized would lure nilgai. WTD were also attracted to the lure stations (Goolsby *et al.* 2017). Of the three artificial lures tested, screwworm lure was the most attractive to nilgai. However, natural nilgai offal was the most attractive of the lures tested with nilgai under field conditions. Progress with a nilgai sprayer to treat tick infestations will be discussed during the presentation.

The planning and refinement of integrated cattle fever tick management programs can benefit from best practices used in areawide pest management programs, which include the development, validation, and experimentation with simulation models (Koul *et al.,* 2008). In this regard, recent efforts involved the application of Fast Fourier Transform analysis to assess the recurrence of SCFT and CFT outbreak activity in the USA (Pérez-de León *et al.,* 2012). It was hypothesized that strategic forecasting by the CFTEP would allow the adaptation of integrated protocols including the use of several methods to decrease the number of, and accelerate the elimination of tick outbreaks. Past and future periods of tick outbreak activity were defined, and potential drivers associated with climatic oscillation signals were identified. A spatially-explicit, individual-based model was developed to simulate ecological and habitat aspects linked to cattle-WTD interactions and the outcomes analyzed in the context of methods followed by the

CFTEP (Wang *et al.,* 2016). The WTD mobility across the landscape resulted in tick refugia. According to the model, these tick refugia contribute to chronic infestation in premises cohabited by WTD and cattle. This tool offers the opportunity to further assess tick-host-landscape interactions and provides the means to assess the efficacy of integrated approaches that could be adopted by the CFTEP to mitigate the economic burden of protracted pasture quarantine.

LAPRU co-leads the Veterinary Pest Genomics Center (VPGC) of the USDA-ARS. This is an initiative that envisions leveraging big data solutions to evaluate risk from, and develop mitigations for invasive and other economically important veterinary pests (https://data.nal.usda.gov/veterinary-pest-genomics-center). Advancing the sequencing of the SCFT genome was one of the foundational projects for the VPGC. The size of the SCFT genome is estimated to be 7.1 Gbp, and to contain around 70% repetitive DNA (Guerrero *et al.*, 2010). A hybrid sequencing and assembly approach was taken to produce the v2.0 assembly of the SCFT genome (Barrero *et al.,* 2017). Genome annotation identified several sequences that can be researched to innovate control technologies. Sequencing of the CFT genome done in collaboration with Texas A&M University will allow comparative genomics analyses (https://entomology.tamu.edu/2017/02/02/texas-cattle-fever-ticks-are-back-with-a-vengeance/).

Translational research based on that information will allow further refinement of reverse vaccinology and mechanism-based screening (Guerrero *et al.,* 2014b; Costa-Júnior *et al.,* 2016; Évora *et al.,* 2017; Ferreira *et al.,* 2017; Gross *et al.,* 2017), among other efforts to develop safer and efficacious interventions for integrated tick management.

Conclusion

Efficacious and more environmentally friendly technologies are required to manage TTBD. The problem with multiple acaricide resistance confers urgency for translational research that can accelerate the research and development of new TTBD control methods. TTBD are complex systems that require an integrated approach to mitigate the burden they cause on animal and human health. Genomics research is helping identify vulnerabilities in TTBD systems that are amenable for the disruption of tick-borne pathogen transmission. The adaptation of precision agriculture to research on TTBD is opening up opportunities to establish the knowledge base to advance integrated tick management strategies.

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