Bovine TB Control Program: Issues to be considered for its final stage.

(Programa de Control para Tuberculosis bovina: Aspectos a considerar para su etapa final).

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Programa de Control de la Tuberculosis bovina: Aspectos a considerar en su etapa final.

Introducción

La Academia Nacional de Agronomía y Veterinaria y el Centro Nacional de Investigaciones Agropecuarias de INTA, Castelar, realizaron una Sesión Pública en la sede de la Academia el día 6 de abril de 2000, destinada a informar sobre avances de investigación en Tuberculosis Bovina en los EEUU y su aplicación en programas de control.

Para tal fin contaron con la participación como disertante del Dr. M.V. Mo Salman, Profesor de Epidemiología Veterinaria, Colorado State University, Fort Collins, Colorado, USA.

El Dr. Salman estaba en el país como experto y consultor en el marco de un proyecto de investigación sobre "Mejoramiento del Diagnóstico de la Tuberculosis Bovina en Rumiantes" proyecto elaborado por los técnicos de los Institutos de Patobiología y Biotecnología del Centro de Investigación en Ciencias Veterinarias y Agronómicas del CNIA-INTA, Castelar, bajo la coordinación del Dr. Jorge Pereira y que se desarrolla con el apoyo de la Agencia Internacional de Energía Atómica (AIEA) de Viena, Austria.

Esta temática tiene sus antecedentes en la ANAyV con un proyecto compartido en el período 1995/1999 entre el Instituto de Patobiología, CICV-INTA, Castelar y la Academia Nacional de Agronomía y Veterinaria, la cual aportó los recursos financieros para la realización del mismo. Dicho proyecto fue coordinado por el Académico Dr. Bernardo J. Carrillo, conjuntamente con los Dres. Jorge Pereira y Lucio Villa y con la participación de los técnicos Dra. Celia Antognoli, Méd. Vet. Sergio Garbaccio y Dra. Alicia Alito del Instituto de Patobiología del INTA, Castelar y de cuyos resultados se informó en comunicación aparte.

Dada la importancia del tema y el nivel del disertante, asistió una calificada concurrencia entre ellos académicos especialistas y profesionales veterinarios de diversas instituciones y de la actividad privada, de la capital y el interior del país.

La apertura del acto estuvo a cargo del Presidente de la ANAyV, Dr. Norberto Ras, quien después de diversas consideraciones sobre la Tuberculosis y su trascendencia como zoonosis, fue secundado por el epidemiólogo Dr. Sergio Duffy de INTA en la presentación del disertante Dr. Salman y de su trayectoria como investigador y consultor internacional.

A continuación disertó el Prof. Salman, recibiendo al finalizar numerosas preguntas que respondió con toda idoneidad, terminando su presentación con los elogios de la concurrencia por la claridad de los conceptos y el nivel de la disertación que se transcribe a continuación en su idioma original para conservar fidelidad.

Disertación del Dr. Mo Salman DVM, Ph.D., DACVPM, F.A.C.E. Professor of Veterinary Epidemiology *

Bovine Tuberculosis Control Program:
Issues to be considered for its final stage
Mr. President,
Colleagues,

It is a great honor and distinction to be received by the Academia Nacional de Agronomía y Veterinaria of Argentina to which I extend my respectful thanks.

Outline:

· Available options for the Bovine TB (BTB) Control Program
· Current measures and status of the USA TB Control Program
· Obstacles to the eradication efforts
· Research findings and their implications in the current eradication efforts
· Our laboratory research activities: current and future directions

What are the current options to control BTB?

I will list options that are familiar to most of you. I will attempt to identify the limitations of these options as I list them:

· Screening and elimination of suspect and infected animals/herds (Test and slaughter option):
· Depends on the sensitivity and specificity of the detection system (skin test and other epidemiological historical background)
· Sacrificing animals and destroying herds that are not infected but they are positive on the detection system (i.e., false positive)
· It is hard to implement in the last stage of the disease eradication program
· The industry has to buy in, otherwise

the program cannot succeed.
· Certification process of herds that are free from the disease
· It requires a highly sensitive system so that the negative herds are surely without the infection. Thus, the specificity of the system will suffer (more false positive herds).
· It requires some incentive for herd owners to maintain certification.
· Animal health authorities in the country should maintain a close monitoring of the "non-certified" herds and encourage the certification process. This will lead to reduction in the number of herds that can spread the infection.
· It is hard to maintain good observations on the non-certified herds. Compliance is a serious problem in these herds.

· Elimination of potential transmission of the disease to human populations through pasteurization and detection of TB lesions in slaughterhouses.
· This option will focus on the public health aspect and ignore the potential losses in cattle production due to this disease.
· It requires laws/regulations for marketing milk and meat in the country.
· It requires a sensitive system for

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detection of suspect TB lesions in slaughterhouses. Training of meat inspectors is an essential part of this system.
· It is a good option combining it with others in the last stage of the eradication phase.

· Trace back infection through the detection of TB lesions in slaughterhouses
· It requires a sensitive system for detection of suspect TB lesions in slaughterhouses. Training of meat inspectors is an essential part of this system.
· It requires an extensive identification system of herd origin in order to be able to trace infection to the original herds.
· It depends on the detection of infection ONLY through slaughter animals and there is a possibility to miss or delay the detection of infection which can lead to a serious problem of spreading the disease.
· It can work well when the infection rate in the country is reaching a low level (i.e. less than 1%)

· Trace back infection through a serological testing of cattle populations in the country.
· This option is valid when there is an existing system for the collection of serum samples for other diseases such as brucellosis.
· It depends on the validity of the used serological test to detect/screen for the infection.
· It is a valid option for a low cost program but it would require an intensive monitoring for the test validity.

· Quarantine infected herds until the disease is cleared.
· This option is used in a low prevalence country with the availability of a highly specific detection system and the absence of the depopulation option.

· It is of value when infected herds are valuable to the cattle industry in the country such as pure breed herds etc.
· It would require an intensive testing and monitoring of these herds to reduce the introduction of the disease to other herds.

· Let the disease take its course (live with it).
· It is a valid option when the disease prevalence is high and a veterinary infrastructure is absent in the country.
· I believe that the disease prevalence will be reduced to a certain level mainly due to poor production performance of infected herds and animals.
· The disease, however, will maintain a high infection rate and the country in general will suffer.

Conclusion/suggestions: Several of these options are combined in order to optimize the overall benefits. The major reasons for choosing some options rather than others are costs and practicality.

What is the current status of BTB in USA?

· The number of infected herds in the USA is currently 3.
· The number of states in which the disease is present is 2.
·The program is strictly dependent on identifying infection through detectable lesions in slaughterhouses. Cash incentive is given to meat inspectors who identify TB lesions if the infection is confirmed. The current level of confirmation of these lesions is 20-30%.
· Culture and/or histopathological findings are considered for the confirmation of infection. A new PCR technique was included last year as part of the confirmatory tests for infection. This PCR that will confirm a histological

lesion with the presence of acid-fast bacteria. Thus, histological preparation of the lesion is still required.

· Both caudal fold and comparative cervical tests are used to declare an animal as a reactor. There are specific Uniform Rules and Methods that should be followed to classify infected herds.

· Indemnity is paid to owners with infected herds if the depopulation option is chosen. The indemnity price, however, is not up to the market price and owners are not happy for this option. Other options are considered to eliminate the infection from specific herds.

· Milk ordinance is in place in only a couple of states. The milk ordinance program would require every dairy herd to have a tuberculin testing (caudal fold) every three-years.

· Due to the impact of other animal species on the spread of the disease, two other BTB programs are in place: Captive/farm cervids and bison. Both of these programs were just recently implemented and passed both the industry and government approval. These two programs, however, use certain modified rules and tests that are adapted from the existing cattle program.

Conclusion: Several progressive steps toward controlling the disease in USA have been accomplished. The disease, however, has not been eradicated and some States are getting new infections rather than maintaining their disease free status.

How far are we from the eradication of the disease in the USA?

It depends on the definition of eradication ... Is it the eradication of Mycobacterium bovis or the eradication of BTB from domesticated cattle? If it is

the latter then I think the country is almost there, if the former then it is far from reaching that goal.

What are the reasons for not reaching the eradication status of the disease in the USA?

· The last stage of the eradication phase is not an easy task due to several reasons such as the lack of interest, reduction in the confidence level of the detection of infection (poor predictive value of positive), difficulty in the location of infected herds, and lack of political and financial support.

· Existing screening and diagnostic tests were developed for a relatively high prevalence level of the disease. When the disease prevalence is low, these tests by their nature will have a poor predictive value of positive. Thus, the proportions of false positive animals/herds are increased. This problem by itself reduces the effectiveness and validity of the eradication program. Thus, there is a need to improve the existing tests to accommodate the low prevalence level of the disease. We will talk about this issue later.

· The bacterium itself has identified a better way to survive by finding a niche in other species particularly other ruminants. Deer, elk, and bison are examples of animals that harbor M. bovis and the bacterium is maintaining a good harmony with nature. Furthermore, we have manipulated the management style of these mainly wild species which increases the opportunity for this bacterium to adapt to these animal species. We have started to manage these wild species in an intensive way so that the environmental conditions for the bacterium to survive are almost perfect.

· The interaction between wild animals and cattle has increased due to

several factors beyond this talk. This interaction has lead to a creation of an environment for the transmission of this bacterium between wild and domesticate animals.

· Low public concerns about the threat of this disease to public health, Unfortunately, the existing monitoring of human TB in the USA identifies the causal bacteria for cases by general category as M.TB complex. Thus, little is known about the impact of M. bovis in human infection.

· Low priority from both government and industry sectors due to low level of the disease.

Conclusion: There is a need to re-evaluate the situation of the existing rules and policy toward the eradication program. Scientifically and socially based approaches need to be explored in order to reach the ultimate goal of eradicating the disease from the USA.

How much research has been done to evaluate options to control/ eradicate BTB?

· During the last two decades, several research projects were conducted in various parts of the world to evaluate diagnostic/screening tests, evaluate the role of mammalian reservoirs, determine potential risk factors associated with the spread of the disease, and determine the source of epidemics and outbreaks of the disease. Most of these efforts, however, were narrowly focused on local geographical areas. For instance, the work in New Zealand was mainly to understand the situation of BTB on the island, the work in Ireland was to determine the role of badgers in the spread of the disease, and the work in Yellowstone was to determine

the role of elk in spreading the disease to cattle.

· The advancement in laboratory techniques particularly in molecular aspects has contributed to several available sensitive tests that can help us in understanding the epidemiology of the disease. The sensitivity of these tests, however, has the disadvantages to derive the wrong conclusion. I will talk later about some of the potential problems we faced in our research due to the high sensitivity of these tests.

· Another area of advancement in science that can help in pursuing our eradication effort is the refinement of surveillance and survey methods to accommodate the needs for detection of diseases with a low level of prevalence. The use of simulation models to determine the best approach to deal with this type of diseases has enhanced our decision making process to select options for controlling these diseases.

In conclusion: Researchers are aware of the need for better approaches to the BTB control programs and I believe that research findings from the last two decades have already been implemented in some countries.

Finally I want to talk about our laboratory and our research activities related to BTB:

Our overall research aim for BTB is to refine existing approaches in controlling the disease utilizing new techniques in diagnostic tests and epidemiological investigations. Specifically, we have invested in the following sections of the disease control program:

1. Development and validation of a multi-antigen panel ELISA as a serological test for screening of infection in

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cattle, other domestic species, wild species, and zoo animals. This work has lead to 4 MS thesis with three published manuscripts. The sensitivity of our ELISA system is in the upper 80s but the specificity is in the lower 60s. Our conclusion from this effort is that we can use 5 antigens that can determine the exposure to Mycobacterium species with varieties of immunity presentation to determine with some certainty the specific exposure to M. bovis. Our findings, however, confirm the previously known speculation that humoral response is not a good way to determine the early stage of exposure or infection with TB. Our ELISA system is currently used as the screening test for infection in elephants, deer, and elk. Our intention is to use this test as the first screening test in a multiple tests system.

2. Use of PCR technique to determine the sources of infection in a large dairy cattle population in Mexico. We have used Random Amplified Polymorphic DNA – Polymerase Chain Reaction (RAPD-PCR) to assess phylogenetic relationships among 400 M.bovis isolates collected from 6 slaughterhouses in Mexico. The aim of this project was to determine the validity and reliability of this technique in the fingerprinting of M.bovis. Isolates were linked to epidemiological data that were collected through a trace back system in these 6 geographical regions of Mexico. Our conclusion is that this technique is TOO sensitive to differentiate these isolates and no phylogenetic clustering could be associated with their epidemiologi-

cal characteristics. Two manuscripts have just recently been published in AJVR (Vol 61, No. 1 January 2000: Feliciano Milian-Suazo, Salman et al. Pages 86-95)

3. Refinement of PCR technique to confirm diagnosis of BTB using formalin fixed tissue. Our aim here is to use PCR as a direct diagnostic test for TB suspect lesions collected on formalin media without processing the samples for histopatholgical reading. We have successfully used this diagnostic test on experimentally spiked tissue samples with M.bovis and we are in the process to validate the test using confirmed TB lesions.

4. Utilization of PCR for detection of M.bovis and other Mycobacterium species in milk and other body fluid samples. Dr. Maria Celia Antognoli is working on this project. She has completed her MS thesis in refining this method and she has used spiked milk to determine the best combination of treatment regimens of milk to demonstrate the validity of her method. She is currently working on the validation of this technique using milk samples from confirmed infected herds in Baja California, Mexico. We are in the process of using the same technique to detect M. avian paratb infection in Colorado dairy herds.

In conclusion, our research effort has lead to several findings that can enhance disease control strategies.

It is now most appropriate to extend my personal thanks to you all for both your presence and attention.

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