↘ **Controlling bovine tuberculosis: a One Health challenge**

PERSPECTIVES | # DOSSIER | # AROUND THE WORLD

EDITORIAL

Eradication of bovine tuberculosis: a One Health issue

From the statistics published by WHO and the declarations made to the OIE, it is painfully obvious that bovine tuberculosis is still a major disease and a cause of concern for a great many countries, as it represents a socio-economic burden that is costly in terms of human lives and resources. This public health and animal health challenge merits special attention through the prism of a One Health *approach.*

The OIE is committed to working in partnership with WHO, FAO and the International Union Against Tuberculosis and Lung Disease to make a significant contribution to improving the situation. We are working together to strengthen the capacity of our Member Countries to combat bovine tuberculosis, notably by publishing the *Roadmap for Zoonotic Tuberculosis*. We are also working to ensure that relevant diagnostic tools and technical standards reflect the latest technical advances, both in the *Terrestrial Animal Health Code* and in the *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*.

> No, bovine tuberculosis is not a disease of the past, including in developed countries. Yes, we must continue to devote the necessary resources to control or even eradicate it.

There is an urgent need to replace the current international standard bovine tuberculin and establish a reference standard for the development of 'second generation' diagnostic tests. This explains why the OIE supports the international collaboration established with the aim of developing and validating a replacement international standard bovine tuberculin. The OIE also supports the research being undertaken to develop innovative approaches to diagnosis and prevention, in particular, through its involvement in the STAR IDAZ platform.

Regarding the challenges facing efforts to control bovine and zoonotic tuberculosis, I must emphasise once again that national coordination of actions and coherence of programmes are preconditions for success. Surveillance,

including in wildlife, and the follow-up of notification reports to the OIE are also of major importance in combating the disease, as is synergy with the network of OIE Reference Laboratories that provide crucial support.

This issue of *Panorama* will, I hope, give you a better understanding of the actions being undertaken by the OIE and the way in which they complement one another. The various testimonies presented here reveal the importance of sharing experiences and the need for cooperation between countries. This issue also highlights the efforts being made throughout the world, especially in low- and middle-income countries, to combat bovine tuberculosis and reduce its impact.

Lastly, this issue of *Panorama* devoted to tuberculosis is, in my view, yet another illustration of the commitment by the FAO/OIE/WHO Tripartite, the Directors General of these three organisations having already formalised their collaboration by signing an agreement on 30 May 2018 [1, 2].

I hope you will find this issue instructive and enjoyable.

Monique Éloit
Director General
World Organisation for Animal Health (OIE)

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'One Health': by protecting animals, we preserve our future

PERSPECTIVES

Roadmap for zoonotic tuberculosis

A 'One Health' initiative to combat zoonotic tuberculosis

AUTHORS

Amina Benyahia[1], Anna S. Dean[2], Ahmed El Idrissi[3], Elisabeth Erlacher-Vindel[4], Simona Forcella[5], Paula I. Fujiwara[6], Glen Gifford[7]*,

Juan Lubroth[8], Francisco Olea-Popelka[9,10] & Gregorio Torres[11]

The above people were members of a core writing team for the *Roadmap for Zoootic Tuberculosis.* See the *Roadmap for Zoonotic Tuberculosis* for a complete list of contributors.

* Corresponding author: g.gifford@oie.int

(1) Scientist, Department of Food Safety and Zoonoses, World Health Organization (WHO).
(2) Technical Officer, Global Tuberculosis Programme, World Health Organization (WHO).
(3) Senior Animal Health Officer, Food and Agriculture Organization of the United Nations (FAO).
(4) Head, Antimicrobial Resistance and Veterinary Products Department, World Organisation for Animal Health (OIE).
(5) Policy Officer, DG SANTE, European Commission, Brussels, Belgium.
(6) Scientific Director, International Union Against Tuberculosis and Lung Disease.
(7) Chargé de mission, Antimicrobial Resistance and Veterinary Products Department, World Organisation for Animal Health (OIE).
(8) Chief Veterinary Officer, Food and Agriculture Organization of the United Nations (FAO).
(9) Associate Professor, Department of Clinical Studies, College of Veterinary Medicine & Biomedical Sciences, Colorado State University, Fort Collins, Colorado, United States of America.
(10) Zoonotic TB Sub-Section, International Union Against Tuberculosis and Lung Disease.
(11) Acting Head of the Science Department, World Organisation for Animal Health (OIE).

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Zoonotic tuberculosis is a form of tuberculosis in humans that is caused by Mycobacterium bovis, a member of a group of related bacteria known as the M. tuberculosis complex. Since animals are the reservoir of zoonotic tuberculosis, reducing the incidence of this form of tuberculosis in animals and humans requires us to manage the risk at its animal source.

Global initiatives to address bovine and zoonotic tuberculosis* are coordinated through a Tripartite (FAO/OIE/WHO) partnership and the International Union Against Tuberculosis and Lung Disease (The Union) [1]. In 2017, the OIE, WHO, FAO, and The Union, jointly launched the first *Roadmap for Zoonotic Tuberculosis* [2, 3, 4, 5, 6], outlining a plan to combat zoonotic tuberculosis using a One Health approach.

The roadmap's three core themes are to:

a) improve the scientific evidence base
b) reduce transmission at the animal–human interface
c) strengthen intersectoral and collaborative approaches.

Ten priority areas are highlighted under these core themes. Addressing these areas will require: improving surveillance and diagnosis, addressing research gaps, improving animal health and food safety to reduce the risk to people, increasing awareness, fostering One Health approaches, and advocating for investment to support the control of bovine and zoonotic tuberculosis.

The OIE contributes to addressing these priority areas through its publication of harmonised international technical standards [7, 8] and related information; an extensive scientific network of Collaborating Centres and Reference Laboratories [9]; its management of a project for the production and evaluation of an international reference standard bovine tuberculin; its management of a global animal disease monitoring and reporting system, WAHIS [10]; and its development of training and capacity-building programmes for Veterinary Services.

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* 'zoonotic TB' refers to disease caused by *M. bovis* infection in people and 'bovine TB' refers to disease caused by *M. bovis* infection in animals

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PERSPECTIVES

Accelerating bovine tuberculosis control in lower-income settings

AUTHORS

Nick Juleff[1]*, Vivek Kapur[2], Shannon Mesenhowski[3], Purvi Mehta[4] & Samuel Thevasagayam[5]

(1) Senior Programme Officer, Agricultural Development, Bill & Melinda Gates Foundation, Seattle, United States of America.
(2) Professor of Microbiology and Infectious Diseases, Huck Distinguished Chair in Global Health, Associate Director Huck Institutes of Life Sciences, The Pennsylvania State University, Pennsylvania, United States of America.
(3) Programme Officer, Agricultural Development, Bill & Melinda Gates Foundation, Seattle, United States of America.
(4) Deputy Director and Head of Asia, Agricultural Development, Bill & Melinda Gates Foundation, Seattle, United States of America.
(5) Deputy Director, Agricultural Development, Bill & Melinda Gates Foundation, Seattle, United States of America.

* Corresponding author: nick.juleff@gatesfoundation.org

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Dairy production in low- and middle-income countries (LMICs) continues to attract substantial development support. This is because the majority of production comes from smallholder

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farmers, and dairy development is a powerful tool for economic growth, food security, nutrition and poverty reduction. Since bovine tuberculosis (bTB) limits dairy productivity and represents a public health threat, accelerating bTB control is a priority for the Bill & Melinda Gates Foundation.

In stark contrast to high-income countries, where bTB is largely controlled in livestock and therefore less important for public health, similar control programmes have not been implemented in most LMICs. This, despite growing evidence of a high and widespread bTB prevalence in LMICs; for example, in Africa and India [1, 2]. Given both the close association of humans with cattle, and the fact that milk is often sold unprocessed in LMICs, there is also considerable risk of zoonotic transmission. However, because of technical and logistical constraints, the true burden of zoonotic tuberculosis in LMICs remains unknown.

Herein lies the key problem: low awareness of bTB means that support for its control remains limited; and limited support means that few resources are available to build awareness. Hence, in LMICs, where disease has the greatest negative impacts, bTB control efforts remain piecemeal and insufficient.

> The true burden of zoonotic tuberculosis in low- and middle-income countries remains unknown

Despite these challenges, we find cause for optimism with a confluence of emerging factors that are likely to increase awareness and provide a renewed urgency to drive bTB control in LMICs.

These factors include:

a) WHO's End Tuberculosis Strategy, and the prioritisation of zoonotic tuberculosis at the global level, along with the launch of the first zoonotic tuberculosis roadmap;

b) recognition that the dairy sector in Africa and India is rapidly transitioning and, while intensification of dairy production in LMICs increases bTB risk, it also provides opportunities for novel interventions;

c) strengthening partnerships between donor organisations, multinational institutions, pharmaceutical industries, dairy organisations, and the governments of countries in which tuberculosis is endemic. Such multidisciplinary, One Health partnerships are essential to promote integrated research, surveillance and control programmes, and the development of evidence-based policy frameworks to accelerate bTB control, improve animal productivity, and protect human health.

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Bovine tuberculosis: global distribution and implementation of prevention and control measures according to WAHIS data

AUTHORS

Kiyokazu Murai[1]*, Paolo Tizzani[2], Lina Awada[2], Lina Mur[2], Neo J. Mapitse[3] & Paula Caceres[4]

(1) Chargé de mission, World Animal Health Information and Analysis Department, World Organisation for Animal Health (OIE).
(2) Veterinary Epidemiologist, World Animal Health Information and Analysis Department, World Organisation for Animal Health (OIE).
(3) Head, Status Department, World Organisation for Animal Health (OIE).
(4) Head, World Animal Health Information and Analysis Department, World Organisation for Animal Health (OIE).

* Corresponding author: k.murai@oie.int
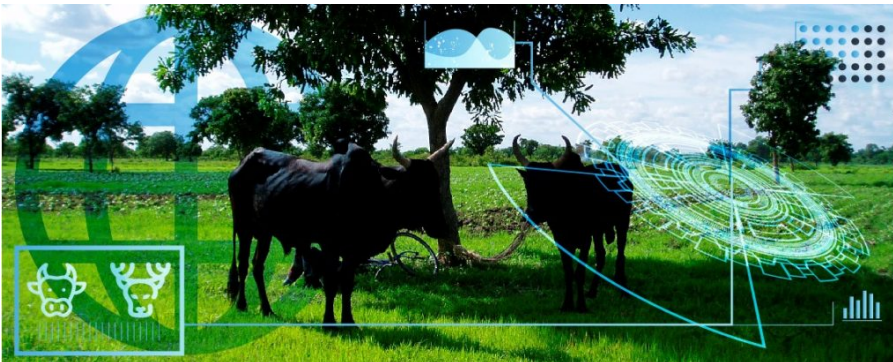
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Forty-four percent of countries reported bovine tuberculosis (bTB) via the OIE World Animal Health Information System (WAHIS) between January 2017 and June 2018. Only a quarter of the affected countries were applying all the relevant control measures. Improved surveillance and accurate reporting by a country's Veterinary Services contributes to the prevention and control of bTB at the animal source.

From January 2017 to June 2018, of the 188 countries and territories reporting their bTB situation to the OIE, 82 countries (44%) were affected, which demonstrates a widespread distribution of the disease (Fig. 1).

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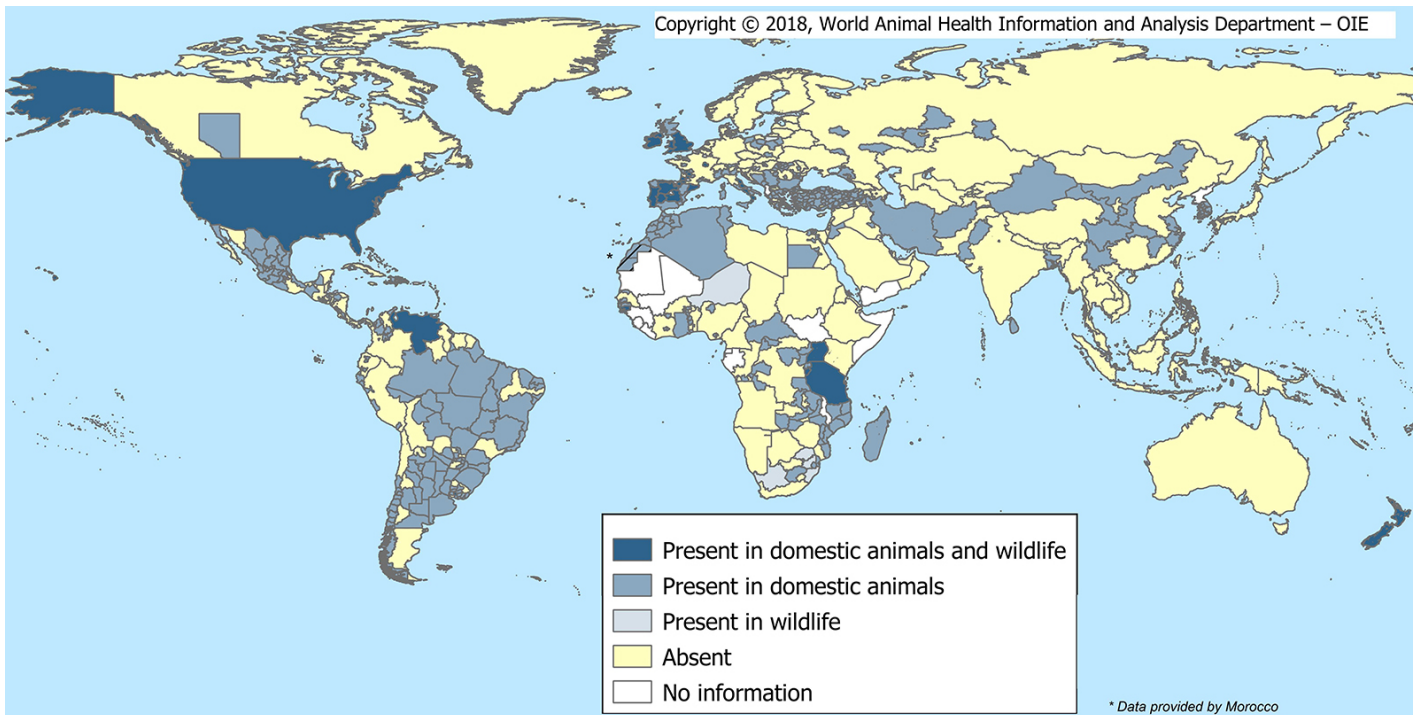
Fig. 1 – Global distribution of bovine tuberculosis in 2017 and first semester of 2018

Among the 82 affected countries, 29 (35.4%) countries reported the presence of bTB in both livestock and wildlife. Two (2.4%) countries reported bTB present only in wildlife, compared to 51 (62.2%) which indicated that only livestock were affected. Moreover, among these 82 affected countries, 66 (80.5%) provided quantitative data for outbreaks via WAHIS, demonstrating relatively good reporting of the global situation of this disease. The persistence of the infection in wildlife poses challenges for disease control in some countries [1], due to the potentially significant impact of wildlife as reservoirs and spillover hosts.

What are we doing to fight bovine tuberculosis?

The implementation of relevant measures is crucial for preventing and controlling bTB at its animal source to avoid its transmission between animals and to humans.

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An analysis of the implementation of prevention and control measures for bTB by country, using WAHIS data, showed that, among the affected countries, 23% had implemented all the relevant control measures. These were: active surveillance, complete or partial stamping-out, and movement control. The majority (62%) of affected countries had implemented some of the relevant measures. However, 3% of them had not applied any of these measures, and therefore require strengthened control efforts.

Among the countries where the disease was reported as absent, the majority (82%) recorded implementing at least one of the relevant prevention measures, namely surveillance and/or border control.

The above data demonstrate a high level of vigilance for bTB by affected and non-affected countries. As outlined in the *Roadmap for Zoonotic Tuberculosis* [2], the collection and reporting of more complete and accurate data is considered one of the priority areas for controlling zoonotic tuberculosis caused by *Mycobacterium bovis.* For this reason, countries are encouraged to continue to maintain and improve their level of bTB surveillance and reporting.

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DOSSIER

Historical data on animal disease outbreaks

The contribution made by the OIE archives

AUTHORS

Aline Rousier[1]* & François Ntsama[2]

(1) Head of the Documentation Cell, World Organisation for Animal Health (OIE).
(2) Chargé de mission, World Animal Health Information and Analysis Department, World Organisation for Animal Health (OIE).

* Corresponding author: a.rousier@oie.int

Since its creation, the OIE has collected data on animal disease outbreaks in its Member Countries. While not all the publications in printed format prior to WAHIS have been digitised as yet, a large number of them are available online in the OIE Documentary Database, presenting a valuable mine of information.

One of the main missions of the OIE, as stated in its Organic Statutes [1], is to collect information from its Member Countries on the presence and distribution of animal diseases and the methods used to control them, the purpose being to avoid the spread of epizootic diseases at the international level.

The original list of nine diseases notifiable to the OIE has expanded considerably over the years to reflect developments in the world animal health situation. Two major changes that have taken place are that two lists – a list of 16 diseases justifying monthly reporting (List A) and a list of 40 diseases to be reported on annually (List B) – were adopted in May 1964 [2] before being combined into a single list in May 2004 [3]. In 2019, the OIE list includes

117 terrestrial and aquatic animal diseases selected according to criteria specified in the *Terrestrial Animal Health Code* and the *Aquatic Animal Health Code*, respectively.

Over time, the procedures related to notifying diseases and implementing control measures came to be refined and harmonised.

OIE archives accessible in various media

Historically, the OIE's publications relating to notifications of animal diseases consisted of the following (Fig. 1):

• the **OIE *Bulletin***, created in 1927, which, up to 1988, published information that included notifications of outbreaks and the annual reports of the Veterinary Services of Member Countries and non-members;
• a weekly publication, during the period 1988–2006 (**_Disease Information_**), containing the notifications received from countries;
• the compilations of **_Annual statistics and the animal health situation in Member Countries_**, which, from 1949, summarised outbreaks by year, disease and country, were superseded in 1985 by a single annual publication, **_World Animal Health_** (since 2015 in digital format only).
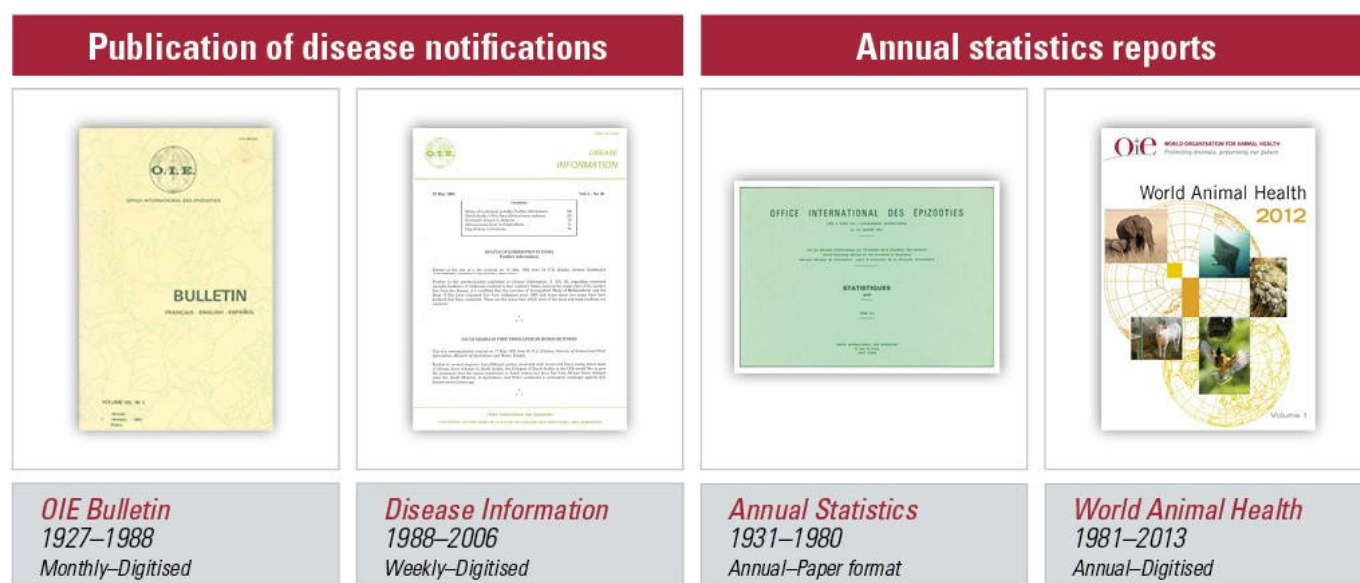
Fig. 1. Historical OIE publications on animal diseases

Since the beginning of the 1980s [4], the OIE has been operating an **international animal disease reporting system** (animal health information system), which has been progressively standardised and computerised. The data collected since 1996 are available online in **World Animal Health**, **HandiStatus II** (1996–2004), **WAHIS** (since 2005) and soon in **its modernised version (OIE-WAHIS)**, due to be launched during 2019.

The example of bovine tuberculosis

Bovine tuberculosis was added to List B in 1968. However, a policy on the subject had started to take shape in the

form of a Recommendation adopted by the International Committee of the OIE in May 1948 [5] and restated in 1950 and 1954. Since 2005, information on bovine tuberculosis has been collected on a six-monthly and annual basis, within the framework of the 'monitoring system' component of the OIE World Animal Health Information System, and can be reported in an immediate notification and subsequent follow-up reports within the framework of the 'early warning system' component.

For information prior to 1968, the *Bulletin* contains reports from Delegates on the statistically based results of the first control measures taken by developed countries at the start of the 20th century, including successful eradication campaigns in Nordic countries [6, 7], but it also sheds light on the progress made in fighting bovine tuberculosis worldwide [8] during the 20th century.

In 2017, the OIE, FAO and WHO joined together to launch the first *Roadmap for zoonotic tuberculosis* [9], based on a One Health approach. One of the priorities of this roadmap is to improve the scientific evidence base by collecting and presenting more complete and accurate data from human and animal populations.

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DOSSIER

The history of *in vivo* tuberculin testing in bovines

(Abstract from manuscript)

AUTHORS

Margaret Good[1]*, Douwe Bakker[2], Anthony Duignan[3] & Daniel M. Collins[4]

(1) Independent Researcher and Private Consultant, Dun Laoghaire, Co. Dublin, Ireland. *Previously affiliated with the Department of Agriculture, Food and the Marine, Dublin, Ireland*.
(2) Department of Animal Health, Faculty of Veterinary Medicine, Complutense University of Madrid, Spain.
(3) Superintending Veterinary Inspector, Department of Agriculture, Food and the Marine, Dublin, Ireland.
(4) Centre for Veterinary Epidemiology and Risk Analysis, UCD School of Veterinary Medicine, University College Dublin, Ireland.

* Corresponding author: mgood2510@gmail.com

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Tuberculosis, which affects multiple species worldwide, is a zoonotic One Health issue. Bovine tuberculosis control commenced in the early 20th century, with scientists collaborating to refine

tuberculin and optimise the skin test methodologies still necessary today, as a simple, technologically undemanding means of detecting infected farmed cattle and protecting humans from infection.

Tuberculosis in context

Tuberculosis (TB) has existed for over three million years, thriving worldwide in multiple species, with zoonotic transmission between animals and humans occurring in both directions. Before the introduction of milk pasteurisation in the 20th century, milk-borne *Mycobacterium bovis* caused mainly extrapulmonary TB, particularly in young children, with significant death rates.

Tuberculin development and standardisation

In 1893, Bang started using Koch's Old Tuberculin in cattle to detect bovine TB (bTB) and it was used thereafter in early bTB control programmes. Throughout most of the 20th century, scientists collaborated worldwide on refining and optimising the production and standardisation of tuberculin of sufficient potency, and on developing various test methodologies with sufficient sensitivity and specificity to detect most infected cattle. The World Health Organization (WHO) and World Organisation for Animal Health (OIE) defined standards for tuberculin production, potency, assay performance and intradermal tests for bovines. Within a few years of commencing a bTB control/eradication programme, clinical TB was rarely seen to cause disease, leading to significant improvements in livestock production.

Notwithstanding the launch of the first-ever roadmap to combat zoonotic TB [1], people still ask if bTB is a problem; if better controls for bTB exist; if alternative sites for conducting the intradermal skin test would be better; if all tuberculins are equal; and why haven't 'better' tests been developed?

Review

These questions prompted the paper, *The History of* In Vivo *Tuberculin Testing in Bovines: Tuberculosis, a 'One Health' Issue*, published in ***Frontiers in Veterinary Science*** [2]. This review tries to succinctly summarise the literature from the late 19th century until today. It focuses on why tuberculin skin tests have been successful; why zoonotic TB is an important One Health concern; why tuberculin skin tests will remain the screening test of choice for farmed livestock for the foreseeable future; and why the reduction of TB is necessary, and too important and urgent to await possible future developments in novel diagnostic assays before addressing the problem.

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DOSSIER

Clear thinking is required to establish a national strategy for bovine tuberculosis control

AUTHORS

Matthew Stone, Deputy Director General, International Standards and Science, World Organisation for Animal Health (OIE).

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*A **Roadmap for Zoonotic Tuberculosis** has recently been developed [1]. **International standards** are in place and updated through the expert network of OIE Members [2]. A strong community of interest focused on disease control holds **international conferences and workshops** to share its strategic, tactical and operational experiences [3]. **All the elements are in place to support the global priority of bovine tuberculosis control.** But it all starts with a national policy, and that **national policy must be founded on a strategic case that appeals to decision-makers**. **Good regulatory practice** in policy development [4] is just as crucial for success as scientific and technical capability in the implementation of animal health programmes.*

It is critically important to establish strategic objectives for a national control programme, because they underpin the activities of the programme. For bovine tuberculosis, these could be:

• **to protect public health**, since bovine tuberculosis is a zoonosis

- **to minimise its impact on animal production** through reducing herd prevalence, thereby contributing to the profitability of the agricultural sector
- **to build domestic and international consumer confidence** in animals and animal products produced under effective animal health and food assurance systems
- **to progressively pursue compartmental[1], zone[2] or national eradication**, when it makes sound economic sense to do so.

The pathways of exposure from animals to humans are well known, but also have cultural specificity that must be acknowledged and managed. Managing the public health risk of exposure through the food chain primarily involves Veterinary Services establishing effective meat hygiene systems, incorporating ante- and post-mortem inspection, and implementing disposition rules for suspicious lesions. Exposure through milk and milk products is effectively managed by pasteurisation; however, alternative approaches must be developed to manage the risks associated with traditional and more recent cultural practices that oppose pasteurising dairy products. Public health risks associated with the occupational exposure of livestock owners and handlers require awareness campaigns and support for best practices.

Animal health programmes that focus on herd health, promoting biosecurity for free herds and prevalence reduction for infected herds, are well known to regulatory veterinarians and their epidemiology advisors, and have proven successful. The test-and-slaughter approach requires herd registration (or, better still, a system providing individual animal identification and traceability); regular screening and confirmatory diagnostic protocols; and epidemiologically sound practices for investigating cases (defining an infection and infectivity timeline, undertaking tracing, investigating at-risk herds). In situations where Veterinary Services lack the capacity for such actions, vaccination can be a useful alternative, particularly in the early stages of a national programme. It can drive down the prevalence of bovine tuberculosis to a level where 'test and slaughter' makes economic sense. Similarly, it can be a challenge to understand those factors and scenarios (which typically occur in limited situations and during the later stages of a programme) that indicate that a stamping-out approach would make better sense. In cases where animals are destroyed, condemned at slaughter or downgraded, fair compensation policies will support the implementation of a stamping-out policy, although they must not incentivise poor biosecurity practices or, worse, illegal or unethical behaviour. The farming community must support the goals of the programme and understand the approach.

The involvement of wildlife presents a particular challenge

The involvement of wildlife in bovine tuberculosis maintenance and the re-exposure of livestock presents a particular challenge. Research must establish the species involved, their demography and ecology, the mechanisms of infection and exposure, and how these can be interrupted, such as through vaccination or, if necessary, wildlife population control.

A national policy of zoning can support targeted risk management, both in the control mechanisms applied for herds and wildlife (e.g. frequency of herd testing, wildlife population management) and in managing the risk of further exposure and disease spread (e.g. movement control policies based on regional prevalence or the risk of wildlife exposure). Zoning may also support export trade assurance.

| A sustained commitment from all stakeholders will support a step-by-step approach

Policy-makers and funders expect an economic rationale to support their decisions. The ultimate disease control objective of eradication may seem natural to veterinarians if it is epidemiologically feasible, but must also be justified economically, considering fiscal and other legitimate policy considerations. Eradication is an ambitious long-term goal, that will require planning a phased approach, building on the lessons learned from implementation in compartments (e.g. semen collection centres, high-biosecurity feedlot operations) and zones selected for their strategic significance and technical feasibility. **A sustained commitment from all stakeholders to a long-term plan, involving regular strategic review, will support a step-by-step approach: moving systematically through prevalence reduction by vaccination, then test and slaughter, the potential ramping up of surveillance to demonstrate freedom, and using stamping-out to accelerate the final stages, as required. Technical capacity must be established to address the challenges that arise at every step of the way, from planning, to implementation, to monitoring and evaluation.**

With the *Roadmap for Zoonotic Tuberculosis*, the building blocks are identified and will be progressively put in place to bring to bear that vital international commitment. Such commitment must support each Member Country as they embark on and sustain a national programme suited to their circumstance. **Success in controlling bovine tuberculosis requires clear thinking and careful planning, starting with designing a programme based on agreed strategic objectives.**

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(1) 'compartment' means an animal subpopulation contained in one or more establishments, separated from other susceptible populations by a common biosecurity management system, and with a specific animal health status with respect to one or more infections or infestations for which the necessary surveillance, biosecurity and control measures have been applied for the purposes of international trade or disease prevention and control in a country or zone. [5]

(2) 'zone' means a part of a country defined by the Veterinary Authority, containing an animal population or subpopulation with a specific animal health status with respect to an infection or infestation for the purposes of international trade or disease prevention or control. [5]

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DOSSIER

The socio-economic costs of bovine tuberculosis

AUTHORS

Antonino Caminiti, Chargé de mission, Science Department, World Organisation for Animal Health (OIE).

Calculating the full socio-economic costs of bovine tuberculosis (bTB) is a complex exercise that requires the evaluation of multiple factors, such as perspective (viewing the impact of the disease through a social lens or a business one); the animal population involved (domestic livestock or wildlife); the zoonotic impact on human health; and especially the context (is the occurrence in a developed or a developing country?).

Costs in developed countries

In developed countries, where the prevalence of bTB is generally low, the direct and indirect costs of bTB are mainly related to trade barriers for live animals and animal products, as well as the financial costs of implementing compulsory bTB eradication programmes. Studies suggested that the majority of the cost of eradication (about 80%) is due to veterinarians performing skin tests [1]. Eradication costs can be so large that some authors have questioned the benefits of such interventions [2]. Conversely, others believe that, when all the benefits are taken into account, including societal benefits, the eradication of bTB is economically viable [3].

Other kinds of costs, such as intangible costs, are rarely assessed in scientific studies, even if their impact can be devastating for rural communities and the farming industry. These costs include, for instance, the impact on the country's reputation, consumer loss of trust and adverse market reactions.

Costs in developing countries

In developing countries, the prevalence of bTB in animals and humans is high because of deficiencies in the implementation of preventive measures (e.g. the scarceness of pasteurisers and lack of controls in animals and meat, due to financial constraints). The costs of bTB are mainly related to livestock production losses, including increased mortality and lower milk and meat production. Estimates of such losses have been produced for countries with a large livestock population, such as Ethiopia [4].

Conclusions

Most of the time, cost evaluations focus primarily on livestock production losses. There is a need for comprehensive studies to estimate the global burden of this disease, including its full cost on society.

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DOSSIER

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Efficacy of BCG vaccine for the control of tuberculosis in domestic livestock and wildlife

AUTHORS

Bryce M. Buddle, AgResearch, Hopkirk Research Institute, Palmerston North, New Zealand.

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Control of bTB remains a difficult problem in many countries, particularly where 'test-and-slaughter' policies cannot be implemented or where wildlife reservoirs of Mycobacterium bovis serve as a recurrent source of infection for domestic livestock. Alternative control measures are urgently required and vaccination is a promising option.

| The use of BCG vaccine in animals has been limited

Although the *M. bovis* bacille Calmette–Guérin (BCG) vaccine has been used in humans for nearly a century, its use

in animals has been limited, principally because protection against tuberculosis has been incomplete and vaccination may result in animals reacting in the tuberculin skin test. However, in the past 25 years, the protection induced by BCG vaccine in animals has been optimised and tests to differentiate infected from vaccinated animals (DIVA) have been developed.

BCG vaccination can moderate the severity of the disease in domestic livestock

Experimental challenge studies in domestic livestock, including cattle, goats and farmed deer, have demonstrated that BCG vaccination can moderate the severity of the disease, while field trials in cattle and goats have indicated that vaccination can also reduce infection. No single vaccine has been shown to be better than BCG in cattle, although combinations of BCG with various subunit tuberculosis vaccines have produced encouraging results and could be applied in the future [1, 2]. Vaccination of cattle with BCG would have greatest application in countries where 'test-and-slaughter' strategies are not affordable or socially acceptable and, in this situation, BCG could play a role in reducing the spread of bTB. Alternatively, vaccination could be integrated with 'test-and-slaughter' control measures, where DIVA tests are used for bTB diagnosis, particularly skin tests utilising specific *M. bovis* antigens [3].

The experimental use of BCG vaccine in wildlife is showing promise

The field testing of BCG vaccine, administered via oral or parenteral routes, in possums and badgers has resulted in significant reductions in the infection of these animals, and a parenteral BCG vaccine has now been licensed for use in badgers in the United Kingdom [4, 5]. In wild boar, feral deer and ferrets, BCG vaccine has been shown to induce significant levels of protection against experimental challenge with bTB, and practical systems for the delivery of oral bait bTB vaccines to wildlife have now been established [2].

In summary, studies in recent years have markedly improved our understanding of the factors influencing BCG vaccine efficacy and, in future, vaccination should be a valuable control measure for bTB in domestic livestock and wild animals.

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DOSSIER

Reverse vaccinology approach for novel bovine tuberculosis vaccines

The Canadian ReVAMP project

KEYWORDS

#bovine tuberculosis, #diagnostic test, #DIVA vaccine, #genomics, #Johne's disease, #paratuberculosis, #proteomics, #ReVAMP, #reverse vaccinology.

AUTHORS

Jeffrey Chen[1], Volker Gerdts[2]* & Andrew Potter[3]**

(1) Molecular Microbiologist, Vaccine and Infectious Disease Organization – International Vaccine Centre (VIDO–InterVac), University of Saskatchewan, Canada.
(2) Associate Director of Research, Vaccine and Infectious Disease Organization – International Vaccine Centre (VIDO–InterVac), University of Saskatchewan, Canada.
(3) Director and Chief Executive Officer, Vaccine and Infectious Disease Organization – International Vaccine Centre (VIDO–InterVac), University of Saskatchewan, Canada.

* Corresponding author: volker.gerdts@usask.ca
** At the time of publication of this article, Dr Andrew Potter had retired and Dr Volker Gerdts is the new Director and Chief Executive Officer of VIDO–InterVac.

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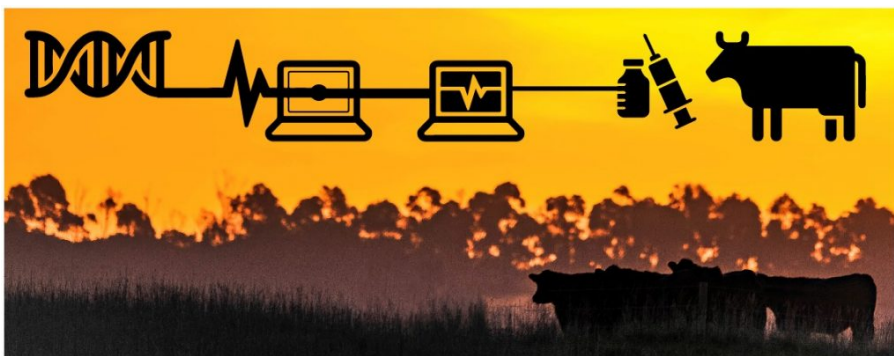
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Test-and-slaughter is the primary method of bovine tuberculosis (bTB) control, but it has encountered growing public scrutiny and disapproval. Moreover, this approach is often untenable in developing nations for social and economic reasons. Therefore, alternative control methods are needed.

Vaccines are widely recognised as the most cost-effective way to prevent infections, but their application to the control of bTB in livestock is limited. Although the live attenuated Bacillus Calmette–Guérin (BCG) vaccine has protected humans against tuberculosis for decades, **there are concerns that its use in livestock will render the tuberculin skin test for bTB diagnosis ineffectual**.

> In Canada, scientists are taking a reverse vaccinology approach to develop new vaccines

To address the urgent need for a bTB vaccine, scientists at VIDO-InterVac, the largest biocontainment research facility in Canada, and collaborators at the University of British Columbia and the University of Calgary are taking a reverse vaccinology approach to develop vaccines for the prevention of mycobacterial diseases in cattle (ReVAMP), including bTB and Johne's disease.

A genomics-based strategy is employed to identify and assess *Mycobacterium bovis* cell-surface and secreted proteins for their potential as bTB vaccine components in experimentally infected calves. The immune responses of calves to *M. bovis infection* are assessed to identify bacterial proteins expressed during infection. Using bioinformatics techniques, the proteins that might provoke an immune response are prioritised for production in

Escherichia coli, tested and developed into novel DIVA[1] vaccine formulations and companion diagnostic tests. In parallel, the competitiveness of bTB DIVA vaccines and companion diagnostics versus the existing test-and-slaughter strategy are being evaluated by investigating public perceptions and industry readiness, commercialisation strategies, and the regulatory systems required for optimal user uptake.

To date, 297 *M. bovis* proteins have been identified, of which 80 have been tested in calves experimentally infected with bTB. This ongoing project is expected to deliver bTB DIVA vaccines, companion diagnostics and a white paper to inform the public, producers and governments of the best strategies to fight bTB.

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(1) DIVA: **d**ifferentiation of **i**nfected from **v**accinated **a**nimals

DOSSIER

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Prevalence of bovine tuberculosis in India

(Abstract from manuscript)

AUTHORS

Sreenidhi Srinivasan[1,2], Laurel Easterling[1,2], Bipin Rimal[2], Xiaoyue Maggie Niu[3], Andrew J.K. Conlan[4], Patrick Dudas[2] & Vivek Kapur[1,2]*

(1) Department of Animal Science, The Pennsylvania State University, United States of America.
(2) The Huck Institutes of the Life Sciences, The Pennsylvania State University, United States of America.
(3) Department of Statistics, Eberly College of Science, The Pennsylvania State University, United States of America.
(4) Disease Dynamics Unit, Department of Veterinary Medicine, University of Cambridge, United Kingdom.

* Corresponding author: vkapur@psu.edu

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Bovine tuberculosis (bTB) is a chronic disease of cattle that affects productivity and represents a major public health threat. Despite the considerable economic costs and zoonotic risk associated

with the disease, accurate estimates of bTB prevalence are lacking in many countries, including India, where national control programmes are not yet implemented and the disease is considered endemic.

To address this critical knowledge gap, we performed a systematic review of the literature and a meta-analysis to estimate bTB prevalence in cattle in India, and provide a foundation for the formulation of rational disease control strategies and the accurate assessment of economic and health impact risks.

The literature search was performed in accordance with PRISMA guidelines and identified 285 cross-sectional studies on bTB in cattle in India across four electronic databases and handpicked publications. Of these, 44 articles were included, contributing a total of 82,419 cows and buffaloes across 18 states and one union territory.

Based on a random-effects (RE) meta-regression model, the analysis revealed a pooled prevalence estimate of 7.3% (95% confidence interval [CI]: 5.6 – 9.5) (see Fig. 4 and Table 7 in the original research article, entitled *Prevalence of bovine tuberculosis in India: a systematic review and meta-analysis* and published in ***Transboundary and Emerging Diseases*** [1]), indicating that there may be an estimated 21.8 million (95% CI: 16.6 – 28.4) infected cattle in India – a population greater than the total number of dairy cows in the United States of America. The analyses further suggest that production system, species, breed, study location, diagnostic technique, sample size and study period are likely moderators of bTB prevalence in India and need to be considered when developing future disease surveillance and control programmes.

Taken together with the projected increase in intensification of dairy production and the subsequent increase in the likelihood of zoonotic transmission, the results of our study suggest that attempts to eliminate tuberculosis from humans will require simultaneous consideration of bTB control in cattle populations in countries such as India.

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DOSSIER

A retrospective study on bovine tuberculosis in cattle in Fiji

(Abstract from manuscript)

AUTHORS

Elva Borja[1,2], Leo F. Borja[3], Ronil Prasad[3], Tomasi Tunabuna[3] & Jenny-Ann L.M.L. Toribio[1]*

(1) University of Sydney, Australia.
(2) Vet Essentials, Fiji.
(3) Ministry of Agriculture, Fiji.

* Corresponding author: jenny-ann.toribio@sydney.edu.au

In recognition of the adverse impacts of bovine tuberculosis (bTB), a Brucellosis and Tuberculosis Eradication and Control (BTEC) programme began in Fiji during the 1980s and has since been sustained by government funding and industry cooperation.

A retrospective study of bTB data from 1999 to 2014 from the BTEC programme was carried out with support from the Government of Fiji (see the original research article entitled *A retrospective study on bovine tuberculosis in cattle in Fiji: study findings and stakeholder responses* and published in ***Frontiers in Veterinary Science*** [1]). It confirmed that bTB is well established in dairy cattle farms in two provinces of Central Division on the main island of Viti Levu, and suggested that the disease is also present among cattle in all or most provinces across three of the four Divisions in the country: Central, Northern and Western[1]. Despite sustained efforts, disease reduction and containment has not been achieved. Reasons include the appropriateness of the protocol and quality assurance when performing the single intradermal test (SID) in cattle, lack of standard procedures for data collection and evaluation, and unregulated movements of stray and owned cattle.

The Fijian Ministry of Agriculture (MOA) actively responded to these findings by revising the use of SID and providing refresher training for staff, as well as imposing cattle movement restrictions by the Biosecurity Authority of Fiji. Furthermore, a stakeholder forum in May 2017 formulated and endorsed a new Fiji BTEC strategy.

Concerned about the potential contribution of zoonotic tuberculosis to the human tuberculosis burden in Fiji, due to practices such as raw milk consumption and levels of extra-pulmonary tuberculosis, the MOA and Fiji Ministry of Health and Medical Services, with support from the University of Sydney Marie Bashir Institute, will conduct a pilot geospatial analysis of human tuberculosis cases and bTB-infected cattle farms to identify high-risk areas for bTB exposure. The contribution of bTB to extra-pulmonary tuberculosis cases in Fiji is unknown because routine diagnostics do not distinguish between pathogen species [2].

Bovine tuberculosis remains a focus for disease control by the Fijian Government. This case study highlights the challenges for bTB control and underlines the importance of technical and social considerations when trying to achieve success in disease control in Fiji.

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(1) Fiji is divided into four major divisions (Central, Eastern, Northern, Western) which are further divided into a total of 14 provinces.

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DOSSIER

Efficacy of oral BCG vaccination in protecting free-ranging cattle

(Abstract from manuscript)

AUTHORS

Graham Nugent[1], Ivor J. Yockney[1], Jackie Whitford[1], Frank E. Aldwell[2] & Bryce M. Buddle[3]*

(1) Manaaki Whenua – Landcare Research, PO Box 40, Lincoln, 7640, New Zealand.
(2) Centre for Innovation, University of Otago, Dunedin, New Zealand.
(3) AgResearch, Hopkirk Research Institute, Palmerston North, New Zealand.

* Corresponding author: bryce.buddle@agresearch.co.nz

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Vaccination of cattle against bovine tuberculosis could be a particularly valuable control strategy in countries faced with intractable ongoing infection from a disease reservoir in wildlife [1].

A field vaccination trial was undertaken in New Zealand which included 1,286 effectively free-ranging cattle stocked at low densities in a remote 7,600 ha area; 55% were vaccinated using a high dose (10^{7-8} colony forming units [cfu]) of *Mycobacterium bovis* BCG (Danish strain 1311) (see the original research article, *Efficacy of oral BCG vaccination in protecting free-ranging cattle from natural infection by* Mycobacterium bovis, published in ***Veterinary Microbiology*** [2]). Vaccine was administered orally in all but 34 cases (where it was injected). The cattle were exposed to natural sources of *M. bovis* infection in cattle and wildlife, most notably the brushtail possum (*Trichosurus vulpecula*). Cattle were slaughtered at 3–5 years of age and inspected for tuberculous lesions, with mycobacteriological culture of tissues from almost all animals. The prevalence of *M. bovis* infection was 4.8% among oral BCG vaccinates, significantly lower than the 11.9% in non-vaccinates.

Vaccination appeared to reduce the incidence of infection, and to slow disease progression substantially in cattle that did become infected. Based on apparent annual incidence, the protective efficacy of oral BCG vaccine was 67.4% for preventing infection, and was higher in cattle slaughtered soon (within 1–2 years) after vaccination. Skin-test reactivity to tuberculin was initially elevated, being high in vaccinates re-tested 70 days after oral vaccination but not in non-vaccinates, although reactor animals had minimal response in gamma-interferon blood tests. However, in re-tests conducted more than 12 months after vaccination, skin-test reactivity among vaccinates did not differ significantly from that in non-vaccinates. These results indicate that oral BCG vaccination could be an effective tool for greatly reducing detectable infection in cattle.

A subsequent similar trial in the same area involving a much lower dose (3×10^5 cfu) of BCG, delivered by injection, reduced the apparent annual incidence of abattoir-detectable infection by 87% [3].

Highlights

- Bovine tuberculosis is difficult to eliminate from livestock where infected wildlife is present.
- Oral BCG vaccination was trialled in free-ranging New Zealand cattle exposed to a combined cattle and wildlife tuberculosis reservoir.
- Vaccination showed 67.4% efficacy in preventing infection and also slowed disease progression in infected cattle.
- Vaccination of livestock could be useful where tuberculosis persists in wildlife reservoirs.

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DOSSIER

BCG-compatible DIVA skin tests for cattle vaccinated against bovine tuberculosis

AUTHORS

H.M. Vordermeier[1,2]*, G. Jones[2], V. Kapur[3] & R.G. Hewinson[1]

(1) Institute for Biological, Environmental and Rural Sciences, Aberystwyth University, United Kingdom.
(2) Animal and Plant Health Agency, Department of Bacteriology, Addlestone, United Kingdom.
(3) The Pennsylvania State University, Department of Animal Sciences, and The Huck Institutes, University Park, Pennsylvania, United States of America.

* Corresponding author: martin.vordermeier@apha.gov.uk

Vaccination with Bacillus Calmette–Guérin (BCG) could be an additional tool to control bovine tuberculosis in cattle. However, to continue with 'test-and-cull' control programmes, BCG-compatible tests to distinguish infected amongst vaccinated animals (DIVA) are required. We summarise herein our recent progress towards the development of a DIVA skin test.

Cattle vaccination could be added to existing control strategies, but the only cattle vaccine candidate available, BCG, does not protect all vaccinated animals and compromises the utility of tuberculin purified protein derivative (PPD) in diagnostic tests. To apply BCG alongside PPD-based test-and-cull approaches, e.g. based on the single intradermal comparative cervical tuberculin test (SICCT), requires replacing or supplementing PPD with BCG-compatible tests to detect infected animals within vaccinated populations.

The discovery that a number of gene regions were deleted from the BCG genome during its attenuation allowed a rational search for DIVA antigens based on antigens encoded by these 'regions of difference'. Two such antigens, ESAT-6 and CFP-10, were shown to fulfil the DIVA criteria [1]. However, although these two DIVA antigens were highly specific in cattle, their sensitivity was inferior to that of PPD. Subsequently, an 'omics'-based antigen mining programme identified the antigen Rv3615c, which when used to complement ESAT-6 and CFP-10 provided significant additional sensitivity without reducing specificity [2]. However, matching DIVA specificity in BCG-vaccinated animals to SICCT specificity in unvaccinated cattle using the blood test format resulted in loss of sensitivity. We correctly hypothesised that the required high specificity could be achieved by using a cocktail of the three antigens as skin test antigens [3]. This cocktail displayed comparable sensitivity to the SICCT, while its specificity in BCG-vaccinated animals matched that of the SICCT in unvaccinated cattle [4].

Further product development led to the generation of a fusion protein composed of all three antigens [5] which exhibited performance equal to that of the protein cocktail, but with a better production and stability profile. A parallel development led to a peptide cocktail representing the same proteins. The next stage in the development of these potentially groundbreaking DIVA reagents is to validate them to OIE standards [6].

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AROUND THE WORLD

▶ OIE ACTIONS

OIE project to replace International Standard Bovine Tuberculin

AUTHORS

Glen Gifford[1]*, Bernardo Alonso[2], Maria Laura Boschiroli[3], Antonino Caminiti[4], Randal Capsel[5], Steven Edwards[6], Glyn Hewinson[7],

Mei Mei Ho[8], Lucia de Juan Ferré[9], Ad Koets[10], Jeanet Van der Goot[11], Martin Vordermeier[12] & Simona Forcella[13]

(1) Chargé de mission, Antimicrobial Resistance and Veterinary Products Department, World Organisation for Animal Health (OIE).
(2) Gerencia de Laboratorios (GELAB), Servicio Nacional de Sanidad y Calidad, Agroalimentaria (SENASA), Buenos Aires, Argentina.
(3) Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES), Unité Zoonoses bactériennes, Laboratoire de santé animale, Maisons-Alfort, France.
(4) Chargé de mission, Science Department, World Organisation for Animal Health (OIE).
(5) National Veterinary Services Laboratories, USDA APHIS Veterinary Services, Ames, Iowa, United States of America.
(6) c/o World Organisation for Animal Health (OIE).
(7) Animal and Plant Health Agency (APHA), Surrey, United Kingdom.
(8) Principal Scientist, Bacteriology Division, MHRA-NIBSC, Potters Bar, United Kingdom.
(9) European Union Reference Laboratory for Bovine Tuberculosis, Centro de Vigilancia Sanitaria Veterinaria (VISAVET), Universidad Complutense, Madrid, Spain.
(10) Senior Scientist – Project Leader, Mycobacterial Infections and Tuberculosis, Central Veterinary Institute; and Head, National Reference Laboratory for Mycobacterial Diseases and Tuberculosis, Wageningen Bioveterinary Research (WBVR), Lelystad, The Netherlands.
(11) Veterinary Epidemiology, Risk Analysis and Statistics, Wageningen Bioveterinary Research (WBVR), Lelystad, The Netherlands.
(12) Team leader (TB Immunology and Vaccinology), Department of Bacteriology, Animal and Plant Health Agency (APHA), Surrey, United Kingdom.
(13) Policy Officer, DG SANTE, European Commission.

* Corresponding author: g.gifford@oie.int

bulletin

An OIE ad hoc Group of bovine tuberculosis (bTB) experts is coordinating a project to evaluate, calibrate and validate a replacement for the OIE's International Standard Bovine Tuberculin (ISBT). The ISBT is used as a reference standard for quality control tests for purified protein derivative (PPD) bovine tuberculins that are used in bTB surveillance, diagnosis and export certification. The current reference standard was produced in 1986 and is becoming depleted, so it must be replaced.

The ISBT replacement project [1] involves participants from OIE Headquarters; an *ad hoc* Group of bTB experts from the OIE Reference Laboratories for bTB (from France, Argentina and the United Kingdom); the United Kingdom National Institute for Biological Standards and Control (NIBSC) for preparation, storage and distribution of the tuberculins; and collaborating scientists from approximately 15 other national laboratories.

In the candidate tuberculin validation studies, two candidate tuberculins will be tested in guinea pigs and cattle, in comparison with the current ISBT, to evaluate and calibrate the candidate tuberculins' potency and specificity, and assess the candidates' overall 'fitness for purpose'.

A preliminary evaluation has been completed with satisfactory results

The laboratory testing is scheduled in two phases. A preliminary evaluation was conducted in guinea pigs, and has now been completed with satisfactory results. A larger-scale international collaborative study is scheduled for September 2018 to June 2019 in which the performance of the two candidate tuberculins will be further assessed in guinea pigs to evaluate potency and specificity, as well as in experimentally infected cattle and naturally sensitised 'reactor' cattle to evaluate 'fitness for purpose'.

When the tests have been completed, provided the data are satisfactory, the *ad hoc* Group will prepare a comprehensive report and submit it for approval/endorsement through the OIE governance processes that include endorsement by experts of the OIE Biological Standards Commission, and adoption by OIE Member Country Delegates at the OIE General Session.

Once the study has been endorsed by the Delegates, the *ad hoc* Group will prepare a summary report for publication in a peer-reviewed scientific journal, and the NIBSC will be able to begin distributing the new ISBT.

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OIE *ad hoc* Group reports

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AROUND THE WORLD

▶ OIE ACTIONS

OIE procedure for Member Country self-declaration of freedom from bovine tuberculosis

AUTHORS

Hernán Daza[1]* & Marija Popović[2]

(1) Chargé de mission, Status Department, World Organisation for Animal Health (OIE).
(2) Chargée de mission, Status Department, World Organisation for Animal Health (OIE).

* Corresponding author: self-declaration@oie.int

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OIE Member Countries may wish to self-declare freedom from an animal disease, for transparency and trade facilitation purposes. At a Member's request, the OIE may publish this claim on a dedicated webpage after an objective and transparent internal review, governed by an established procedure.

Publication of the self-declaration does not imply OIE official endorsement of the claim, but it acknowledges the country's conformance to the relevant documented evidence of the Member's compliance with the relevant international standards.

By joining the OIE, a Member Country undertakes to notify animal disease events that it detects on its territory. This

notification reflects how well a country fulfils its obligation of transparency and enables the progress of its disease control programmes, including its ability to maintain its disease-free status, to be monitored [1].

When a Member Country declares itself or a zone or compartment free from an OIE listed disease [2] or another animal disease,[1] OIE standards provide for the Member to inform the OIE of this achievement by submitting the self-declaration accompanied by documented evidence of compliance with the provisions of the *Terrestrial Animal Health Code (Terrestrial Code)* or the *Aquatic Animal Health Code (Aquatic Code)*. At the Member's request, the OIE may then publish the self-declaration on its website, thereby enabling the Member to enhance the visibility of its animal health situation. The submitted documents should follow the Standard Operating Procedure for publication of self-declarations, a procedure that includes a technical screening based on the information available in WAHIS and on the relevant requirements of the OIE *Codes*.

OIE Member Countries interested in making self-declarations of country or zone freedom from infection with *Mycobacterium tuberculosis complex* in bovids are invited to review the OIE provisions in Article 8.11.4. of the *Terrestrial Code*. According to these requirements, Members have to provide evidence of the following: the disease is notifiable, regulatory measures have been implemented for early detection of the infection, a surveillance programme based on regular testing of all herds in the country or zone has been in place for the required period, and a surveillance programme is in place to detect the infection through ante- and post-mortem inspections of bovids. Additionally, and according to its disease situation, a country or zone may be considered historically free from infection with *M. tuberculosis* complex in specified animal categories when the requirements of point 1 *a)* of Article 1.4.6. have been met for the relevant animal categories.

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(1) The OIE does not publish self-declarations for diseases that are included in the OIE official recognition procedures, namely: bovine spongiform encephalopathy (BSE), foot and mouth disease (FMD), contagious bovine pleuropneumonia (CBPP), African horse sickness (AHS), peste des petits ruminants (PPR) and classical swine fever (CSF)

For more information on the publication of self-declarations on the OIE website,
please contact the OIE at: self-declaration@oie.int

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AROUND THE WORLD

▶ NETWORK INITIATIVES

Improving the coordination of research into bovine tuberculosis: the STAR–IDAZ IRC

AUTHORS

Stefano Messori[1]*, Alex Morrow[2] & Glen Gifford[3]

(1) Secretariat for STAR-IDAZ IRC; Chargé de mission, Science Department, World Organisation for Animal Health (OIE).
(2) Secretariat for STAR-IDAZ IRC; Department of Environment, Farming & Rural Affairs (DEFRA), United Kingdom.
(3) Chargé de mission, Antimicrobial Resistance and Veterinary Products Department, World Organisation for Animal Health (OIE).

* Corresponding author: s.messori@oie.int

The Strategic Alliance for Research on Infectious Diseases of Animals and Zoonoses–International Research Consortium on Animal Health (STAR–IDAZ IRC) is a self-sustained network of public and private research funders and programme owners. STAR–IDAZ's aim is to maximise funding for coordinated animal health research and to contribute to new and improved animal health strategies and control tools for priority diseases/infections/issues. The STAR–IDAZ IRC Secretariat is co-hosted by the World Organisation for Animal Health (OIE).

The STAR–IDAZ IRC is establishing expert working groups to analyse gaps in research and to draft research roadmaps and project summaries for specific diseases and issues. The previously formed Global Research Alliance

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on Bovine Tuberculosis (GRAbTB) serves as the STAR–IDAZ IRC Working Group for Bovine Tuberculosis (bTB).

The STAR–IDAZ IRC Secretariat and GRAbTB jointly organised a workshop in Birmingham, the United Kingdom, on 11–12 December 2017, to develop three research roadmaps to coordinate and guide bTB research.[1] The first day of the workshop was devoted to overview presentations and break-out group discussions to highlight continuing research projects. This was to provide background information before starting work on the STAR–IDAZ IRC research roadmaps for:

- vaccines
- diagnostics
- epidemiology and control.

Draft roadmaps were developed by the GRAbTB with the support of the STAR–IDAZ IRC Secretariat before the meeting. In break-out discussion groups, the experts were asked to build on these draft roadmaps, identifying potential key missing challenges, information and tools, and to consider if there might be alternative or novel pathways, as well as other start and end points and dependencies to take into account.

_____

(1) This workshop was held shortly after the October 2017 launch of the *Roadmap for Zoonotic Tuberculosis*, which identified research as one of the key priorities to address zoonotic tuberculosis caused by *Mycobacterium bovis*.

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Bovine tuberculosis research roadmaps and project summaries

AROUND THE WORLD

▶ NETWORK INITIATIVES

OIE Reference Laboratories for Bovine Tuberculosis

AUTHORS

Bernardo Alonso[1], Maria Laura Boschiroli[2]* & Glyn Hewinson[3]

(1) Gerencia de Laboratorios (GELAB), Servicio Nacional de Sanidad y Calidad Agroalimentaria (SENASA), Buenos Aires, Argentina.
(2) Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES), Unité Zoonoses bactériennes, Laboratoire de santé animale, Maisons-Alfort, France.
(3) Animal and Plant Health Agency (APHA), New Haw, Addlestone, Surrey, Weybridge, United Kingdom.

* Corresponding author: Maria-laura.BOSCHIROLI@anses.fr

The OIE has a network of experts and Reference Laboratories that are designated to pursue the scientific and technical problems relating to named diseases, such as bovine tuberculosis [1].

There are three OIE Reference Laboratories for Bovine Tuberculosis. They are located at the Animal and Plant

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Health Agency (APHA) in the United Kingdom, the Agency for Food, Environmental and Occupational Health & Safety (ANSES) in France, and the National Food Safety and Quality Service (SENASA) in Argentina. Each of these laboratories is also a national reference laboratory for their country.

The designated experts in the Reference Laboratories provide training, expert advice and scientific and technical assistance to personnel from Member Countries. In addition, they coordinate scientific and technical studies in collaboration with other laboratories or organisations.

The OIE Bovine Tuberculosis Reference Laboratories have the facilites and expertise to perform a broad range of specialised laboratory tests that are used in bovine tuberculosis diagnosis, as well as research to study host–bacterium interactions. The Reference Laboratory experts are also experienced in dealing with diverse epidemiological situations within their respective countries. Consequently, the OIE Bovine Tuberculosis Reference Laboratory network experts can offer their expertise and advice on a broad range of topics, including molecular methods for studying complex epidemiological aspects of bovine tuberculosis, which may involve multi-host transmission cyles between domestic livestock and wildlife.

The activities of the Bovine Tuberculosis Reference Laboratories are summarised in annual reports. These reports are intended to help raise awareness among scientists, other stakeholders, and the public of the scope of the laboratory expertise and advice that are available from the Reference Laboratories to support scientists from OIE Member Countries who work on bovine tuberculosis.

OIE Reference Laboratories for Bovine Tuberculosis

Dr Bernardo Alonso
Gerencia de Laboratorios (GELAB) del Servicio Nacional de Sanidad y Calidad Agroalimentaria (SENASA)
Avda A. Fleming 1653
1640 Martínez
Pcia de Buenos Aires
Argentina
Tel. +54-11 48 36 19 92 / 11 73
balonso@senasa.gov.ar

Dr María Laura Boschiroli-Cara
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)
Unité Zoonoses bactériennes
Laboratoire de santé animale
23, avenue du Général de Gaulle
94706 Maisons-Alfort Cedex
France
Tel. +33-1 49 77 13 00
maria-laura.boschiroli@anses.fr

Prof. Glyn Hewinson
Animal and Plant Health Agency

Woodham Lane
Addlestone
Surrey, KT15 3NB
United Kingdom
Tel. +44-1932 34 11 11
glyn.hewinson@apha.gov.uk

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AROUND THE WORLD

▶ NETWORK INITIATIVES

Mycobacterium bovis infection of wildlife in France

Assessment through a national surveillance system, Sylvatub (Abstract from manuscript)

AUTHORS

Édouard Réveillaud[1], Stéphanie Desvaux[2], Maria-Laura Boschiroli[3]*, Jean Hars[2], Éva Faure[4], Alexandre Fediaevsky[5], Lisa Cavalerie[5], Fabrice Chevalier[5], Pierre Jabert[5], Sylvie Poliak[6], Isabelle Tourette[7], Pascal Hendrikx[1] & Céline Richomme[8]

(1) Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES), Unité Coordination et appui de la surveillance, Maisons-Alfort, France. *Current address for Édouard Réveillaud: Direction régionale de l'alimentation de Nouvelle-Aquitaine, Limoges, France.*
(2) Office national de la chasse et de la faune sauvage (ONCFS), Direction de la recherche et de l'expertise (DRE), Auffargis, France.
(3) Université Paris-Est – ANSES, Laboratoire national de référence pour la tuberculose, Maisons-Alfort, France.
(4) Fédération nationale des chasseurs (FNC), Issy-les-Moulineaux, France.
(5) Direction générale de l'alimentation (DGAL), Bureau de la santé animale, Paris, France.
(6) Association française des directeurs et cadres des laboratoires vétérinaires publics d'analyses (Adilva), Paris, France.
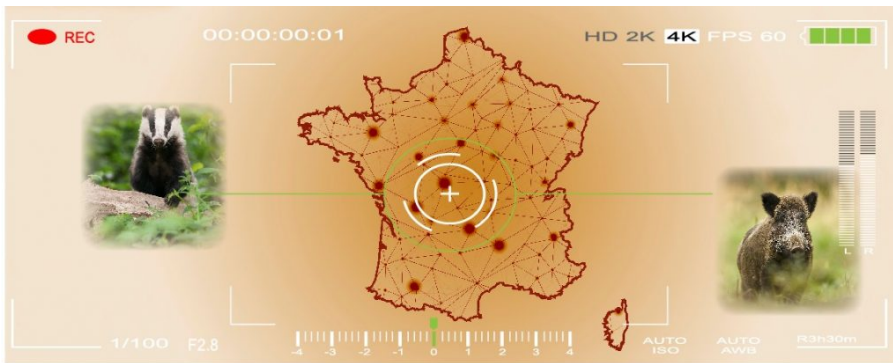(7) Fédération nationale des groupements de défense sanitaire (GDS France), Paris, France.
(8) Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES), Laboratoire de la rage et de la faune sauvage de Nancy, Malzéville, France.

* Corresponding author: maria-laura.boschiroli@anses.fr

PANORAMA 2019-1

Mycobacterium bovis infection was first described in free-ranging wildlife in France in 2001, and was subsequently detected in hunter-harvested ungulates and badgers in areas where outbreaks of bovine tuberculosis (bTB) were also detected in cattle. Increasing concerns about bTB in wildlife led the General Directorate for Food (DGAL) and the main French institutions involved in animal health and wildlife management to establish a national surveillance system for bTB in free-ranging wildlife.

This surveillance system is known as **Sylvatub**. The system coordinates the activities of various national and local partners. The main goal of Sylvatub is to detect and monitor *M. bovis* infection in wildlife through a combination of passive and active surveillance protocols, adapted to the estimated risk level in each part of the country. Event-based surveillance relies on *M. bovis* identification (molecular detection) in:

a) gross lesions detected in hunter-harvested ungulates
b) ungulates that are found dead or dying
c) road-killed badgers.

Additional targeted surveillance of badgers, wild boar and red deer is carried out on samples from trapped or hunted animals in at-risk areas.

With the exception of one unexplained case in a wild boar, *M. bovis* infection in free-living wildlife has always been detected in the vicinity of bTB outbreaks in cattle, with the same genotype of the infectious *M. bovis* strains. Since 2012, *M. bovis* has been actively monitored in these infected areas and detected mainly in badgers and wild boar, with apparent prevalence rates of 4.57–5.14% and 2.37–3.04%, respectively, depending on the diagnostic test used (culture or polymerase chain reaction), the sample collection period and the area concerned. Sporadic infection has also been detected in red and roe deer.

This surveillance has demonstrated that *M. bovis* infection in France involves multiple hosts in different areas (Fig. 1), including cattle and wildlife. However, prevalence rates are lower than those observed in badgers in the United Kingdom or in wild boar in Spain.
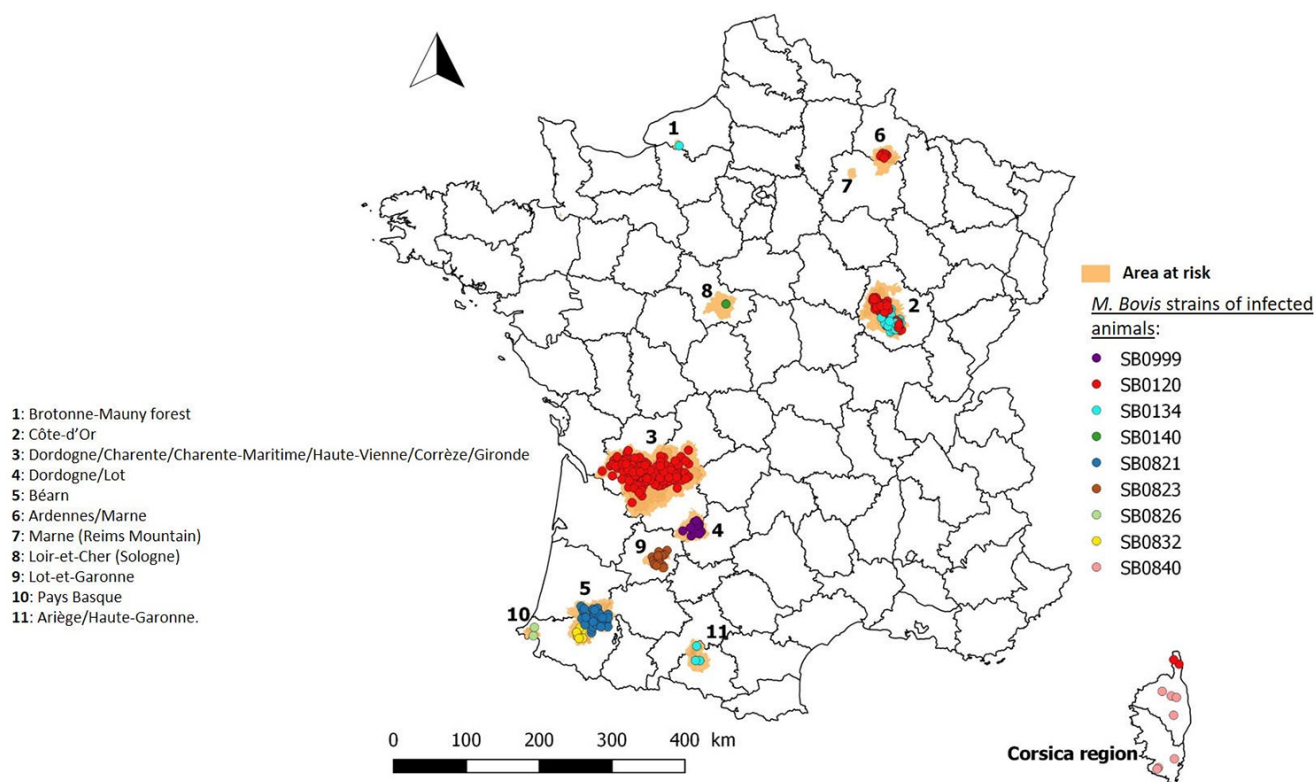
bulletin

1: Brotonne-Mauny forest
2: Côte-d'Or
3: Dordogne/Charente/Charente-Maritime/Haute-Vienne/Corrèze/Gironde
4: Dordogne/Lot
5: Béarn
6: Ardennes/Marne
7: Marne (Reims Mountain)
8: Loir-et-Cher (Sologne)
9: Lot-et-Garonne
10: Pays Basque
11: Ariège/Haute-Garonne.

Fig. 1. Location of Mycobacterium bovis strains in wildlife in France

DOI of the original research article published in *Frontiers in Veterinary Science*:

https://doi.org/10.3389/fvets.2018.00262

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AROUND THE WORLD

▶ SUCCESS STORIES

Lessons learned from Australian success during the successful eradication of bovine tuberculosis

AUTHORS

Simon J. More[1]*, Brian Radunz[2] & Ron J. Glanville[3]

(1) Professor of Veterinary Epidemiology and Risk Analysis, School of Veterinary Medicine, University College Dublin, Ireland.
(2) Ex-CVO of the Northern Territory, PO Box 678, Howard Springs, Northern Territory, Australia.
(3) Ex-CVO of Queensland, Biosecurity Advisory Service, PO Box 476, Woodend, Victoria, Australia.

* Corresponding author: simon.more@ucd.ie

Australia is one of very few countries to have successfully eradicated bovine tuberculosis (bTB). The last known bTB case was recorded in 2002, following a 27-year national eradication campaign. Despite ongoing intensive surveillance, no further cases of Mycobacterium bovis have been found, either in domestic or wild animal populations. Numerous lessons can be learned

from the success of the eradication campaign which may be relevant to other countries.

The following is a brief overview of key lessons learned during Australia's Brucellosis and Tuberculosis Eradication Campaign (BTEC), as outlined by More *et al.* [1], which were both technical and non-technical in nature:

• **A compelling rationale**. The Australian cattle industry is highly export-oriented, and there were real concerns before the start of BTEC that bTB might threaten international trade. This was a compelling rationale for eradication, both nationally and also for individual farmers.

• **A clear, agreed outcome**. Across both government and industry, there was a shared purpose with a common goal; namely, the eradication of *bovis* from the Australian cattle and buffalo population.

• **A government–industry partnership**. Genuine industry commitment proved crucial to BTEC's success. BTEC decision-making was a partnership between government and industry, with the cattle industry actively involved at all levels of management, including nationally, regionally and on individual farms. Cost-sharing between the industry and government was also an important feature throughout BTEC, using industry funds collected through levies. These arrangements evolved during BTEC, with the cattle industry covering 50% of programme costs (operations, compensation, additional assistance measures) during the latter half of the programme.

• **A business model**. BTEC was underpinned by detailed forward planning, including multi-annual strategic plans and annual operational plans.

• **Technical standards**. Key features of BTEC included consistent and transparent technical standards and a strict regulatory regime. Improving livestock traceability through the introduction of the tail-tag system linked to property identification codes was an important element of the control and eradication programme. The programme was also underpinned by applied research.

• **Abattoir surveillance**. This was the primary method of surveillance to detect herds not previously known to be infected, and a number of strategies were used to maximise its sensitivity.

• **Effective elimination of residual infection**. Many risk-based approaches were used to minimise infection risk, including risk classification of herds and regions, pathways for herd classification, risk-based movement/trading and the elimination of uncontrolled animals. Controls on infected herds were tightened as the programme progressed, and an ongoing risk of residual infection was assumed until all cattle exposed to infected animals had been slaughtered.

• **Objective measures of progress**. Area and herd classification were used throughout BTEC, providing clear evidence of progress towards eradication.

Information about the overall Australian programme is available, both in the lay [2] and scientific [1, 3] literature.

The final round of testing on the last quarantined infected property in Queensland, Australia

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AROUND THE WORLD

▶ SUCCESS STORIES

Bovine tuberculosis in Western Canada (2016)

Case response overview

KEYWORDS

#Alberta, #bovine tuberculosis, #Canada, #disease freedom, #*Mycobacterium bovis*.

AUTHORS

Noel Harrington, Veterinary Programme Specialist, Policy and Programs Branch, Animal Health Directorate, Canadian Food Inspection Agency (CFIA), Canada.

The response objective of the Canadian Food Inspection Agency (CFIA) is to determine the extent and origin of the disease in Canadian livestock populations and take action to eradicate the disease where confirmed. This includes the destruction of all susceptible exposed animals and the identification and investigation of all epidemiologically associated herds.

In September 2016, the CFIA responded to a case of bovine tuberculosis (bTB) detected in a mature beef cow from a cow-calf operation in Alberta, Canada. Due to the farm's production practices, which include the regular use of community pasture, numerous additional cattle herds were investigated and subject to herd testing. In total,

145 herds were investigated: approximately 34,000 cattle were tested and 12,000 exposed cattle were ordered to be destroyed. The livestock aspect of the investigation was closed in April 2018. In collaboration with wildlife authorities, active wildlife surveillance to ensure disease freedom will continue through 2020.

© Canadian Food Inspection Agency (CFIA)

Despite the extensive investigation, only the index herd was found to be infected, with six positive animals identified, giving an apparent herd prevalence of 1.6%. Whole-genome sequencing analysis demonstrated that all infected animals shared the same strain of *Mycobacterium bovis* that is most genetically related to a strain last recovered in Mexico in 1997, and not linked to previous animal or human cases in Canada. The investigation examined several routes of exposure or introduction; however, a definitive source of infection was not identified.

Given the outcome of the case response, Alberta continues to be considered officially free from bTB. The bTB-free status of all other Canadian provinces also remains in place.

The strength of Canada's bTB programme and the case response supported uninterrupted international market access for Canadian cattle and beef meat products during the course of the response, which mitigated any impacts on the overall Canadian cattle sector.

The cooperation of individual producers involved in the response and the engagement with their industry associations were vital to the effectiveness of the CFIA's response.

The case highlights the challenges with response capacity and the need for ongoing surveillance for a disease that has become increasingly rare in Canada as a result of longstanding eradication efforts.

Additional information

Behind the scenes during the bovine tuberculosis (TB) outbreak investigation (video series)

AROUND THE WORLD

▶ SUCCESS STORIES

The Irish experience of the tuberculin test in bovine tuberculosis eradication

AUTHORS

Margaret Good[1]* & Anthony Duignan[2]

(1) Independent Researcher and Private Consultant, Dun Laoghaire, Co. Dublin, Ireland. *Previously affiliated with the Department of Agriculture, Food and the Marine, Dublin, Ireland*.
(2) Superintending Veterinary Inspector, Department of Agriculture, Food and the Marine, Dublin, Ireland.

* Corresponding author: mgood2510@gmail.com

Control and eradication of bovine tuberculosis (bTB) is desirable for animal welfare, socio-economic and zoonotic reasons. Tuberculin potency affects test sensitivity and specificity. Therefore, accurate potency determination is critical for test performance. Eradication of bTB will undoubtedly continue to require a multifaceted approach if it is to be successful.

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The Irish national bTB eradication programme commenced in 1954 with 80% herd and 17% animal (22% cows) prevalence rates [1]. **The single intradermal comparative tuberculin test using avian and mammalian tuberculin purified protein derivatives (PPDs)** addressed non-specific sensitisation by abundant environmental mycobacteria. Skin testing requires minimal technology (Fig. 1) and, being safe, allows testing from birth [1, 2]. Progress was dramatic to 1965 but stalled at ~30,000 reactors removed/year until 2000 (Fig. 2).

Programme milestones

- 1974, first tuberculous badger detected, by the 1980s infected badgers found countrywide;
- 1975-1976, programme interruption (fewer reactors);
- 1976-1977, bovine replaced human tuberculin PPD (more sensitive and specific);
- 1978-1979, tuberculin potency fell, affecting bTB detection (initiated routine potency assay on infected cattle as critical quality control);
- 1980, tuberculin supplier changed;
- 1989, TB investigation unit (now CVERA) founded to investigate bTB and improve eradication, using science-informed policy in a national context;
- 1990, endemically infected badgers recognised as tuberculosis maintenance host (culled since 2003 when epidemiological investigation associated them with bTB breakdowns);
- 1991, interferon-γ assay (using tuberculin) used in bTB herds to remove additional infected cattle (legally recognised 2005);
- 1992, PPD potency standardised for Irish programme at bovine 30,000 IU/ml, avian 25,000 IU/ml (giving optimal sensitivity/specificity). Studies showed imprecise guinea pig bio-assay potency estimates and a significant fall in the number of infected cattle detected using low potency tuberculin but if standard potency maintained there was no apparent impact from changing supplier/manufacturer [1, 3].

> Clinical bovine tuberculosis and human zoonotic tuberculosis are now uncommon in Ireland

The Irish programme uses tuberculin PPD and optimal test methodologies for bTB eradication; considers disease epidemiological profile, controls non-bovine maintenance hosts, pursues rigorous quality controls (including tuberculin potency assay), evaluates surveillance protocols, test performance, policy efficacy and outcomes, and is modified reflecting findings and scientific advances [2, 3]. Clinical bTB and human zoonotic tuberculosis [4] are now uncommon.

Fig. 1. Testing cattle: clip sites mid-neck; measure skin thickness; inject tuberculin – avian and bovine; 72-hours later measure and compare responses [2, 3]. ©A. Duignan
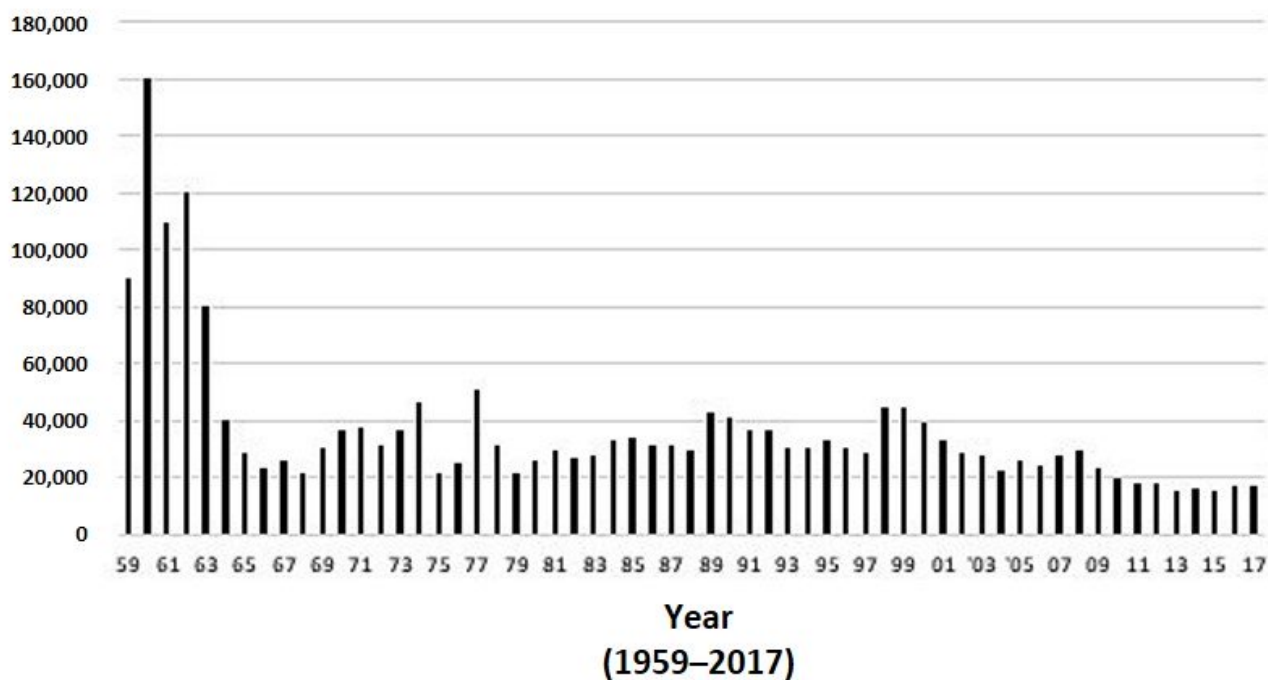
Number of animals

**Year
(1959–2017)**

Fig. 2. Number of animals removed annually 1959 to 2017 inclusive under the Irish bovine tuberculosis eradication programme

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AROUND THE WORLD

▶ THEMATIC EVENTS

The United Nations High-Level Meeting on tuberculosis

Its importance for zoonotic and bovine tuberculosis

AUTHORS

Paula I. Fujiwara[1]* & Francisco Olea-Popelka[2]

(1) Scientific Director, International Union Against Tuberculosis and Lung Disease, Paris, France.
(2) Associate Professor, Department of Clinical Studies, College of Veterinary Medicine & Biomedical Sciences, Colorado State University, Fort Collins, Colorado, United States of America.

* Corresponding author: pfujiwara@theunion.org

Photo: © Daryan Shamkhali – Unsplash

Each year, the United Nations General Assembly convenes heads of state and government to

discuss solutions to relevant issues. These representatives then endorse a political declaration on the topic that serves as a global framework for action.

On 26 September 2018, the United Nations (UN) held a High-Level Meeting (HLM) on tuberculosis (TB), the infectious disease that currently kills the most people worldwide [1]. This HLM was the culmination of nearly two years' work since it was originally proposed in December 2016.

Relevant input for the political declaration was coordinated by the 'Stop TB' Partnership and the World Health Organization (WHO). Staff of the International Union Against Tuberculosis and Lung Disease (the Union) were in charge of developing the TB community's five key priority actions to be included in the political declaration developed by the UN country missions. These were to [2]:

1. reach all people by closing the gaps in TB diagnosis, treatment and prevention
2. transform the tuberculosis response to be equitable, rights-based, and people-centred
3. accelerate the development of essential new tools to end TB
4. invest the funds necessary to end TB
5. commit to decisive and accountable global leadership, including regular UN reporting and review.

Bovine and zoonotic tuberculosis were included in the UN political declaration

Bovine and zoonotic tuberculosis (caused by *Mycobacterium bovis*) were included in the declaration, based on **two key advocacy efforts.**

1. The fourth edition of *The Global Plan to End TB: the Paradigm Shift 2016–2020* identified key populations at risk, which included people who live and work with livestock [3].
2. The Tripartite of the World Organisation for Animal Health (OIE), the World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations (FAO) collaborated with the Union to produce a multisectoral *Roadmap for Zoonotic Tuberculosis* in 2017, based on the WHO Strategic and Technical Advisory Group's previous recognition of zoonotic tuberculosis as a priority [4].
The availability of these two documents convinced the UN missions to include both bovine and zoonotic tuberculosis in the political declaration.

The two key points on bovine and zoonotic tuberculosis in the 16-page political declaration [5] are found in paragraphs 5 and 17:

Paragraph 5. '*Recognize other recent high-level commitments and calls for action against tuberculosis, including against its multidrug-resistant and **zoonotic** forms, made by global, regional and sub-regional bodies and meetings, including the Delhi End TB Summit held from 12 to 17 March 2018*.'

Paragraph 17. '*Recognize the enormous, often catastrophic, economic and social impacts and burden of tuberculosis for people affected by the disease, their households, and affected communities, and that the risk and impact of tuberculosis can vary depending on demographic, social, economic and environmental circumstances, and, in order to make the elimination of tuberculosis possible, prioritizing, as appropriate, notably through the involvement of communities and civil society and in a non-discriminatory manner, high-risk groups as well as other*

people who are vulnerable or in vulnerable situations, such as women and children, indigenous peoples, health care workers, migrants, refugees, internally displaced people, people living in situations of complex emergencies, prisoners, people living with HIV and AIDS, people who use drugs particularly those who inject drugs, miners and others exposed to silica, urban and rural poor, underserved populations, undernourished people, individuals who face food insecurity, ethnic minorities, **people and communities at risk of exposure to bovine tuberculosis**, *people living with diabetes, people with mental and physical disabilities, people with alcohol use disorders, and people who use tobacco, recognizing the higher prevalence of tuberculosis among men.'*

This recognition by the United Nations of the importance of tuberculosis as a major cause of morbidity and mortality will serve to energise the entire tuberculosis community, including those addressing its zoonotic and bovine forms.

In two articles published in 2018, one in *Frontiers in Public Health* [6] and another in *The Lancet: Infectious Diseases* [7], the **practical actions** that need to be taken between now and 2025 as part of the *Roadmap for Zoonotic Tuberculosis,* to 'improve the scientific evidence base, reduce transmission at the animal–human interface and strengthen intersectoral and collaborative approaches' were highlighted.

On 4 October 2018, the **G20 Health Ministers' Meeting** at Mar del Plata, Argentina, issued its own declaration, recognising the contribution of the Tripartite to '*address the threats of zoonotic diseases and improve animal health sector capacities and implement One Health, multi-sectoral approaches to accelerate health security*' [8].

Finally, the Seventh International Conference on *Mycobacterium bovis (M. bovis* 2020) will be held in Galway, Ireland, where plans are being made to further highlight and discuss the remaining zoonotic tuberculosis challenges and opportunities to be addressed if we are to accomplish the milestones outlined in the *Roadmap for Zoonotic Tuberculosis*.

Momentum is building. Now is the time to take the words of the United Nations Political Declaration as the starting point for human and veterinary communities to join together to end tuberculosis by 2030, as stipulated in Sustainable Development Goal 3 [9].

http://dx.doi.org/10.20506/bull.2019.1.2930

Stop TB Partnership website

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AROUND THE WORLD

▶ THEMATIC EVENTS

Use of BCG vaccination for bovine tuberculosis control

Jerusalem workshop

AUTHORS

Ben J. Marais[1], Bryce M. Buddle[2] & Charles Greenblatt[3]*

(1) The Marie Bashir Institute for Infectious Diseases and Biosecurity, the University of Sydney, Australia.
(2) AgResearch, Hopkirk Research Institute, Palmerston North, New Zealand.
(3) Department of Microbiology and Molecular Genetics,The Institute for Medical Research Israel-Canada, The Hebrew University of Jerusalem, Israel.

* Corresponding author: charlesg@ekmd.huji.ac.il

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*Bovine tuberculosis (bTB) is an intractable problem in settings where 'test-and-cull' policies are not affordable or socially acceptable, or in areas where Mycobacterium bovis infection is sustained by wildlife reservoirs. Given the limited efficacy of traditional bTB containment methods in these countries, it seems important to re-assess the value of bacille Calmette-Guérin (BCG) vaccination. BCG has been used in humans for nearly 100 years, but its use in animals is limited [1]. A bTB workshop held in Jerusalem considered key bTB knowledge gaps and innovative solutions, with a specific focus on BCG vaccination [2]. **Table I** presents an overview of bTB knowledge gaps and research needs identified at the workshop.*

BCG vaccination of cattle

Studies have demonstrated that BCG vaccination of cattle can be a valuable tool in bTB control [3, 4]. A major constraint has been potential positive reactions with the traditional tuberculin skin test. However, these concerns have been addressed with new tests that utilise *M. bovis* antigens not expressed by BCG [5]. Potential impacts on bTB diagnosis are also less relevant in settings that do not export cattle and where 'test and cull' is not a control option.

BCG vaccination of camels

The dromedary camel (*Camelus dromedarius*) is important for the livelihood of many pastoral communities and camel milk is traditionally consumed raw. Camel tuberculosis has been reported in multiple countries [6, 7, 8]. There is a need both to develop more sensitive and specific tests for bTB surveillance and diagnosis and to assess BCG efficacy against bTB in domesticated camels.

BCG vaccination of wild animals

Vaccination of reservoir species aims to decrease bTB transmission among wildlife and spill-back to domestic animals. Baits containing oral BCG vaccines have been successfully used in possums in New Zealand [3], badgers in Ireland [9], and wild boar in Europe [10]. African buffalo (*Syncerus caffer*) are a major bTB reservoir species [11] and play an important role in bTB spillover to other wildlife [11], including rare and endangered species such as black rhinoceros (*Diceros bicornis*) [12] and African wild dog (*Lycaon pictus*) [L.M. De Klerk-Lorist, personal communication]. The potential wildlife conservation value of BCG vaccination requires further exploration.

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Table I. – Bovine tuberculosis knowledge gaps and research needs identified at the Jerusalem workshop

Knowledge gap	Research need
Poorly quantified bTB prevalence in humans, cattle, camels, water buffaloes and relevant wildlife	• Existing bTB* surveillance data provide local snapshots, but fail to provide a global overview of the situation. • Poor communication between human and animal health branches of government limit the exchange of relevant surveillance data. • African buffalo and American bison are important bTB reservoirs, but the contribution of water buffalo in Asian settings is poorly documented. • bTB is not restricted to bovines. It may be a significant problem in domestic camels, but the prevalence is unknown. • Good surveillance data are essential to prioritise intervention sites, especially if current BCG*** vaccine trials in cattle demonstrate success.
What to do when 'test and cull' is not an option?	• 'Test and cull' is unfeasible in settings where it is not economically viable, where cultural or religious objections exist, or where wild animal reservoirs exist in protected species. • Settings where infected cows are long-lived pose the greatest risk, since they could spread infection for prolonged periods of time. More studies should track the natural history of disease and epidemic spread of bTB in settings where infected animals cannot be culled.
Use of BCG vaccination to reduce bTB in domestic animals and wildlife reservoirs	• Proof of principle BCG vaccine studies have demonstrated significant bTB protection in cattle and in wildlife, such as possums in New Zealand and badgers in Great Britain/Ireland. • Oral BCG vaccination has shown good protection against TB** in humans and bTB in cattle, but large-scale cattle studies are lacking and few studies have investigated its value in problematic wildlife reservoirs. • Novel BCG formulations and pragmatic delivery methods require consideration in affected animal species. • Limited research has investigated how *M. bovis* infection spreads within local ecosystems and how this can be contained. The conservation value of BCG vaccination in iconic wildlife species, for instance, the African buffalo, and spill-over carnivore species such as lions and African wild dogs, has not been considered.

* bTB: bovine tuberculosis, mostly caused by *Mycobacterium bovis*

** TB: tuberculosis, mostly caused by *M. tuberculosis*

*** BCG: *M. bovis* bacille Calmette-Guerin

Conclusion

Following a review of the efficacy and safety of BCG vaccination for bTB control in domestic livestock and wildlife [3], there is scope to assess the ability of creative BCG vaccine delivery strategies to limit zoonotic disease risk and to consider the conservation value of BCG vaccination in key affected wildlife, such as the African buffalo and associated 'spill-over' species.

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Acknowledgements

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AROUND THE WORLD

▶ THEMATIC EVENTS

The Seventh International Conference on *Mycobacterium bovis*

Galway, Ireland, 8–11 June 2020

AUTHORS

The Scientific Committee of the Seventh International Conference on *Mycobacterium bovis**

(1) School of Veterinary Medicine, University College Dublin (UCD), Belfield, Dublin 4, D04 W6F6, Ireland.
(2) Department of Agriculture, Food and the Marine (DAFM), Agriculture House, Kildare Street, Dublin 2, DO2 WK12, Ireland.

* Corresponding author: egormley@ucd.ie

The Seventh International Conference on Mycobacterium bovis (M. bovis 2020 for short) will take place in Galway, Ireland from 8 to 11 June 2020.

The Seventh International Conference on *Mycobacterium bovis* will gather together scientists, policy-makers, veterinarians and industry stakeholders from around the world with the aim of identifying constraints and providing practical solutions for the control and eradication of *M. bovis*.

Themes which are applicable to countries at various stages of control and eradication will be covered including –

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zoonotic tuberculosis, breeding for genetic resistance, vaccination of cattle, vaccination of wildlife, diagnostics techniques, programme policies, stakeholder involvement, surveillance strategies in cattle and wildlife and biosecurity.

Galway, the cultural heart of Ireland, has officially been designated as European Capital of Culture for 2020. The host of activities that are sure to whet your appetite include world renowned theatre, street performers, traditional Irish music and dance. Experience nature along the magnificent Wild Atlantic Way which stretches over 2,500 km of rugged coastline with spectacular scenery from County Donegal to the north and County Cork to the south. Staying in Galway, why not immerse yourself in the spectacular beauty and traditional Irish culture of Connemara.

We look forward to extending a *céad míle fáilte* ('a hundred thousand welcomes') to you all.

For more information, please visit www.mbovis2020.com

RESOURCES

▶ JOINT PUBLICATIONS

Taking a multisectoral, One Health approach: a tripartite guide to addressing zoonotic diseases in countries
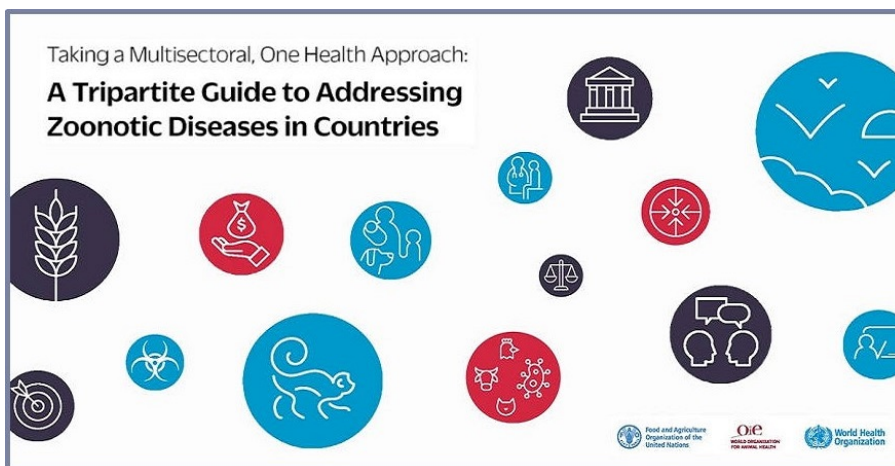
Zoonotic diseases – those diseases that can spread between animals and people – have major impacts on human health. Every year, nearly 60,000 people die from rabies, and other zoonotic diseases such as avian influenza, Ebola or Rift Valley fever constitute additional threats. These diseases do not only affect human health, but also animal health and welfare, causing lowered productivity (milk or egg quality and safety, etc.), or death, and consequently affecting farmers' livelihoods and countries' economies.

As global trade and travel expands, zoonotic diseases are increasingly posing concerns worldwide. Every day, new health challenges emerge at the human-animal-environment interface. To face these threats, collaboration, coordination, communication, and concerted action between different sectors are needed, using a multisectoral, One Health approach. However, many countries lack the capacity to implement such collaboration. The Tripartite organisations – the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE), and the World Health Organization (WHO) – have published this guide in order to support countries in filling these gaps.

Building multisectoral, One Health bridges to strengthen national capacities

This guide, referred to as the *Tripartite Zoonoses Guide (TZG)*, provides principles, best practices and options to assist countries in achieving sustainable and functional collaboration at the human-animal-environment interface. It

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is flexible enough to be used for other health threats; for example, food safety and antimicrobial resistance. By using the TZG and its associated operational tools (which are currently being developed), countries can build or strengthen their national capacities in:

- Multisectoral, One Health coordination mechanisms
- Strategic planning and emergency preparedness
- Surveillance and information sharing
- Coordinated investigation and response
- Joint risk assessment for zoonotic disease threats
- Risk reduction, risk communication and community engagement
- Workforce development.

Options for monitoring and evaluating the function and impact of these activities are additionally included to support countries in their efforts to make improvements in their zoonotic disease frameworks, strategies and policies. Moreover, taking the One Health approach presented in the *TZG* helps countries to make the best use of limited resources and reduces indirect societal losses, such as impacts on livelihoods of small producers, poor nutrition, and restriction of trade and tourism.

By working collaboratively across sectors and disciplines, human and animal lives are saved, livelihoods are secured, and our global health systems are improved in a sustainable way. The Tripartite organisations encourage countries to use the *TZG* to achieve these goals by taking a One Health approach to address zoonotic diseases.

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RESOURCES

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OIE resources on bovine and zoonotic tuberculosis

OIE portal on bovine tuberculosis >>>>>

OIE portal on zoonotic tuberculosis >>>>>

RESOURCES

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OIE technical standards for diagnostic tests and vaccines for bovine tuberculosis

AUTHORS

Glen Gifford[1]*, Gregorio Torres[2], Sara Linnane[3], Elisabeth Erlacher-Vindel[4] & Matthew Stone[5]

(1) Chargé de mission, Antimicrobial Resistance and Veterinary Products Department, World Organisation for Animal Health (OIE).
(2) Acting Head, Science Department, World Organisation for Animal Health (OIE).
(3) Scientific Editor, Science Department, World Organisation for Animal Health (OIE).
(4) Head, Antimicrobial Resistance and Veterinary Products Department, World Organisation for Animal Health (OIE).
(5) Deputy Director General, International Standards and Science, World Organisation for Animal Health (OIE).

* Corresponding author: g.gifford@oie.int
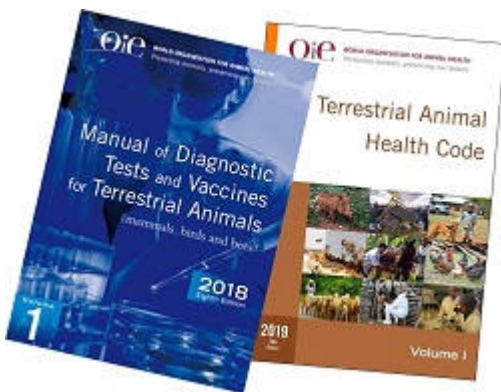
The World Organisation for Animal Health (OIE) is an intergovernmental, animal health, standard-setting organisation that develops and publishes science-based standards for animal health and welfare programmes, as well as technical standards for the manufacturing and quality control of diagnostic tests and vaccines for use in the diagnosis, prevention and control of animal diseases, including bovine tuberculosis.

The technical standards for diagnostic tests and vaccines are developed and updated collaboratively, through an extensive network of scientific experts in OIE Collaborating Centres and Reference Laboratories throughout the world, and in consultation with Member Country Delegates who review and approve the final texts through a vote at the OIE General Session, which is held in Paris in May of each year.

These adopted standards are published in the *Terrestrial Animal Health Code (Terrestrial Code)* and the *Manual of*

Diagnostic Tests and Vaccines for Terrestrial Animals (Terrestrial Manual).

Bovine tuberculosis is covered in the *Terrestrial Code* Chapter 8.11. Infection with *Mycobacterium tuberculosis* complex [1] and the *Terrestrial Manual* Chapter 3.4.6. Bovine tuberculosis [2].

Chapter 8.11, Infection with *Mycobacterium tuberculosis* complex, of the ***Terrestrial Code*** provides an overview of the animal health standards and requirements for demonstrating freedom from bovine tuberculosis or notifying its presence within a country, zone, compartment or herd, and lists the agreed procedures for ensuring safe international movement of animals and animal products. These recommendations are intended to help manage the human and animal health risks associated with animals infected with a member of the *Mycobacterium tuberculosis* complex (*M. bovis, M. caprae* and *M. tuberculosis)*.

Chapter 3.4.6, Bovine tuberculosis, of the ***Terrestrial Manual*** provides a detailed description of the disease and recommended laboratory methods to identify the causative agent, as well as the internationally accepted diagnostic techniques for official disease control and eradication programmes and international trade. This chapter also outines the technical standards for manufacturing and testing bovine tuberculosis vaccines and diagnostic tests.

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RESOURCES

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OIE technical standards for manufacturing and quality control of veterinary vaccines

KEYWORDS

#Manual of Diagnostic Tests and Vaccines for Terrestrial Animals, #technical standard, #Terrestrial Animal Health Code, #vaccine, #World Organisation for Animal Health (OIE).

The OIE aims to prevent and control animal diseases including zoonoses, facilitate safe international trade in animals and animal products, and contribute to the improvement of animal health and welfare services worldwide.

These global animal health objectives are achieved through a variety of means, including the collaborative development and publication of technical standards for manufacturing and quality control of veterinary vaccines.

This technical reference is a compilation of selected vaccine-related Chapters from the *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* and the *Terrestrial Animal Health Code*. It is intended to serve as a readily

accessible technical resource for vaccine manufacturers and regulatory officials, to advance global awareness and implementation of the established science-based standards for the quality, safety and efficacy of veterinary vaccines.

We hope that this reference will prove useful to vaccine manufacturers and regulatory officials to help them to maximise the quality and availability of veterinary vaccines that are required for the prevention and control of animal diseases.

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Plurithematic issue of the *Scientific and Technical Review*, 2018

The plurithematic issue of the Scientific and Technical Review, 2018, contains 22 articles, two of which relate particularly to bovine tuberculosis. Both articles are described and summarised below.

• **Isolation and analysis of the molecular epidemiology and zoonotic significance of *Mycobacterium tuberculosis* in domestic and wildlife ruminants from three states in India**. Authors: F. Mukherjee, V.S. Bahekar, S.Y. Pasha, P. Kannan, A. Prasad, S.K. Rana, A. Kanani, G.K. Sharma, D. Premalatha & V.A. Srinivasan – doi:10.20506/rst.37.3.2902.

The majority of tuberculosis cases in ruminants are caused by *Mycobacterium bovis* (*MB*). However, in this study, the authors reported the isolation of *Mycobacterium tuberculosis* (*MT*) from bovine milk, nasal swabs and postmortem tissue samples collected from cattle and buffaloes in the states of Telangana, Maharashtra and Gujarat in India in the period from 2010 to 2015. The isolates were confirmed as *Mycobacterium* due to their growth characteristics and colony morphology in a commercial liquid medium Mycobacterial Growth Indicator Tube (MGIT)™ employing the BD BACTEC™ MGIT™ 960 system and the Lowenstein-Jensen (LJ) medium supplemented with glycerol but not with sodium pyruvate, and BD-DIFCO™ Middlebrook 7H10 agar containing oleic albumin dextrose catalase (OADC). These isolates were initially identified as members of the *M. tuberculosis* complex (MTC) using a commercial nested polymerase chain reaction (PCR) kit based on the

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IS*6110* MTC specific nucleotide sequence. The isolates were confirmed as *MT* using three commercial line probe assay kits, were further genotyped, and the spoligotypes identified were of East African Indian (EAI) 3_IND, EAI5, Central-Asian (CAS) 1_DELHI, U and T1 lineages. Two *MT* isolates from one antelope (*Antilope cervipara*) and one gazelle (*Gazella bennettii*) from Gujarat, which were identified previously, were spoligotyped during this study and identified as belonging to EAI3_IND and EAI5 lineages, respectively. The epidemiological significance and zoonotic implications of regional presence and documentation of the same or two different spoligotypes in different species within the family Bovidae as well as humans is discussed.

• **Antibacterial activity of silver nanoparticles against field and reference strains of *Mycobacterium tuberculosis*, *Mycobacterium bovis* and multiple-drug-resistant tuberculosis strains**. Authors: A. Selim, M.M. Elhaig, S.A. Taha & E.A. Nasr – doi:10.20506/rst.37.3.2888.

This study aims to investigate the antimycobacterial activity of silver nanoparticles (AgNPs) by determining the minimal inhibitory concentration (MIC) of AgNPs, using the microplate Alamar blue assay. The AgNPs were chemically synthesised and their form and size were characterised by ultraviolet-visible absorption spectrophotometry, transmission electron microscopy and X-ray diffraction. The reference strains of *Mycobacterium bovis* and *Mycobacterium tuberculosis* H37Rv, and one multiple-drug-resistant (MDR) strain of *M. tuberculosis* were tested, as well as clinical isolates of *M. bovis* and *M. tuberculosis.* The AgNPs were tetrahydral with a few spherical particles and an average particle size of 50 nm. The mycobacterial strains were varied with MICs of AgNPs. Both reference strains of *M. tuberculosis* and *M. bovis,* in addition to the MDR strain of *M. tuberculosis*, were successfully inhibited by AgNPs at MICs of 1 µg/ml, 4 µg/ml and 16 µg/ml, respectively, whereas clinical isolates of *M. bovis* and *M. tuberculosis* were inhibited at MIC values of 4–32 µg/ml and 1–16 µg/ml, respectively. The AgNPs showed an *in vitro* chemotherapeutic effect against *Mycobacterium* spp. Thus, they can be used to treat tuberculosis not only in humans but also in animals, and may be useful in tuberculosis prevention and control strategies worldwide.

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Roadmap for zoonotic tuberculosis
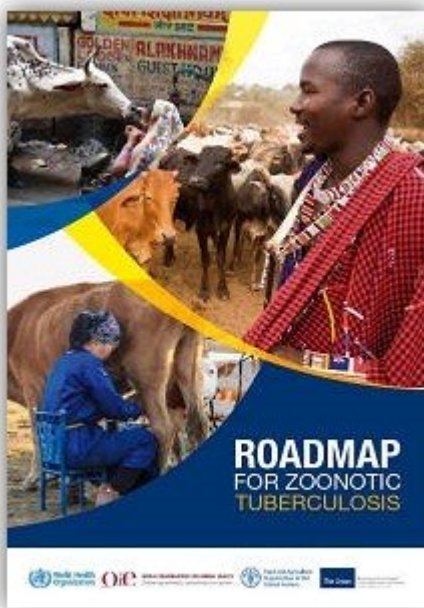
World Health Organization (WHO), Food and Agriculture Organization of the United Nations (FAO) and World Organisation for Animal Health (OIE) joint publication.
2017
ISBN 978-92-95108-51-6

Zoonotic tuberculosis (TB) is a form of TB in people predominantly caused by the bacterial species, *Mycobacterium bovis*, which belongs to the *M. tuberculosis* complex. The implications of zoonotic TB go beyond human health. The organism is host-adapted to cattle, where it is referred to as bovine TB, and it also causes TB in other animal species including wildlife. Bovine TB has an important economic impact and threatens livelihoods.

The time is right for a bold and concerted effort to collectively address zoonotic and bovine TB, framed within the multidisciplinary United Nations Sustainable Development Goals (SDGs) 2016–2030 and WHO's *End TB Strategy* which seek to end the global TB epidemic by 2030. The *Strategy* calls for the diagnosis and treatment of every person with TB, and this must include zoonotic TB. This is supported by the Stop TB Partnership's *Global Plan to End TB 2016–2020 – The Paradigm Shift*, which identifies people at risk of zoonotic TB as a neglected population deserving greater attention.

The human burden of disease cannot be reduced without improving standards of food safety and controlling bovine

TB in the animal reservoir. A One Health approach recognises the interdependence of the health of people, animals and the environment, and the engagement of all relevant sectors and disciplines. The declaration made by the leaders of the G20 forum in July 2017, *G20 Leaders' Declaration: Shaping an Interconnected World,* calls for a One Health approach to tackling the spread of antimicrobial resistance and highlights the need to foster research and development for TB.

The first steps towards formally conceptualising this roadmap began in April 2016 in Geneva at a meeting co-organised by WHO and The International Union Against Tuberculosis and Lung Disease (The Union), with contributions from leading international organisations for human and animal health, academic institutions, and non-governmental organisations. With this roadmap, we call for concerted action through broad engagement across political, financial and technical levels, including government agencies, donors, academia, non-governmental organisations and private stakeholders. This roadmap lays down ten priorities grouped into three core themes. To end the global TB epidemic by 2030, action must begin today. Milestones are defined for the short-term, by 2020, and medium-term, by 2025.
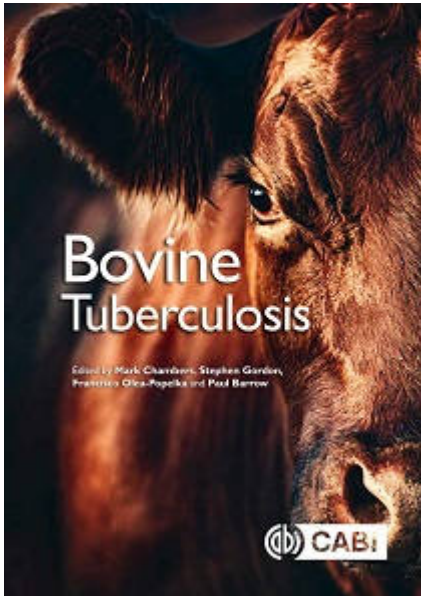
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Perspective: Roadmap for zoonotic tuberculosis: a One Health initiative to combat zoonotic tuberculosis

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Bovine tuberculosis

1st Edition, 2018
Edited by Mark Chambers, Stephen Gordon, F. Olea-Popelka & Paul Barrow
Published by CABI c/o Robert Taylor
Information: info@cabi.org

This book provides an essential, comprehensive treatise on bovine tuberculosis and the bacterium that causes it, *Mycobacterium bovis*. Bovine tuberculosis remains a major cause of economic loss in cattle industries worldwide, exacerbated in some countries by the presence of a substantial wildlife reservoir. It is a major zoonosis, causing human infection through consumption of unpasteurised milk or by close contact with infected animals.

Following a systematic approach, expert international authors cover epidemiology and the global situation; microbial virulence and pathogenesis; host responses to the pathogen; and diagnosis and control of the disease.

Aimed at researchers and practising veterinarians, this book is essential for those needing comprehensive information on the pathogen and disease, and offers a summary of key information learned from human tuberculosis research.

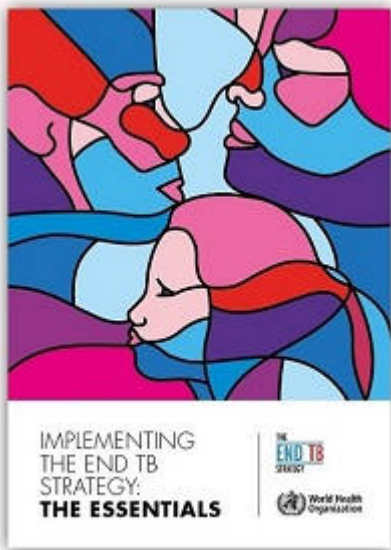**Table of contents**
1: Bovine tuberculosis: worldwide picture

[Order the book from the CABI Bookshop]

RESOURCES

► EXTERNAL PUBLICATIONS

Implementing the End TB Strategy: the essentials

The aim of this document is to guide actions that are needed at the national level to adapt, launch and implement the World Health Organization's End TB Strategy. The Strategy, approved by the 67th World Health Assembly in 2014, is designed to achieve a health-related target under the United Nations Sustainable Development Goal 3 that calls for ending the TB epidemic. Pursuing this ambitious but achievable goal will require new ways of working, building on the national and global efforts of the past two decades and seizing the opportunity to draw in many new stakeholders to join the endeavour.

This document was developed by the WHO's Global TB Programme. It has benefited from the collective inputs of WHO's Strategic and Technical Advisory Group for Tuberculosis and in-depth consultations with many stakeholders during the two-year development of the Strategy and during the year after its approval. It also builds on the early experiences of countries preparing to introduce the Strategy.

This document, designed for use mainly by national TB programmes (NTPs) and equivalents within Ministries of health, is intended for all stakeholders engaged in TB care and prevention. The NTPs must engage with a wide range of stakeholders to implement the Strategy. Using this document as a starting point, country officials may need to prepare detailed national operational guidance on the implementation of the Strategy to meet the needs of

diverse stakeholders.

As countries adapt and implement the End TB Strategy and share their experiences, WHO will provide additional guidance and tools and revise The Essentials as appropriate. This is therefore a 'living' document and will be enriched by supplementing it further with country examples and case studies available online.
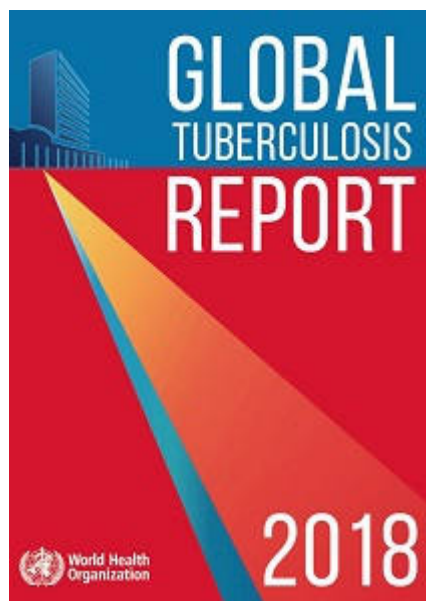
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Global Tuberculosis Report, 2018

World Health Organization (WHO)
2018
ISBN 978-92-4-156564-6

The aim of the WHO Global Tuberculosis Report is to provide a comprehensive and up-to-date assessment of the tuberculosis epidemic, and of progress in prevention, diagnosis and treatment of the disease at global, regional and country levels.

[Download the document from the WHO website]

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