# Controlling bovine tuberculosis: a One Health challenge

# PERSPECTIVES | # DOSSIER | # AROUND THE WORLD

*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.

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

| Knowledge gap | Research need |
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| | |
|---|---|
| **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.<br>• Poor communication between human and animal health branches of government limit the exchange of relevant surveillance data.<br>• African buffalo and American bison are important bTB reservoirs, but the contribution of water buffalo in Asian settings is poorly documented.<br>• bTB is not restricted to bovines. It may be a significant problem in domestic camels, but the prevalence is unknown.<br>• 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.<br>• 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.<br>• 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.<br>• Novel BCG formulations and pragmatic delivery methods require consideration in affected animal species.<br>• 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.

## Acknowledgements

## AROUND THE WORLD

▶ THEMATIC EVENTS

# Use of BCG vaccination for bovine tuberculosis control

## Jerusalem workshop

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## REFERENCES

1. Waters W.R., Palmer M.V., Buddle B.M. & Vordermeier H.M. (2012). – Bovine tuberculosis vaccine research: historical perspectives and recent advances. *Vaccine*, **30** (16), 2611–2622. https://doi.org/10.1016/j.vaccine.2012.02.018.

2. Buddle B.M., Vordermeier H.M., Chambers M.A. & de Klerk-Lorist L.M. (2018). – Efficacy and safety of BCG vaccine for control of tuberculosis in domestic livestock and wildlife. *Front. Vet. Sci.*, **5** (Art 259). https://doi.org/10.3389/fvets.2018.00259.

3. Buddle B.M., Parlane N.A., Wedlock D.N. & Heiser A. (2013). – Overview of vaccination trials for control of tuberculosis in cattle, wildlife and humans. *Transboundary Emerg. Dis.,* **60** (Suppl. 1), S136–S146. https://doi.org/10.1111/tbed.12092.

4. Nugent G., Yockney I.J., Whitford J., Aldwell F.E. & Buddle B.M. (2017). – Efficacy of oral BCG vaccination in protecting free-ranging cattle from natural infection by *Mycobacterium bovis*. *Vet Microbiol.,* **208**, 181–189. https://doi.org/10.1016/j.vetmic.2017.07.029.

5. Vordermeier H.M., Jones G.J., Buddle B.M. & Hewinson R.G. (2016). – Development of immuno-diagnostic reagents to diagnose bovine tuberculosis in cattle. *Vet. Immunol. Immunopathol.*, **181**, 10–14. https://doi.org/10.1016/j.vetimm.2016.02.003.

6. Wernery U. & Kaaden O.R. (2002). – Infectious diseases in camelids. Berlin: Blackwell Science, pp 23–373.

7. Zubair R., Khan A.M.Z. & Sabri M.A. (2004). – Pathology in camel lungs. *J. Camel Sci.*, **1**, 103–106.

8. Ahmad I., Kudi C.A., Babashani M., Chafe U.M., Yakubu Y. & Shittu A. (2019). – Tuberculosis in dromedary camels slaughtered in Nigeria: a documentation of lesions at postmortem. *Trop. Anim. Health Prod.*, **51** (1), 73–78. https://doi.org/10.1007/s11250-018-1661-0.

9. Gormley E., Ní Bhuachalla D., O'Keeffe J., Murphy D., Aldwell F.E., Fitzsimons T. *et al.* (2017). – Oral vaccination of free-living badgers (*Meles meles*) with bacille Calmette Guerin (BCG) vaccine confers protection against tuberculosis. *PLoS One*, **12** (1), e0168851. https://doi.org/10.1371/journal.pone.0168851.

10. Gortázar C., Beltrán-Beck B., Garrido J.M., Aranaz A., Sevilla I., Boadella M. *et al.* (2014). – Oral re-vaccination of Eurasian wild boar with *Mycobacterium bovis* BCG yields a strong protective response against challenge with a field strain. *BMC Vet. Res.*, **10**, 96. https://doi.org/10.1186/1746-6148-10-96.

11. Hlokwe T.M., De Klerk-Lorist L.M. & Michel A.L. (2016). – Wildlife on the move: a hidden tuberculosis threat to conservation areas and game farms through introduction of untested animals. *J. Wildlife Dis.*, **52** (4), 837–843. https://doi.org/10.7589/2015-10-281.

12. Miller M.A., Buss P.E., van Helden P.D. & Parsons S.D.C. (2017). – *Mycobacterium bovis* in a free-ranging black rhinoceros, Kruger National Park, South Africa, 2016. *Emerg. Infect. Dis.*, **23** (3), 557–558. https://doi.org/10.3201/eid2303.161622.

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