

Tuberculosis in South American camelids – surveillance and control policy in England

An invited presentation given by the Animal and Plant Health Agency (APHA), for veterinary practitioners, pathologists and diagnosticians

Camelid Symposium organised by the British Society of Veterinary Pathology (BSVP), Bristol, 24 May 2023



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Outline

- 1. Susceptibility of South American Camelids to *Mycobacterium bovis* infections and disease distribution in GB
- 2. Epidemiology of camelid TB in GB
- 3. Diagnosis of *M. bovis* infections
- 4. TB surveillance, control policy and legislation in England



Camelid susceptibility to infection

- Camelids are susceptible to infections with *Mycobacterium bovis* (bovine TB bacterium) and other bacteria of the MTB complex, such as *M. microti* (vole TB bacterium)
- Infection with these organisms can give rise to clinical disease and typical pathology (tuberculosis – 'TB') in camelids
- Highly variable incubation period (from a few weeks to a lifetime), but rapid deterioration tends to occur once first clinical signs become apparent
- *M. bovis* infections rarely diagnosed in their natural habitats in South America. Most cases have occurred in camelids living in close association with infected cattle or humans (Fowler 1996, Rev. Sci. Tech. OIE).
- First documented case of *M. bovis* infection in the UK was reported in Ilamas in Southeast Wales (Barlow et al. 1999, Veterinary Record).

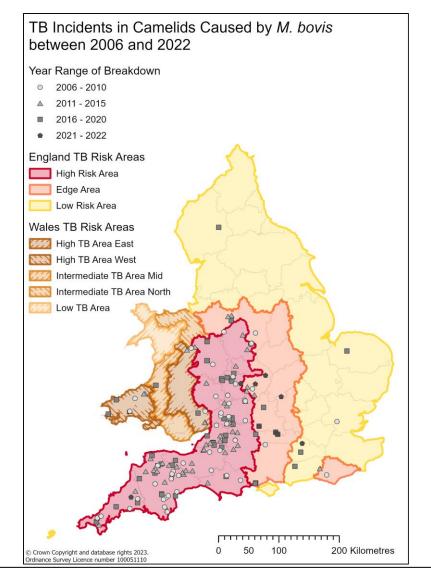


Early reports of natural *M. bovis* infection outside the UK

Country	Year of disclosure	Species affected	Comments		
The Netherlands	1988	Alpaca	Dinkla et al. (1991) - imported stock. 12/13 alpacas in a holding affected with extensive pulmonary TB.		
Rol	2004	Alpaca	Ryan et al. (2008) - Local strain of <i>M. bovis.</i> Infected cattle and badgers in the locality (high bTB incidence area).		
Spain	2009	Alpaca	 García-Bocanegra et al. (2010) Index herd in an endemic bTB area of Andalucía. Several animals were affected, with secondary spread to another alpaca herd. Alpacas infected with a strain of <i>M. bovis</i> commonly found in the local cattle herds and wildlife. 		
USA	1970s to date	Alpacas, llamas	Bleem et al. (1993), Fowler (2010) – isolated sporadic incidents in zoos and on private farms.		
Argentina	?	Alpaca	Argentinean animal health authorities (pers. comm.) Animals co-grazing with infected cattle herds.		
NZ	2000, 2004	Alpaca	P. Livingstone, NZ Animal Health Board (pers. comm.) Probably wildlife vector-related (ferrets or possums).		

Occurrence and distribution in GB

- A small number of laboratory-confirmed TB incidents (or 'breakdowns') are recorded each year in camelid herds in GB
- Variable severity and duration. Some incidents have resulted in high attack rates and a large proportion of the infected herds removed as TB test-positive animals, suspected clinical cases, direct contacts and, in extreme cases, ending with total or near-total depopulation
- A proportion of these incidents are clearly related to the movement of subclinically infected camelids between herds, without private TB testing
- But the majority are 'within homerage' and arise in areas of endemic TB in cattle and badgers (e.g. High Risk and Edge Areas of England)



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Annual number of culture-confirmed new TB incidents on camelid premises in GB (1999-2013)

Year of disclosure	Infected herds (with > 1 dead or culled animal)	Type of herd infected (herd with > 1 culled animal)	Location of affected herds		
			Gwent (2 llama holdings), Gloucestershire (alpaca), Herefordshire		
1999-2003	5	2x alpaca 3x llama	(llama), Somerset (alpaca)		
2004	1*	alpaca	Devon		
2005	1	llama	Avon		
2006	2 (1)	1x alpaca 1x llama (1) 2x alpaca (2) 1x llama	Sussex (alpaca), Devon (llama)		
2007	3 (3)	(1)	Carmarthenshire (llama), Powys (alpaca), Dorset (alpaca)		
2008	11 (6)	9x alpaca (4) 2x llama (2)	Carmarthenshire (llama), Devon (1 llama, 1 alpaca), Avon (2), Cornwall, Gloucestershire (3), Herefordshire, Worcestershire		
2009	12 (6)	all alpacas	Devon (3), Derbyshire, Gloucestershire (2), Shropshire, Somerset (2), Staffordshire, Worcestershire (2)		
2010	15 (6)	all alpacas	Devon (4), Cornwall (3), Gloucestershire, Hampshire, Monmouthshire, Staffordshire (2), Warwickshire, Worcestershire (2)		
2011	6 (4)	all alpacas	Cornwall, Dorset, Gloucestershire (2), South Gloucestershire (near Bristol), Warwickshire		
2012	14(5)	11x alpacas (4) 2x llama 1x 'mixed' (1)	Carmarthenshire, Cheshire, Devon (4), Somerset(2), Staffordshire, Warwickshire c , West Midlands, West Sussex, Wiltshire, Worcestershire		
2013	10(6)	9x alpacas (5), 1 x 'mixed' (1)	Ceredigion, Cornwall, Devon, Gloucestershire (3), North Somerset (2), Shropshire, Vale of Glamorgan.		

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(*) No culture possible, but typical histopathology and PCR positive for MTB complex

Results of TB surveillance in camelids (England)

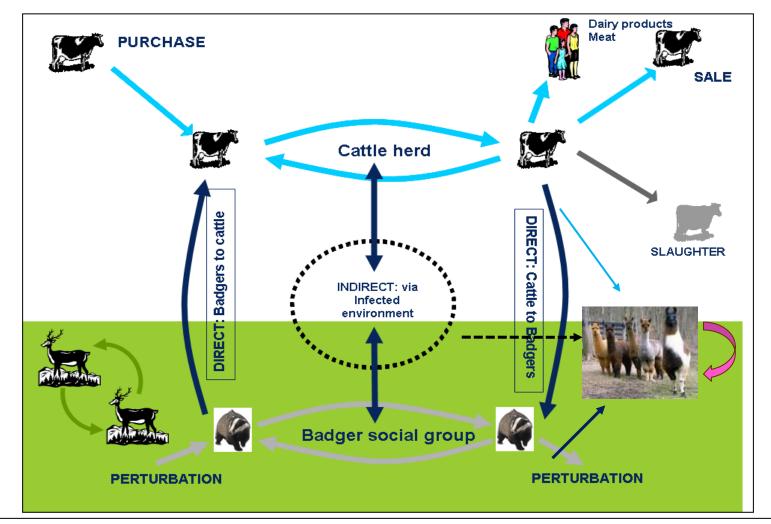
	2019	2020	2021
Number of ante-mortem TB tests performed (of which antibody tests)	9,433 (3,282)	5,290 (2,778)	6,343 (2,768)
Number of TB testing events in herds (of which antibody tests)	542 (302)	420 (243)	398 (217)
Total TB test-positive camelids removed by APHA (%)	207 (2.2%)	199 (3.8%)	92 (1.5%)
Animals undergoing bacteriological culture (<i>M. bovis</i> - positive results)	81 (30)	35 (7)	83 (12)
New laboratory-confirmed TB incidents in camelid herds	10	3	2
Camelid herds under TB restriction at year's end (for any reason)	76	84	78

Official data extracted from official statistics in non-bovine domestic species published by Defra – <u>https://www.gov.uk/government/statistical-data-sets/other-tb-statistics</u>



Epidemiology of bovine TB in GB (1) – role of camelids

Mycobacterium bovis transmission cycle



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Epidemiology of bovine TB in GB (2) – transmission pathways

- Direct contact with *M. bovis*-infected animals:
 - camelid to camelid (aerosols, grooming, milk-borne?, in-utero?)
 - cattle (domestic maintenance host) or other susceptible domestic animals
 - badgers (main wildlife maintenance host) and potentially wild deer in localised areas
- Indirect contact:
 - pasture, equipment, feedstuffs, water, soil contaminated by secretions/excreta from infectious animals
- Introduction of undetected infected animals in a camelid herd:
 - purchases, loaned/hired breeding males, drive-by mating, etc.
- Camelid TB is also a zoonosis:
 - very rare (low, but not negligible, risk)
 - close contact with infected animals or their carcases (inhalation of bacteria shed by infectious animals, spitting of gastric contents?
 - contamination of skin cuts/abrasions during clinical/PM examination
 - two documented cases in GB, involving an alpaca owner in Cornwall (pulmonary TB) and a PVS treating alpacas (cutaneous TB granuloma)



Epidemiology of bovine TB in GB (3)

- No investigations in GB have conclusively established a link between a TB breakdown as a result of infection transmitting between cattle and camelids in either direction
- However, it would seen reasonable to assume that both species pose a potential risk to each other either via direct, or indirect (wildlife, contaminated shared environment) transmission
- Camelids not considered to play a significant role in the epidemiology and maintenance of TB in cattle (spill-over hosts, potentially amplifiers of infection within the camelid population and other species)



Clinical signs

Clinical cases:

- Infected animals may not show any clinical signs
- Variable incubation period (few weeks to several years or a lifetime)
- Once first clinical signs appear, affected animals deteriorate rapidly
- Clinical signs (when present) are not specific/pathognomonic:
 - chronic loss of condition and appetite
 - dyspnoea, chronic cough (not responsive to treatment)
 - enlarged superficial lymph nodes
 - sudden death
- Post-mortem examination by PVS is strongly recommended for all camelids dying of unexplained reasons (APHA scanning surveillance on camelid submissions)



Gross pathology

- Macroscopic lesions predominantly found in respiratory tract and associated lymph nodes
- Liver and abdominal (hepatic, mesenteric) LNs often involved too
- White/cream extensive caseous necrosis
- Little mineralisation
- Pulmonary lesions are often very extensive and cavitation is common
- More unusual presentations, e.g. tuberculous mastitis

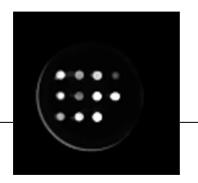


Diagnosis of *M. bovis* infections in camelids (1)

Ante-mortem (immunological) tests

- Intradermal comparative (or single) tuberculin test of cell-mediated immunity
 - official TB screening test internationally, but
 - has a poor diagnostic sensitivity in camelids
 - must be supplemented with TB antibody tests
- Serum antibody testing: three kits validated and available for statutory and private TB testing of camelids in GB
 - Chembio Diagnostics Dual Path Platform test (DPPVetTB)
 - IDEXX ELISA
 - Enfer Scientific's multiplex ELISA (Enferplex)
- Interferon-γ blood assay not available in camelids





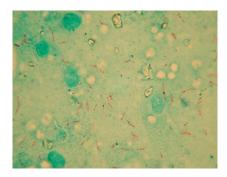


Diagnosis of *M. bovis* **infections in camelids (2)**

Post mortem (direct detection) tests

- Gross pathological findings at PME
- Ziehl-Neelsen staining / histopathology
- *M. bovis* RT-PCR test on <u>fresh/frozen</u> PM tissue specimens:
 - > primary TB confirmatory test for all non-bovine tissue samples at APHA since March 2022
 - results within three weeks of submission (usually 1-2 weeks)
- Bacteriological culture currently only performed on PM tissue samples if:
 - PCR test failure (very rare), or
 - PCR +ve result (to enable whole-genome sequencing and phylogenetic analysis of isolates to support epidemiological investigations)







Tuberculin skin test (1) – protocol

- Requires a meticulous technique
- Careful measurement of skin thickness before and after injection
- Bovine and avian PPD tuberculins injected <u>intradermally</u> (left and right <u>axillary region</u>)
- Comparative measurement of skin reactions 72 hrs. post-injection
- 'Reactor': positive (>2mm rise) bovine PPD reaction > avian PPD reaction
- No 'inconclusive reactor' range
- A minimum 90-day interval between tests, to account for de-sensitisation and any false -ve animals infected shortly before the previous test
- Single (bovine PPD only) injection to increase sensitivity in herds with laboratory-confirmed TB incidents
- Diagnostic sensitivity in camelids under field conditions in GB is lower than that reported in the literature (< 25%)
 - > poor predictive value of a negative result







Tuberculin skin testing (2) – protocol

- Tuberculin skin test
 - injection site: axilla (x 2)
 - use 1ml syringes, 25G-26G needles and Vernier calipers
 - mark with a broken cross using a permanent marker pen, before measuring and injecting tuberculin







Tuberculin skin test (3) – practicalities

- If statutory testing: APHA will instruct relevant VDP to arrange test with keeper
- If private testing: PVS (OV) must first obtain written authorisation from APHA (complete TN184 'Request to Test' form)
- Individual identification required for all animals being tested for TB
- Do not separate tested animals
- Good handler is key
- Standing or cast animal on side
- Risks to TB tester:
 - kicking
 - scratching
 - spitting
 - 'cushing'

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TB antibody testing policy

- Chembio Dual Path Platform (DPP) test
- IDEXX ELISA test
- Enferplex test
- SureFarm Ltd (voluntary camelid TB surveillance scheme)

Both performed at APHA Starcross

APHA Starcross (statutory testing only)

➢ High sens. (2-spot) or High spec. (4-spot) test interpretation, depending on the circumstances

- Usually deployed as combinations of two antibody tests to maximise:
 - diagnostic sensitivity (parallel testing of infected herds) or
 - diagnostic <u>specificity</u> (serial testing of unrestricted, but suspected herds)
- Owner/PVS can choose the two tests (out of the three available) to be run by APHA
- Blood samples taken 10-30 days after tuberculin injection to benefit from antibody 'boosting effect' due to an anamnestic response to PPD tuberculin antigens in infected animals and maximise diagnostic sensitivity
 - > this is mandatory for statutory antibody testing, strongly recommended if private

TB testing and control legislation applicable to camelids (1)

The Tuberculosis in Animals (England) Order 2021 (legislation.gov.uk)

- Art. 1: Part 2 applies to camelids (as well as bovines and other non-bovine farmed mammals)
- Art. 2: "camelid" any species of South American camelid incl. llama, alpaca, vicuña, guanaco
- Arts. 5&6: duty to notify suspicion of TB in live camelids or in carcases to APHA
- Art. 7: powers of veterinary inspectors to investigate the existence of TB on camelid premises by detaining, examining, marking and testing/taking samples from suspected animals / carcases
- Art. 8: powers to test camelid herds for TB (and keeper's obligation to facilitate this).
- Art. 10: prohibition to test/treat camelids for (or vaccinate it against) TB without APHA's written consent
- Art. 12: powers of veterinary inspectors to require adoption of certain precautions to contain the spread of infection (e.g. herd movement restrictions, C&D, safe disposal of manure, etc.)
- Art. 17: duty to notify the identification of *M. bovis* by laboratory examination of samples taken from a camelid



TB testing and control legislation applicable to camelids (2)

The Tuberculosis (Non-bovine animals) Slaughter and Compensation (England) Order 2017 (legislation gov.uk)

- Compensation for camelids and other non-bovine farm animals removed for TB control reasons in GB is determined under relevant legislation for each country
- In England this Order directs that TB in camelids (and other non-bovine farmed mammals) is included within the diseases for which the Minister may cause an animal to be slaughtered under section 32 of the <u>Animal Health Act 1981</u>
- The Schedule to this Order sets out the amount of compensation payable in respect of each species and category of animal slaughtered. For camelids:
 - a. £750 for an animal 18 months old or younger
 - b. £750 for a non-breeding animal over 18 months old
 - c. £1,500 for a stud male or a breeding female over 18 months old

Surveillance for TB in camelids in GB

- Incidence of *M. bovis* infection in camelids is relatively low and sporadic
- Spillover (and potentially amplifier) hosts
- No compulsory system of herd registration, animal ID or movement records in GB
- Routine TB testing of all camelid herds at the government's expense would be disproportionate and probably not cost-effective
- Therefore, surveillance for TB in camelids is through:
 - a. investigation of suspected clinical cases and lesions of TB reported to APHA,
 - b. scanning surveillance of diagnostic submissions to APHA labs, and
 - c. targeted testing by APHA of specific herds (or animals) at elevated risk of *M. bovis* infection/exposure
 - d. privately-funded (skin and/or antibody) TB testing, which can be voluntary (e.g. private sales), or a statutory requirement (e.g. camelid breeders wishing to export stock to the EU must have a TB surveillance plan in place)



APHA investigation of suspected *M. bovis* infections

- Reports of clinical signs in live animals (suspected 'clinical case')
- Suspicious gross lesions of TB at PM examination (inc. scanning surveillance at APHA laboratories)
- Herds with epidemiological links to a known infected herd (TB incident investigations, inc. tracings)
- Following positive results to a private TB test, which must be notified to APHA:
- Statutory targeted TB testing of camelids instigated by APHA:
 - contiguous to a cattle/other livestock farm affected by laboratory-confirmed TB incident
 - co-located with infected cattle herds
 - enhanced TB surveillance (radial testing) areas in the Low Risk Area of England
 - confirmed TB hotspots in the Low Risk Area of England
 - TB source and spread tracings from infected herds.



Herd TB movement restrictions

Applied in the following scenarios:

- Suspected clinical cases awaiting further examination/testing by APHA
- Post-mortem cases: TB-like lesions pending confirmatory test results at APHA
- Following confirmation of *M. bovis* infection in PM samples by an APHA laboratory (PCR test or culture)
- Reactors to a statutory or private tuberculin skin test
- Seropositive animals on a statutory or private antibody TB test
- Camelids co-located with cattle or other livestock with laboratory-confirmed *M. bovis* infection
- A statutory TB test instructed by APHA becoming overdue



Actions in the event of a TB incident

- Statutory TB testing scenarios apply once suspicion of TB is raised or confirmed in a camelid herd (see: <u>TB in camelids - Bovine TB | TB Hub</u>)
- Herds with one or more test reactors and/or animals with laboratory-confirmed *M.* bovis infection require statutory repeat ('short-interval') skin herd testing at least 90-days following removal of the last reactor
- As soon as possible after confirmation of *M. bovis* infection by positive PCR testing (or culture), supplement the skin test with a combination of two antibody tests
 - Further rounds of antibody parallel testing at APHA's discretion
- APHA case vet can also remove non-reactors as direct contacts (DCs)
- All test reactors, any DCs and suspect clinical cases removed with compensation
- Possible partial-/whole-herd slaughter of persistently infected incidents
- Source and spread tracings (and radial/CON testing)
- Lift movement restrictions following two successive skin herd tests with -ve results

Prevention / risk mitigation measures

- Investigate suspicious/unexplained deaths in the herd through PME and notify APHA immediately if private vet suspects TB in the herd (legal requirement)
- Avoid direct/indirect contact with neighbouring/co-located TB-susceptible livestock (e.g. over farm boundaries, shared grazing, shared equipment)
- Minimise direct/indirect contact with badgers/wild deer or their excretions/secretions on farm
- Be aware of the risk posed by animals moved on to the farm (e.g. purchases, 'drive-by' matings, returns from shows):
 - source any animals carefully, quarantine them on arrival from another farm or show, and arrange/request a private anamnestic pre- and/or post-movement TB antibody test



Further information & advice

- Voluntary TB surveillance scheme, with testing provided by APHA (dual DPPVetTB + IDEXX test) and Surefarm Ltd (Enferplex test only)
 - details on how the scheme operates can be found at the British Alpaca Society's website: <u>www.bas-uk.com</u> or <u>www.surefarm.co.uk</u>)
- APHA Vet Gateway: instructions for PVS
 http://apha.defra.gov.uk/External_OV_Instructions/TB_Camelids_Instructions/Ancillary_Testing/index.htm
- Help and support for those affected by TB in alpacas and llamas, from the <u>Camelid TB support and research group (http://www.alpacatb.com/</u>)
- TB Advisory Service (TBAS): <u>https://www.tbas.org.uk/</u> or <u>info@tbas.org.uk</u>
 - free, bespoke advice on practical, cost-effective measures to build resilience of herds to TB through on-farm advisory visits and telephone advice
 - camelid keepers in England are eligible for a free farm survey by an experienced TBAS advisor

FB ADVISORY SERVICE

available for herds currently TB-free and those sustaining a TB incident.



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