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Review Article

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Mycobacterium caprae infection across species: A one health perspective on domestic animals, wildlife, and humans

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Abstract

Mycobacterium caprae (M. caprae), a member of the *Mycobacterium tuberculosis* complex (*MTBC*), is an emerging zoonotic pathogen of increasing concern in both veterinary and public health sectors. While traditionally associated with caprine tuberculosis, *M. caprae* has been reported in a wide range of domestic animals, wildlife species, and humans across Europe, Asia, and Africa. Its broad host range highlights the importance of adopting a One Health framework to understand and mitigate its transmission dynamics. In livestock, *M. caprae* infection leads to significant economic losses due to trade restrictions, decreased productivity, and the need for culling. Wildlife reservoirs, including deer, wild boar, and other ungulates, complicate eradication efforts and create persistent sources of infection. Human cases, often linked to zoonotic exposure through unpasteurized dairy products or direct animal contact, emphasize the public health risks associated with cross-species transmission. Despite its growing significance, *M. caprae* remains underdiagnosed and frequently misidentified as other *MTBC* members, limiting accurate surveillance and control. Limitations of conventional diagnostic methods and inconsistent use of molecular typing have contributed to underdiagnosis and misclassification, obscuring both burden and transmission pathways. This review synthesizes current knowledge on the pathogen's ecology, epidemiology, diagnostic challenges, and control implications from a One Health perspective. A coordinated One Health approach, integrating veterinary, medical, and ecological perspectives, is essential for the effective detection, prevention, and control of *M. caprae* infections globally.

Keywords: Tuberculosis, *Mycobacterium caprae,* Epidemiology, Wildlife, One Health, Molecular typing

List of abbreviations

The following abbreviations are used in the review:

AMR	Antimicrobial resistance
EU	European Union
IFN-γ	Interferon-gamma
LJ	Lowenstein–Jensen
M.caprae	Mycobacterium caprae

MIRU-VNTR	Mycobacterial Interspersed Repetitive Units–Variable Number Tandem Repeats
MTBC	Mycobacterium tuberculosis complex
OHCEA	One Health Central and Eastern Africa
PZA	Pyrazinamide
RD4	Region of Difference 4
SACIDS	Southern African Centre for Infectious Disease SurveilLance
SNP	Single Nucleotide Polymorphism
TB	Tuberculosis
TST	Tuberculin skin test
UVGI	Ultraviolet germicidal irradiation
WGS	Whole genome sequencing

1. Introduction

Tuberculosis (TB) remains one of the most serious infectious diseases worldwide, affecting both humans and animals. It is a chronic granulomatous disease characterized by long-term persistence, insidious progression, and the ability to cross species barriers [1]. Caused by members of the *Mycobacterium tuberculosis* complex (*MTBC*), the primary disease-causing species within this group include *M. tuberculosis*, *M. africanum*, *M. bovis*, and *M. caprae.*

M. caprae has emerged over the last two decades as an important multi-host pathogen that affects domestic livestock, a range of wild animals, and humans [2-4]. Historically considered a subspecies of *M. bovis, M. caprae* is genetically distinct and has been documented repeatedly. It causes bovine-like tuberculosis in goats and cattle and establishes infection reservoirs in wildlife such as wild boar and red deer [5-7]. From a One Health viewpoint, *M. caprae* exemplifies the interconnectedness of animal, human, and environmental health. Transmission occurs at multiple interfaces: between livestock (notably goats and cattle) via close contact and shared housing or pasture; between wildlife and livestock, where overlapping grazing or contaminated environments allow spillover and maintenance; and to humans, primarily through occupational exposures, direct contact with infected animals, or consumption of unpasteurized dairy products in areas where animal TB is not fully controlled. These multi-directional transmission pathways complicate control efforts and underline the need for integrated surveillance and intervention [3, 8-10].

Recent genomic and epidemiological studies have highlighted how animal trade, farm management practices, and wildlife ecology shape the regional distribution and persistence of *M. caprae*. One Health investigations in Europe have revealed long-term circulation of clonal lineages across livestock, wildlife, and occasionally humans, indicating both cryptic transmission chains and spillover events that standard livestock-only control programs can fail to capture (e.g, Bulgarian whole-genome sequencing phylogeography in cattle; Italy genotyping combining spoligotyping/ exact tandem repeat; occupational cases in Greece) [11-13]. Accurate detection and characterization of *M. caprae* are therefore essential but remain challenging. Conventional diagnostic tools used for bovine tuberculosis such as the tuberculin skin test (TST), culture, and post-mortem examination can indicate infection but usually lack species-level resolution. Molecular typing approaches are critical to distinguish *M. caprae* from other members of the *M. tuberculosis* complex, to trace epidemiological links, and to guide targeted control strategies (e.g. the Region of Difference 4 (RD4) variants study; comparative genomics of *M. bovis and M. caprae*) [14, 15]. However, current research on *M. caprae* is limited in scope: most studies are restricted to certain European countries, with little data from Africa, Asia, or Latin America where caprine and bovine TB remain endemic (Tunisia study; Peru case report) [16]. Moreover, diagnostic limitations in wildlife, under-reporting of zoonotic human cases, and frequent misclassification of isolates as *M. bovis* or *M. tuberculosis* contribute to major gaps in our understanding of the true global burden and epidemiology of *M. caprae* infections. For example, the European Union (EU) 2023

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zoonoses report points out that TB cases of zoonotic origin are highly likely to have been underestimated because many member states do not routinely distinguish *M. bovis* and *M. caprae* from *M. tuberculosis* in human TB cases [17].

2. Characteristic traits of *M. caprae*

M. caprae is an acid-fast, non-motile, non-spore-forming rod that is normally 0.2–0.6 µm wide and 1.0–10 µm long. Some strains generate smooth colonies, while others form rough colonies. The color of the colonies can vary from white to orange or pink [18]. The actual structure of the *MTBC* is uncertain due to the various taxonomic and nomenclatural alterations that have occurred among its species [19].

The species now known as *M. caprae* was originally described as *M. tuberculosis subsp. caprae* due to its initial identification from goats that had spread TB lesions [20], subsequently renamed as *M. bovis subsp. caprae* in accordance with Rule 27(3) of the Bacteriological Code [21]. The name *M. bovis subsp. caprae* proposed by Niemann [22] is not valid, since the type strain was not placed in two publicly available service collections in different nations when it was published [23] and finally promoted to the rank of species as *M. caprae* comb. nov., sp. nov.

M.caprae (ca′prae.): The name comes from the Latin feminine genitive noun caprae, meaning “of the goat,” referring to Capra, the host species from which the organism was first isolated. The description is identical to that provided for M. tuberculosis subsp. Caprae (Aranaz et al., 1999) [20]. Moreover, isolates exhibit a particular variant of the gyrB gene, where nucleotide 1311 is a G and nucleotide 1410 is a C. The type strain is gM-1^T (=CIP 105776^T =ATCC BAA-824^T) and displays the phenotypic and genotypic features assigned to this taxon [24].

M. caprae exhibits a particular set of phenotypic, biochemical, genetic, and genomic traits [25]. Phenotypic traits of the caprine mycobacterial isolates are poor hydrolysis of Tween 80 after 10 days and sensitivity to pyrazinamide (PZA) [26]. Biochemical characteristics include a lack of niacin accumulation, absence of nitrate reduction, no growth on Lebek’s medium, and the ability to grow in the presence of 2 mg/ml thiophen-2-carboxylic acid hydrazide [24].

3. Epidemiology

3.1. Host range susceptibility

M. caprae exhibits a broad host range, capable of infecting humans as well as domestic and wild animals across multiple regions, as summarized in Table 1 [27, 28]. *M. caprae* was first recognized as the predominant pathogen responsible for tuberculosis in goats [24], but it has also been reported in a variety of domestic and wild animal species and its role in wildlife in the epidemiology is increasingly recognized. Between 2003 and 2014, *M. caprae* was isolated from 55 animals in Portugal, including 29 goats, 21 cattle, 1 sheep, and 4 wild boars [29]. Phylogenetic studies suggest that the most recent common ancestor of *M. caprae* in goats dates back to approximately 100 years ago, with frequent host transitions between goats, wild boars, and humans, likely driven by mixed farming practices, extensive animal management, and close human-animal interaction [10]. Moreover, the pathogen has been identified in both sheep and goats, indicating direct interspecies transmission between these animals [30]. Notably, an outbreak of tuberculosis caused by *M. caprae* was reported in Croatia, where both children and cattle from a small dairy farm were found to be infected, and the bacterium was isolated from both hosts [31].

In addition to traditional livestock, *M. caprae* has also been isolated from less common hosts. In Spain, the first case of TB caused by *M. caprae* in a dromedary camel was reported [3], and in Slovenia, the bacterium was detected in two bison and one dromedary camel housed in a zoo [32]. In Italy, although *M. caprae* has been detected in only about 9% of cattle isolates, it has been rarely reported in red deer [33], and for the first time, the genotype SB0866 with Mycobacterial Interspersed Repetitive Units–Variable Number Tandem Repeats (MIRU-VNTR) profile 4,1,5,4,4,11,4,2,4,3,8,7 was isolated from an adult sow [34]. Additionally, the first reported instance of *M. caprae* infection in a domestic cat in the United Kingdom occurred in a castrated male Bengal breed [35].

In the Iberian Peninsula, the bacterium was isolated from a fox in an area where recent outbreaks had affected cattle and goat herds, indicating its spread among wild carnivores [9]. The bacterium has also been reported in red deer (Cervus elaphus) within Austria’s western states of Tyrol and Vorarlberg. In 2008, the prevalence of *M. caprae* in red deer was found to be up to 23% [36, 37], and *M. caprae* subtype Lech-tal was identified in a red fox (Vulpes vulpes) shot by a hunter in 2018 in the western part of Austria [38]. Additionally, *M. caprae*

has been isolated from wild boar and roe deer, though not from bison populations in the Bieszczady Mountains in Southeast Poland [39]. Another concerning occurrence was reported in the Bieszczady Mountains region in a wild boar (Sus scrofa) [40]. Importantly, research has shown that infected wild boars can sustain the circulation of *M. caprae* strains within their populations and potentially transmit the infection to domestic goats. *M. caprae* infection was reported in a captive Borneo elephant (Elephas maximus borneensis) imported directly from Borneo Island after being orphaned [41]. This interspecies transmission compromises the effectiveness of TB eradication campaigns in livestock and poses a significant public health risk [8].

M. caprae represents a significant public health concern due to its zoonotic potential and the likelihood of transmission between animals and humans. Spain, which reports the highest number of zoonotic tuberculosis cases in humans annually in the EU, also documented notable *M. caprae* activity between 2018 and 2022, underscoring its ongoing role in human and animal TB [42]. However, due to limitations in diagnostic methods for accurately identifying *MTBC* strains, the reported cases of *M. caprae* infection in humans likely underestimate the true extent of the issue. The first bacteriologically confirmed case of human infection with *M. caprae* in Poland was reported in November 2012, involving a 46-year-old male [43]. Relatively few known cases of autochthonous humans have been discovered outside of continental Europe [6]. Human illness caused by *M. caprae* has only been documented in a few number of cases, primarily from Turkey and Central and Southern European nations [44-46]. Additionally, it has been identified as a causative agent of tuberculosis in humans in both Peru and northern Algeria, highlighting the critical need for species-level identification of *MTBC* members to ensure effective management and treatment of zoonotic TB [47, 48]

3.2. Patterns of infection spread among hosts

The main pathways for *M. caprae* infection are the consumption of unpasteurized dairy products and direct contact with infected animals. Reported cases involved 13 occupational exposures (seven goat farm workers, three cattle farm workers, two slaughterhouse workers, and one individual handling animal remains for fodder production), two family members of cattle owners, and five migrants from regions where unpasteurized milk consumption is common (four from the Sahel region and one from Sub-Saharan Africa, with one specifically reporting the consumption of unpasteurized milk) [49]. Pigs typically become infected through the ingestion of unpasteurized milk or dairy by-products from infected cows, as well as unsterilized slaughterhouse waste. An incident reported on a family farm in the Czech Republic confirmed the transmission of *M. caprae* to domestic pigs through the consumption of contaminated cow's milk [50].

The detection of similar *M. caprae* genotypes in both red deer and cattle suggests that domestic cattle may have become infected over time through contact with free-ranging red deer, which have attained the position of maintenance hosts [51, 52]. Notably, *M. caprae* can be excreted in the feces of naturally infected red deer, indicating that red deer can play a role in the transmission and spread of the disease [53]. Cattle may contract the infection when the environment near to feeding areas is contaminated by excretions from infected wildlife, such as feces, urine, pus, or sputum. Extended crowding of red deer at feeding areas creates ideal conditions for close contact between individuals, increasing the risk of intraspecies transmission [36, 51, 52]. Another possible source of infection could be wildlife winter feeding locations, when contaminated food and salt licks are accessible. The likelihood of disease transmission between wildlife and domestic animals is influenced by several factors, such as species-specific behavior, herd management practices, and the virulence of the pathogen. A key contributor to transmission risk is the environmental persistence of mycobacteria, which can remain viable in soil and bedding materials for extended periods, even lasting several years [54, 55]. In Andalusia, the regions with the highest density of goat farms corresponded closely with the geographic distribution of human cases. Human *M. caprae* isolates were recovered from five Andalusian hospitals that routinely performed species-level identification of members of the *M. tuberculosis* complex. Most cases were associated with direct or indirect contact with livestock, particularly goats and cattle, or with individuals originating from countries where consumption of unpasteurized dairy products is common. In the majority of patients, tuberculosis involved the respiratory tract, indicating that airborne transmission from infected animals (via inhalation of aerosolized bacilli during close contact or handling of livestock) was the predominant route of

infection, while ingestion of contaminated milk or dairy products represented a secondary but possible transmission pathway [31, 49].

4. Insights into the pathogenesis and virulence mechanisms of *M. caprae*

M. caprae causes tuberculosis primarily in goats, sheep and other ruminants, but can spill over to cattle, wildlife, and humans [56]. Its pathogenesis follows the general *MTBC* paradigm: after inhalation or ingestion, bacilli are phagocytosed by macrophages, where they resist killing and establish infection, forming granulomas which may later caseate. Although *M. caprae* does not appear to carry unique classical toxins, comparative genomics has revealed several virulence-associated features shared with *M. bovis* and *M. tuberculosis* [57]. Key among these are conserved type VII secretion (ESX) systems, especially ESX-1 and ESX-5, which are involved in secretion of proteins like ESAT-6/CFP-10 that mediate phagosomal escape, modulation of immune responses, and virulence [58, 59]. Also, the lipid metabolism / stress-response gene families (e.g. those linked to mycolic acids, cell envelope lipids) are highly conserved and likely crucial for persistent infection and resistance to host defenses [58, 60]. Another locus of interest is the RD4, which is present in *M. caprae* (in many, but shows heterogeneity among isolates) but absent in *M. bovis*; this region appears to include genes involved in trehalose-containing glycolipid synthesis, which may affect virulence by influencing the cell envelope's properties and immune evasion [61]. Mutations or deletions in certain antigenic proteins, variation in host T-cell epitopes, and differences in peptidoglycan assembly also correlate with the variation in lesion severity, host range, and transmissibility among *M. caprae* isolates [57, 62]. Altogether, *M. caprae's* virulence arises not from novel toxins but from the capacity to modulate the immune response, survive in hostile intracellular environments, and adapt its envelope and secreted antigen repertoire to different hosts.

M. caprae infection in humans presents as pulmonary tuberculosis in most cases [43], but extrapulmonary forms, such as tuberculous meningitis, which is the most serious form of extrapulmonary tuberculosis, are relatively more *ulosis* infections. *M. caprae* causes tuberculosis in both animals and humans via similar intracellular survival and immune-modulating mechanisms.

However, in humans, it tends to show different tissue preferences, reflecting partial host adaptation and genomic divergence from *M. bovis* and *M. tuberculosis* [46, 63-65].

5. Comprehensive diagnostic approaches for the detection of *M. caprae*

Diagnostic approaches for *M. caprae* rely on a combination of clinical evaluation, post-mortem examination, and laboratory testing [66].

5.1. Clinical and pathological features across species

M. caprae infection exhibits a wide clinical and pathological spectrum depending on the host species, route of infection, and disease stage, but it generally reflects the chronic and granulomatous nature of the disease. In domestic cats, infection may present as systemic illness with respiratory involvement, pyogranulomatous bronchopneumonia, and renal lesions, with histopathology revealing necrotizing granulomas containing moderate numbers of acid-fast bacilli in lymph nodes; infection often occurs via the respiratory tract, with hematogenous dissemination to other organs [35, 67]. In domestic ruminants such as cattle and goats, infection typically presents as a chronic, progressive condition, and many cases remain subclinical for long periods, with lesions often detected only at slaughter or postmortem examination [67]. Experimentally infected goats were euthanized and developed extensive tuberculous lesions in the lungs and respiratory lymph nodes [68]. while naturally infected cattle in endemic regions may exhibit lesions in the lungs, liver, intestines, and regional lymph nodes following alimentary or aerosol exposure, with histology showing sparse acid-fast bacilli but strong immunohistochemical positivity for mycobacterial antigens [69]. In camels, the disease manifests with progressive weight loss, dull coat, and lethargy, typically noted within two weeks prior to euthanasia. Necropsy findings include ascites, hydrothorax, and hydropericardium, along with numerous nodules measuring 0.5–3 cm in diameter scattered throughout the spleen and liver. Marked generalized lymph node enlargement is evident, particularly in the mesenteric and mediastinal nodes. The distribution of these gross lesions reflects systemic involvement [3].

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In wildlife reservoirs, lesion patterns vary by species. In red foxes, disseminated disease may result in severe emaciation, blindness, depression, markedly enlarged lymph nodes with caseous necrosis, thickened pericardium with purulent exudate, discrete pulmonary granulomas, and multifocal caseopurulent renal necrosis [9]. In red deer, lesions are most often located in the head lymph nodes, especially the medial retropharyngeal nodes, reflecting oral exposure; severity ranges from small granulomas to coalescing abscesses and generalized tuberculosis with lesions up to 200 mm in diameter [70].

Table 1. Comparative overview of *M. caprae* cases across regions and hosts.

Region	Host Species Reported	Critical considerations	References
Southern Europe (Spain, Italy, Portugal)	Goats, cattle, sheep, dromedary camel, domestic sow, wildlife	**Spain** reports the largest number of documented zoonotic TB (M. caprae) in humans within the EU. **In Portugal**, isolates recovered between 2003 and 2014 demonstrated infection across multiple species, highlighting a broad host involvement. **In Italy**, the genotype SB0866 of *M. caprae* was first detected in an adult sow.	[3, 29, 33]
Central Europe (Austria's western states of Tyrol and Vorarlberg, Slovenia)	Red deer, red fox, bison, dromedary camel	**In Austria**, red deer exhibited a high prevalence of *M. caprae* (up to 23%), and the Lech-tal subtype of the bacterium was additionally identified in a red fox, highlighting its circulation in both wild cervids and carnivores. **In Slovenia** In Slovenia, cases of *M. caprae* were identified in zoo animals, including two bison and one dromedary camel.	[32, 36, 38, 39]
Western Europe (Croatia, United Kingdom)	Cattle, goats, domestic cat Sporadic human cases	**In Croatia**, human cases are uncommon but have been occasionally reported, with some outbreaks traceable to livestock exposure. **In the United Kingdom**, the first confirmed *M. caprae* case occurred in a cat.	[31, 35]
Southwest corner of Europe (Iberian Peninsula)	Goats, wild boars, foxes, humans	Host transitions occur between livestock, wildlife, and humans.	[9, 10]
Poland (Bieszczady Mountains)	Wild boar, roe deer, humans; not detected in bison	No cases have been detected in bison.	[39, 40, 43]
Czech Republic	Cattle, pigs	Transmission of *M. caprae* to domestic pigs can occur via consumption of cow's milk contaminated with the pathogen.	[50]
Asia (Borneo)	Borneo elephant (captive)	Documented infection in a captive Borneo elephant.	[41]
Turkey	Humans	Relatively few human cases have been identified.	[44-46]
Latin America (Peru)	Humans	*M. caprae* has been identified as a causative agent of human TB, emphasizing the importance of species-level identification within the *MTBC*.	[47]
Africa (Northern Algeria)	Cattle, humans	*M. caprae* has been observed in humans as a zoonotic pathogen transmitted from cattle to humans.	[48]

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Wild boar commonly develop yellowish tubercles (1–5 mm) in submandibular, mediastinal, and tracheobronchial lymph nodes [39]. *M. caprae* was also recovered from the sputum of an elephant presenting with low-grade fever (99.9 °F), loss of appetite, progressive weight loss, and a productive cough [41]. In humans, *M. caprae* does not exhibit distinctive clinical manifestations, which can make it difficult to recognize as the causative agent of tuberculosis. These clinical manifestations are indistinguishable from those of *M. tuberculosis*. Pulmonary forms are most common, with chronic cough, fever, night sweats, and weight loss [49], while extrapulmonary involvement may include lymphadenitis, peritoneal TB, skeletal TB, genitourinary TB, and Tuberculous meningitis is the most serious form of extrapulmonary tuberculosis in children, especially infants [44, 65]. As in animals, gross pathology in human cases reveals caseous necrotizing granulomas, and histopathology shows classic tuberculous architecture with central necrosis and epithelioid cell layers, though definitive species identification requires microbiological culture and molecular typing [64, 71].

5.2. Conventional and molecular methods for laboratory diagnosis

The laboratory diagnosis of *M. caprae* in animals and humans involves a combination of ancillary, immunological, and molecular methods to ensure accurate detection and differentiation within the *MTBC, as* summarized in Table 2 [72].

Screening for *MTBC* infection typically begins with the TST, which serves as the primary diagnostic tool to detect cell-mediated immune responses to mycobacterial antigens. However, the sensitivity of the TST may be limited under certain conditions, such as early stages of infection, immunosuppression, or exposure to environmental mycobacteria. The interferon-gamma (IFN-γ) assay is generally regarded as more sensitive than the TST, providing an earlier and more reliable indication of infection. Nonetheless, both assays are unable to distinguish *M. caprae* from other members of the *MTBC* [73, 74].

M. caprae is a slow-growing, non-motile, acid-fast bacillus. On Lowenstein–Jensen (LJ) or Middlebrook 7H10/7H11 media, colonies of *M. caprae* generally appear rough, dry, and cream to buff-colored, resembling those of *M. bovis*. Growth typically occurs after 3 to 8 weeks of incubation at 37 °C, and unlike *M. bovis*, *M. caprae* can also grow, though weakly, at 42 °C. Microscopically, the organism appears as slender, slightly curved rods, which stain red with Ziehl–Neelsen due to the high mycolic acid content in their cell wall [75-77]. Biochemically, *M. caprae* is niacin-negative, nitrate-negative, pyrazinamidase-positive, and catalase-negative at 68 °C, features that help distinguish it from *M. tuberculosis* and *M. bovis.* It is also susceptible to pyrazinamide, in contrast to *M. bovis*, which shows natural resistance to this drug [44, 78]. These biochemical and growth traits, in combination with molecular analyses such as spoligotyping or region of difference (RD) typing, are essential for accurate identification and differentiation of *M. caprae* within the *MTBC*.

In both animals and humans, molecular detection of *MTBC* from clinical specimens or culture isolates using real-time PCR provides a rapid and highly sensitive diagnostic approach. Targets such as *IS6110* and *IS1081,* which are multicopy insertion sequences, enable efficient detection of *MTBC* DNA, even in samples with low bacterial load. The *gyrB* gene, encoding the DNA *gyrase subunit B*, contains sequence polymorphisms that allow for reliable species differentiation within the *MTBC*, including *M. caprae*, *M. bovis*, and *M. tuberculosis*. Similarly, amplification of the mpb64 gene, which encodes an immunogenic protein specific to *MTBC* species but absent in BCG strains, serves as an additional confirmatory marker for active infection. The combination of these genetic targets in multiplex or real-time PCR assays enhances diagnostic specificity and enables rapid species-level identification, supporting both clinical diagnosis and epidemiological tracing [64, 79-82].

Genotyping methods such as spoligotyping, IS6110-RFLP, and MIRU-VNTR are essential for epidemiological tracing, with MIRU-VNTR providing higher discriminatory power than spoligotyping. To distinguish *M. caprae* from other *MTBC* members, [83] discovered an additional *M.caprae*-specific single nucleotide polymorphism (SNP) at position 690 bp of the lepA gene. Genetic fingerprinting identifies unique characteristics of caprine mycobacterial isolates. By using first-generation membranes and direct variable repeat-spoligotyping, as described by [84], they constructed a homogeneous cluster that is clearly identified by the lack of

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spacers 1, 3–16, 30–33, and 39–43. Additionally, caprine mycobacterial isolates are separated from M. bovis isolates by RFLP typing linked to IS6110, polymorphic GC-rich sequences, and direct repetitions [85, 86]. At the genomic level, it was first demonstrated that MTC species differed based on whether or not they have regions of differentiation (RD). RD9, RD7, RD8, RD10, RD5, RD6, RD12, RD13, and N-RD25 are absent from caprine isolates [87, 88]. Although a standardized panel of loci has not yet been established due to variations in allelic diversity among strains, MIRU-VNTR has shown high discriminatory power for *M. caprae*, enabling differentiation between closely related isolates and tracing transmission routes. Among the most informative loci for *M. caprae* differentiation are VNTR3232, QUB11a, ETR-B, and ETR-A, which provide strong resolution for epidemiological investigations [89].

6. Control and prevention of *M. caprae*: A one health perspective

The control and prevention of *M. caprae* infection require an integrated One Health approach combining veterinary, environmental, and human health strategies. As a zoonotic member of the *MTBC*, *M. caprae* can be transmitted directly between animals and humans or indirectly via contaminated environments, food products, or shared resources [90]. Routine surveillance of livestock, particularly goats and sheep, is essential for early detection and interruption of transmission chains. Veterinary programs should incorporate tuberculin skin testing, interferon-γ release assays, bacteriological culture, and molecular tools such as whole-genome sequencing (WGS) to differentiate *M. caprae* from other *MTBC* members [91].

Table 2. Summary of diagnostic approaches for *M. caprae*.

Diagnostic category	Key information
General diagnostic approach	Diagnosis in animals and humans relies on ancillary tests, immunological assays, culture, and molecular methods.
TST	Primary screening tool for *MTBC* infection.
IFN-γ	More sensitive than TST; offers an earlier indication of infection. Still unable to differentiate *M. caprae* from other *MTBC* members.
Culture characteristics	Slow-growing, non-motile, acid-fast bacilli. Rough, dry, cream to buff-colored colonies on LJ or Middlebrook media. Growth in 3–8 weeks at 37 °C. Unlike *M. bovis*, *M. caprae* can also grow, though weakly, at 42 °C.
Microscopic features	Slender, slightly curved, acid-fast rods stained by Ziehl–Neelsen due to high mycolic acid content.
Biochemical tests	*M. caprae* is niacin-negative, nitrate-negative, pyrazinamidase-positive, and catalase-negative.
Molecular detection	Real-time PCR targeting IS6110 and IS1081 enables rapid and sensitive *MTBC* detection. mpb64 gene amplification confirms *MTBC* infection; gyrB polymorphisms allow species differentiation among *M. caprae*, *M. bovis*, and *M. tuberculosis.*
Genotyping methods	Spoligotyping, IS6110-RFLP, and MIRU-VNTR are used for epidemiological studies; MIRU-VNTR offers the highest discriminatory power.
Species-specific markers	An *M. caprae*-specific SNP is identified at position 690 bp of the lepA gene.
Spoligotype pattern	Characterized by the absence of spacers 1, 3–16, 30–33, and 39–43, forming a distinct cluster.
Differentiation from *M. bovis*	Achieved through IS6110-RFLP, polymorphic GC-rich sequences (PGRS), direct repeat analysis, and specific RD deletions.
MIRU-VNTR for *M. caprae*	Reliable for genotyping *MTBC*, including *M. bovis* and *M. caprae*. No universal locus panel exists due to allelic diversity. Highly discriminatory for *M. caprae*; informative loci include **VNTR3232, QUB11a, ETR-B, and ETR-A**, which are useful for tracing transmission chains.

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In humans, clinical suspicion should be raised in tuberculosis cases with a history of occupational animal contact or consumption of unpasteurized dairy products, and laboratory capacity for subspecies identification should be strengthened.

Environmental contamination is a critical yet often underestimated factor in the epidemiology of *M. caprae* infections. Farms and grazing areas where domestic livestock interact with wildlife species such as badgers, wild boars, and deer pose a high transmission risk due to the shedding of infectious bacilli in feces, nasal secretions, and saliva [92]. The pathogen can persist for extended periods in soil, water, and organic matter while maintaining infectivity [93], enabling sustained transmission among livestock and wildlife. Breaking this environmental transmission cycle requires rigorous sanitation and disinfection measures targeting contaminated reservoirs. Effective strategies include alternating the use of ethyl alcohol, sodium hypochlorite, and 20% lime milk for cleaning animal housing, equipment, and transport vehicles [94]. Weekly treatments of barns and exercise areas with 2% sodium hydroxide or quicklime help reduce microbial load. Monthly disinfection of sewage systems and cesspits using bleaching powder further limits persistence. The installation of permanent disinfection stations at farm entry and exit points, with bimonthly replenishment, enhances biosecurity [95].

In confined settings such as veterinary clinics, hospitals, and prisons, airborne transmission risk can be reduced through natural ventilation, with upper-room ultraviolet germicidal irradiation (UVGI) serving as a supplementary measure in poorly ventilated environments [96]. Incorporating these environmental control measures alongside regular monitoring is essential for mitigating the persistence and spread of *M. caprae* in agricultural and communal environments.

From an animal health perspective, test-and-slaughter or test-and-segregate policies remain central to removing infected livestock, alongside biosecurity measures that restrict herd mixing, regulate animal movement, and prevent wildlife access to feed and water sources through interventions such as raised troughs and anti-badger fencing [97]. While complete eradication of *MTBC* from wildlife is generally unfeasible, vaccination campaigns, such as BCG immunization of badgers in the United Kingdom, have shown potential in reducing bacterial shedding [98]. Several studies have demonstrated the efficacy of BCG vaccination in reducing tuberculosis caused by *M. caprae* in animal models. In goats naturally exposed to *M. caprae*, a field trial showed that BCG vaccination lowered the prevalence of tuberculous lesions, with efficacy ranging from 53% to 75% depending on lesion location, indicating reduced disease severity and bacterial spread [99]. Similarly, in wild badgers, BCG vaccination not only reduced the risk of disease in vaccinated individuals but also provided indirect protection to unvaccinated cubs when a substantial proportion of their social group was immunized [100]. These results align with findings from wildlife and livestock tuberculosis control programs where BCG vaccination helped reduce bacterial shedding and transmission risk, supporting its use as a valuable tool in integrated control strategies against *MTBC* in animals.

Food safety is a critical element of prevention, as unpasteurized dairy products are a well-documented vehicle for zoonotic TB, including *M. caprae* [101]. Mandatory milk pasteurization, as implemented in Canada since 1991, has markedly reduced the risk of foodborne *MTBC* transmission [102]. Hygiene protocols for milking equipment, birthing areas, and personnel should be enforced to prevent contamination, while ensuring disinfectant residues do not enter the milk supply [103].

Public health control measures should prioritize targeted screening of high-risk occupational groups and travelers from endemic regions. Although human *M. caprae* infections are rare, a Canadian case in an elderly immigrant from Ukraine with a history of animal farming, reported by Riopel [104], demonstrates its zoonotic potential. The patient developed pulmonary tuberculosis, the isolate was fully susceptible to first-line drugs, and no secondary cases occurred, yet the outcome was fatal. Such cases, typically acquired abroad, highlight the importance of screening protocols that incorporate travel and occupational histories, support subspecies-level *MTBC* identification, and include diagnostic approaches for both pulmonary and extrapulmonary disease. The WHO–OIE–FAO Roadmap for Zoonotic Tuberculosis aims to reduce TB mortality by 95% and incidence by 90% by 2035, but persistent environmental reservoirs and cross-species transmission remain significant barriers [105]. Special attention should be given to vulnerable populations, including those with HIV infection, for whom environmental exposure

can accelerate disease progression and complicate treatment [106]. Progress toward these targets will depend on sustained coordination between veterinary and human health sectors, enhanced environmental surveillance, public awareness campaigns, and the application of molecular epidemiology to identify and interrupt transmission routes.

7. Future directions for surveillance of *M. caprae*

Future research on *M .caprae* infection should prioritize genomic surveillance to enhance the detection of transmission clusters, trace cross-species spillover events, and monitor the emergence of drug-resistant strains, building on established whole-genome sequencing (WGS) frameworks for zoonotic tuberculosis. Robust surveillance systems are essential for identifying emerging disease threats and antimicrobial resistance (AMR), guiding treatment and mitigation strategies, evaluating the effectiveness of current control measures, and informing evidence-based policy and regulation. These systems typically operate at national or subnational levels and monitor infections and AMR in animals, farm workers, the general human population, and at the interfaces linking livestock, humans, wildlife, and the environment [13, 107]. Strengthening interdisciplinary One Health collaborations including veterinarians, medical professionals, microbiologists, epidemiologists, and wildlife ecologists is vital for early detection, coordinated outbreak response, and the development of effective control policies for zoonotic tuberculosis [108]. Experiences from initiatives such as the Southern African Centre for Infectious Disease Surveillance (SACIDS), One Health Central and Eastern Africa (OHCEA), and AfriqueOne in Tanzania demonstrate how multisectoral partnerships can enhance infectious disease surveillance, including for mycobacterial infections. Therefore, advancing the One Health approach through strong intersectoral collaboration among stakeholders, governmental sectors, and communities is essential to address the complex factors shaping the health and well-being of humans, animals, and ecosystems [109].

8. Conclusion

M. caprae is emerging as a notable pathogen within the interconnected One Health framework of humans, animals, and the environment. Its persistence in multi-host systems demonstrates that eradication strategies focusing solely on livestock are insufficient. Wildlife reservoirs and ecological factors must be considered in long-term control policies. Advances in molecular epidemiology, including whole-genome sequencing, offer promising tools to improve surveillance and trace transmission pathways. However, their routine application remains limited in many regions. Building stronger links between veterinary, medical, and environmental sectors will be critical to closing diagnostic and epidemiological gaps. Ultimately, controlling *M. caprae* requires moving beyond traditional species-specific frameworks toward a truly integrated One Health strategy.

Author contributions

The authors conducted the research and data analysis, and were responsible for writing and approving the review. All authors have thoroughly reviewed the work and provided their consent to the final version.

Conflicts of interest

All authors declare no conflicts of interest.

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Data availability

Data will be available on request.

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