THE CURRENT KNOWLEDGE OF TUBERCULOSIS IN PINNIPEDS

Ailin Sosa Drouville[1], Martha Patricia Rincón-Díaz[2], Soledad Barandiaran[3], María Soledad Leonardi[1]

[1] Instituto de Biología de Organismos Marinos (IBIOMAR-CONICET), Puerto Madryn, Chubut, Argentina.

[2] Centro para el Estudio de Sistemas Marinos (CESIMAR-CONICET), Puerto Madryn, Chubut, Argentina.

[3] Instituto de Investigaciones en Producción Animal (INPA-CONICET-UBA), Ciudad Autónoma de Buenos Aires, Buenos Aires, Argentina.

Correspondencia: Ailin Sosa Drouville, Bvd. Brown 2915, (U9120ACD) Puerto Madryn, Chubut, Argentina

Email: ailinsosa@cenpat-conicet.gob.ar

SUMMARY

Infectious diseases and zoonoses, particularly, are in the spotlight after the COVID-19 pandemic. Under this scenario, the One Health approach becomes of fundamental relevance to understanding, analyzing, interpreting, and, ideally, preventing future scenarios of the spread of infectious agents. It is estimated that about 60% of human infectious diseases are caused by zoonotic agents. A clear example is zoonotic tuberculosis caused by pathogenic mycobacteria grouped within the *Mycobacterium tuberculosis* complex (MTBC). MTBC affects humans, livestock, and wildlife, and according to the World Health Organization, tuberculosis is one of the diseases with the most significant increase in the number of cases worldwide. The present study reviews current knowledge on tuberculosis in pinniped populations. *Mycobacterium pinnipedii*, a member of the MTBC, has been reported in different pinniped species.

KEYWORDS: infectious diseases, Mycobacterium Tuberculosis complex, pinnipeds, presences, tuberculosis, zoonoses

INTRODUCTION

Infectious diseases in general and zoonoses in particular are in the spotlight after the COVID-19 pandemic. In this scenario, the *One Health* approach to understanding, analyzing, interpreting, and, ideally, preventing future scenarios of infectious agent spread becomes of fundamental relevance. Approximately 60% of human infectious diseases are estimated to be caused by zoonotic agents (Dafale et al., 2020; Jones et al., 2008; Karesh et al., 2012). The advancement of the livestock frontier, habitat fragmentation, consumption of wildlife, large-scale animal production, and the use of animals as a tourist resource are some of the many human activities that facilitate the spread and introduction of pathogens into new host species (Karesh et al., 2012; Uhart, 2021). Tuberculosis (TB) is a clear example. According to the World Health Organization (WHO), tuberculosis is one of the diseases with the most significant increase in cases worldwide (World Health Organization, 2023). Currently, it is the second leading cause of death from infectious diseases and is among the top 10 causes of death reported by the WHO. However, it is not known what represents cases infected with particularly zoonotic TB. According to the WHO, 10 million people contract tuberculosis annually. Despite being a preventable and curable disease, tuberculosis kills 1.5 million people every year, making it one of the leading causes of death from infectious diseases.

Zoonotic tuberculosis is a worldwide disease caused by bacteria from the *Mycobacterium tuberculosis* complex (MTBC) different from *Mycobacterium tuberculosis* and *Mycobacterium africanum* and is present worldwide. These bacteria can infect a wide range of species, including pinnipeds and humans, for which zoonotic transmission of the MTBC has been reported (Kiers et al., 2008; Miller & Olea-Popelka, 2013; Vagene et al., 2022). Species typically associated with human tuberculosis are *M. tuberculosis* and *M. africanum* (Supply et al., 2013), and those considered adapted to infect both domestic and wild animals are *M. bovis* (cattle), *M. caprae* (sheep and goats), *M. microti* (rodents), *M. mungi* (striped mongoose, *Mungos mungo*), *M. orygis* (members of the family Bovidae), *M. pinnipedii* (seals and sea lions), *Dassie bacillus* (cape hyrax, *Procavia capensis*), and *Chimpanzee bacilli* (chimpanzees) (Jagielski et al., 2016). All these species have zoonotic character and are also very similar genetically (>99%) (Brites et al., 2018; Chiner-Oms et al., 2019). These mycobacteria have become established in different wildlife populations (Corner, 2006) and tend to spread when environmental, host, and pathogen characteristics change (Humblet et al., 2009). In particular, there are several papers in which pathogenic bacteria belonging to MTBC have been found in pinnipeds around the world (Cousin et al., 1993; Kats et al., 2022; Kiers et al., 2008; Kriz et al., 2011; Sacristan et al., 2021).

In this context, understanding infectious diseases such as TB in marine mammal populations is paramount for protecting human and animal health. As a first approach to this understanding, it is essential to know the presence of MTBC in pinnipeds populations worldwide and map the geographical distribution of cases, as well to document the techniques commonly used to detect this disease and the current geographical gaps in its detection in pinnipeds. Mapping the distribution of cases of infected pinnipeds within the species global distribution allows to determine whether there are information gaps associated with certain geographical regions. It is important to note the various techniques used to detect TB, providing easy access and synthesizing the most significant number of methods. The information gathered here allow the implementation of specific management measures according to geographical regions, thus contributing to public health and scientific knowledge in this field.

Aim and objectives of the review

In this review, we summarise cases of tuberculosis in pinnipeds reported in scientific literature worldwide as a first step towards understanding the geographical distribution of this disease and its potential zoonotic risk.

We therefore aimed to map the geographical distribution of cases and identify geographical gaps in the detection of MTBC in this group of marine mammals. We also recorded whether the animals were in captivity or not, and if it was possible to identify the bacterial species associated with MTBC in the papers reviewed. In addition, we classify the different detection techniques.

Primary question:

What is the current global geographic coverage of MTBC detection in pinniped species? Are there geographical gaps in detecting the complex in wild populations worldwide? Which tuberculosis detection techniques are used in pinniped species? Are they used on captive or wild specimens?

Methods

Literature search and selection

The literature search included studies published in indexed scientific journals that reported TB in wild and captive pinnipeds since 1900.

We followed the Collaboration for Environmental Evidence (CEE) guidelines to identify the primary systematic review question in combination withthe PRISMA protocol for literature selection (Collaboration for Environmental Evidence, 2013) (Table 1). The study search was conducted by title and abstract in English using the NIH (www.nih.gov), Dimensions (https://app.dimensions.ai), and Scopus (www.scopus.com) databases. In addition, a supplementary search of studies referenced in the selected literature was conducted using Google Scholar (www.scholar.google.com). The literature search was conducted in all databases using four strings with the keywords Mycobacterium tuberculosis complex, TB, pinnipeds, infectious diseases, presence, tuberculosis, and zoonoses (Supplementary Material Table S1). Boolean operators and wildcards were considered in the strings according to the default setting of each database.

Table 1: Definition of components of the primary systematic review question as per the Collaboration for Environmental Evidence (CEE) guidelines

Subject Population	**Exposure**	**Biological outcome measures**	**Comparators**	**Designs**
Pinnipeds	MTBC	Presence	• Species of pinnipeds with MTBC sampled tissue • Study location • Detection technique	Any observational study that provides evidence of the presence of bacteria belonging to the Mycobacterium tuberculosis complex (MTBC) in pinnipeds.

A total of 133 references were identified in the search after removal of duplicate studies (Figure 1). Two co-authors conducted an initial independent screening of the literature based on the title and abstract to eliminate spurious literature, with 96.87% agreement in literature selection. If agreement on a particular study was not reached during the independent screening, the co-authors engaged in dialogue to accept or reject a study, considering the components of the research question described in Table 1. We selected a total of 41 studies at this first screening. Then, a second independent full-text screening was carried out to identify studies that did not aim to identify MTBC in pinnipeds (Figure 1). These studies were excluded, leaving a final selection of 31 studies that were considered relevant to our objectives.

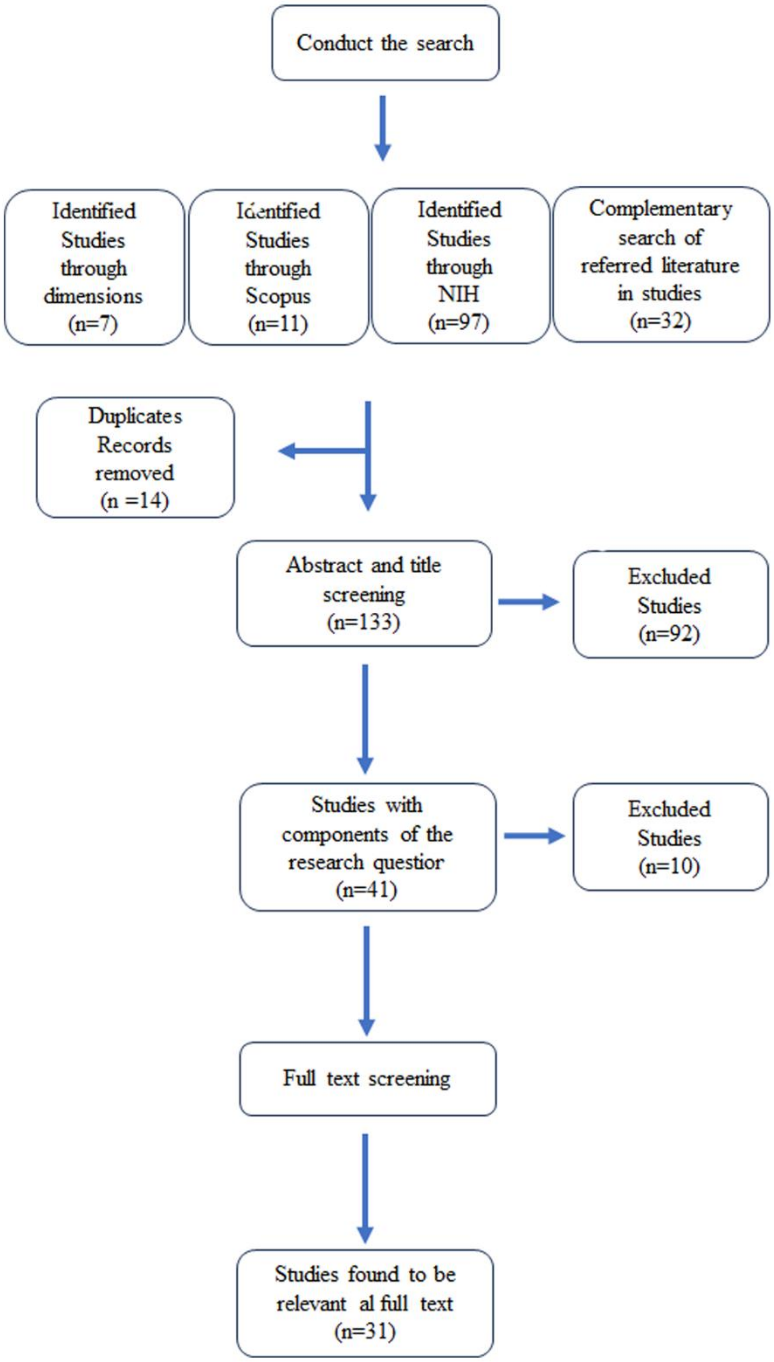

Figure 1. Flow diagram of literature search strategy and screening

Data extraction

Two co-authors independently extracted data from selected studies using a structured data extraction form. We extracted information about the studied pinniped species, country of the study site, year of publication, year of sampling, sampled tissue, population status categorized as captive or wild, presence of MTBC and bacterial species, and identification techniques. The consistency of extracted information from the two co-authors was compared with no discrepancies, except for minor differences related to one article, which was eliminated by a joint decision and agreement between the co-authors.

RESULTS

Literature search

The systematic review included 31 studies published over 109 years, from 1913 to 2022. It showed that MTBC bacteria were present in different species of pinnipeds in different world regions. The first case of pinniped tuberculosis was reported in 1913 in the United States in a capuchin seal (Cystophora cristata) (Blair 1913), and the second in 1956 in a Californian sea lion (Zalophus californianus) in a zoo in Germany (Ehlers 1965). Since 1987, cases of pinnipeds infected with *Mycobacterium tuberculosis* complex have been reported in Europe, America, and Australia (Bastida et al. 1999; Bernardelli et al. 1996; Cousins et al. 1990; Gutter et al. 1987). Since then, cases of tuberculosis have been reported in captive and free-ranging pinnipeds in various parts of the world (Cousin et al. 1990; Kiers et al. 2008; Martins Melo et al. 2019; Moser et al. 2008; Thompson et al. 1993).

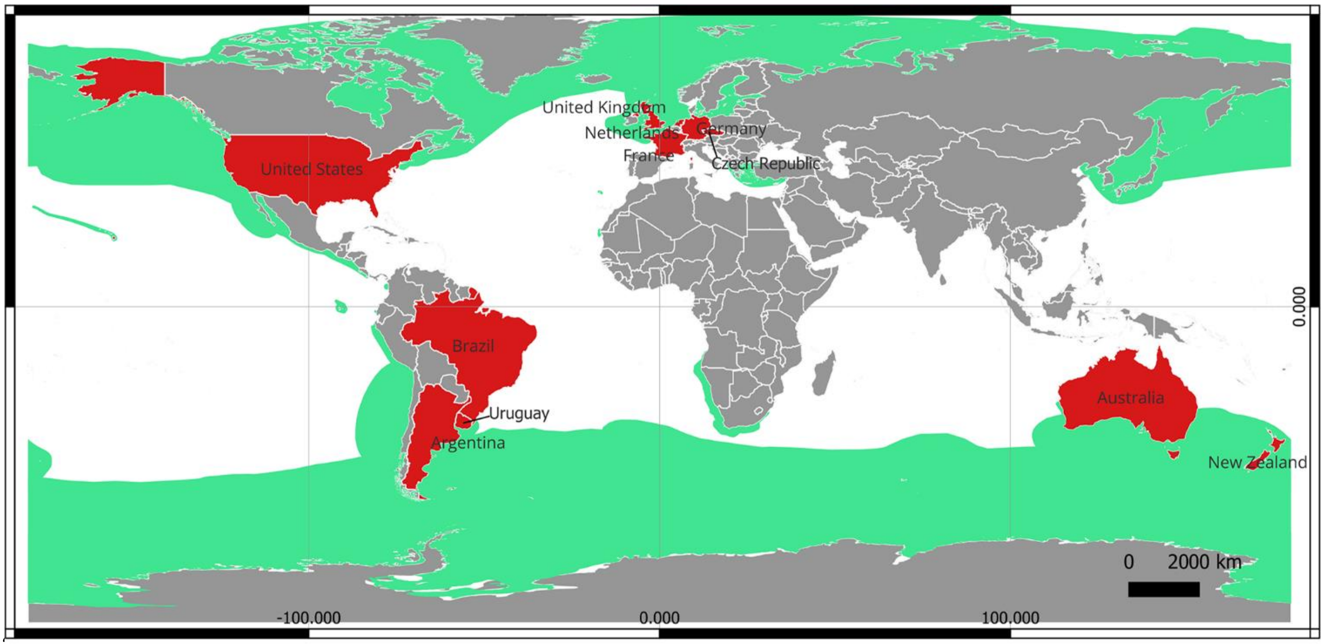

Figure 2: (●) distribution of all pinniped species worldwide, (●) countries where pinniped species infected with bacteria belonging to MTBC were found. Pinniped species distribution was extracted from the UICN Red List 2023.

What is the current global geographic coverage of MTBC detection in pinniped species?

In our review, 3 species of bacteria belonging to the *Mycobacterium tuberculosis* complex were documented 11 pinniped species (Figure 2, Table 2 and Table S2) among 11 different countries. Australia and Argentina stand out as the countries with the most studies documenting TB in pinnipeds, with 7 studies, respectively. Among the 11 countries, New Zealand stands out by reporting infections in wild and captive individuals of five pinniped species (*Arctocephalus forsteri, Arctocephalus tropicalis, Hydrurga leptonyx, Mirounga leonina, Phocarctos hookeri*). Notably, infected individuals exclusively recorded in the wild were studied in Latin American countries such as Brazil, Argentina, and Uruguay (Table 2).

Are there geographical gaps that need to be considered in detection of the complex in wild populations worldwide?

We identified notable global information gaps in the MTBC detection. There are several countries in the American, European, Asian, and African continents and Antartida with the presence of pinniped species and in which no cases of infected pinnipeds with bacteria belonging to MTBC have been reported (Figure 2).

Which tuberculosis detection techniques are used in pinniped species? Are they used on captive or wild specimens?

We identified 18 techniques used to detect TB in pinnipeds, with some techniques being more used than others for specific stages in the detection process. Across all literature review, bacterial culture was conducted in the first detection stages, in 27.6% (n = 45) of the 163 documented cases, each defined as combining a studied species with a particular detection technique per studied reviewed. Following the bacterial cultures, the use of nineTB detection methods represented 43.6% (n = 71) of the total cases as the second stage of the detection process (Table 3). From these last cases, 37 were carried out through polymerase chain reaction (PCR) tests. In cases where the bacteria are isolated by bacterial culture, further methods are used to detect TB species. At least one of the TB species detection techniques were used in 26% of the total cases found (n = 42 cases), with spoligotyping as the most commonly used technique within this group (n = 10 cases) (Table 3). Finally, we found few cases (n = 8) in which an earliest radiologic sign test was conducted. All identified techniques were used in individuals of wild populations in reviewed studies. Most techniques were tested in captive individuals, except for the bioquimic test, sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), Immunoperoxidase test, Mycobacterial Interspersed Repetitive Units (MIRU), variable number tandem repeats (VNTR) and 3D Computed Tomography. A total of 16 infected pinnipeds were confirmed with bacteria belonging to the MTBC. In 36 cases, the involved species could be differentiated, with 31 cases identified as *M. pinnipedi,* 1 case identified as *M. smegmatis* and 4 as *M. bovis*, a mycobacteria adapted to infect primarily terrestrial animals (Table S2)

Certain techniques have the advantage of being able to detect tuberculosis in living individuals, such as the Tuberculin skin test, Serological test and IGRA. These techniques are mostly utilized in individuals captured, in order to treat sick individuals as soon as possible and prevent contagion (Table 3).

Table 2. Summary of studies on pinniped species with tuberculosis detected and reported in wild or captivity populations worldwide.

Country	Number of studies	Number of studied species	Species	Number of studies per population status		
				Wild	Captivity	Wild and captivity
Argentina	7	3	*Arctocephalus australis*, *A. tropicalis*, *Otaria flavescens*	7		
Australia*	7	3	*A. forsteri*, *A. pusillus*, *Neophoca cinera*	4	3	1
Brazil	4	1	*O. flavescens*	4		
Czech Republic	1	1	*O. flavescens*		1	
France	1	1	*O. flavescens*		1	
Germany	3	2	*O. flavescens*, *Zalophus californianus*		3	
Netherlands	1	1	*O. flavescens*		1	

New Zealand	5	5	*A. forsteri, A. tropicalis, Hydrurga leptonyx, Mirounga leonina, Phocarctos hookeri*	4		1
United Kingdom	2	2	*A. australis, Z. californianus*		2	
United States*	1	1	*Cystophora cristata*			
Uruguay	5	2	*A. australis, O. flavescens*	3	2	
Total	32	11				

The asterisks in some countries (*) denotes no information provided about population status detailed.

Table 3. Tuberculosis detection techniques used in the cases found for pinniped species in the literature review.

Detection technique	Technique name	Number of cases*	Case percentage	Wild	Captive	Wild and captive	Source+
Bacterial culture	Bacterial culture	45	27.6	29	14	2	1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 12, 14, 15, 16, 18, 19, 20, 21, 22, 23, 24, 25, 26, 29, 31
TB detection	Bioquimic test	3	1.8	3			10, 19, 25
	Serological test	6	3.7	3	3		3, 4, 5, 15, 17
	Tuberculin skin test	8	4.9	1	7		11, 18, 22, 24, 26, 29
	Interferon-gamma release assay (IGRA)	2	1.2	1	1		11, 26
	Pathogenicity tests	4	2.5	2	2		18, 21, 24
	Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE)	2	1.2	2			23
	Western blotting	5	3.1	3	2		21, 23, 24
	Immunoperoxidase test	3	1.8	3			23, 25
	Polymerase chain reaction (PCR)	37	22.7	27	8	2	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 15, 16, 19, 20, 23, 25, 26, 31

Species TB detection	Mycobacterial Interspersed Repetitive Units (MIRU)	1	0.6	1			26
	Spoligotyping	17	10.4	9	6	2	1, 2, 4, 5, 7, 9, 11, 14
	Variable number tandem repeats (VNTR)	5	3.1	5			19
	Fluorescent amplified fragment length polymorphism (FAFLP)	8	4.9	4	2	2	14
	Restriction fragment length polymorphism (RFLP)	5	3.1	1	2	2	1, 3, 20, 23
	Restriction enzyme analysis (REA)	6	3.7	4	2		21, 23, 24, 30
Earliest radiologic sign	3D Computed Tomography	3	1.8	3			5, 13
	Thoracic radiography/ digital Rx	5	3.1	3	2		11, 26, 29
Total		163	100				

*Each case represents the combination of each studied species and used technique per reviewed studied.

+Reference numbers for each source of information are listed in Table S2.

DISCUSSION

This review found that only 11 countries worldwide have records of pinnipeds infected with bacteria from the MTBC. Information gaps were identified, as there are regions with large pinniped populations, such as Chile, Peru, the Galapagos, Antarctica, and the Arctic, where no cases have yet been documented. These gaps may be due to a lack of research in these areas, where, until now, no records of TB in pinnipeds have been found, or because research has not documented the presence of MTBC bacteria in pinnipeds. In addition, remote locations such as Antarctica and the Arctic, where various species of pinnipeds live, present significant research challenges due to their inaccessibility, which may contribute to the lack of TB records in these locations.

In 2003, *M. pinnipedii* was described as the causative agent of tuberculosis in pinnipeds (Cousin et al., 2003). This species is the only marine member of the MTBC, infecting other domestic and wild mammals and humans (Cousin et al., 2003; Kiers et al. 2008). *Mycobacterium pinnipedii* is one of the most aggressive mycobacteria in the complex and poses the greatest risk to humans (Bastida et al., 2020). It has been reported in at least 9 species of pinnipeds (*Otaria flavescens, Artocephalus tropicalis, Artocephalus australis, Artocephalus forsteri, Artocephalus pusillus, Neophoca cinera, Mirounga leonina, Phocarctos hookeri, Hydrurga leptonyx*) (Arbiza et al., 2012; Cousins et al., 2006; Jurczynski et al., 2011; Kiers et al., 2008; Kriz et al., 2011; Moser et al., 2008; Roe et al., 2019; Silva-Pereira et al., 2019). Surprisingly, the species *M. bovis*, whose primary host is cattle, was also identified in both captive and free-ranging pinnipeds.

MTBC species are highly transmissible, and there are reports from several zoos of transmition from pinnipeds to keepers and from keepers to other zoo species (Jurczynski et al.. 2012; Kiers et al., 2008; Lacave et al., 2009; Moser et al., 2008). These reports demonstrate its high zoonotic potential and interspecies transmissibility. In addition, Bastida et al. 2020 suggested that TB may have been transmitted to human populations in the southern tip of South America thousands of years ago through the practice of capturing and consuming these marine mammals.

Tuberculosis is transmitted by direct inhalation of expectorated bacteria from the respiratory tract and/or secretions of an actively infected individual (Sakamoto et al. 2012). Pinnipeds infected with tuberculosis have respiratory tract involvement, supporting inhalation as the most common route of transmission (Arbiza, et al. 2012; Kiers et al. 2008; Roe et al., 2019). In most of the positive cases of TB, lesions and/or granulomas were found in the lymph nodes, lungs, mediastinum, pleura, liver, and/or spleen (Kriz et al., 2011; Roe et al., 2019; Sacristan et al., 2021).

Various techniques have been developed to detect bacteria belonging to the MTBC in pinnipeds. In most of the studies reviewed, samples were first collected for bacterial culture in order to isolate bacteria from both living and dead individuals. Once the bacterial colony was established, various TB detection methods were used. Some TB detection techniques confirm the presence of the disease but do not allow for the identification of the MTBC. The bacteriological cultured followed by molecular techniques to identify the specific MTBC species were the most commonly used. The bacteriological cultured followed by molecular techniques to identify the specific MTBC species were the most commonly used. However, species isolation is not always possible due to the need for a certain concentration of bacteria (Kats et al., 2022). Once TB is confirmed, infected individuals are isolated, and if there is no improvement, euthanasia is considered to prevent the further spread of the bacteria (Jurczynski et al., 2011). The protocol to be used will depend on the country in which the infected individual is located.

In general the choice of techniques depends on the type of cost involved and whether the study involves living or dead individuals.

In addition to TB, there are other infectious diseases of zoonotic origin in pinnipeds that pose significant risks to public health, such as leptospirosis, trichinosis, salmonellosis, and avian influenza (Avalos-Téllez et al., 2016; Gamarra-Toledo et al., 2023; Hermosilla et al., 2018; Pasqualetti et al., 2018;). Recently, the first infection and massive mortality associated with highly pathogenic avian influenza (HPAI) was reported in common sea lions in Peru (Gamarra-Toledo et al., 2023). This disease has spread rapidly in South America, affecting not only pinnipeds but also birds and other marine mammals (Campagna et al., 2023; Plaza et al., 2023). The risk of transmission to humans has not been studied yet in this geographic area.

In conclusion, our review highlights the importance of pinnipeds as hosts and/or vectors of zoonotic pathogens, establishing their role as essential sentinel animals for detecting environmental health problems and public health risks. Our results indicate that zoonotic TB is present in several regions of the world; however, we identified important geographical information gaps in areas with the presence of pinniped, despite these animals having a greater risk of zoonoses. Detecting TB in pinnipeds is particularly important in tourist areas where there is close interaction between the human and wild populations of pinnipeds.

REFERENCES

Allison, M.J., Mendoza, D. & Pezzia, A. (1973). Documentation of a case of Tuberculosis in Pre-Columbian America. American Review of Respiratory Disease, 107, 985-991.

Arbiza, J., Blanc, A., Castro-Ramos, M., Katz, H., Ponce de León, A. & Clara, M. (2012). Uruguayan pinnipeds (Arctocephalus australis and Otaria flavescens): evidence of influenza virus and Mycobacterium pinnipedii infections. New Approaches to the Study of Marine Mammals 2, 151-182.

Arriaza, B.T., Salo, W., Auferheride, A.C. & Holcomb, T.A. (1995). Pre-Columbian tuberculosis in Northern Chile: molecular and skeletal evidence. American Journal Physical Anthropology, 98, 37-45.

Arrieta, M. A., Bordach, M. D. L. A. & Mendonça, O. J. (2011). Tuberculosis precolombina en el noroeste argentino (NOA): El cementerio de Rincón Chico 21 (RCH 21), Santa María, Catamarca. Intersecciones en Antropología, 12, 245-260.

Avalos-Téllez, R., Carrillo-Casas, E. M., Atilano-López, D., Godínez-Reyes, C. R., Díaz-Aparicio, E., Ramírez-Delgado, D., Ramirez-Echenique, M. F., Leyva, M., Suzan, G., & Suárez-Güemes, F. (2016). Pathogenic Leptospira serovars in free-living sea lions in the Gulf of California and along the Baja California coast of Mexico. Journal of Wildlife Diseases, 52, 199-208.

Bastida, R. O., Quse, V., Martinoli, M. P., & Zangrando, A. F. J. (2020). First record of tuberculosis lesions in zooarchaeological samples of otariid pinnipeds. New aspects of the pre-European origin of human tuberculosis in South America and dissemination mechanisms of Mycobacterium pinnipedii in the Southern hemisphere.

Revista de Arqueología, 24. 227-253.

Bastida, R., Loureiro, J., Quse, V., Bernardelli, A., Rodríguez, D., & Costa, E. (1999). Tuberculosis in a wild subantarctic fur seal from Argentina. Journal of Wildlife Diseases, 35, 796-798.

Bernardelli, A. (1996). Tuberculosis in sea lions and fur seals from the south-western Atlantic coast. Revue scientifique et technique, 15, 985-1005.

Bishop, C. R., Athens, J. W., Boggs, D. R., Warner, H. R., Cartwright, G. E., & Wintrobe, M. M. (1968). Leukokinetic studies: XIII. A non-steady-state kinetic evaluation of the mechanism of cortisone-induced granulocytosis. The Journal of Clinical Investigation, 47, 249-260.

Blair, W. R. (1913). Report of the veterinarian. Annual Report of the New York Zoological Society, 74.

Boletín del Ministerio de Salud Argentina N°6: Tuberculosis y Lepra 2023. https://bancos.salud.gob.ar/recurso/boletin-ndeg-6-tuberculosis-y-lepra-en-la-argentina.

Bos, K. I., (…), & Krause, J. (2014). Pre-Columbian mycobacterial genomes reveal seals as a source of New World human tuberculosis. Nature, 514, 494-497.

Brites, D., Loiseau, C., Menardo, F., Borrell, S., Boniotti, M. B., Warren, R., ... & Gagneux, S. (2018). A new phylogenetic framework for the animal-adapted Mycobacterium tuberculosis complex. Frontiers in Microbiology, 9, 2820.

Castiñeira Estévez, A., López Pedreira, M., Pena Rodríguez, M., & Liñares Iglesias, M. (2002). Manifestaciones radiológicas de la tuberculosis pulmonar. Medicina Integral, 39, 192-206.

Chiner-Oms, Á., Sánchez-Busó, L., Corander, J., Gagneux, S., Harris, S. R., Young, D., Gonzales Candelas, F. & Comas, I. (2019). Genomic determinants of speciation and spread of the Mycobacterium tuberculosis complex. Science Advances, 5, eaaw3307.

Corner, L. A. (2006). The role of wild animal populations in the epidemiology of tuberculosis in domestic animals: how to assess the risk. Veterinary Microbiology, 112, 303-312.

Cousins, D., Thoen, C. O., Steele, J. H., & Gilsdorf, M. J. (2006). Tuberculosis in fur seals and sea lions caused by Mycobacterium pinnipedii. In Mycobacterium bovis Infection in Animals and Humans. Eds C. O. Thoen, J. H. Steele, M. J. Gilsdorf. Ames Blackwell Publishing, 258-270.

Cousins, D. V., Bastida, R., Cataldi, A., Quse, V., Redrobe, S., Dow, S., Duignan, P., Murray, A., Dupont, C., Ahmed, N., Collins, D. M., Butler, W.R., Dawson, D., Rodríguez, D., Loureiro, J., Romano, M. I., Alito, A., M. Zumarraga, M. & Bernardelli, A. (2003). Tuberculosis in seals caused by a novel member of the Mycobacterium tuberculosis complex: Mycobacterium pinnipedii sp. nov. International Journal of Systematic and Evolutionary Microbiology, 53, 1305-1314.

Cousins, D. V., Francis, B. R., Gow, B. L., Collins, D. M., McGlashan, C. H., Gregory, A., & Mackenzie, R. M. (1990). Tuberculosis in captive seals: bacteriological studies on an isolate belonging to the Mycobacterium tuberculosis complex. Research in Veterinary Science, 48, 196-200.

Cousins, D.V. (1987). ELISA for detection of tuberculosis in seals. Veterinary Record, 121, 305.

Dafale, N. A., Srivastava, S., & Purohit, H. J. (2020). Zoonosis: an emerging link to antibiotic resistance under “One Health Approach”. Indian Journal of Microbiology, 60, 139-152.

Ehlers, K. (1965). Records of the hooded seal, Cystophora cristata Erxl, and other animals at Bremerhaven Zoo. International Zoo Yearbook, 5, 148-149.

European Food Safety Authority, European Centre for Disease Prevention and Control, European Union Reference Laboratory for Avian Influenza, Adlhoch, C., Fusaro, A., Gonzales, J. L., Kuiken, T., Mirinaviciute, G., Niqueux, E., Stahl, K., Staubach, C., Terregino, C., Broglia, A., Kohnle, L. & Baldinelli, F. (2023). Avian influenza overview March–April 2023. EFSA Journal, 21, 8039.

Fiorito, C., Marfil, J., Falzoni, E., Vivot, MM., Zumárraga, M., Lombardo, D. & Barandiaran, S. (2020). Tuberculosis in wild South American sea lions Otaria flavescens stranded in Chubut, Argentina. Diseases of Aquatic Organisms, 142, 33-40.

Fereidouni, S., Munoz, O., Von Dobschuetz, S., & De Nardi, M. (2016). Influenza virus infection of marine mammals. Ecohealth, *13*, 161-170.

Gamarra-Toledo, V., Plaza, P. I., Inga, G., Gutiérrez, R., García-Tello, O., Valdivia-Ramírez, L., Huamán-Mendoza, D., Nieto-Navarrete, J. C., Ventura, S. & Lambertucci, S. A. (2023). First mass mortality of marine mammals caused by highly pathogenic influenza virus (H5N1) in South America. bioRxiv.

Guichón, R. A., Buikstra, J. E., Stone, A. C., Harkins, K. M., Suby, J. A., Massone, M., Prieto lglesias, A., Wilbur, A., Constantinescu, F. & Rodríguez Martín, C. (2015). Pre-Columbian tuberculosis in Tierra del Fuego: Discussion of the paleopathological and molecular evidence. International Journal of Paleopathology, 11, 92-101.

Hermosilla, C., Hirzmann, J., Silva, L. M., Scheufen, S., Prenger-Berninghoff, E., Ewers, C., Häussermann V., Försterra, G., Poppert, S. & Taubert, A. (2018). Gastrointestinal parasites and bacteria in free-living South American sea lions (Otaria flavescens) in Chilean Comau Fjord and new host record of a Diphyllobothrium scoticum-like cestode. Frontiers in Marine Science, 5, 459.

Hunter J.E., Duignan, P. J., Dupont, C., Fray, L., Fenwick, S. G., Murray, A. (1998). First report of potentially zoonotic tuberculosis in fur seals in New Zealand. 1998. New Zeal Med J 111: 130-131.

IUCN <Red List version year>. The IUCN Red List of Threatened Species. <Red List version>. https://www.iucnredlist.org. Accessed: 15/1/2024

Jagielski, T., Minias, A., van Ingen, J., Rastogi, N., Brzostek, A., Żaczek, Dziadek J. (2016). Methodological and clinical aspects of the molecular epidemiology of Mycobacterium tuberculosis and other mycobacteria. Clinical Microbiology Reviews, 29, 239-290.

Jones, K. E., Patel, N. G., Levy, M. A., Storeygard, A., Balk, D., Gittleman J. L. & Daszak, P. (2008). Global trends in emerging infectious diseases. Nature, 451, 990-993.

Jurczynski, K., Lyashchenko, P. K., Scharpegge, J., Fluegger, M., Geraldine Lacave, G., Irmgard Moser, I., Sonia Tortschanoff, S., & Greenwald, R. (2012). Use of multiple diagnostic tests to detect Mycobacterium pinnipedii infections in a large group of South American sea lions (Otaria flavescens). Aquatic Mammals, 38, 43.

Karesh, W. B., DPhil, A., D., Lloyd-Smith, J. O., Lubroth, J., Dixon, M. A., Bennett, M., Aldrich, S., Harrington, T, Formenty, P., Loh, E. L., Machalaba, C. C., Thomas, M. J., Heymann, D. L. (2012). Ecology of zoonoses: natural and unnatural histories. The Lancet, 380, 1936-1945.

Kiers, A., Klarenbeek, A., Mendelts, B., Van Soolingen, D., & Koëter, G. (2008). Transmission of Mycobacterium pinnipedii to humans in a zoo with marine mammals. The International Journal of Tuberculosis and Lung Disease, 12, 1469-1473.

Klaus, H. D., Wilbur, A. K., Temple, D. H., [e], Buikstra, J. E., Anne C. Stone, A. C., Fernandez, M., Wester, C., Tam, M. E. (2010). Tuberculosis on the North coast of Peru: skeletal and molecular paleopathology of late pre-Hispanic and postcontact mycobacterial disease. Journal of Archaeological Science, 37, 2587-2597.

Kriz, P. Kralik, P., Slany, M., Slana, I., Svobodova, J., Parmova, I., Barnet,V., Jurek, V., Pavlik, I. (2011.) Mycobacterium pinnipedii in a captive Southern sea lion (Otaria flavescens): a case report. Veterinary Medicine, 56, 307-313.

Lacave, G., Malliot, A., Alerte, V., Boschiroli, M. L., & Lecu, A. (2009). Atypical case of Mycobacterium pinnipedii in a Patagonian sea lion (Otaria flavescens) and tuberculosis cases history review in pinnipeds. In EAAM Mycobacterium pinnipedii Workshop Report. Duisburg Zoo (Duisburg, 2009).

Loeffler, S. H. de Lisle, G. W., Neill, M. A., Collins, D. M., Price-Carter, M., Paterson, B., & Crews, K. B. (2014). The seal tuberculosis agent, Mycobacterium pinnipedii, infects domestic cattle in New Zealand: epidemiologic factors and DNA strain typing. Journal of Wildlife Diseases, 50, 180-187.

Melo, A. M., da Silva Filho, R. P., von Groll, A., Reis, A. J., do Carmo Guimarães, J. D. L., Perdigão, J., ... & Xavier, M. O. (2019). Tuberculosis caused by Mycobacterium pinnipedii in a wild South American sea lion Otaria flavescens stranded in southern Brazil. Diseases of Aquatic Organisms, 133, 189-194.

Miller, M. & Olea-Popelka, F. (2013). One Health in the shrinking world: Experiences with tuberculosis at the human–livestock–wildlife interface. Comparative Immunology, Microbiology and Infectious Diseases, 36,263-268

Moser, I., Prodinger, W. M., Hotzel, H., Greenwald, R., Lyashchenko, K. P., Bakker, D., Gomis, D., Seidler, T., Ellenberger, C., Hetzel, U., Wuennemann K. & Moisson, P. (2008). Mycobacterium pinnipedii: transmission from South American sea lion (Otaria byronia) to Bactrian camel (Camelus bactrianus bactrianus) and Malayan tapirs (Tapirus indicus). Veterinary Microbiology, 127, 399-406.

Pasqualetti, M. I., Fariña, F. A., Krivokapich, S. J., Gatti, G. M., Daneri, G. A., Varela, E. A., Lucero, S., Ercole, M. E, Bessi, C., Winter M. & Ribicich, M. M. (2018). Trichinella spiralis in a South American sea lion (Otaria flavescens) from Patagonia, Argentina. Parasitology Research, 117, 4033-4036.

Roe, W. D., Lenting, B., Kokosinska, A., Hunter, S., Duignan, P. J., Gartrell, B., Rogers, L., Collins, D. M., Lisle, G. W., Gedye, K., & Price-Carter, M. (2019). Pathology and molecular epidemiology of Mycobacterium pinnipedii tuberculosis in native New Zealand marine mammals. PloS one, 14, e0212363.

Silva-pereira, T. T. Silva-Pereira, T. T., Ikuta, C. Y., Zimpel, C. K., Camargo, N. C., de Souza Filho, A. F., Ferreira Neto, J. S., Heinemann, M. B. & Guimarães, A. M. (2019). Genome sequencing of Mycobacterium pinnipedii strains: genetic characterization and evidence of superinfection in a South American sea lion (Otaria flavescens). BMC genomics, 20, 1-13.

Society for Marine Mammalogy. (2024). List of Marine Mammal Species and Subspecies. Recuperado de https://marinemammalscience.org/science-and-publications/list-marine-mammal-species-subspecies/

Supply, P, (…) Roland Brosch, R. (2013). Genome analysis of smooth tubercle bacilli provides insights into ancestry and pathoadaptation of the etiologic agent of tuberculosis. Nature Genetics, 45, 172–179.

Thompson, P. J., Cousins, D. V., Gow, B. L., Collins, D. M., Williamson, B. H., & Dagnia, H. T. (1993). Seals, seal trainers and mycobacterial infection. American Review of Respiratory Disease, 147, 164-167.

Uhart, M.M. (2021). Redefinir nuestra relación con la naturaleza para evitar futuras pandemias. Actualizaciones en Sida e Infectología.

Vågene, Å. J., Honap, T. P., Harkins, K. M., Rosenberg, M. S., Giffin, K., Cárdenas-Arroyo, F., Leguizamón, L. P., Arnett, J., Buikstra, J.E., Herbig, A., Krause, J., Stone, A. C. & Bos, K. I. (2022). Geographically dispersed zoonotic tuberculosis in pre-contact South American human populations. Nature communications, 13(1), 1195.

World Health Organization, https://bit.ly/33PN0YJ, 2022.

Zmak, L., Obrovac, M., Jankovic makek, M., Perko, G., & Trkanjec, J. T. (2019). From Peruvian mummies to living humans: first case of pulmonary tuberculosis caused by Mycobacterium pinnipedii. The International Journal of Tuberculosis and Lung Disease, 23, 1283-1285.

SUPPLEMENTARY MATERIAL

Table S1. The strings with all databases and the works found.

	Strings	Databases	N° studies
1	“Mycobacterium Tuberculosis complex” OR “tuberculosis” OR “TB” AND “Pinnipeds” AND “zoonoses” OR “infectious disease” AND “presence”	Dimensions	0
	("Mycobacterium Tuberculosis complex" OR tuberculosis OR TB) AND " Pinnipeds" AND (zoonoses OR "infectious disease") AND presence	Scopus	3
	("Mycobacterium Tuberculosis complex" OR tuberculosis OR TB) AND Pinnipeds AND (zoonoses OR "infectious disease") AND presence	NIH	9
2	"Mycobacterium Tuberculosis complex" OR "tuberculosis" OR "TB" AND "Pinnipeds" AND " zoonoses" OR "infectious disease"	Dimensions	6
	"Mycobacterium Tuberculosis complex" OR "tuberculosis" OR "TB" AND "Pinnipeds" AND " zoonoses" OR "infectious disease"	Scopus	11
	("Mycobacterium Tuberculosis complex" OR tuberculosis OR TB) AND Pinnipeds AND (zoonoses OR "infectious disease")	NIH	79
3	"Mycobacterium Tuberculosis complex" OR “tuberculosis” OR “TB” AND Pinnipeds AND “zoonoses” OR "infectious diseases"	Dimensions	6
	"Mycobacterium Tuberculosis complex" OR “tuberculosis” OR “TB” AND “Pinnipeds” AND “zoonoses” OR "infectious diseases"	Scopus	11

	("Mycobacterium Tuberculosis complex" OR tuberculosis OR TB) AND Pinnipeds AND (zoonoses OR "infectious diseases")	NIH	63
	"Mycobacterium Tuberculosis complex" OR “tuberculosis” OR “TB” AND Pinnipeds AND “zoonoses” OR "infectious diseases" AND “presence”	Dimensions	0
4	"Mycobacterium Tuberculosis complex" OR “tuberculosis” OR “TB” AND Pinnipeds” AND “zoonoses” OR "infectious diseases" AND “presence”	Scopus	3
	("Mycobacterium Tuberculosis complex" OR tuberculosis OR TB) AND Pinnipeds AND (zoonoses OR "infectious diseases") AND presence.	NIH	9

Table S2: Species of pinnipeds infected with bacteria belonging to the MTBC. Reference numbers for each source of information are in parentheses.

Species	Country	Authors	Sampled year	Sampled tissue	Population status	MTBC species	Identification techniques
O. flavescens	Uruguay	Zumarraga et al. 1999 (1)	1991-1996	Not specified	Captivity	MTBC	Bacterial culture, PCR, RFLP, spoligotyping
O. flavescens	Argentina	Fiorito et al. 2020 (2)	2013-2018	Lymph nodes, lungs	Wild	MTBC	Bacterial culture, PCR, spoligotyping
O. flavescens	France	Lacave et al. 2009 (3)	2008	Lymph nodes, lungs	Captivity	M. pinnipedii	Bacterial culture, PCR, RFLP, serological test
O. flavescens	Germany	Moser et al. 2008 (4)	2001-2006	Lymph nodes, lungs	Captivity	M. pinnipedii	Bacterial culture, PCR, spoligotyping, serological test
O. flavescens	Germany	Jurczynski et al. 2011 (5)	2008	Blood, sputum, thoracic CT imaging, lymph nodes	Captivity	M. pinnipedii	3D computed tomography, PCR, spoligotyping, serological test
O. flavescens	Brazil	de Amorim et al. 2014 (6)	2011	Lymph node, lung	Wild	M. pinnipedii	Bacterial culture, PCR
O. flavescens	Brazil	Silva-Pereira et al. 2019 (7)	2011	Lymph node, lung	Wild	M. pinnipedii	Bacterial culture, PCR, spoligotyping

O. flavescens	Brazil	Sacristán et al. 2021 (8)	2017	Cervical abscess, nasal, oral, and rectal swabs, urine, blood, lung, lymph node	Wild	M. pinnipedii	Bacterial culture, PCR
O. flavescens	Brazil	Martins Melo et al. 2019 (9)	2016	Lung, fibrinous exudate, thoracic fluid	Wild	M. pinnipedii	Bacterial culture, PCR, spoligotyping
O. flavescens	Uruguay	Arbiza et al. 2012 (10)	2001-2005	Lung, lymph nodes, spleen, liver	Wild	M. pinnipedii	Bacterial culture, PCR, bioquimic test
O. flavescens	Netherlands	Kiers et al. 2008 (11)	2006	Lung, lymph nodes, liver, spleen, blood	Captivity	M. pinnipedii	Bacterial culture, PCR, spoligotyping, tuberculin skin test, thoracic radiographs, IGRA
O. flavescens	Czech Republic	Kriz et al. 2011 (12)	2009	Lungs, lymph nodes, pleura,faecal and oral swabs	Captivity	M. pinnipedii	Bacterial culture, PCR
O. flavescens	Argentina	Bastida et al. 2020 (13)	Not specified	Vertebrae	Wild	M. pinnipedii	Digital Rx, 3D external computed tomography
O. flavescens	Argentina	Cousin et al. 2003 (14)	1985-2000	Lungs, lymph nodes, liver	Wild	M. pinnipedii	Bacterial culture, PCR, FAFLP, spoligotyping
O. flavescens	Uruguay	Cousin et al. 2003 (14)	1985-2000	Lungs, lymph nodes, liver	Captivity	M. pinnipedii	Bacterial culture, PCR, FAFLP spoligotyping

O. flavescens	Argentina	Bernardeli et al. 1996 (15)	Not specified	Lungs, lymph nodes	Wild	M. bovis	Bacterial culture, PCR, serological test
O. flavescens	Uruguay	Castro Ramos et al. 2006 (16)	2001-2004	Lungs, lymph nodes, liver, pleura	Wild	M. pinnipedii	Bacterial culture, PCR
O. flavescens	Uruguay	Kats et al. 2022 (17)	2009-2013	Blood, nasal, vaginal, oral and rectal swabs	Wild	MTBC	Serological test
A. tropicalis	Argentina	Bastida et al. 1999 (18)	1996	Lung, lung swabs	Wild	MTBC	Bacterial culture, pathogenicity tests, tuberculin skin test
A. tropicalis	Argentina	Cousin et al. 2003 (14)	1985-2000	Lungs, lymph nodes, liver	Wild	M. pinnipedii	Bacterial culture, PCR, FAFLP, spoligotyping
A. tropicalis	Argentina	Zumarraga et al. 1999 (1)	1991-1996	Not specified	Wild	MTBC	Bacterial culture, PCR, RFLP, spoligotyping
A. tropicalis	New Zealand	Roe et al. 2019 (19)	1999-2017	Lungs, lymph nodes, mediastinum, pleura, liver, spleen	Wild	M. pinnipedii	Bacterial culture, PCR, VNTR
A. australis	Argentina	Cousin et al. 2003 (14)	1985-2000	Lungs, lymph nodes, liver	Wild	M. pinnipedii	Bacterial culture, PCR, FAFLP, spoligotyping
A. australis	United Kingdom	Cousin et al. 2003 (14)	1985-2000	Lungs, lymph nodes, liver	Captivity	M. pinnipedii	Bacterial culture, PCR, FAFLP, spoligotyping

A. australis	Argentina	Zumarraga et al. 1999 (1)	1991-1996	Not specified	Wild	MTBC	Bacterial culture, PCR, RFLP, spoligotyping
A. australis	Uruguay	Castro Ramos et al. 2006 (16)	2001-2004	Lungs, lymph nodes, liver, pleura	Wild	M. pinnipedii	Bacterial culture, PCR
A. australis	Uruguay	Arbiza et al. 2012 (19)	2001-2005	Lung, lymph nodes, spleen, liver	Wild	M. pinnipedii	Bacterial culture, bioquimic test, PCR
A. australis	Argentina	Romano et al. 1995 (20)	Not specified	Lung, lymph nodes, liver	Wild	MTBC	Bacterial culture, PCR, RFLP
A. australis	Argentina	Bastida et al. 2020 (13)	Not specified	Vertebrae	Wild	M. pinnipedii	Digital Rx, 3D external computed tomography
A. australis	Uruguay	Kats et al. 2022 (17)	2009-2013	Blood, nasal, vaginal, oral and rectal swabs	Wild	MTBC	Serological test
A. forsteri	New Zealand	Cousin et al. 2003 (14)	1985-2000	Lungs, lymph nodes, liver	Wild and captivity	M. pinnipedii	Bacterial culture, PCR, FAFLP, spoligotyping
A. forsteri	New Zealand	Cousin et al. 1990 (21)	1986	lungs, lymph nodes	Wild	M. bovis	Bacterial culture, pathogenicity tests, REA, Western blot
A. forsteri	Australian	Forshaw et al. 1991 (22)	1986	Lungs, lymph nodes, liver, kidney, spleen, brain, blood	Captivity	MTBC	Bacterial culture, tuberculin skin test

A. forsteri	New Zealand	Roe et al. 2019 (19)	1999-2017	Lungs, lymph nodes, mediastinum, pleura, liver, spleen	Wild	M. pinnipedii	Bacterial culture, PCR, VNTR
A. forsteri	Australian	Cousin et al. 1993 (23)	1990-1991	Lungs, lymph nodes, pleura, heart and kidney	Wild	MTBC	Bacterial culture, PCR, REA, RFLP, SDS/PAGE, western blotting, immunoperoxidase test
A. forsteri	Australian	Thompson et al 1993 (24)	1986-1988	Not specified	Captivity	M. bovis	Bacterial culture, pathogenicity test, western blotting, tuberculin skin test, REA
A. pusillus	Australian	Cousin et al. 2003 (14)	1985-2000	Lungs, lymph nodes, liver	Wild	M. pinnipedii	Bacterial culture, PCR, FAFLP, spoligotyping
A. pusillus	Australian	Forshaw et al. 1991 (22)	1986	Lungs, lymph nodes, liver, kidney, spleen, brain, blood	Captivity	MTBC	Bacterial culture, tuberculin skin test
A. pusillus	Australian	Woods et al. 1995 (25)	1992	Lungs, lymph nodes, liver, pleura, spleen	Wild	MTBC	Bacterial culture, PCR, immunoperoxidase test, bioquimic test
A. pusillus	Australian	Boardman et al. 2014 (26)	2012	Lungs, lymph nodes, pleura	Wild	M. pinnipedii	Bacterial culture, PCR, MIRU, tuberculin skin test, IGRA, thoracic radiographs

N. cinera	Australian	Cousin et al. 2003 (14)	1985-2000	Lungs, lymph nodes, liver	Wild and captivity	M. pinnipedii	Bacterial culture, PCR, FAFLP, spoligotyping
N. cinera	Australian	Forshaw et al. 1991 (22)	1986	Lungs, lymph nodes, liver, kidney, spleen, brain, blood	Captivity	MTBC	Bacterial culture, tuberculin skin test
N. cinera	Australian	Cousin et al.1993 (23)	1990-1991	Lungs, lymph nodes, pleura, heart, kidney	Wild	MTBC	Bacterial culture, immunoperoxidase test, PCR, SDS/PAGE, western blotting, REA
N. cinera	Australian	Thompson et al 1993 (24)	1986-1988	Not specified	Captivity	M. bovis	Bacterial culture, pathogenicity test, western blotting, tuberculin skin test, REA
M. leonina	New Zealand	Roe et al. 2019 (19)	1999-2017	Lungs, lymph nodes, mediastinum, pleura, liver, spleen, blood	Wild	M. pinnipedii	Bacterial culture, PCR, VNTR
C. cristata	United States	Blair 1913 (27)	Not specified	Not specified	Not specified	MTBC	Not specified
Z.californianus	Germany	Ehlers 1965 (28)	1956	Not specified	Captivity	MTBC	Not specified
Z.californianus	United Kingdom	Gutter et al. 1987 (29)	1984	Biopsy the abscessed	Captivity	M.smegmatis	Bacterial culture, tuberculosis skin test, thoracic radiographs

P. hookeri	New Zealand	Roe et al. 2019 (19)	1999-2017	Lungs, lymph nodes, mediastinum, pleura, liver, spleen	Wild	M. pinnipedii	Bacterial culture, PCR, VNTR
P. hookeri	New Zealand	Roe et al. 2006 (30)	2005	Lungs, lymph nodes	Wild	M. pinnipedii	REA
P. hookeri	New Zealand	Lenting et al. 2019 (31)	2000-2017	Not specified	Wild	M. pinnipedii	Bacterial culture, PCR
H. leptonyx	New Zealand	Roe et al. 2019 (19)	1999-2017	Lungs, lymph nodes, mediastinum, pleura, liver, spleen	Wild	M. pinnipedii	Bacterial culture, PCR, VNTR