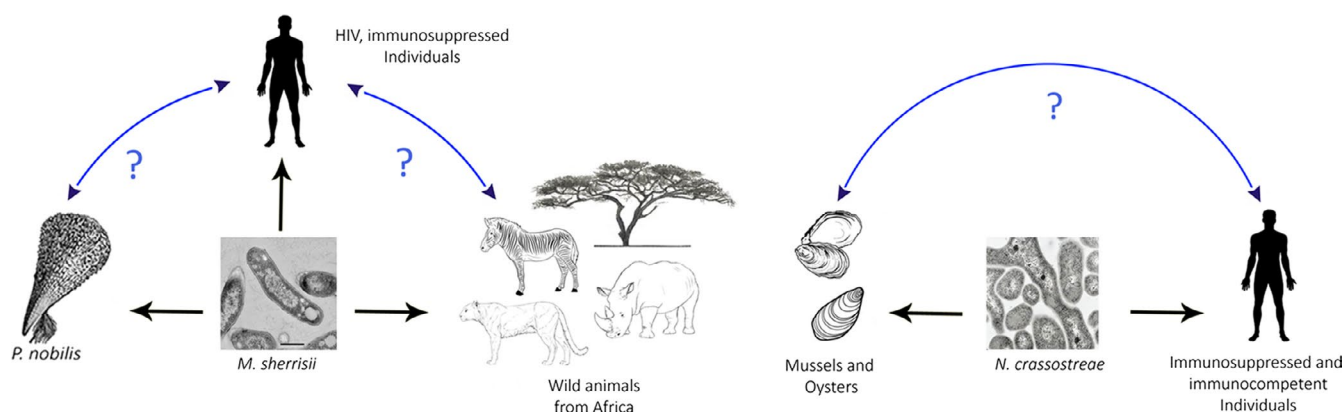


# Nocardiosis and mycobacteriosis of bivalves: “Yet-to-emerge” zoonoses of public concern?

To the editor:

Novel zoonotic pathogens are among the greatest challenges to global health security (Bird & Mazet, 2018). Accordingly, the key event to succeed in fighting zoonoses is detecting “yet-to-emerge” novel pathogens from animal reservoirs and human population as quickly as possible (Bird & Mazet, 2018). Among the characteristics these pathogens must express, to make us suspect their potential danger, the sudden change of their biology, a jump of host species, the involvement in episodes of illness not detected previously, even if on a simple local scale, are underlined (Bird & Mazet, 2018). In this context, *Nocardia crassostreae* and *Mycobacterium sherrisii* seem to be excellent candidates to “yet-to-emerge” zoonotic pathogens of possible public concern (Figure 1). In late nineteenth century, *N. crassostreae* was recognized as a new species, responsible for the so-called summer mortality outbreaks occurring in the bivalve molluscs *Crassostrea gigas* in several embayments in Canada and USA (Friedman et al., 1998). Lesions were characterized by focal areas of brown discoloration on the mantle or raised green or yellow nodules in the adductor muscle, gills, heart and mantle. Histological observation revealed dense clumps of branching, Gram-positive, acid-fast filamentous bacteria, surrounded by both haemocytic capsules and nodules (Friedman et al., 1998). Later, the disease appeared in Europe in summer 2006, causing an extensive mortality of *C. gigas* in Lake Grevelingen, the Netherlands (Engelsma, Roozenburg, & Joly, 2008). In 2013, the first report of *N. crassostreae* in a bivalve host of different genus and species, *M. galloprovincialis* and in a new geographic area, the Mediterranean Sea, was described (Carella et al., 2013). In this case, the lesions were observed most frequently in the connective tissue surrounding the digestive tract, with scattered multifocal lesions resulting from formation of haemocytic

nodules (Carella et al., 2013). Concomitantly, the first case of human nocardiosis by *N. crassostreae* was recorded in an immunocompromised patient with non-Hodgkin's lymphoma, showing abscess-like lesions in the left psoas muscle extending outward and producing a multiloculated abscess in the left lumborum muscle (Taj-Aldeen et al., 2013). Finally, Igbaseimokumo et al. (2016) recently reported the first human infection of *N. crassostreae* in an immunocompetent patient suffering of a brain abscess. As far as *M. sherrisii* is concerned, it belongs to the *Mycobacterium simiae* complex, a heterogeneous group of Non-Tuberculous Mycobacteria (NTM) considered relevant emergent pathogens, which only recently have made the transition from environmental to pathogenic bacteria (Steffani-Vallejo, Brunck, Acosta-Cruz, Montiel, & Barona-Gómez, 2018). The first strains of *M. sherrisii* were isolated from HIV-infected human patients born in Africa and appeared later in Italy (Tortoli, Mariottini, & Mazzarelli, 2007), Argentina (Barrera, Palmero, Paul, & Lopez, 2010) Singapore (Ho et al., 2012) and USA (Lee, Myers, Singh, & Kansal, 2013). The clinical pictures differ in that is prevalently disseminated, or both pulmonary and disseminated, in HIV-infected patients, whereas it is mainly pulmonary in other patients (van Ingen et al., 2011). The first isolations of this mycobacterium in wild animals were recorded in Africa by Botha, Gey van Pittius, and Helden (2013) and again in Africa in 2017, there was the first isolation from a sick lion with tuberculous-like lesions (Gcebe & Hiokwe, 2017). Finally, very recently, *M. sherrisii* has been involved in mass mortality events affecting the bivalve Pen shell *Pinna nobilis*, recorded in two different regions of Italy, Campania and Sicily, in the Mediterranean Sea (Carella et al., 2019). The origins of disease caused by *M. sherrisii* remains an area of investigation. In general, NTM are in soils, dust and natural waters.



**FIGURE 1** A schematic view of the known (black arrows) and hypothetical (blue line with arrowheads) infections route of both *Mycobacterium sherrisii* (left) and *Nocardia crassostreae* (right) [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

**Impact**

- Emerging Zoonotic pathogens are among the greatest challenges to global health security. Key event to succeed in fighting zoonoses is detecting "yet-to-emerge" zoonotic pathogens as quickly as possible.
- *Nocardia crassostreae* and *Mycobacterium sherrisii* are both emerging pathogens of bivalve molluscs and humans which (a) increased their pathogenicity and virulence, (b) expanded their hosts range and (c) extended the geographical area in which the episodes of illness linked to them occurred, both in invertebrates and in vertebrates.
- It is suggested to monitor both pathogens in a systematic and globalized way to increase knowledge on their zoonotic potential.

Thus, drinking water, dust/water aerosol and biofilms are considered the major infection source for both humans and animals (Honda, Viridi, & Chan, 2018). However, NTM infections are among the most common chronic disease of aquatic animals, which along with terrestrial wild animals could represent environmental reservoirs and interspecies source of infection (Honda et al., 2018; Figure 1). In conclusion, according to available data, both *N. crassostreae* and *M. sherrisii* 1) quickly increased their pathogenicity and virulence, 2) expanded their hosts range and 3) extended the geographical area in which the episodes of illness linked to them occurred, both in invertebrates and in vertebrates, including humans. Furthermore, they are both multidrug-resistant organism (Taj-Aldeen et al., 2013; Tortoli, 2014). Overall, these data suggest, in our opinion, to monitor such emerging pathogens in a systematic and globalized way, and to increase the research on their biology, pathogenicity, virulence and zoonotic potential.

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**CONFLICT OF INTEREST**

The authors declare no conflict of interest.

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**REFERENCES**

- Barrera, L., Palmero, D., Paul, R., & Lopez, B. (2010). Grupo de investigación de *M. simiae*. Disease due to *Mycobacterium simiae* and *Mycobacterium sherrisii* in Argentina. *Medicina (B Aires)*, 70, 343–346.
- Bird, B. H., & Mazet, J. A. K. (2018). Detection of emerging zoonotic pathogens: An integrated one health approach. *Annual Review of Animal Biosciences*, 6, 121–139. <https://doi.org/10.1146/annurev-animal-030117-014628>
- Botha, L., Gey van Pittius, N. C., & Helden, P. D. (2013). Mycobacteria and disease in southern Africa. *Transboundary and Emerging Diseases*, 60, 147–156. <https://doi.org/10.1111/tbed.12159>
- Carella, F., Aceto, S., Pollaro, F., Miccio, A., Iaria, C., Carrasco, N., ... De Vico, G. (2019). A mycobacterial disease is associated with the silent mass mortality of the pen shell *Pinna nobilis* along the Tyrrhenian coastline of Italy. *Scientific Reports*, 9, 2725. <https://doi.org/10.1038/s41598-018-37217-y>
- Carella, F., Carrasco, N., Andree, K. B., Lacuesta, B., Furones, D., & De Vico, G. (2013). Nocardiosis in Mediterranean bivalves: First detection of *Nocardia crassostreae* in a new host *mytilus galloprovincialis* and in *ostrea edulis* from the Gulf of Naples (Italy). *Journal of Invertebrate Pathology*, 114, 324–328. <https://doi.org/10.1016/j.jip.2013.10.001>
- Engelsma, M. Y., Roozenburg, I., & Joly, J. P. (2008). First isolation of *Nocardia crassostreae* from Pacific oyster *Crassostrea gigas* in Europe. *Diseases of Aquatic Organisms*, 80, 229–234. <https://doi.org/10.3354/dao01938>
- Friedman, C. S., Beaman, B. L., Chun, J., Goodfellow, M., Gee, A., & Hedrick, R. P. (1998). *Nocardia crassostreae* sp. nov., the causal agent of nocardiosis in Pacific oysters. *International Journal of Systematic Bacteriology*, 48, 237–246. <https://doi.org/10.1099/00207713-48-1-237>
- Gcebe, N., & Hiokwe, T. M. (2017). Non-tuberculous Mycobacteria in South African wildlife: Neglected pathogens and potential impediments for bovine tuberculosis diagnosis. *Frontiers in Cellular and Infection Microbiology*, 7, 15. <https://doi.org/10.3389/fcimb.2017.00015>
- Ho, J., Balm, M., Huggan, P., Chew, N., Venkatachalam, I., & Archuleta, S. (2012). Immune reconstitution inflammatory syndrome associated with disseminated *Mycobacterium sherrisii* infection. *International Journal of STD & AIDS*, 23, 369–370.
- Honda, J. R., Viridi, R., & Chan, E. D. (2018). Global Environmental nontuberculous mycobacteria and their contemporaneous man-made and natural niches. *Frontiers in Microbiology*, 9, 2029.
- Lee, S. M., Myers, R. A., Singh, K., & Kansal, S. (2013). Disseminated *Mycobacterium sherrisii* Infection in a US-Born, HIV-infected patient. *Journal of the International Association of Providers of AIDS Care*, 12(4), 245–246.
- Steffani-Vallejo, J. L., Brunck, M. E., Acosta-Cruz, E. Y., Montiel, R., & Barona-Gómez, F. (2018). Genomic insights into *Mycobacterium simiae* human colonization. *Standards in Genomic Sciences*, 13, 1. <https://doi.org/10.1186/s40793-017-0291-x>
- Taj-Aldeen, S. J., Deshmukh, A., Doiphode, S., Wahab, A., Allangawi, M., Almuzruchi, A., & .... (2013). Molecular identification and susceptibility pattern of clinical *Nocardia* species: Emergence of *Nocardia crassostreae* as an agent of invasive nocardiosis. *Canadian Journal of Infectious Diseases and Medical Microbiology*, 24(2), e33–e38.
- Tortoli, E. (2014). Microbiological features and clinical relevance of new species of the genus mycobacterium. *Clinical Microbiology Reviews*, 27(4), 727–752. <https://doi.org/10.1128/CMR.00035-14>

Tortoli, E., Mariottini, A., & Mazzealli, G. (2007). *Mycobacterium sherrisii* isolation from a patient with pulmonary disease. *Diagnostic Microbiology and Infectious Disease*, *57*, 221–223.

van Ingen, J., Tortoli, E., Selvarangan, R., Coyle, M. B., Crump, J. A., Morrissey, A. B., & ..... Dick van Soolingen, D. (2011). *Mycobacterium*

*sherrisii* sp. nov., a slow-growing non-chromogenic species. *International Journal of Systematic and Evolutionary Microbiology*, *61*, 1293–1298.