

# *Mycobacterium chimaera* infections associated with heater-cooler units (HCU): closing another loophole in patient safety

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In 2011, invasive cardiovascular and disseminated infections by a slowly-growing non-tuberculous mycobacterium, *Mycobacterium chimaera*, were detected in patients who had undergone cardiothoracic surgery in Switzerland. *M. chimaera* was subsequently detected in the water tanks of heater-cooler units (HCUs) used to regulate the temperature of patients' blood in the cardiopulmonary bypass circuit, and in air samples from the operating room when the HCUs were running [1]. This report led investigators in other countries to look for similar cases among cardiothoracic surgery patients exposed to such devices. From 2014 onwards up to April 2015, cases of invasive cardiovascular infection by *M. chimaera* potentially linked to HCUs were consecutively detected in the Netherlands, Germany and the United Kingdom (UK) [2] and hereafter in the United States (US) [3]. An epidemiological link with use of a specific model of HCUs, the 3T device (LivaNova, UK; formerly Sorin, Germany), was confirmed by the detection of *M. chimaera* in these devices across affected cardiothoracic surgery centres [4]. Observational and experimental studies showed that exhaust air from contaminated HCUs can transmit aerosols with *M. chimaera* to the operating field under ultraclean laminar air flow ventilation [5,6].

Environmental testing at the manufacturing site identified contamination with *M. chimaera* of water tanks of LivaNova/Sorin 3T HCUs, as well as of water from the pump assembly area of the facility [4]. In April 2016, the preliminary results of an analysis of the whole genome sequence of outbreak-related *M. chimaera* isolates showed 'almost identical genome sequences' among clinical isolates from patients in three European countries and environmental isolates from 3T devices in the affected hospitals and at the device manufacturing site. These findings supported the hypothesis of a common-source, multi-country outbreak related to intrinsic contamination of 3T devices manufactured before September 2014 [4]. Recently, a study of

whole-genome sequences of clinical isolates from *M. chimaera* infected open-heart surgery patients and from HCUs from hospitals in Pennsylvania and Iowa, US, reportedly showed few single nucleotide polymorphism (SNP) differences between outbreak-related isolates as compared with hundred-fold larger SNP differences between outbreak-related isolates and an epidemiologically unrelated isolate [7]. However, the full results of the analysis of whole-genome sequence data in relation to the epidemiological data from the outbreak investigations in Europe and the US have not been published to date\*.

In this issue of *Eurosurveillance*, the first case of *M. chimaera* pleural infection in a lung transplant recipient from Australia is reported, together with results of environmental investigations that indicate frequent contamination with *M. chimaera* of HCU devices used in hospitals across Western Australia, suggesting that the outbreak extends beyond Europe and the US [8]. This report tests potential source hypotheses by whole-genome sequencing of clinical and environmental *M. chimaera* isolates. Of particular interest is the finding that the genomes of isolates from HCUs across four hospitals clustered in two groups, each composed of isolates differing by less than 17 SNPs. It remains to be seen whether these *M. chimaera* genotypes match those from HCUs in Europe and the US. Of note, a clinical isolate from the infected patient potentially exposed to one of the contaminated HCUs did not match environmental genotypes and showed over 600 SNPs differences from the isolates recovered from the devices. Although, in this case, the results were found sufficient to rule out the HCU as the source of infection, the authors recognise the limitation of their sampling method based on single colony genome analysis, which may have missed mixed-strain populations that were present in the tested samples. Furthermore, the whole-genome comparative analysis of a larger collection of *M. chimaera* isolates, including from sporadic

infections and environmental reservoirs worldwide, is awaited. It should reveal the genetic population structure of *M. chimaera* and ascertain the extent of common source contamination of HCUs as well as the fraction of HCU-associated infections attributable to the 3T device. Of note, the sharing before publication of genome sequence data on this emerging pathogen through public repositories, as advocated for improving public health investigations of international epidemics [9,10], has been recently implemented by several investigators [7]\*.

In a second study in this issue, the occurrence of *M. chimaera* infection associated with treatment by extracorporeal membrane oxygenation (ECMO) devices was explored in a retrospective descriptive clinical study combined with prospective environmental sampling at a German supra-regional ECMO centre [11]. ECMO also uses thermoregulatory devices and is regarded as a potential further source for *M. chimaera* infections in a group of severely ill and often immunocompromised patients. However, in contrast to HCUs used in cardio-thoracic surgery, ECMOs are air-tight and closed systems, plausibly precluding the release of aerosols. Contamination with *M. chimaera* of water tanks from ECMO thermoregulatory devices from two manufacturers was documented, but no room air contamination was found. No patients with *M. chimaera* infection linked to ECMO devices were identified during the period of intensive care. A limitation of this single-centre study is the relatively short patient follow-up. Further prospective studies should elucidate the clinical relevance, if any, of *M. chimaera* contamination of ECMO devices.

Recognising the health hazard associated with mycobacterial contamination of HCUs used in cardio-thoracic surgery, national authorities in Europe and the US have issued health alerts to surgical facilities. They call for increased vigilance, active surveillance and implementation of risk mitigation measures such as removal of the HCU from the operating room to a side room as well as implementation of the updated decontamination and cleaning protocol as provided by the device manufacturer, or product recall [2,3,12,13]. The true extent of the 3T device-associated *M. chimaera* infections has not yet been determined and it is likely to remain underestimated. Jointly with experts from various European countries, the European Centre for Disease Prevention and Control (ECDC) developed a clinical and environmental investigation protocol based on available experience [14]. Still, both clinical and environmental surveillance face technical challenges as (i) symptoms of invasive *M. chimaera* infection can occur more than 5 years after surgery, (ii) the clinical presentation is non-specific and can be indolent, (iii) diagnosis of *M. chimaera* infections by mycobacterial culture is slow and of low sensitivity unless infected tissue is obtained by invasive sampling, and (iv) identification of mycobacteria at the species level requires specialised DNA sequence-based testing. Thus far, no direct

nucleic-acid amplification or metagenomics assay has been proposed for the rapid detection of *M. chimaera* in clinical or environmental samples.

An improved understanding of the risk determinants associated with the use of HCUs and the extent of the *M. chimaera* outbreak are critical for appropriate communication to healthcare providers and patients and for raising their awareness. Risk assessments at hospital level and the timely diagnosis and treatment of *M. chimaera* infection among exposed patients, as well as close collaboration between device manufacturers and regulatory agencies to ensure safe use of the HCUs are essential to close this patient safety loophole [2,12,15]. Further to this incident of contamination of devices during manufacturing, growing evidence of contamination of HCUs with diverse non-tuberculous mycobacteria and other opportunistic pathogens suggests a wider aerosol-borne infectious hazard from water-containing devices used in surgery that will require further risk assessment before and after putting such devices into clinical use [4,16].

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#### \*Authors' correction

Upon the authors' request, the following corrections were made on 21 November 2016, after publication date:

The sentence 'However, whole-genome sequence data from the outbreak investigations in Europe and the US have not been published to date.' has been corrected to read 'However, the full results of the analysis of whole-genome sequence data in relation to the epidemiological data from the outbreak investigations in Europe and the US have not been published to date.'

The sentence 'To the best of our knowledge, the sharing before publication of preliminary genome sequence data on this emerging pathogen through public repositories, as advocated for improving public health investigations of international epidemics [9,10], has not yet been implemented.' has been corrected to read 'Of note, the sharing before publication of genome sequence data on this emerging pathogen through public repositories, as advocated for improving public health investigations of international epidemics [9,10], has been recently implemented by several investigators [7].'

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#### Conflict of interest

None declared.

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#### Authors' contributions

Both authors contributed to the drafting and reviewing of the manuscript.

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#### References

1. Sax H, Bloemberg G, Hasse B, Sommerstein R, Kohler P, Achermann Y, et al. Prolonged Outbreak of Mycobacterium chimaera Infection After Open-Chest Heart Surgery. Clin Infect Dis. 2015;61(1):67-75. DOI: 10.1093/cid/civ198 PMID: 25761866
2. European Centre for Disease Prevention and Control (ECDC). Invasive cardiovascular infection by Mycobacterium chimaera potentially associated with heater-cooler units used during cardiac surgery. 2015. Stockholm: ECDC. 30 Apr 2015. Available

- from: <http://ecdc.europa.eu/en/publications/Publications/mycobacterium-chimaera-infection-associated-with-heater-cooler-units-rapid-risk-assessment-30-April-2015.pdf>
3. Centers for Disease Control and Prevention (CDC). Nontuberculous Mycobacterium (NTM) Infections and Heater-Cooler Devices Interim Practical Guidance: Updated October 27, 2015. Atlanta: CDC. 27 Oct 2015. Available from: <http://www.cdc.gov/hai/pdfs/outbreaks/cdc-notice-heater-cooler-units-final-clean.pdf>
  4. Haller S, Höller C, Jacobshagen A, Hamouda O, Abu Sin M, Monnet DL, et al. Contamination during production of heater-cooler units by Mycobacterium chimaera potential cause for invasive cardiovascular infections: results of an outbreak investigation in Germany, April 2015 to February 2016. *Euro Surveill.* 2016;21(17):30215. DOI: 10.2807/1560-7917.ES.2016.21.17.30215 PMID: 27168588
  5. Götting T, Klassen S, Jonas D, Benk Ch, Serr A, Wagner D, et al. Heater-cooler units: contamination of crucial devices in cardiothoracic surgery. *J Hosp Infect.* 2016;93(3):223-8. DOI: 10.1016/j.jhin.2016.02.006 PMID: 27101883
  6. Sommerstein R, Rüegg C, Kohler P, Bloemberg G, Kuster SP, Sax H. Transmission of Mycobacterium chimaera from Heater-Cooler Units during Cardiac Surgery despite an Ultraclean Air Ventilation System. *Emerg Infect Dis.* 2016;22(6):1008-13. DOI: 10.3201/eid2206.160045 PMID: 27070958
  7. Perkins KM, Laws A, Hasan NA, Strong M, Halpin AL, Rodger RR, et al. Notes from the Field: Mycobacterium chimaera Contamination of Heater-Cooler Devices Used in Cardiac Surgery - United States. *MMWR Morb Mortal Wkly Rep.* 2016;65(40):1117-8. DOI: 10.15585/mmwr.mm6540a6 PMID: 27740609
  8. Robinson JO, Coombs GW, Speers DJ, Keehner T, Keil AD, D'Abrera V, et al. Mycobacterium chimaera colonisation of heater-cooler units in Western Australia, 2015: investigation of possible iatrogenic infection using whole genome sequencing. *Euro Surveill.* 2016;21(46):22640.
  9. Delaunay S, Kahn P, Tatay M, Liu J. Knowledge sharing during public health emergencies: from global call to effective implementation. *Bull World Health Organ.* 2016;94(4):236-236A. DOI: 10.2471/BLT.16.172650 PMID: 27034513
  10. World Health Organization (WHO). Developing global norms for sharing data and results during public health emergencies. Statement arising from a WHO Consultation held on 1-2 September 2015. [Internet]. WHO: Geneva. Sep 2015. Available from: [http://www.who.int/medicines/ebola-treatment/blueprint\\_phe\\_data-share-results/en/](http://www.who.int/medicines/ebola-treatment/blueprint_phe_data-share-results/en/)
  11. Trudzinski FC, Schlotthauer U, Kamp A, Hennemann K, Muellenbach RM, Reischl U, et al. Clinical implications of Mycobacterium chimaera detection in thermoregulatory devices used for extracorporeal membrane oxygenation (ECMO), Germany, 2015 to 2016. *Euro Surveill.* 2016;21(46):22641.
  12. U. S. Food and Drug Administration. UPDATE: Mycobacterium chimaera Infections Associated with LivaNova PLC (formerly Sorin Group Deutschland GmbH) Stöckert 3T Heater-Cooler System: FDA Safety Communication [Internet]. 2016 [updated 14 Oct 2016; cited 2016 24 Oct 2016]. Available from: <http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm520191.htm>.
  13. Group S. 3T Field Safety Notice Update - October 13, 2016. [Accessed 24 Oct 2016]. Available from: <http://www.livanova.sorin.com/products/cardiac-surgery/perfusion/hlm/3t>
  14. European Centre for Disease Prevention and Control (ECDC). EU protocol for case detection, laboratory diagnosis and environmental testing of Mycobacterium chimaera infections potentially associated with heater-cooler units: case definition and environmental testing methodology. Stockholm: ECDC. Aug 2015. Available from: <http://ecdc.europa.eu/en/publications/Publications/EU-protocol-for-M-chimaera.pdf>
  15. Centers for Disease Control and Prevention (CDC). Contaminated Devices Putting Open-Heart Surgery Patients at Risk. Atlanta: CDC. 13 Oct 2016. Available from: <http://www.cdc.gov/media/releases/2016/p1013-contaminated-devices-.html>
  16. U. S. Food and Drug Administration (FDA). FDA's Ongoing Investigation of Nontuberculous Mycobacteria Infections Associated with Heater-Cooler Devices. Silver Spring: FDA. 13 Oct 2016. Available from: <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/CardiovascularDevices/Heater-CoolerDevices/ucm492590.htm>

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