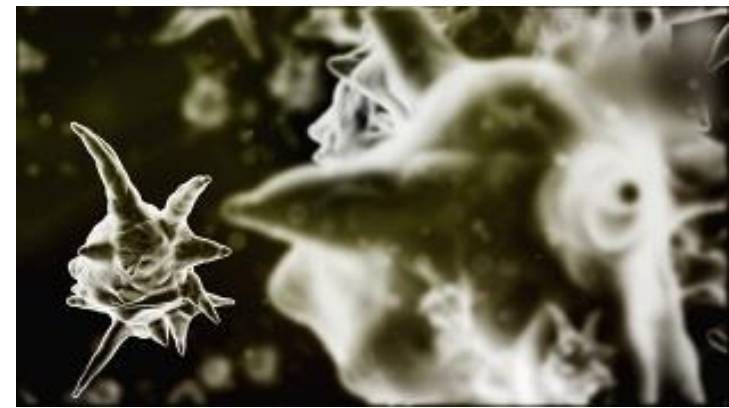




***Mycobacterium chimera* ako príčina endokarditíd po kardiochirurgických výkonoch**

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Mycobacterium chimera



- *Mycobacterium chimera* je netuberkulózne mykobakterium (Mycobacterium avium complex) identifikované v roku 2004
- Vyskytuje sa v pôde a vo vode, je možná formácia biofilmu
- Virulencia je nízka: *M. chimera* vzácnne spôsobuje infekcie u zdravých pacientov, riziková sú imunokompromitovaní pacienti
- «**Slow Grower**»: Symptómy sa prejavujú s odstupom 3 mesiacov až 5 rokov od momentu iničiálnej expozície, často preto ako kauza nebýva brané do úvahy.
- **Všetky prípady invazívnych kardiovaskulárnych infekcií nahlásených doteraz boli spojené s používaním 3T HCUs.**



Joint_WHO2

RAPID RISK ASSESSMENT

Invasive cardiovascular infection by *Mycobacterium chimaera* associated with the 3T heater-cooler system used during open-heart surgery

18 November 2016

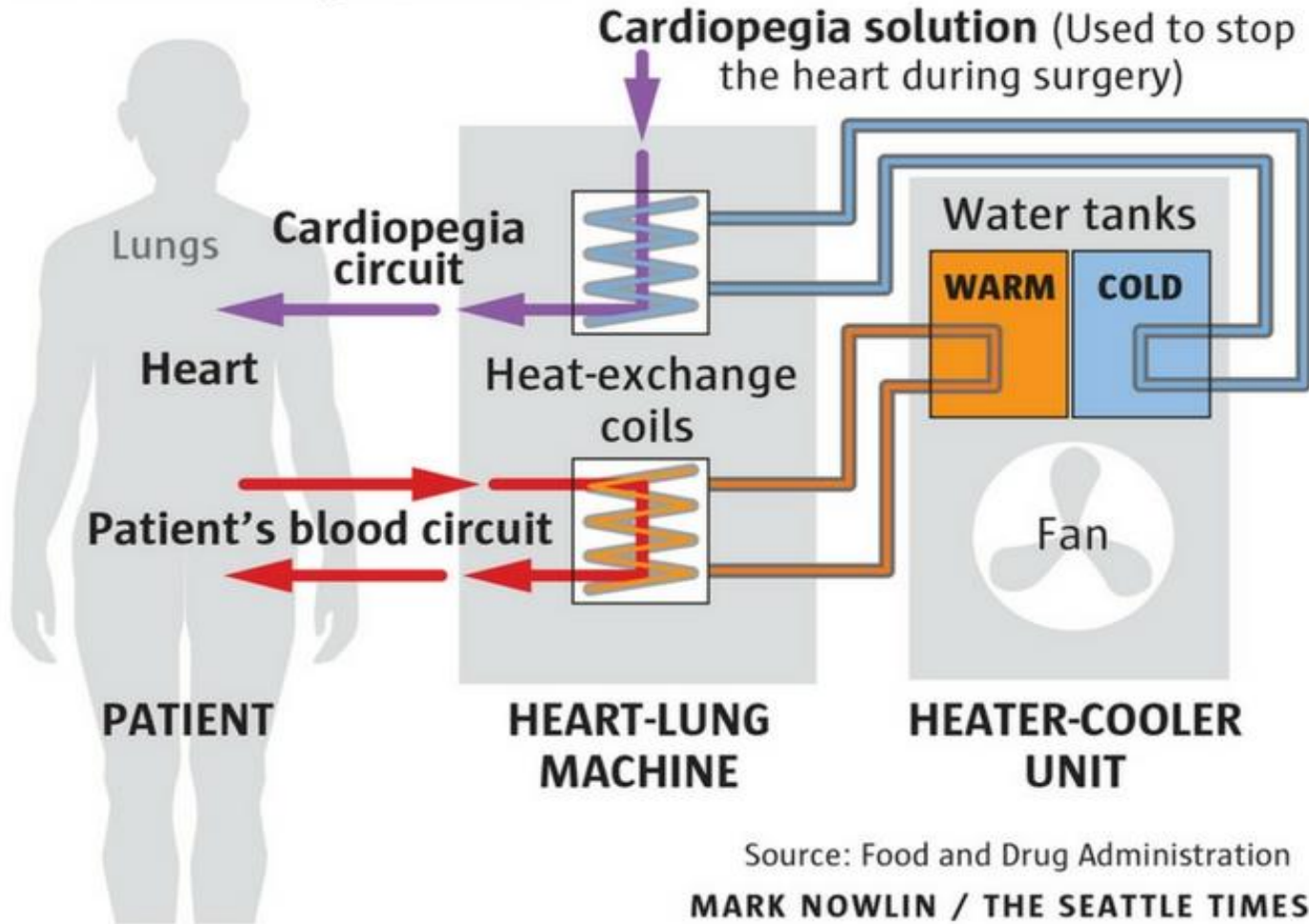
Conclusions and options for response

Fifty-two cases of invasive cardiovascular infection caused by *Mycobacterium chimaera* have been detected in patients who had previously undergone open-heart surgery in seven countries in Europe (France, Germany, Ireland, the Netherlands, Spain, the UK and Switzerland) since 2011. Cases have also been reported in the US, Canada, Australia and Hong-Kong Special Administrative Region.

Isolation of *M. chimaera* in heater-cooler units (HCU) and in air samples suggests aerosolisation of water from the HCU in the operating room as the most likely source of infection. Contamination of the 3T heater-cooler system at the manufacturing site in Germany, has been identified as the most plausible source, which explains most but not all of invasive *M. chimaera* infections linked to this device. Contamination during use at the hospital as well as involvement of other heater-cooler system models are also possible.

Heater-cooler devices

Heater-cooler units are used to regulate blood temperature during heart surgery. Federal health officials on Thursday warned that some devices have the potential to spread life-threatening infections.



Transmission of *Mycobacterium chimaera* from Heater–Cooler Units during Cardiac Surgery despite an Ultraclean Air Ventilation System

Rami Sommerstein, Christian Rüegg, Philipp Kohler, Guido Bloemberg, Stefan P. Kuster, Hugo Sax

Heater–cooler units (HCUs) were recently identified as a source of *Mycobacterium chimaera* causing surgical site infections. We investigated transmission of this bacterium from HCUs to the surgical field by using a thermic anemometer and particle counter, videotape of an operating room equipped with an ultraclean laminar airflow ventilation system, and bacterial culture sedimentation plates in a non-ventilated room. Smoke from the HCU reached the surgical field in 23 s by merging with ultraclean air. The HCU produced on average 5.2, 139, and 14.8 particles/min in the surgical field at positions Off, On/oriented toward, and On/oriented away, respectively. Culture plates were positive for *M. chimaera* ≤ 5 m from the HCU in the test room. These experiments confirm airborne transmission of *M. chimaera* aerosols from a contaminated HCU to an open surgical field despite ultraclean air ventilation. Efforts to mitigate infectious risks during surgery should consider contamination from water sources and airflow-generating devices.

airflow is superior in reducing surgical site infections in vascular patients (8), Brandt et al. reported an increase in surgical site infections in orthopedic surgery after use of laminar airflow systems (9). The hazard of horizontal airflow disrupting laminar airflow has been studied for forced-air warming systems that prevent hypothermia (10–12). Although these devices contaminate ultra-clean air ventilation systems, no definite link to an increased risk for surgical site infection has been established (10–12).

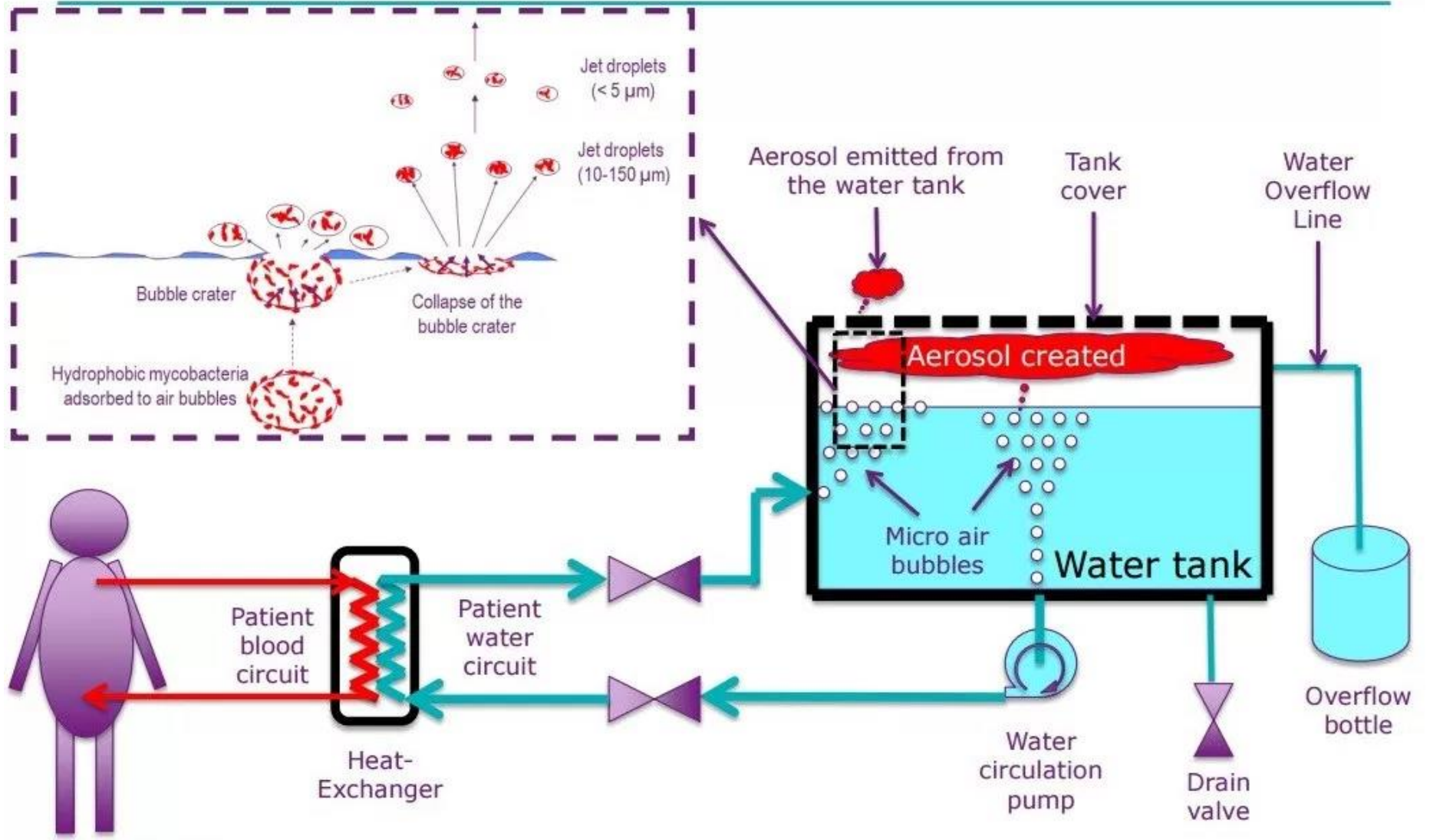
The considerable horizontal airflow generated by heater–cooler units might disrupt vertical ultraclean airflow, which could be a potential mechanism for transmission of pathogens from a contaminated heater–cooler unit to a surgical site. Thus, we conducted a series of technical and microbiological experiments to investigate the potential airborne transmission pathway of pathogens, such as *M. chimaera*, from a contaminated heater–cooler unit to the surgical field.



Heater – Cooler Units

- HCUs : regulácia teploty krvi a cardioplegického roztoku mimotelového obehu počas kardiochirurgických výkonov
- Ako výmenník tepla je používaná filtrovaná voda, nikdy neprichádza do kontaktu s krvou pacienta!
- Cirkulácia **nie je vzduchotesná**, chladenie vody je umožňované ventilátorom, takže dochádza ku vzniku a šíreniu sa kontaminovaného aerosolu.
- HCUs sú obvykle umiestnené v operačnej sále.

Prenos infekcie: Aerosol



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

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Enviromentálne testy

- **Najpravdepodobnejším zdrojom infekcie M. chimaera boli 3T HCUs contaminované v priebehu výrobného procesu v mieste produkcie v Nemecku.**
- **2014 : Testovanie v mieste výrobného procesu preukázalo kontamináciu M. chimaera vo výrobnej linke a vodných zdrojoch v mieste výroby, následne boli aplikované nové dezinfekčné normy a kontaminácia nebola viac preukázaná.**
- **HCUs boli distribuované do celého sveta, nie je jasné či ku kontaminácii došlo behom výrobného procesu alebo v mieste používania kvôli použitiu kontaminovanej vody z kohútika.**
- **Kultivačné vyšetrenie vzoriek vzduchu z operačných sál kde tieto 3T HCUs boli používané preukázalo prítomnosť M. chimaera, potvrdzujúc produkciu infikovaného aerosolu týmito zariadeniami.**
- **3T HCU-produkovaný aerosol obsahujúci M. chimaera sa dokáže dostať k operačnému stolu napriek ultračistému laminárnemu prúdeniu.**
- **Bola detekovaná taktiež kontaminácia HCUs používaných v extracorporálnych membránových oxygenátoroch (ECMO): v tomto prípade sa nepreukázala kontaminácia okolitého vzduchu pravdepodobne vďaka vzduchotesnosti membrán.**



Stanovenie rizika:

Riziko invazívnej infekcie spôsobenej M. Chimaera u pacientov po kardiochirurgickom výkone na otvorenom srdci bolo odhadnuté 0.4 – 16 per 10 000 patient-years [2,13].

Ak vezmeme do úvahy riziko 1.2% pre infekciu v mieste chirurgického výkonu v prvom roku po valvuloplastike a kumulatívnu 5 – ročnú incidenciu prostetickej endokarditídy, ktorá je 3.2–5.7% [30], riziko invazívnej infekcie spôsobenej M. Chimaera je považované za **nízke**.

«Cost vs Benefit»

Benefit udržovania primeranej teploty prostretníctvom HCU prevažuje nad rizikom prenosu infekcie spojenej s používaním týchto zariadení.



Typ infekcie

- Endokarditidy, infekcie cievnych protéz, disseminované inf.
- Sternálna osteomyelitis
- Pneumonia u predisponovaných pacientov – CHOPN
- Variabilne dlhé obdobie od chirurgického výkonu po objavenie sa symptómov: 3 mesiace – 5 rokov?
(medián 19 mesiacov)

Healthcare-associated prosthetic heart valve, aortic vascular graft, and disseminated *Mycobacterium chimaera* infections subsequent to open heart surgery

Philipp Kohler¹, Stefan P. Kuster¹, Guido Bloemberg², Bettina Schulthess^{2,3}, Michelle Frank⁴, Felix C. Tanner⁴, Matthias Rössle⁵, Christian Böni⁶, Volkmar Falk^{7,8}, Markus J. Wilhelm⁷, Rami Sommerstein¹, Yvonne Achermann¹, Jaap ten Oever⁹, Sylvia B. Debast¹⁰, Maurice J.H.M. Wolfhagen¹⁰, George J. Brandon Bravo Bruinsma¹¹, Margreet C. Vos¹², Ad Bogers¹³, Annerose Serr¹⁴, Friedhelm Beyersdorf¹⁵, Hugo Sax¹, Erik C. Böttger^{2,3}, Rainer Weber¹, Jakko van Ingen^{16†}, Dirk Wagner^{17†}, and Barbara Hasse^{1†*}

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Diagnóza a terapia:



- Diagnóza je zdĺhavá, často sa na M. Chimera nemyslí vzhľadom na dlhé obdobie od chir. výkonu
- Neexistuje test ktorý potvrdí že pacient bol v kontakte s M. Chimera
- Diagnostika je laboratórna: mikrobiologická kultivačná metóda, vyžaduje 2 mesiace.
- Terapia je zložitá, vyžaduje kombináciu ATB a chirurgickej revízi
- Významné percento zlyhania a fatálneho outcome

ECDC TECHNICAL DOCUMENT

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

August 2015

A target-specific assay for rapid and quantitative detection of chimaera DNA in environmental and clinical specimens

Enrique Zozaya-Valdes, Jessica L. Porter, John Coventry, Janet A.M. Fyfe, Glen P. Carter, Anders Goncalves da Silva, Torsten Seemann, Paul D.R. Johnson, Andrew J. Stewardson, Ivan Bastian, Sally A. Roberts, Benjamin P. Howden, Deborah A. Williamson, Timothy Stinear

doi: <https://doi.org/10.1101/105213>

Mycobacterium chimaera is an opportunistic environmental mycobacterium, belonging to the *Mycobacterium intracellulare* complex. Although most commonly associated with pulmonary disease, there has been growing awareness of invasive *M. chimaera* infections following cardiac surgery. Investigations suggest world-wide spread of a specific *M. chimaera* clone, associated with contaminated hospital heater-cooler units used during the surgery. Given the global dissemination of this clone, its potential to cause invasive disease, and the laboriousness of current culture-based diagnostic methods, there is a pressing need to develop rapid and accurate diagnostic assays, specific for *M. chimaera*. Here, we assessed 354 mycobacterial genome sequences and confirmed that *M. chimaera* is a phylogenetically coherent group. *In silico* comparisons indicated six DNA regions present only in *M. chimaera*. We targeted one of these regions and developed a TaqMan qPCR assay for *M. chimaera* with a detection limit of 10 CFU in whole blood. *In vitro* screening against DNA extracted from 40 other mycobacteria and 22 bacterial species from 21 diverse genera confirmed *in silico* predicted specificity for *M. chimaera*. Screening 33 water samples from heater cooler units with this assay highlighted the increased sensitivity of PCR compared to culture, with 15 of 23 culture negative samples positive by *M. chimaera* qPCR. We have thus developed a robust molecular assay that can be readily and rapidly deployed to screen clinical and environmental specimens for *M. chimaera*.



Odporúčania:



- 1. aplikácia čistiacich a dezinfekčných protokolov odporúčaných výrobcom
- 2. Ak je to možné odstránenie HCU z operačných sál, alebo aspoň umiestniť HCU čo najďalej od pacienta a operačného stola.
- 3. Vyhýbať sa používaniu vody z vodovodného kohútika (FDA 2015)
- 4. Zváženie náhrady HCU vyrobených pred rokom 2014

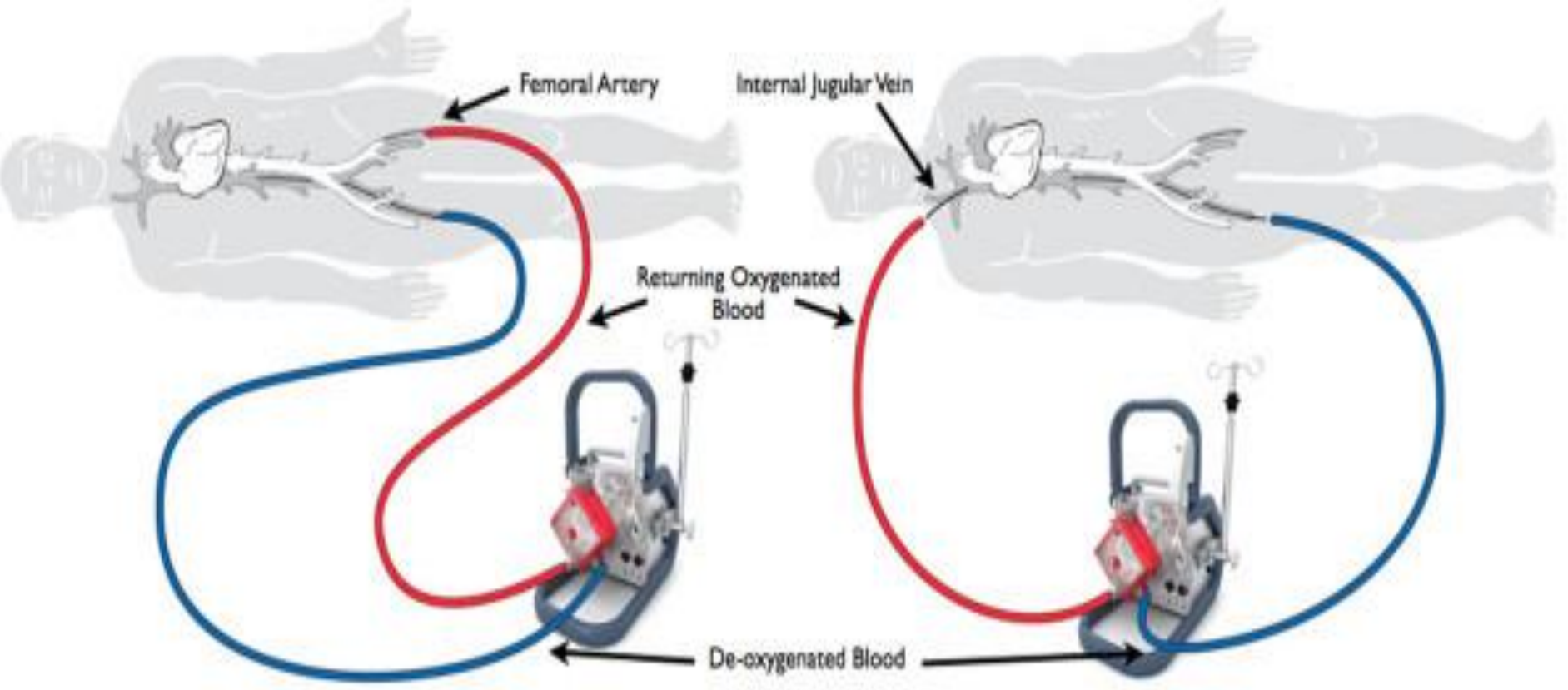


- Be aware that heater-cooler devices are important in patient care. In appropriately selected patients, the benefits of temperature control during open chest cardiothoracic procedures generally outweigh the risk of infection transmission associated with the use of these devices.
- Strictly adhere to the cleaning and disinfection instructions provided in the manufacturer's device labeling. Ensure you have the most current version of the manufacturer's instructions for use readily available for staff who interact with these devices.
- **DO NOT** use tap water to rinse, fill, refill or top-off heater-cooler water tanks since this may introduce NTM organisms. Use only water that has been passed through a filter of less than or equal to 0.22 microns. When making ice needed for use in the heater-cooler, use only water that has been passed through a filter of less than or equal to 0.22 microns. Deionized water and sterile water created through reverse osmosis are not recommended because they may promote corrosion of the metal components of the system.
- Direct and/or channel the heater-cooler's exhaust vent(s) away from the surgical field and toward an operating room exhaust vent to mitigate the risk of aerosolized heater-cooler tank water reaching the sterile field.
- Establish regular cleaning, disinfection and maintenance schedules for heater-cooler devices according to the manufacturer's instructions to minimize the risk of bacterial growth and patient infection.
 - Follow a comprehensive quality control program for maintenance, cleaning, and disinfection of heater-cooler devices. This may include written procedures for monitoring adherence to the program and documenting set up, cleaning, and disinfection processes before and after use.
- Immediately remove from service heater-cooler devices that show discoloration or cloudiness in the fluid lines/circuits. This may indicate bacterial growth. Consult your hospital infection control officials to perform the appropriate follow up measures and report events of device contamination to the manufacturer.
- Consider performing environmental, air, and water sampling and monitoring if heater-cooler contamination is suspected. Environmental monitoring requires specialized expertise and equipment to collect and process samples, which may not be feasible in all facilities.
- Health care facilities should follow their internal procedures for notifying and evaluating patients if they suspect infection associated with heater-cooler devices.
- Review the communications from the Centers for Disease Control and Prevention:

ECMO: ExtraCorporeal Membrane Oxygenation

VA-ECMO

VV-ECMO



Clinical implications of *Mycobacterium chimaera* detection in thermoregulatory devices used for extracorporeal membrane oxygenation (ECMO), Germany, 2015 to 2016

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Mycobacterium chimaera, a non-tuberculous mycobacterium, was recently identified as causative agent of deep-seated infections in patients who had previously undergone open-chest cardiac surgery. Outbreak investigations suggested an aerosol-borne pathogen transmission originating from water contained in heater-cooler units (HCUs) used during cardiac surgery. Similar thermoregulatory devices are used for extracorporeal membrane oxygenation (ECMO) and *M. chimaera* might also be detectable in ECMO treatment settings. We performed a prospective microbiological study investigating the occurrence of *M. chimaera* in water from ECMO systems and in environmental samples, and a retrospective clinical review of possible ECMO-related mycobacterial infections among patients in a pneumological intensive care unit.

We detected *M. chimaera* in 9 of 18 water samples from 10 different thermoregulatory ECMO devices; no mycobacteria were found in the nine room air samples and other environmental samples. Among 118 ECMO patients, 76 had bronchial specimens analysed for mycobacteria and *M. chimaera* was found in three individuals without signs of mycobacterial infection at the time of sampling. We conclude that *M. chimaera* can be detected in water samples from ECMO-associated thermoregulatory devices and might potentially pose patients at risk of infection. Further research is warranted to elucidate the clinical significance of *M. chimaera* in ECMO treatment settings.

- **Filtered tap water, which was commonly used to fill the thermoregulatory devices for ECMO treatment, was subjected to microbiological examinations at three different time points (several weeks apart), but neither bacterial nor mycobacterial pathogens were detected.**

• **Ďakujem za pozornosť!**

