

Original Article

The Heater Cooler as a Source of Infection from Nontuberculous Mycobacteria

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Abstract: Nosocomial infections acquired during the course of cardiac surgery and hospitalization can have devastating patient consequences. The source of these infections is often difficult to determine which complicates eradication efforts. Recently it has become apparent that the heater-cooler devices used in conjunction with cardiopulmonary bypass may become contaminated with bacteria that are normally found in hospital water sources. The culprit organisms are nontuberculous mycobacteria which coat the intrinsic surfaces found within the circuits of the heater-coolers. Aerosolization

of the bacteria occurs during normal heater-cooler operation which can disperse the organisms throughout the operating room. The bacteria are slow-growing and may not present for months, or years, following exposure which makes epidemiological determination a challenge. The ensuing report summarizes a recent outbreak in these infections that have been reported both in Europe and the United States, along with efforts to reduce the risk for patient infection. **Keywords:** cardiac surgery, cardiopulmonary bypass, heater-cooler device. *JECT. 2016;48:55–59*

In 2013, a group from University Hospital of Zurich Switzerland reported two cases of infective endocarditis that developed from nontuberculous mycobacteria (NTM) in patients who had previously undergone cardiac surgery (1). In both patients, the culprit organism was *Mycobacterium chimaera*, a slow-growing mycobacteria. Although the source of the mycobacteria remained elusive, the authors stated that the water supply within the operating room (OR) needed to be considered. Gene sequencing revealed that in both cases the strains of *M. chimaera* were identical, which resulted in the hospital undergoing an extensive evaluation to determine if a nosocomial link was possible. Since *M. chimaera* is predominantly found in water supplies this became a focus for the investigatory team that was made up of clinicians, microbiologists, technicians, and hospital administrators. A prospective

evaluation of all aspects of care administered to patients was undertaken along with a retrospective review of histopathological records of all *M. chimaera* isolates within the hospitals since 2006. The investigators identified six patients who had met case definition criteria and all were found to have undergone cardiac surgery for valvular or aortic reconstruction surgery, or a combination of the two (2). After an exquisite and exhaustive review, they identified the source of bacteria as originating in contaminated water found in heater-cooler devices (HCD) used in conjunction with cardiopulmonary bypass (CPB). Additional cases were identified both in Germany and the Netherlands for disseminated *M. chimaera* infection with airborne contamination originating from the HCD as the cause (3). In the summer and fall of 2014, the Food and Drug Administration (FDA) received reports from a single hospital where four patients had died from *Mycobacterium abscessus*, but not all had undergone cardiothoracic surgery procedures. *Mycobacterium abscessus* is also found in water and is a rapidly growing, Gram-positive *Mycobacterium*, as opposed to *M. chimaera* that is a slow-growing organism. Since the initial report national safety alerts concerning the use of HCD have been issued

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in several countries¹ bringing this serious and devastating occurrence to the minds of all clinicians involved in the conduct of cardiac surgery.

HEATER-COOLER DEVICES

CP temperature controller is the official term that the FDA uses to identify and regulate HCD. They are categorized as Class II devices and require 510(k) premarket notification for review and clearance. They use compressors to adjust the temperature of water, i.e., contained in tanks within the devices. The water is then pumped through tubing connected to the device and flows, in a recirculating pattern, external to the system. The tubing is connected to heat exchangers located in the CPB circuit in both oxygenator and cardioplegia devices, and through water-filled blankets placed on the OR bed. Each HCD may contain several circuits that allow independent control of temperature for different devices. In some devices, the circuit perfusate, cardioplegia solution, and OR bed blankets can all be simultaneously maintained at different temperatures. Although the trend is moving toward a single HCD to serve multiple functions within an OR, it is not uncommon for several devices to be used in a single room. All HCD are considered “open” systems, which refers to the necessity of filling the tanks with water at a functional level capacity. However, the circuits connected to the CPB components and OR bed are considered “closed” since no water comes in contact with either the perfusate or cardioplegia solutions nor the patient. The heat exchangers contain thermally conductive barriers that facilitate the conductive transfer of heat across the medium. The internal components of HCD are generally not readily observable and are obscured by the casings that surround the units. The devices may contain an insulating barrier to reduce thermal loss as well as reduce noise generated from the compressors. The labeling for all HCD states that they are cleared for a maximum use of 6 hours by the FDA. The Instructions-For-Use (IFU) are documents that contain operational information as well as specific instructions for cleaning and disinfection processes specific for each device.

There are presently six manufacturers who produce and market HCD in the United States (Table 1). Although the

function of temperature regulation is similar between devices, there is significant variability in operation and, hence a need to carefully follow individual manufacturers operating instructions. Because of the inherent design characteristics, all devices are capable of aerosol formation and the potential for NTM infection. The cleaning and disinfection protocols also vary and failure to follow the IFU may result in inadequate decontamination and/or early degradation of the device components. The cleaning process for most HCD follows the Environmental Protection Agency National Primary Drinking Water standards reducing CFU to 500 CFU per 100 mL of water.² Furthermore, human factor elements also play a role in device maintenance with failure to follow the manufacturers’ IFU resulting in subadequate cleaning and contamination of the units.

The FDA is working with HCD manufactures to identify appropriate test conditions that should be used to evaluate the effectiveness of the cleaning and disinfection processes. The devices that will be tested include those that have not left the manufacturing facility, as well as those that are, and have been, used in clinical situations. The test procedures will include simulations that test the devices under a variety of conditions including worst-case scenarios, such as testing units that have been used clinically and have undergone repeated cleaning and disinfection procedures. The test environments should also include testing where the end-users conduct cleaning and disinfection processes listed in the manufactures IFU, and the devices are used according to labeling instructions. To assess the adequacy for disinfection procedures manufactures should follow the validation process using criteria published by the FDA for Class II medical washing devices.³ These guidelines assess multiple levels of disinfection that reduce vegetative organisms, such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella*, and NTM species, at a minimum of a 6-log kill to show high level decontamination.

In December 2015, one manufacturer of HCD was issued a warning letter from the FDA that resulted from inspections conducted at facilities managed by the company both in Europe and the United States (FDA Warning Letter to LivaNova).⁴ The company was cited for a variety of reasons including failure to validate a process that demonstrated that the testing for disinfection and drying of the devices. Although some of the findings may seem

¹European Centre for Disease Prevention and Control. Invasive cardiovascular infection by *Mycobacterium chimaera* potentially associated with heater-cooler units during cardiac surgery. Issue Date: April 30, 2015. Gov.uk Medical Safety Alert, Heater-cooler devices used in Cardiac surgery—risk of infection with *Mycobacterium* species. Issue Date: June 11, 2015. U.S. Food and Drug Administration. Nontuberculous mycobacterium infections associated with heater cooler devices. Issue Date: October 15, 2015. CDC. Non-tuberculous mycobacterium (NTM) infections associated and heater cooler devices interim practical guidance. Updated: October 27, 2015.

²Environmental Protection Agency Guide to Safe Drinking Water, <https://www.epa.gov/ground-water-and-drinking-water/table-regulated-drinking-water-contaminants>.

³Class II Special Controls Guidance Document: Medical Washers and Medical Washers-Disinfectors, <http://www.fda.gov/RegulatoryInformation/Guidances/ucm073357.htm>.

⁴FDA Warning Letter to LivaNova formerly Sorin Group, <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm479684.htm>.

Table 1. List of various HCDs used in the United States as of June 2016.

Manufacturer Location and Device	Reservoir Number	Disinfection Interval (Days)	Preventative Maintenance Service	Estimated U.S. Market Share (%)	Features
LivaNova, PLC Arvada, CO, and 3T™	3	14	Yearly or after 1,000 operation hours	60	3-circuit control
Cincinnati Sub-Zero, LLC Sharonville, OH, and Hemotherm® 400MR, CE	2	30	None stated	13	Remote control capability
Terumo Cardiovascular, Ann Arbor, MI, and TCM, TCM11*	2	7	None stated	10	Automatic ice maker
Terumo Cardiovascular and Dual Cooler Heater*	1	7	None stated	8	External ice required
Maquet Getinge Group Wayne, NJ, and HCU 20*, 30*, 40	2	7	Yearly or after 1000 operation hours	6	3-circuit control Automatic ice maker
CardioQuip, LLP Bryan, TX, and MCH 1000(i)™	1	90	Yearly or after 500 operation hours	1	External ice required Optional modules
Terumo Cardiovascular and HX2™*	2	7	None stated	1	2-circuit controls External ice required
Medtronic BioCal and 370*	1	None listed	Yearly	1	External ice required

HCDs, heater cooler devices.

*No longer manufactured.

like minor infractions (failure to address documentations and record-keeping), the outbreak of NTM infections has emphasized the critical importance of strict adherence to all regulatory requirements. The HCD in question were not recalled and no warnings were issued to users of these devices in the United States. The company, as well as other manufacturers of HCD, has been proactive in updating the IFU on cleaning and disinfecting procedures, and has published resources to aid users in reducing the risk for contamination.⁵

SPREAD OF CAUSATIVE ORGANISMS BY HCD

The fact that HCD could serve as sources of infection in the OR environment was not unknown to clinicians. Weitkemper et al. stated that HCD have the potential to increase the risk of infection when water from these devices comes in contact with a patient undergoing cardiac surgery (4). The NTM are widely distributed in nature and are found in both soil and water, including drinking systems in private and public locations including health-care facilities. They thrive in aqueous environments and grow rapidly in the temperatures commonly used within HCD. One aspect of their adaptability is to form a biofilm on the surface of materials used in HCD. Once this biofilm has formed, it is mostly resistant to standard disinfectants making these extremely difficult to eradicate. When these biofilms have been identified the only way to completely remove them is by disassembly, replacing the affected tubing, and completing a thorough disinfection (5). Assessing the adequacy of cleaning should be accomplished by testing for the microbial load in the HCD. Garvey has recently

shown that completing a decontamination cycle following an initial replacement of internal tubing, with weekly testing of for microbiological organisms, will maintain safe levels of water quality within the devices (5). However, after NTM organisms have impregnated the surfaces of HCD they can be liberated by the normal agitation created by the recirculation pumps used to move water throughout the device. The agitation creates bubbles within the circuit whereby NTM have been shown to attach to water droplets as the fluid moves through the device. These droplets then burst when exposed to atmosphere creating a bio-aerosol and once airborne are distributed throughout the OR by the action of exhaust and cooling fans found in the HCD (6). This airborne dissemination is directly related to the time that the HCD are turned on and in use, as well as the total operating time. Although the infections have occurred in a variety of patients, the most susceptible group seems to be those undergoing valvular procedures and in those receiving vascular grafts.

Patients who have developed NTM infections from HCD have experienced serious illness including death. The clinical symptoms shown in these slow-growing NTM may occur several years after exposure to the infected HCD. The long latency period combined with the rare occurrence rate has made the clinical presentation difficult to epidemiologically link to a nosocomial source. However, the excellent reporting by Sax, Kohler, and others in Europe has unequivocally identified NTM as the culprit organisms originating from HCD (2,3,7,8).

INTERNATIONAL AND LOCAL RESPONSE

After publication of the European findings and the examination of the deaths that have occurred in the

⁵LivaNova, formerly Sorin Group, <http://www.livanova.sorin.com/products/cardiac-surgery/perfusion/hlm/3t>.

United States attributed to NTM infections, a number of international organizations charged with patient and consumer safety, issued alerts (9–15). In October 2015, both the CDC and FDA in the United States issued safety communications. In June 2016, the FDA convened a Circulatory Devices Advisory Panel as part of the Medical Devices Advisory Committee to examine the current data on NTM infections and advise the Committee on possible actions. Both authors of this document participated as representatives of the perfusion community. Although the risk for developing NTM infections is low, actions can be immediately undertaken to reduce and mitigate the risk for all patients exposed to HCD. Therefore, the following recommendations are being suggested by the authors as part of an overall plan to improve patient safety. Further guidelines from the manufacturers and regulatory agencies should be followed when they are released.

RECOMMENDATIONS TO LIMIT THE OCCURRENCE OF NTM INFECTIONS IN THE OR

1. All HCD will be maintained using hospital, federal and state regulatory policies, and in accordance with manufacturer's labeled use.
2. All HCD should be used in accordance with established policies by the facility and by the manufacturer's IFU.
3. All policies and procedures for cleaning and disinfecting HCD devices will follow the manufacturer's IFU.
4. A "Checklist" for cleaning and disinfecting HCD will be completed at the scheduled intervals for each device, and will be maintained by each hospital according to bioengineering guidelines.
5. Clinical competencies should be established for all individuals involved in cleaning and disinfecting HCD as part of facility required annual continuing education.
6. Identification and documentation of each HCD by serial number will be maintained for each clinical procedure for which they have been used.
7. Document utilization of HCD in non-cardiac procedures, such as liver transplantation, lung transplantation, vascular surgery and ECMO, following the same standards for use for cardiac surgical procedures.
8. All water to be used for HCD will undergo filtration using a 0.2-micron filter.

SUGGESTED RECOMMENDATIONS TO LIMIT THE OCCURRENCE OF NTM INFECTIONS IN THE OR (NOT POSSIBLE IN ALL SITES)

1. Monitor HCD for bacterial growth through heterotrophic plate count, *Pseudomonas* and coliform bacteria, based on hospital infectious disease recommendations.
2. Reduce open entry points on oxygenator venous reservoirs by closing all luer ports not necessary for venting,

and omitting the use of syringes as "funnels" for the delivery of solutions either during priming of the circuit or throughout the case.

3. Where possible position heart–lung machine in the laminar flow area of the OR table.
4. Limit turning HCD on to the times when needed.
5. Position HCD at the end of the OR bed at patient's feet.
6. Do not empty tubing attaching HCD to heat exchanger(s) until after the patient has left the OR.
7. Use gas evacuation system to capture air circulated at the HCD exhaust fan into hospital waste system.
8. Omit the use of non-disposable mounting system (holders) for oxygenators and cardioplegia heat exchange couplers.
9. At regular disinfection and cleaning cycles sterilize quick-disconnects (Hansen Couplers, W.W. Grainger, Inc., Lake Forest, IL) according to hospital policy for instrumentation.

ADDITIONAL CONSIDERATIONS FOR LIMITING THE OCCURRENCE OF NTM INFECTIONS IN OR

1. Consider an alternate location of HCD outside of the OR.
2. Place HCD in encased housing.
3. When system is in use place blanket over exhaust area of HCD, assuring that the device does not malfunction by limiting exhaust and over-heating.

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