

PENNSYLVANIA DEPARTMENT OF HEALTH

2015- PAHAN -322 -12-11-ADV

PADOH and PSA Guidance Regarding Nontuberculous Mycobacterium (NTM) Infections among Patients Undergoing Open Heart Surgeries on Cardiopulmonary Bypass.



DATE:	12/11/2015
TO:	Health Alert Network
FROM:	Karen M. Murphy, PhD, RN, Secretary of Health
SUBJECT:	Pennsylvania Department of Health (PADOH) and Pennsylvania Patient Safety Authority (PSA) Guidance Regarding Nontuberculous Mycobacterium (NTM) Infections among Patients Undergoing Open Heart Surgeries on Cardiopulmonary Bypass.
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Please see the attached guidance from the Pennsylvania Department of Health (PADOH) and Pennsylvania Patient Safety Authority (PSA) regarding Nontuberculous Mycobacterium (NTM) Infections Among Patients Undergoing Open Heart Surgeries on Cardiopulmonary Bypass.

Pennsylvania Department of Health (PADOH) and Pennsylvania Patient Safety Authority (PSA) Patient Safety Communication: Nontuberculous Mycobacterium (NTM) Infections among Patients Undergoing Open Heart Surgeries on Cardiopulmonary Bypass — PADOH Interim Recommendations for Hospitals

Situation:

Bacteria can contaminate heater-cooler units (HCU) used in conjunction with cardiopulmonary bypass (CPB) machines. Recent investigations have recovered Nontuberculous mycobacterium (NTM), specifically *M. chimaera*, from:

- 1) Water samples and swabs taken of HCUs,

- 2) Operating room air samples while the HCU is running but not when the HCU is off, and
 - 3) Patients with clinical infections who have undergone open heart surgeries on CPB.
- The epidemiological and microbiological findings from investigations in Europe and Pennsylvania convincingly support the conclusion that exposure to contaminated HCUs is associated with NTM infection among patients undergoing open heart surgery on CPB.

Background:

NTM grow slowly and are commonly found in soil and water, including tap water. NTM are usually not harmful, but can cause infections in patients who have had invasive health care procedures and those with weakened immune systems. NTM may enter the body through the lungs by breathing, through the gut by eating or drinking, or through the skin by a cut or wound contaminated by water or dirt containing NTM. NTM are not contagious and are not spread from person to person. As the name suggests, NTM or Nontuberculous mycobacterium are different from the bacteria that cause TB (*Mycobacterium tuberculosis*). Treatments for NTM exist; however, infections can be life-threatening especially among immunocompromised patients or patients with significant co-morbidities.

HCUs are commonly used during cardiothoracic surgical procedures to warm and cool a patient's blood during cardiopulmonary bypass. Blood does not come into direct contact with the water in the HCU. Transmission likely occurs during surgery by the production of aerosols (fine spray) of contaminated water coming from the HCU.

Earlier this year, Sax et al. published a description of six patients with prosthetic valve endocarditis or vascular graft infection due to *M. chimaera*.¹ The investigation also cultured *M. chimaera* from water circuits of HCU and from air samples collected when HCU were in use. Molecular fingerprinting linked the environmental isolates to the clinical isolates of two clusters of case patients.

On 15 June 2015, Sorin Group Deutschland GMBH issued a Field Safety Notice² that stated, "Without vigilant performance of the disinfection and maintenance procedures per the Instructions for Use [IFU], organisms can multiply in a heater cooler device and potentially form biofilm. ... [T]here is a possibility that bacteria can become aerosolized when the heater cooler device is operated and serve as a source of contamination. ... [F]luid leakage from the device or aerosolization generated by a contaminated water circuit during device operation may create conditions in which the organisms could potentially contact the patient and subsequently contaminate the surgical site." The Field Safety Notice also provided users with the latest IFU, dated February 2015, and detailed two different pathways containing additional disinfection, maintenance procedures and surveillance recommendations depending on the facility's past practices.³

On 15 October 2015, the Food and Drug Administration (FDA) issued a Safety Communication⁴ to, "... heighten awareness about infections associated with heater-cooler devices and [provide] steps health care providers and health facilities can take to mitigate risks to patients." The guidance in the Safety Communication applied to all HCUs, not just those manufactured by Sorin Group Deutschland GMBH. Among 32 HCU specific medical device reports filed with FDA between 2010 and 2015 in which HCU contamination or patient infection was reported, 25 were filed in the year 2015.

On 21 October 2015 the Centers for Disease Control and Prevention (CDC) published interim practical guidance⁵ about NTM infections and heater-cooler devices to echo concerns about "...the possible association between NTM infections and use of heater-cooler devices and to provide guidance on identifying patients with infection."

Subsequent to new awareness of the risk of NTM infection among patients undergoing open heart surgeries on CPB, two Pennsylvania hospitals (Wellspan York Hospital and Penn State Hershey Medical Center) detected separate clusters of patients with NTM infections. The details of these investigations and subsequent patient notification processes are available here: <http://www.wellspan.org/yorkopenheart> and <http://www.pennstatehershey.org/open-heart>.

Assessment:

PADOH and PSA consulted with infection control and patient safety experts, reviewed IFU from three HCU manufacturers, guidance issued by domestic and European government agencies and considered investigation findings.

Although sometimes associated with severe disease, at this time, NTM infections appear to occur very infrequently among persons undergoing an open-heart surgery and potentially exposed to a contaminated HCU (approximately 1 in 10,000 procedures to possibly 1 in 100 procedures).

At this time, the potential for aerosolization of bacteria from HCUs has only been demonstrated with the Sorin 3T HCU; however, there is consensus among experts and manufacturers that bacterial contamination and colonization of HCUs is likely if not maintained properly. Guidance from FDA, CDC and manufacturers stress fastidious adherence to IFU. PADOH and PSA do not currently have data to validate or refute the efficacy of HCU manufacturers' disinfection procedures to prevent NTM contamination, colonization and transmission. Any deviation from manufacturers' IFU may not be justified by science, may void warranties, and have unanticipated consequences.

PADOH and PSA observed significant differences in IFU from one version to the next published by the same manufacturer and between manufacturers. IFU also varied depending on prior maintenance and disinfection history. In addition, language from manufacturers was frequently ambiguous ("should" vs. "must") and some IFU were permissive of, but did not recommend, certain things (use of materials, chemical additives, procedures). PADOH and PSA also observed engineering differences that might predispose certain units to increased risk of biofilm formation and aerosolization of bacteria (e.g., blind segments of internal tubing, overflow tubes with low flow). Differences included:

1. Water source and characteristics (e.g., filtered, sterile, distilled, deionized, water hardness);
2. Method of bacterial control (periodic chemical disinfection [e.g., bleach], continuous circulation of bacteriostatic/bacteriocidal agent [hydrogen peroxide], periodic self-clean cycle involving circulation of hot water followed by a deep freeze cycle);
3. Addition of other chemicals to the water reservoir (USP-grade propylene glycol);
4. Water drainage schedule;
5. Disinfection schedule;
6. Schedule for addition and monitoring of concentrations of additives;
7. Tubing replacement schedule;
8. Degree of field-serviceability and ability to visually inspect the device for biofilm and water turbidity;
9. Inclusion of in-line water filters within machine and their maintenance (e.g., metal screens in HCU water path);
10. Method for cleaning of HCU fans;
11. Ability to connect auxiliary cooling units or directly add ice to water reservoirs;
12. Guidance for placement of the HCU inside or outside of the OR and positioning relative to the patient and nearby walls; and

13. Bacteriologic surveillance.

It is important to note that none of the reviewed IFU include a mechanical or enzymatic cleaning procedure beyond the water agitation that occurs with pump operation and drainage. One manufacturer has announced intentions to offer a mechanical debridement and chemical disinfection service for machines thought to be contaminated.

In addition, investigation findings also suggest that non-disposable devices connected to the HCU water path may serve as a potential reservoir for bacteria (e.g., cardioplegia device without disposable water path, paddle wheel visual flow indicators, reusable patient blankets). These devices may or may not have their own disinfection and maintenance procedures and may or may not be exposed to the bacterial control methods employed by connected HCUs.

PSA analysts queried the Pennsylvania Patient Safety Reporting System (PA-PSRS) for events related to heater-cooler use. Although no event reports mentioned infection as an outcome, 10 reported patient safety events between 2004 and 2015 provided insight into clinical practices that could result in increased risk of producing an aerosol, including water leakage at hose connections and water spillage upon disconnection of hoses and fittings. Water may spray if hoses are disconnected from fittings under pressure while the HCU is in use. Furthermore, leaks near HCU fans or exhausts might increase the potential for aerosolization.

HCUs are not semi-critical or critical devices. They are not sterile. While EPA drinking water standards have been proposed for acceptable heterotrophic plate counts (HPCs) for surveillance purposes, at this time, PADOH and PSA are unaware of data to suggest a safe threshold level of bacterial contamination under which aerosolization of bacteria, and potential transmission, might occur. Culturing NTM is challenging; NTM are slow-growing and faster-growing bacteria and fungi can overgrow NTM colonies. The use of HPCs may be an acceptable proxy for the suitability of water in the HCU; however, additional research in this area is needed.

Recommendations:

At this time, estimates of risk are imprecise; however, the rate of NTM infections appears to be small (approximately 1:10,000 to possibly 1:100) among patients undergoing open heart surgery on CPB. Hospitals must assess their equipment and procedures and take appropriate action to minimize impact on patients. Patients and providers should not delay cardiac surgeries after appropriate informed consent. At this time, there are several important unknowns. It is unknown whether risk of NTM infection can be completely eliminated given the paucity of data with which to validate device engineering and manufacturers' most recent IFU. The degree to which only certain models of HCUs will aerosolize bacteria or whether all HCUs have the potential to aerosolize bacteria is also not known. In addition, the ability of stated disinfection procedures to adequately decontaminate a colonized machine is unknown. At this time, manufacturers' IFU provide the best available guidance to hospitals for device maintenance. Strictly adhere to the cleaning and disinfection instructions provided in the manufacturer's IFU. Ensure you have the most current version of the manufacturers' IFU readily available to promote adherence. PADOH and PSAs assessment identified multiple factors that may promote bacterial colonization of HCUs. Beyond maintenance of the device, PADOH recommends a comprehensive approach to risk assessment and mitigation. Assess the physical device, physical ergonomics, clinical environment, individual, team and organizational behaviors that may increase the risk of bacterial colonization and subsequent aerosolization of bacteria. Implement interventions using a hierarchy of controls (elimination/substitution, engineering controls, and administrative controls). At this time, PADOH cannot recommend the elimination or substitution of one HCU over another unless there is evidence (visible, bacteriologic or epidemiologic) to suggest bacterial colonization or transmission. PADOH will continue

to work with federal partners (e.g., CDC, FDA) and manufacturers to better understand the risk of infection and how best to implement effective controls.

Additional recommendations from PADOH include:

1. Assessment

- a.** Identify all HCUs, associated devices connected to the water path, previous and current standard operating procedures (SOPs) and stakeholders (e.g., perfusionist, surgeon, surgical services manager, surgical nurse, biomedical engineering, central processing manager, infection control, hospital epidemiologist, and patient safety officer).
- b.** Assess current status of HCUs and attached devices. Where possible, visibly inspect internal and external hoses, fittings and reservoirs. Refer to manufacturer's guidance to determine whether and how to access internal components for visual inspection.
- c.** Evaluate the interplay of HCU disinfection procedures and those of attached devices. Can one device act as a bacterial reservoir for other attached devices?
- d.** Assess current and former SOPs relative to manufacturer's IFU with special attention to domains enumerated above. Does documentation exist to substantiate compliance with manufacturer's directions?
- e.** Identify and assess the expertise needed for proper implementation of infection control procedures and surveillance.
- f.** Assess existing training program.
- g.** Evaluate existing workflow to identify challenges and available resources (e.g., production pressure, team backup, device backups).
- h.** If substantive changes are made to existing equipment or equipment is replaced, be sure to assess impact of those changes. Consider using PSAs assessment tool:⁶
http://patientsafetyauthority.org/EducationalTools/PatientSafetyTools/ergonomics_inf/Pages/home.aspx.

2. Controls

- a.** Implement maintenance, disinfection and replacement schedule according to strictest interpretation of manufacturer's IFU.
- b.** Implement a process to periodically ensure you have the most current version of the manufacturers' IFU, can identify changes in guidance, assess the impact of those changes on your processes, and can implement those changes.
- c.** Do not use tap water. Use a 0.2 micron filter to mechanically disinfect water added to the HCU. Sterile water, distilled water or deionized water should only be used if consistent with manufacturer's IFU.
- d.** Implement appropriate safeguards to minimize spillage and ensure that units are not "topped-off" inappropriately (e.g., with unfiltered tap water).
- e.** Verify the appropriateness and concentration of additives used for bacterial control.
- f.** Carefully consider the impact of any decision to move the HCU outside of the operating room. While some units have remote control panels, moving the HCU outside the operating room poses significant logistical challenges. Hoses should not be routed through propped open operating room doors. Bulk heads mounted in the operating room enabling remote operation should also be cleaned and disinfected. In addition, the added length of tubing might impact the volume of fluid required for proper operation and the heat transfer

properties of the system. If the HCU is moved outside the operating room, seek and implement validated manufacturer protocols that address these concerns.

- g.** Move the HCU away from patient and sterile surfaces (e.g., draped mayo stands). HCU exhaust should point toward the operating room exhaust vents. Be sure to comply with manufacturer's IFU and minimum distance from surfaces (e.g., walls).
- h.** Although some institutions have built enclosures for their heater-cooler devices, at this time PADOH cannot recommend engineering controls that have not been vetted by the manufacturer.
- i.** Implement a quality assurance program to re-assess entire system related to operation and maintenance of HCUs and act upon findings.
- j.** Implement a training program and develop job action sheets.
- k.** Consult with the HCU vendor and other stakeholders (e.g., FDA, CDC and PADOH) to raise concerns and answer unresolved questions about device and process.

3. Bacteriologic surveillance

- a.** Implement a device tacking system that logs which unit was used for every patient and their on-pump times.
- b.** Implement a water quality sampling program. If not specified by the manufacturer, interim guidance includes monthly heterotrophic plate counts. At a minimum, water should meet EPA drinking water standards.
- c.** If not specified by the manufacturer, consult PADOH for guidance on NTM specific cultures and air sampling if a cluster of infections is suspected or if device assessments suggest possible contamination (see reporting guidance below). Environmental monitoring requires specialized expertise and equipment to collect and process samples, which may not be feasible in all facilities.

4. Patient surveillance

- a.** Disseminate information to relevant clinical staff and ensure appropriate index of suspicion and that they have methods in place to diagnose mycobacterial infections in patients who have been exposed to HCUs. The NTM bacteria (specifically *M. chimaera*) observed in most of the associated case-patients is very slow growing. Special equipment/procedures may be necessary (e.g., biopsy vs. swab, AFB isolator tube)
- b.** Conduct prospective and retrospective surveillance using proposed case definition (See Appendix A.)
- c.** In facilities in which open heart surgery on bypass is performed, conduct retrospective case finding by cross-referencing microbiology NTM culture data with operative databases. Report identified cases as noted below.

5. Reporting and taking machines out-of-service

- a.** HCUs with discoloration, visible biofilm, visibly turbid water, or machines with water cultures outside of EPA limits for drinking water should be removed from service immediately and sequestered until further directed by PADOH.
- b.** Report any visible biofilm, turbid water or positive culture results from a HCU immediately to your local health department, PADOH Bureau of Epidemiology (717-787-3350) and to PADOH Division of Acute and Ambulatory Care as an infrastructure failure via PA-PSRS. Notify the manufacturer, file a FDA MedWatch Report

(<https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home>) and inform your local health department (if applicable).

- c.** Report any departure from the IFU to PADOH Division of Acute and Ambulatory Care as an infrastructure failure via PA-PSRS. Also file a FDA MedWatch report, inform the Pennsylvania Department of Health Bureau of Epidemiology (717-787-3350) and your local health department (if applicable).
- d.** Health care practitioners, facilities and laboratories are required to report an unusual occurrence of a disease (e.g., NTM) or outbreak pursuant to 28 Pa. Code § 27.3(b), “A person... shall report an unusual occurrence of a disease, infection or condition not listed as reportable... or defined as an outbreak, within 24 hours... .” Notify PADOH of all patients with NTM meeting the surveillance case definition (See Appendix A.) Report cases to your local health department or to 1-877-PA-HEALTH.

Appendix A. Proposed Case Definition

All case patients must meet the following clinical criteria with onset of symptoms occurring two weeks to four years after having had an open heart surgery requiring cardiopulmonary bypass.

Clinical Signs and Symptoms:

- Localized infection, including but not limited to:
 - Prosthetic valve endocarditis
 - Prosthetic vascular graft infection
 - Sternotomy wound infection
 - Mediastinitis
 - Other deep organ space infection (e.g., empyema, pocket infection around LVAD or other implantable device)
- Disseminated infection, resulting in:
 - Bacteremia
 - Embolic and immunologic manifestations (splenomegaly, arthritis, osteomyelitis, bone marrow involvement with cytopenia, chorioretinitis, cerebral vasculitis, myocarditis, hepatitis, nephritis)

Laboratory Criteria:

Bacteria must be detected from an invasive sample (e.g., blood, pus, tissue biopsy or implanted prosthetic material; NOT from sample collected via bronchoscopy).

Exclusion criteria:

Isolated pneumonitis or tracheobronchitis (e.g., isolate obtained on bronchoscopy) is NOT sufficient to meet clinical criteria for infection.

Case Classification	Laboratory Criteria
Probable Case	<p><i>Mycobacterium chimaera</i>, <i>Mycobacterium avium complex</i> (MAC), <i>Mycobacterium-avium-intracellulare-scrofulaceum</i> (MAIS) complex or <i>Mycobacterium avium intracellulare</i> detected in an invasive sample by:</p> <p>Culture and identification (e.g., hybridization DNA probes, HPLC, MALDI-TOF mass spectroscopy, PCR restriction analysis, DNA sequencing of 16S rRNA gene along with a second target; contact PADOH for additional information.)</p>
Suspect Case	<p>Nontuberculous Mycobacterium (NTM) detected in an invasive sample by:</p> <p>Culture and identification (e.g., hybridization DNA probes, HPLC, MALDI-TOF mass spectroscopy, PCR restriction analysis, DNA sequencing of 16S rRNA gene along with a second target; contact PADOH for additional information.)</p> <p>OR</p> <p>Histopathology consistent with non-caseating granuloma and foamy/swollen macrophages with/without acid fast bacilli in deep organ tissue.</p>

Appendix B. Local Health Department Phone Numbers

- i. Pennsylvania Department of Health: 877-PA-HEALTH (877-724-3258)
- ii. Allegheny County Health Department: 412-687-2243; After Hours: 412-687-2243
- iii. Allentown Health Bureau: 610-437-7760; After Hours 610-437-7760
- iv. Bethlehem Bureau of Health: 610-865-7087; After Hours 610-865-7187
- v. Bucks County Department of Health: 215-345-3318; After Hours: 888-245-7210
- vi. Chester County Health Department: 610-344-6225; After Hours: 610-733-4919
- vii. Erie County Department of Health: 814-451-6700, 24 Hours/7 Days
- viii. Montgomery County Department of Health: 610-278-5117; After Hours: 610-275-1222
- ix. Philadelphia Department of Public Health, Division of Disease Control: 215-685-6740, After Hours: 215-686-4514
- x. Wilkes-Barre City Health Department: 570-208-4268; After Hours: 570-208-4268
- xi. York City Bureau of Health: 717-849-2299; After Hours: 717-324-6591

References:

1. Sax H, Bloemberg G, Hasse B, et al. Prolonged Outbreak of Mycobacterium chimaera Infection After Open-Chest Heart Surgery. Clin Infect Dis 2015;
2. Sorin Group Deutschland GMBH. Field Safety Notice: Cardiac Surgery Mycobacterium Risks Disinfection and Cleaning of Sorin Heater Cooler Devices [Internet]. 2015 [cited 2015 Nov 12]; Available from: http://www.livanova.sorin.com/products/cardiac-surgery/perfusion/hlm/3t#product_download_area
3. Sorin Group Deutschland GMBH. Heater-Cooler System 3T --- Operating Instructions [Internet]. 2015; Available from: http://www.livanova.sorin.com/products/cardiac-surgery/perfusion/hlm/3t#product_download_area
4. Food and Drug Administration. Nontuberculous Mycobacterium Infections Associated with Heater- Cooler Devices: FDA Safety Communication [Internet]. 2015 [cited 2015 Nov 11]; Available from: <http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm466963.htm>
5. Centers for Disease Control and Prevention. Non-tuberculous Mycobacterium (NTM) Infections and Heater-Cooler Devices Interim Practical Guidance: Updated October 27, 2015 [Internet]. 2015. Available from: <http://www.cdc.gov/HAI/pdfs/outbreaks/CDC-Notice-Heater-Cooler-Units-final-clean.pdf>
6. Davis, J. Equipment, Environment, and Ergonomics: An Enigma of Infection Risk Pa Patient Saf Advis 2015 Mar;12(1):37-40.

The Pennsylvania Department of Health is responsible for planning and coordinating health resources throughout the Commonwealth. It licenses and regulates a variety of health facilities, such as hospitals, nursing homes, ambulatory surgical facilities and other in-patient and out-patient facilities. Its mission is to promote healthy lifestyles, prevent injury and disease, and to assure the safe delivery of quality health care for all Pennsylvanians.

The Pennsylvania Patient Safety Authority is an independent state agency charged with taking steps to reduce and eliminate medical errors by identifying problems and recommending solutions that promote patient safety in hospitals, ambulatory surgical facilities, birthing centers, abortion facilities and nursing homes, primarily through data collection, education and training. PSAs role is non-regulatory and non-punitive.

Categories of Health Alert messages:

Health Alert: conveys the highest level of importance; warrants immediate action or attention.

Health Advisory: provides important information for a specific incident or situation; may not require immediate action.

Health Update: provides updated information regarding an incident or situation; unlikely to require immediate action.

<p>This information is current as of December 11, 2015, but may be modified in the future. We will continue to post updated information regarding the most common questions about this subject.</p>
