Agenda

- Overview of Heater-Cooler Device Issue
- NTM Infection Incidence
- Chronology of Events and Communications
- Risk Management Implications
- Q&A
Milestones in NTM research

• 1882: Robert Koch: Mycobacterium tuberculosis
• 1882-1900: birds, reptiles, fish, environment
  – “Atypical M. tuberculosis”
• 1900-1950 Sporadic case reports
  – Strains were given names: Battey, Ryan, Mx, IP, …
• 1953: Buhler & Pollak: cavitary NTM lung disease
  – “Yellow bacillus” 2 patients, cavitary disease = M. kansasii
• 1980s: Nodular bronchiectatic lung disease
  – Lady Windermere syndrome
• 1980s: disseminated M. avium disease in HIV/AIDS patients
The birth of M. chimaera

- Enrico Tortoli, 2004
- MAC-A 16S-23S ITS sequevar
  - Stands out within “MAC-X”
- Separate species: M. chimaera
  - Genetic features of Mav + Min
- 10 pulmonary isolates, 1 urine
- 7/10 had M. chimaera lung disease
- “virulence greater than other MAC organisms”

M. Chimaera reality check

- Germany
- Retrospective analysis
- 166 ‘M. intracellulare’ isolates
- 143 (86%) were M. chimaera
- 97 patients with M. chimaera
- 3 (3.3%) M. chimaera lung disease
- All true M. intracellulare isolates caused severe pulmonary infections (?)

Schweickert B. et al., Emerg Infect Dis 2008
M. chimaera, an epidemic species?

- Pub Med
  - 34 papers in 11.5 years
  - 26 cases of disease
- Local data
- The year this far: 81 MAC patients
  - 48 M. avium
  - 15 M. chimaera
  - 13 M. intracellulare
  - 5 other MAC
- Same ratio as last 4 years
The story changes…

- 11 patients (10 M, 1 F)
- Mean age 58 years (1-74)
- Valve replacement surgery (+ dissection)
  - 8 endocarditis, 2 dissem., 1 localized
  - Immunocompetent
  - 6 already died
- All in centers with HCU inside the OR

The story continues…

- Public Health: England, October 6, 2015
- 13 possible cases
- Investigation started
- UK ref lab joins EU typing effort
An then, on October 27, 2015…

- USA!

**Non-tuberculous Mycobacterium (NTM) Infections and Heater-Cooler Devices**

**Interim Practical Guidance: Updated October 27, 2015**

**Purpose:**

CDC has identified a need for increased vigilance for NTM infections by health departments, healthcare facilities, and individual healthcare providers. [FDA recently issued a Safety Communication on Nontuberculous Mycobacterium Infections Associated with Heater-Cooler Devices](https://www.cdc.gov/ntm/index.html) that addresses issues regarding the proper use and maintenance of these devices. CDC has been working with the FDA and local and state health departments to investigate heater-cooler units associated with NTM infections and/or found to be contaminated with NTM. This CDC communication is to (a) raise awareness among health departments, healthcare facilities, and healthcare providers of the possible association between NTM infections and use of heater-cooler devices and (b) to provide guidance on identifying patients with infection.
2016

UPDATE: Mycobacterium chimaera Infections Associated with LivaNova PLC (formerly Sorin Group Deutschland GmbH) Stöckert 3T Heater-Cooler System: FDA Safety Communication

The FDA is updating its June 1, 2016 Safety Communication (//MedicalDevices/Safety/AlertsandNotices/ucm504213.htm) to provide new information about *Mycobacterium chimaera* (M. chimaera) infections associated with the use of the 3T in U.S. patients who have undergone cardiothoracic surgeries. This communication also contains updated recommendations to help prevent the spread of infection related to the use of these devices.

October 13, 2016
Audiences:
- Health care providers who use 3T Heater-Cooler System
- Primary care providers who are responsible for the ongoing care of patients who have undergone cardiothoracic surgery
- Patients who have undergone cardiothoracic surgery
- Hospital staff who are responsible for operating and maintaining 3T Heater-Cooler System
- Health care facilities that perform procedures using the 3T Heater-Cooler System

Medical Specialties: Cardiothoracic Surgeons, Cardiovascular Surgeons, Orthopedic Surgeons, Neurosurgeons, General Surgeons, Anesthesiologists, Infection Control, Infectious Disease Physicians, Pediatrics, Primary Care, and Intensive Care Physicians

Product: The Stöckert 3T Heater-Cooler System (3T), manufactured by LivaNova PLC (formerly Sorin Group Deutschland GmbH), is intended to provide temperature-controlled water to 1) oxygenator heat exchangers, 2) cardioplegia (paralysis of the heart) heat exchangers, and/or 3) warming/cooling blankets to warm or cool a patient during cardiopulmonary bypass procedures lasting six hours or less.

The Centers for Disease Control and Prevention (CDC) has informed us that Stöckert 3T Heater-Cooler devices manufactured by LivaNova PLC (formerly Sorin Group Deutschland GmbH) may have been contaminated with *Mycobacterium chimaera* (M. chimaera) in the manufacturing process, and that patients for whom these devices were used during cardiac surgery may be at risk of developing infections. On Thursday, Oct. 13, CDC will publish information in the *Morbidity and Mortality Weekly Report* detailing its research about this potential device-related infection risk and issue a Health Advisory.

October 12, 2016

**The Issue**

The CDC has informed us that Stöckert 3T Heater-Cooler devices manufactured by LivaNova PLC (formerly Sorin Group Deutschland GmbH) may have been contaminated with *Mycobacterium chimaera* (M. chimaera) in the manufacturing process, and that patients for whom these devices were used during cardiac surgery may be at risk of developing infections. On Thursday, Oct. 13, CDC will publish information in the *Morbidity and Mortality Weekly Report* detailing its research about this potential device-related infection risk and issue a Health Advisory.

**Embargoed for Media Until Thursday, Oct. 13, at 1 PM ET**
Tainted Heart-Surgery Machine Said to Infect 12 in Pennsylvania

By SABRINA TAVERNISE

WASHINGTON — A device used during open-heart surgery that infected at least 12 patients at a Pennsylvania hospital last year was probably tainted at the plant in Germany where it was made, a federal investigation has found.

The device, called a heater-cooler machine, uses water to regulate the temperature of patients having heart surgery. The water does not come into contact with the patient, but bacteria can be transmitted through the air from the device’s exhaust vent.

That seems to be what happened to 12 heart patients at a hospital in York last year. The heater-cooler machine was contaminated with Mycobacterium chimaera, bacteria that can be found in soil and water. Six patients died, though officials said it was not clear whether the infection was the primary cause. The infection was identified at other hospitals, too.

It was not clear at the time exactly how people had been infected. So disease sleuths from the Centers for Disease Control and Prevention and the Pennsylvania Health Department took samples from 11 patients and five devices from hospitals in Pennsylvania and Iowa, two of the states where clusters of infections had been identified. There were also infections in Europe.

The investigators found that all of the samples had the same genetic fingerprint, a sure sign that the infections came from the same place, probably the plant in Germany.

The highly specialized devices, called Sorin Stöckert 3Ts, are used in about 60 percent of the 250,000 heart bypass procedures that require such machines each year, and there are few alternatives.

But Dr. Michael Bell, an expert at the C.D.C., said that the risk of infection from the device was very low — from about 1 in 100 to 1 in 1,000 in hospitals where at least one infection had been identified — and that the agency was recommending that medical staff and patients be aware of the problem, not stop using the devices.

The bacteria are not usually harmful, but they can infect patients who are seriously ill or who have compromised immune systems, causing fever, weight loss, joint pain and energy loss. But the infection is slow, growing over months or years, and it can be treated if it is caught.

LivaNova, the London-based company that owns the German manufacturer, said it was “proactively and voluntarily contacting 3T heater-cooler users to inform them of the new information.”
Why M. chimaera?

A. Because it is well adapted to survival at body temperature
B. Because it is resistant to commonly used disinfectants
C. Pure coincidence, right place-right time story
D. Because it is good at biofilm formation on metal surfaces
The mycobacterial cell wall

- Outer membrane (like Gram neg’s)
- Mycolic acids
- Extremely hydrophobic
- Preference for surface attachment
  - Biofilms (resistance!)
- Prefer aerosolization from water
- Disinfectant resistance
- Heat resistance (M. avium, M. xenopi)
- Hence NTM thrive in – and spread from – treated tap water systems!
The story continues…

• There is an (ongoing?) outbreak of M. chimaera endocarditis/severe disease
• Related to cardiac surgery in ORs with Sorin 3T heater cooler units
• NTM highly able to cause instrument-related outbreaks
• Why M. chimaera? Unknown still, but work is ongoing
• Other than that, M. chimaera is not an epidemic species
Joint Cardiac and Thoracic Surgery Society Statement on Mycobacterium Chimaera Infections Related to Heater-Cooler Devices Used in Cardiac Surgery

The worldwide cardiothoracic surgery community is aware of the public health issue with recent heater-cooler infection findings traced to a manufacturing facility and has actively engaged in understanding the cause and developing measures to lower the risk and occurrences of these infections. To date, *Mycobacterium chimaera* infections related to heater-cooler devices have been reported in Europe and North America (i.e., Germany, the Netherlands, Switzerland, the United Kingdom, the United States, and Canada).

Cardiac and thoracic surgery societies throughout the world are united in efforts to share information, including practices, protocols, and mitigation strategies that have been deployed and utilized by our members, their institutions, and other health care experts, especially infectious disease experts. Cardiothoracic surgeons remain committed to offering a safe environment for patients.

In issuing this statement, our goals are to 1) communicate with the global cardiothoracic surgery community and its patients regarding protocols that have been developed, and 2) offer information from credible sources.

A US Centers for Disease Control and Prevention (CDC) Health Advisory and a US Food and Drug Administration Safety Communication provide detailed approaches for health care providers, hospitals, health departments, and patients. The undersigned societies support the CDC’s advice that patients who have undergone cardiac surgery and are at risk of *M. chimaera* infection should be informed about the infection, provided a list of possible symptoms, and urged to seek early medical advice should these symptoms develop. In addition, we suggest that you review your consent processes for patients who are about to undergo cardiac surgery in order to help ensure that these kinds of potential risks are covered.

You can access more heater-cooler infection information at [www.sts.org/news/infections-related-heater-cooler-devices](http://www.sts.org/news/infections-related-heater-cooler-devices). You also may want to view the 1-hour CDC webinar “Invasive NTM Infections and Heater-Cooler Units.”

At the upcoming STS Annual Meeting in Houston (January 21-25, 2017), a special symposium will be offered on the heater-cooler situation. This symposium will include presentation of data, reflect policy from various constituents, and offer a panel discussion of clinical implications featuring cardiothoracic surgeons and infectious disease experts. More details will be available as they develop.

Sincerely,

Joseph E. Bavaria, MD
President, The Society of Thoracic Surgeons

[www.sts.org](http://www.sts.org)
When to think about *M. chimaera*

- Patients with cardiopulmonary bypass with heater cooler exposure AND
  - Nonfocal but progressive/severe systemic symptoms of fatigue, myalgias, night sweats or fever
  - Culture negative endocarditis
  - Labs with transaminitis/elevated alkaline phosphatase, cytopenias, kidney injury not otherwise explained. Lab abnormalities can be minor despite disseminated infection
  - Retinal exam may be suggestive
  - Tissue biopsy with findings of granulomas or sarcoid in a patient with heater cooler exposure
  - Any culture with *Mycobacterium avium* complex, *M intracellulare/chimaera*
Nontuberculous Mycobacterial Infections Associated with Heater-Cooler Devices

Emily K. Shuman, MD
Assistant Professor, Division of Infectious Diseases
Associate Hospital Epidemiologist, Department of Infection Prevention and Epidemiology
Assistant Medical Director, Occupational Health Services
Outline

• Overview of nontuberculous mycobacteria (NTM)/Mycobacterium chimaera
• Review of the literature on NTM infections associated with heater cooler devices
• UMHS process for evaluation of patients with symptoms concerning for NTM infection
Overview of NTM

- NTM are free-living organisms that are ubiquitous in the environment (e.g., water, soil)
- Mycobacteria = acid-fast bacilli
- Special culture techniques are required to isolate and identify mycobacteria
M. chimaera

- Part of the M. avium complex (MAC)
- Slowly growing organism
- Typically susceptible to antimicrobials including azithromycin, moxifloxacin, rifampin, ethambutol, and amikacin
  - Prolonged treatment with 3-4 antimicrobials required
University Hospital, Zurich - 2012

- 6 cases of *M. chimaera* infection
  - All underwent cardiac surgery with cardiopulmonary bypass and placement of implant (valve, graft)
  - Infections developed 1.5-3.6 years after surgery
  - Symptoms and clinical findings:
    - Fever, fatigue
    - Splenomegaly, 5/6 ocular emboli
    - Pancytopenia, acute kidney injury, LFT elevation
    - Positive cultures: 4/6 cardiac tissue, 2/6 blood, 2/6 bone, 1/6 sputum, 1/6 urine, 1/6 bone marrow
    - Imaging: 5/6 endocarditis
  - Outcomes: 3/6 required valve replacement, 1/6 required surgical debridement, 2/6 died despite combination antimicrobials

Sax et al, Clin Infect Dis, 2015
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y</th>
<th>Date of Index Surgery</th>
<th>Latency, y</th>
<th>Heart Surgery</th>
<th>Implant</th>
<th>Material</th>
<th>Manifestations</th>
<th>Positive Cultures for Mycobacterium chimaera</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1&lt;sup&gt;1&lt;/sup&gt;</td>
<td>58</td>
<td>Aug 2008</td>
<td>2.9</td>
<td>Mitral valve reconstruction</td>
<td>29 mm C-E physio mitral annulopexy ring (model 4480; serial no. 1712653, lot no. 08E134)</td>
<td>Layers of Ethiglof Sewing ring with layers of silicone covered by polyester knit fabric</td>
<td>Endocarditis, splenomegaly, pancytopenia, hepatitis, renal involvement</td>
<td>Blood, cardiac tissue prosthesis, sputum</td>
<td>Granulomatous hepatitis, nephritis</td>
</tr>
<tr>
<td>Patient 2&lt;sup&gt;2&lt;/sup&gt;</td>
<td>51</td>
<td>Jan 2010</td>
<td>1.5</td>
<td>Composite graft for aortic dissection</td>
<td>25 mm ATS composite graft (serial no. 408588, lot no. 823A826); 8 mm GAF Gel weave x protein (serial no. 0011779877; lot no. 101 1387/1A 1677)</td>
<td>Heart valve: pyrolytic carbon; Graft: double woven velour</td>
<td>Endocarditis, pancytopenia, splenomegaly, hepatitis, pulmonary, ocular emboli</td>
<td>Blood, sputum, bone marrow, urine</td>
<td>Granulomatous myocarditis, pneumonia, nephritis, involvement of aorta</td>
</tr>
<tr>
<td>Patient 3</td>
<td>64</td>
<td>June 2009</td>
<td>3.6</td>
<td>Mitral valve reconstruction</td>
<td>32 mm x 2 mm Carpentier ring (model 445, serial no. 0944171, lot no. 0950552)</td>
<td>Layers of Ethiglof Sewing ring with layers of silicone covered by polyester knit fabric</td>
<td>Endocarditis, pancytopenia, splenomegaly, hepatitis, renal involvement, ocular emboli</td>
<td>Cardiac tissue and prosthesis, bone (wrist)</td>
<td>Granulomatous osteomyelitis</td>
</tr>
<tr>
<td>Patient 4</td>
<td>49</td>
<td>Oct 2009</td>
<td>3.4</td>
<td>Aortic valve replacement</td>
<td>26 mm ATS Open Pivot AP Series Heart Valve (model 565424; serial no. 409100)</td>
<td>Heart valve: pyrolytic carbon graft; double woven velour</td>
<td>Endocarditis, pancytopenia, splenomegaly, hepatitis, ocular emboli, pacemaker pocket infection</td>
<td>Cardiac tissue and prosthesis, deep tissue samples of pacemaker pocket</td>
<td>Granulomatous hepatitis, myositis</td>
</tr>
<tr>
<td>Patient 5</td>
<td>61</td>
<td>May 2012</td>
<td>1.7</td>
<td>Aortic root and arch replacement</td>
<td>ATS AVG (model 302A023; serial no. 823707); 26 mm grafts as elephant trunk (model 150028-50; serial no. 14262231, lot no. 11J19)</td>
<td>Valve: pyrolytic carbon; Hemashield Woven Double Velour Graft; Elephant trunk: collagen coated external velour polyester graft</td>
<td>Vascular graft infection, Bone (vertebral and sternum osteomyelitis), Spleenomegaly, Ocular emboli</td>
<td>Vertebral bone</td>
<td>Granulomatous osteomyelitis</td>
</tr>
<tr>
<td>Patient 6</td>
<td>63</td>
<td>March 2012</td>
<td>1.8</td>
<td>Aortic root and arch replacement</td>
<td>Medtronic Freestyle Aortic Valve (model 13502995; serial no. 2222)</td>
<td>26 x 8 mm, 50 cm</td>
<td>Vascutek, serial no. 0001159091, lot no. 104368 1367</td>
<td>Vascular graft infection, splenomegaly, hepatitis, renal failure, multifocal choroiditis</td>
<td>Cardiac tissue and prosthesis</td>
</tr>
</tbody>
</table>
University Hospital, Zurich - 2012

- *M. chimaera* cultured from water and air samples from Sorin Stockert 3T heater-cooler device used for cardiopulmonary bypass

Sax et al, Clin Infect Dis, 2015
Elsewhere in Europe - 2014

• Four cases identified in Germany and the Netherlands, including a 1 year old child
• Median duration from surgery to diagnosis of infection was 21 months (range, 5-40 months)
• Similar clinical presentation, lab, and echo findings
  – Night sweats and weight loss
  – CRP and LDH elevation

Kohler et al, Eur Heart J, 2015
European cohort: clinical findings

Kohler et al, Eur Heart J, 2015
European cohort: susceptibility testing

### Table 2 Phenotypic drug susceptibility testing of 15 M. chimaera isolates of the 10 study patients

<table>
<thead>
<tr>
<th>Samples date Material</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral ring</td>
<td>30.06.11</td>
<td>27.07.11</td>
<td>10.05.12</td>
<td>20.03.13</td>
<td>07.02.14</td>
<td>06.03.13</td>
<td>13.06.13</td>
<td>06.01.14</td>
<td>10.09.14</td>
<td>14.01.14</td>
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<tr>
<td>Bone marrow</td>
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<tr>
<td>Urine</td>
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<tr>
<td>Bone Wrist</td>
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<tr>
<td>Mitral ring</td>
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<tr>
<td>Cardiac tissue</td>
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<tr>
<td>Pocket tissue</td>
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<tr>
<td>Vertebral bone</td>
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<tr>
<td>Urine</td>
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<tr>
<td>Cardiac tissue</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>Clarithromycin</th>
<th>Moxifloxacin</th>
<th>Linezolid</th>
<th>Amikacin</th>
<th>Rifampicin</th>
<th>Rifabutin</th>
<th>Ethambutol</th>
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<tbody>
<tr>
<td>1</td>
<td>≤4</td>
<td>2.5</td>
<td>ND</td>
<td>20</td>
<td>&gt;1&lt;20</td>
<td>&gt;0.1&lt;2</td>
<td>≤5</td>
</tr>
<tr>
<td>2</td>
<td>≤4</td>
<td>2.5</td>
<td>16</td>
<td>20</td>
<td>&gt;1&lt;20</td>
<td>0.4</td>
<td>≤5</td>
</tr>
<tr>
<td>3</td>
<td>≤4</td>
<td>2.5</td>
<td>ND</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>≤5</td>
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<tr>
<td>4</td>
<td>≤4</td>
<td>0.5</td>
<td>16</td>
<td>4</td>
<td>4</td>
<td>0.4</td>
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<td>0.4</td>
<td>≤5</td>
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<td>6</td>
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<td>7</td>
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<td>16</td>
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<td>2</td>
<td>0.5</td>
<td>≤5</td>
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<tr>
<td>8</td>
<td>≤4</td>
<td>2.5</td>
<td>16</td>
<td>4</td>
<td>4</td>
<td>0.5</td>
<td>≤0.25</td>
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<td>9</td>
<td>2</td>
<td>4</td>
<td>16</td>
<td>4</td>
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<td>2</td>
<td>4</td>
<td>16</td>
<td>4</td>
<td>2</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>

Data are minimum inhibitory concentrations, in mg/L. ND, not done, minimum inhibitory concentrations, MICs. MGIT method applied in Patients 1–6, the broth dilution method has been applied in Patients 7–10.

Kohler et al, Eur Heart J, 2015
European cohort: outcomes

Kohler et al, Eur Heart J, 2015
Germany - 2015

- 5 additional cases identified through active case finding

**Table 1**
Cases with symptomatic *Mycobacterium chimaera* infection, notified between April 2015 and February 2016, Germany (n=5)

<table>
<thead>
<tr>
<th>Case number</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Cardiac surgery centre</th>
<th>Type of surgery (exposure)</th>
<th>Prosthetic material</th>
<th>Site of Infection</th>
<th>Death due to Infection</th>
<th>Incubation period (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>80</td>
<td>Male</td>
<td>A</td>
<td>Aortic valve replacement</td>
<td>Yes</td>
<td>Endocarditis</td>
<td>No</td>
<td>&lt;1</td>
</tr>
<tr>
<td>2</td>
<td>75</td>
<td>Male</td>
<td>B</td>
<td>CABG</td>
<td>No</td>
<td>Spondylodiscitis</td>
<td>No</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>65</td>
<td>Male</td>
<td>C</td>
<td>Aortic valve replacement</td>
<td>Yes</td>
<td>Valvular aortic endocarditis, paravalvular leak and abscess</td>
<td>Yes</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>67</td>
<td>Male</td>
<td>C</td>
<td>CABG and aortic valve replacement</td>
<td>Yes</td>
<td>Paravalvular abscess</td>
<td>No</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>53</td>
<td>Male</td>
<td>C</td>
<td>Aortic valve replacement</td>
<td>Yes</td>
<td>Endocarditis and cerebral abscesses</td>
<td>No</td>
<td>3</td>
</tr>
</tbody>
</table>

CABG: coronary artery bypass grafting.

\(^{a}\) Time between exposure to open chest surgery involving use of an HCU and clinical diagnosis.

\(^{b}\) Currently in palliative care.

\(^{c}\) Endocarditis lenta and change of aortic valve in September 2013.

Haller et al, Euro Surveill, 2016
Germany - 2015

• *M. chimaera* cultured from new heater-cooler units at manufacturing site

Haller et al, Euro Surveill, 2016
4 Dead After Being Infected by a Device in Surgery at a Pennsylvania Hospital

By SABRINA TAVERNSE  OCT. 26, 2015

At least eight people who received treatment at a hospital in York, Pa., have developed an infection from a medical device used during open-heart surgery, hospital and health officials said. Four of those who were infected have died, though officials said it was not clear whether the infection was the primary cause.

WellSpan York Hospital said Monday it was notifying about 1,300 current and former patients of possible exposure to potentially harmful bacteria during open-heart surgeries performed over nearly four years, from Oct. 1, 2011, to July 24, 2015. The hospital said the infection had been identified in less than 1 percent of patients who had open-heart surgery during the period.

The Food and Drug Administration said it had received 32 reports of infected patients or bacterial contaminations associated with the devices, which are used to heat and cool a patient’s blood during heart surgery. Of those, 25 were reported this year. Eight of the reported infections happened in the United States; the rest were contracted in Europe. It was not clear if those American cases were at York Hospital.
• 3 patients with *M. chimaera* infection after undergoing cardiac surgery with implanted valve or graft 16-26 months previously (all at outside institutions)
  – Similar clinical presentation to European cohort
    • 2/3 had chorioretinitis
    • 3/3 had noncaseating granulomas with negative cultures on bone marrow biopsy
    • 2/3 died

Tan et al, Open Forum Infect Dis, 2016
US Experience

• 24 cases at four healthcare systems as of 7/24/16
  – Surgical procedures:
    • Prosthetic valve/ring: 46%
    • Vascular graft: 29%
    • LVAD: 21%
    • Heart transplant: 13%
    • CABG: 4%
  – Mean age 60, 88% male
  – Mean time to diagnosis: 1.6 years (range, 0.1-6.3 years)
  – 83% deep-seated, often with dissemination
  – 8 cases identified though lookback and provider notification, none through notification of ~10,000 patients

Appenheimer et al, ID Week #2392
Table 1. Clinical characteristics of probable cases (N=18) of severe *M. chimaera* infection associated with cardiopulmonary bypass surgery, UK

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All cases N=18</th>
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<tbody>
<tr>
<td>Female, n (%)</td>
<td>5 (28)</td>
</tr>
<tr>
<td>Median age (range), y</td>
<td>63 (7-81)</td>
</tr>
<tr>
<td><strong>Type of surgery, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Aortic valve replacement</td>
<td>14 (77)</td>
</tr>
<tr>
<td>Mitral valve replacement</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Aortic valve replacement and homograft to pulmonary valve (redo)</td>
<td>1 (6)</td>
</tr>
<tr>
<td><strong>Site of infection, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Sternal osteomyelitis</td>
<td>2 (11)</td>
</tr>
<tr>
<td>Anterior mediastinal abscess</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Spinal osteomyelitis and discitis</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>5 (28)</td>
</tr>
<tr>
<td>Endocarditis, aortic root abscess</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Endocarditis, disseminated infection</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Disseminated infection</td>
<td>3 (17)</td>
</tr>
<tr>
<td><strong>Median time between surgery and presentation (range), y</strong></td>
<td>115 (0-25-51)</td>
</tr>
<tr>
<td><strong>Median time between presentation and first mycobacterial culture (range), d</strong></td>
<td>85 (6-457)</td>
</tr>
<tr>
<td><strong>Outcome, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>9 (50)</td>
</tr>
<tr>
<td>Recovered</td>
<td>2 (11)</td>
</tr>
<tr>
<td>Remains unwell and on treatment</td>
<td>7 (38)</td>
</tr>
<tr>
<td><strong>Median time between culture and death (range), d</strong></td>
<td>71 (14-567)</td>
</tr>
</tbody>
</table>

Chand et al, Clin Infect Dis, 2016
Evaluation of Patients with Symptoms Concerning for NTM Infection

• From patient letter:

Symptoms of an NTM infection may include:

- Night sweats
- Muscle aches
- Weight loss

- Unexplained fever
- Drainage or redness of surgical wound

To discuss any symptoms you’re experiencing, or if you have other questions or concerns, we established a Hotline at (855) 336-5900. Representatives are available Monday through Friday from 8 a.m. to 5 p.m. There is more information at http://umhealth.me/2eml7K8.
Evaluation of Patients with Symptoms Concerning for NTM Infection

Adult Screening Questions

Are you currently having any of the following symptoms for at least 1 week?

1. Fever (temperature > 100.4°F):
   a. How often have you had fevers?
   b. How long have you had fevers?
2. Chills (more severe than feeling a bit cool, lasting at least 5 minutes and not relieve with extra heat/blankets):
   a. How often have you had chills?
   b. How long have you had chills?
3. Drenching night sweats (severe enough to consider changing pajamas and/or sheets):
   a. How often have you had night sweats?
   b. How long have you had night sweats?
4. Pain, redness, or drainage from the site of your open heart surgery:
   a. How long have these symptoms been present?
5. Fatigue that cannot be explained by activity or lack of sleep:
   a. Has the fatigue limited your ability to perform routine daily activities (e.g., household chores)?
   b. How long has the fatigue been present?
6. Unintentional weight loss of more than 10 pounds:
   a. How much weight have you lost?
7. Unexplained change in vision or presence of "floaters" in visual field (not related to another medical condition):
   a. How long have you noticed problems with your vision?
8. Have you experienced muscle aches?
   a. How long have the muscle aches been present?
9. Any other symptoms that you are concerned about?
10. Any other ongoing health concerns or complaints?
NTM Screening Process

1. Patient calls MLine number and leaves contact information.
2. Patient is contacted by NP/PA or other provider from relevant service. MiChart screening questionnaire is completed (see separate document). Patients who have positive symptom screen will be offered evaluation in appropriate surgical clinic. Positive symptom screen consists of the following:
   a. Answers “yes” to any one of questions 1-4 from screening questionnaire.
   b. Answers “yes” to any two questions including 5-8 from screening questionnaire.
3. Patient is evaluated in the appropriate surgical clinic if indicated based on screening questionnaire. Patients answering “yes” to 3 or more questions should receive expedited evaluation (within 1-2 weeks). The following evaluation should be performed in the appropriate surgical clinic:
   a. Complete physical examination
   b. Laboratory evaluation: CBC, comprehensive metabolic panel, ESR, CRP, routine blood cultures x 2 sets, AFB blood cultures
   c. Imaging: echocardiogram (if symptoms are new since last echo or no echo within 6 months- please use clinical judgment)
   d. Other imaging based on symptoms (e.g., ultrasound or CT for abdominal pain)
4. Patient is referred to ID clinic if both of the following criteria are met:
   a. Symptoms are confirmed on evaluation in heater-cooler clinic.
   b. Significant laboratory or imaging abnormalities are noted, including any of the following:
      i. Low cell counts (WBC, platelets)
      ii. Elevated LFTs
      iii. Elevated ESR, CRP
      iv. Positive blood cultures
      v. Vegetation on echocardiogram
Evaluation of Patients with Symptoms Concerning for NTM Infection

• Additional information:
  – For patients with surgical site infection, any tissue obtained during debridement or other surgical intervention should be sent for AFB cultures
  – Referral to ophthalmology should be considered for patients with visual symptoms
Summary

- NTM infection associated with exposure to heater-cooler devices is a relatively rare but serious complication
  - Risk of infection estimated to be 1/100-1/1,000
    - Association with implanted valve or graft
    - Mortality rates ~50% in case series even with appropriate treatment
- Infection can be localized to the surgical site or disseminated
- Diagnosis of NTM infection is challenging and requires a high index of suspicion
  - Delayed onset of vague symptoms (up to 6 years)
  - Requires multimodality testing (laboratory, imaging, biopsy)
- Treatment is complex and requires prolonged multidrug antibiotic therapy +/- surgical intervention
Questions?