

# City Wide ID Conference

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# CHIEF COMPLAINT(S)

60's year old male presenting with:  
Dizziness and right sided hemiparesis

- PMH: Atrial fibrillation (Admits to not taking warfarin for AC), HTN, Prior ETOH abuse (d/c 1 month prior), Severe mitral regurgitation
- PSx: Mitral valve repair 6 years ago, prosthetic mitral valve replacement 2 years ago. C-scope within 5 years WNL.
- Social History: Born in VA. Office worker in Philadelphia. No outdoors exposure. Former ETOH abuse. No tobacco use or IVDU. No recent dental work.
- Allergies: NKDA
- Medications: ?Warfarin, Insulin, Metoprolol, Aspirin

# Patient Case

- **4 days Pre-Admission:** Patient presents with low grade fevers at home and URI symptoms. ED obtains NEGATIVE flu swab. CXR WNL. Discharged with supportive care.
- 
- **Day 1:** Patient re-presents to ED with sudden onset right sided weakness and dysarthria. Stroke alert called and patient admitted to NICU for full neurologic work up. Given tPA emergently. CT scan head negative. MRI brain possible small midbrain infarct, later corrected by radiology as normal study.
  - **Day 2:** Overnight in the NICU, patient develops fever up to 102.5 degrees and leukopenia (WBC 3)- growing concern for meningitis. Blood cultures obtained prior to initiation vancomycin, ceftriaxone, and ampicillin.

# Physical Exam

- VS: T 98.6 -> 101.2, HR 61, BP 155/95, RR 20, 96% RA
- GENERAL: Oriented to person, place, and time. Does not appear distressed. Not making eye contact.
- HENT: Normocephalic, atraumatic, **poor dentition**.
- EYES: **+Dysconjugate gaze** (improving), **+Scleral icteris**, PERRL, EOMI
- NECK: **Supple**
- CV: Normal rate and **irregularly irregular rhythm**. A **murmur** is present.
- PULM/CHEST: Effort normal and breath sounds normal.
- ABD: Abdomen is soft, he has no distension. There is no tenderness.
- MSK: No Edema. Strength and ROM WNL.
- LYMPH: No cervical adenopathy.
- NEURO: AAOx3, **+dysarthria**, **+mild R facial droop**. VF grossly intact to confrontational testing. +RUE pronator drift. Strength 5/5 throughout.
- SKIN: Skin is warm and dry. No rash noted, noes, splinter hemorrhages.

# Laboratory Findings

- WBC 3 (52% PMN, 28% lymphocytes)
- Hgb 11.2
- Plt 188
- INR 1.42
- Cr 1.4
- Alk Phos 643
- AST 140/ ALT171
- TB 3.3/ DB 2.1

# Patient Case

- **Day 3:**
  - LP performed: CSF protein 36, glucose 54, WBC 0, 2 RBC, OP 24, biofire panel negative, ctx neg.
  - LFTs noted to be rising. Patient has no known biliary disease. Abdominal US neg.
  - Blood cultures obtained again. Antibiotics stopped.
  - TTE performed 2/2 A.fib without AC and concern for endocarditis given persistent fevers and worsening leukopenia (WBC 0.9/ANC 470)

# Echocardiography

## 1. TTE

- Left atrium is moderately dilated.
- Mildly decreased left ventricular systolic function with global hypokinesis.
- Concentric, left ventricular hypertrophy.
- Normal right ventricular size.
- No evidence of a patent foramen ovale.
- Prosthetic mitral valve appears normal.
- Focal calcification of the aortic valve with mild aortic regurgitation

## 2. TEE

- Several vegetations noted on the atrial surface of the mitral prosthesis, the largest is a ovoid structure measuring approximately 9mm x 5mm on the mid segment of the anterior leaflet.
- Several smaller more mobile grape like vegetations and a circular lesion on the posterior leaflet near its tip measuring about 3mm.
- Moderately decreased left ventricular systolic function with global hypokinesis.
- The clinically suspected endocarditis is documented to infect both leaflets of the mitral prosthesis.



- **Day 5:** Patient still febrile off antibiotics with positive results of TEE, patient is started on IV cefepime and vancomycin for possible endocarditis. **Consulted ID.** Gentamicin added for prosthetic valve endocarditis. Hold rifampin 2/2 rising LFTs. **Consult CT surgery.** Ask to hold cultures longer than 5 days. All sets so far negative.
- **Day 6:** Due to worsening LFTs, **GI consulted** and MRCP performed to rule out biliary obstruction.
- **Day 9:** Due to persistent rise in LFTs, liver biopsy performed and consistent with **chronic granulomatous hepatitis**, likely DILI vs. sarcoidosis. Thought to be due to antibiotics so cefepime, vancomycin and gentamicin discontinued; started on IV daptomycin and full anticoagulation. Blood cultures are persistently negative.
- **Day 10:** Discharged with plan for 6 weeks of IV daptomycin

# Review

- 60's yo M presenting with dysarthria and right sided weakness, w/u CVA. Persistent fevers with transaminitis and pancytopenia, found to have culture negative endocarditis.

# Discussion

- Differential diagnosis for culture negative prosthetic valve endocarditis with liver, renal, and possibly bone marrow involvement

- **1 months later:** Still with fevers at rehab; transferred back to TJUH and had repeat TEE demonstrating improvement in MV vegetation on antibiotics and full AC. However, patient still with fevers and pancytopenia. A **bone marrow biopsy** performed by hematology demonstrated hypercellular marrow without dysplasia, granulomas, and negative cultures.
- Pancytopenia thought to be 2/2 daptomycin so transitioned to IV vancomycin. CBC improved, fevers subsided. Discharged to rehab.
- **3 weeks later:** Returned to hospital with fevers from rehab again. Stopped vancomycin (now has had 6 weeks of IV antibiotics cumulatively) without clinical improvement and negative infectious work up. Fevers down trending. Hospice discussion with family.
- Entire infectious work up repeated and found negative. 1x Anti-cardiolipin IgG positive (titer 47), ANA + x2 with 1:160, and negative infectious workup (coxiella, bartonella, legionella, routine blood cultures (held 10 days) and fungal blood cultures. AFB cultures sent but predicted to have low yield. Discharged home.

- **3 weeks later:** Brought to hospital by wife with failure to thrive, anorexia, weight loss. Labs show hemolytic anemia with schistocytes, pancytopenia. Denied fevers at this time.
- TEE: Compared with 1 month ago, the anterior mitral leaflet vegetation is more extensive and there now is a vegetation on the posterior leaflet at the area of contact with the anterior leaflet vegetation. The LV is somewhat less dynamic.
- During this hospital stay **AFB blood culture positive MAC** (3 weeks after initial culture drawn). Sent for speciation and susceptibilities.

# Discussion

- What antimicrobial therapy should we start now that we have an organism?
- What MAC species do we expect to be identified?
- What further testing should we perform at this time?
- How did the patient obtain this infection?

- Send out AFB confirmed ***Mycobacterium chimaera*** by 16S rDNA sequencing. All routine blood cultures are NGTD.
- **3 months after initial presentation:**
  - Started on azithromycin 600 qday
  - Rifabutin 150mg PO qday
  - Ethambutol 15 mg/kg PO qday
  - Moxifloxacin 400mg PO qday.
- **This month:** Unfortunately presents again to hospital with fevers, pancytopenia and AKI. TTE repeated this month demonstrates "bioprosthetic mitral valve with irregular echodensities that appear to rock" as well as moderate to severe MS. CT surgery states he is a very high risk surgical candidate. Family decision pending.

**Microbiology Data:**9/22 AFB BCX: **MAC**9/22 AFB BCX: **MAC** (susceptibilities pending. Sent out 10/26/17)

10/16 AFB BCX: NGTD

10/17 AFB BCX: **AFB isolated**10/17 AFB BCX: **AFB isolated**

ANTIMICROBIAL	(mcg/mL)	INTERP
AMIKACIN	32	
CIPROFLOXACIN	16	
CLARITHROMYCIN	4	S
ETHAMBUTOL	16	
ETHIONAMIDE	10	
ISONIAZID	4	
LINEZOLID	32	R
MOXIFLOXACIN	4	R
RIFAMPIN	8	
RIFABUTIN	0.5	
STREPTOMYCIN	32	

# *Mycobacterium chimaera*

- Nontuberculous mycobacteria named in 2004 based on 16S rRNA gene sequencing
- MALDI is unable to distinguish *M. chimaera* from other members of MAC complex
- Typically less virulent than *M. avium* and *M. intracellulare*
- Associated most commonly with pulmonary infections in the past
- Infections with this organism are on the rise in patients with history of cardiothoracic surgeries (aortic grafts or valvular surgeries) in US and Europe



# Endovascular infections with *M. chimaera*

- Several reported cases in the US and Europe
- Present with typical symptoms of endocarditis: fevers, chills, weight loss, fatigue, +/- heart failure symptoms
- Presentation typically months to years after initial cardiac surgery
- Often mistaken for sarcoidosis due to disseminated nature of the disease and mild improvement with steroid therapy initially
- Treatment typically involved 4 drug therapy
- Frequently susceptible to clarithromycin, intermediate to moxifloxacin and linezolid
- Infection remains difficult to eradicate even with surgical intervention
- **We suspect the original source of the this infection was the heater-cooler device used during cardiopulmonary bypass during his open heart surgery in 8/2015.**

# References

- Tan et al; Disseminated *Mycobacterium chimaera* Infection After Cardiothoracic Surgery, *Open Forum Infectious Diseases*, Volume 3, Issue 3, 1 May 2016, ofw131, <https://doi.org/10.1093/ofid/ofw131>
- Achermann et al; *Prosthetic Valve Endocarditis and Bloodstream Infection Due to Mycobacterium chimaera*. J. Clin. Microbiol. **June 2013** vol. 51 no. 6 **1769-1773**

# Contamination of Heater-Cooler Units with *Mycobacterium* *chimaera*

Mitchell Sternlieb, MD

PGY 5-ID fellow

Thomas Jefferson University Hospital.

# Chimaera

- "a thing of immortal make, not human, lion-fronted and snake behind, a goat in the middle, and snorting out the breath of the terrible flame of bright fire."  
-Homer, *Illiad*
- Organism so named due to genetic relatedness and distinction from several members of the MAC, and a sequevar of *M. intracellulare*-  
Tortolli et al, 2004.



<http://harrypotter.wikia.com/wiki/Chimaera>

# Epidemiology of infection

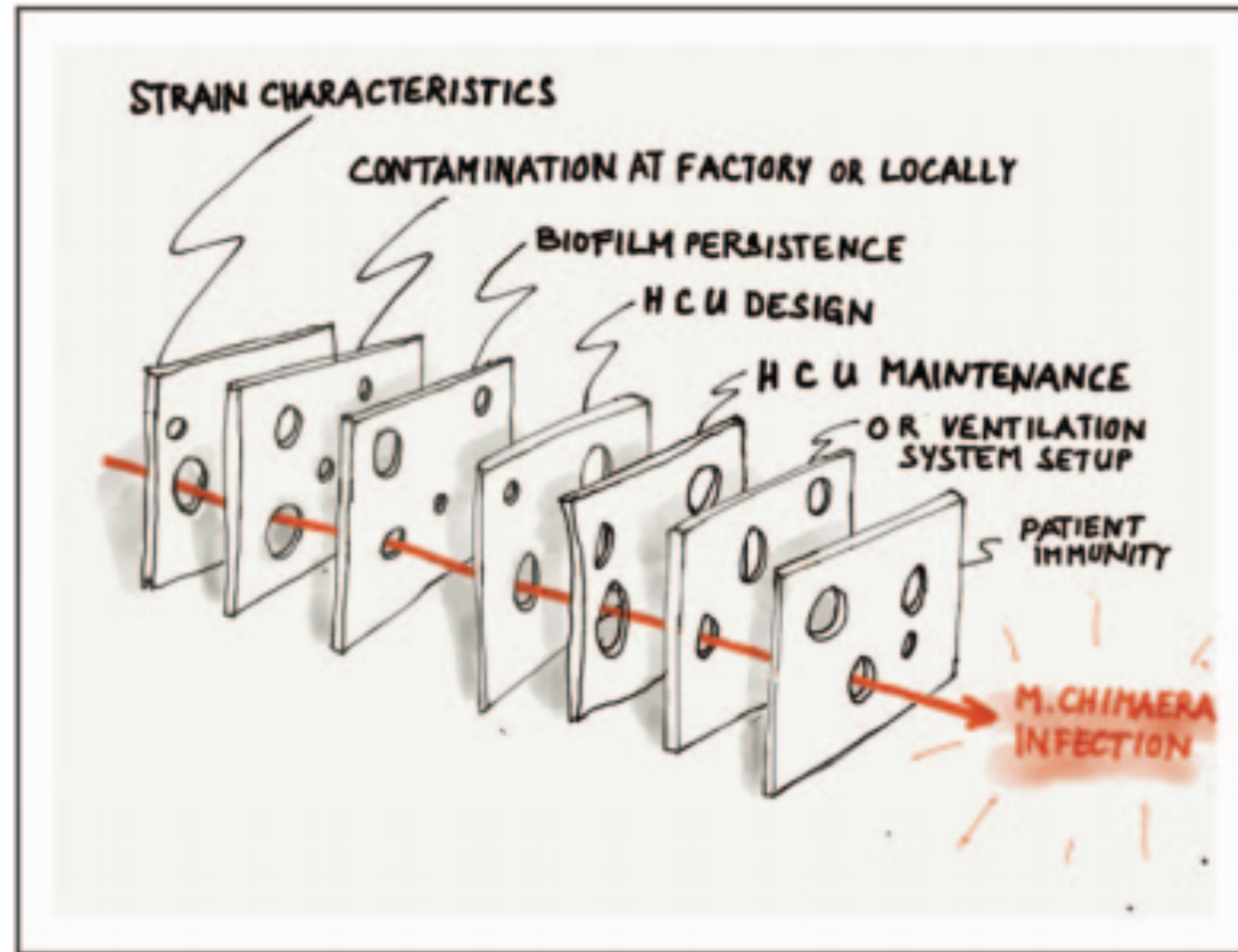
- 2011 initial reports in Switzerland, The Netherlands and Germany of *M. chimaera* infections following cardiac surgery.
  - Air sampling from Swiss outbreak detected the organism.
- Spring 2014 Federal office of Public Health in Switzerland further reported on this.
- Spring 2015 additional Swiss cases.
- July 2015, cluster of cases identified in a hospital in PA. Cluster also noted in Iowa. Genome sequencing showed close genetic relatedness between *M. chimaera* isolates.
- Epidemiologic analyses revealed all patients had exposure to the LivaNova (Formerly Stockert, Formerly Sorin) 3T Heater-Cooler Unit.

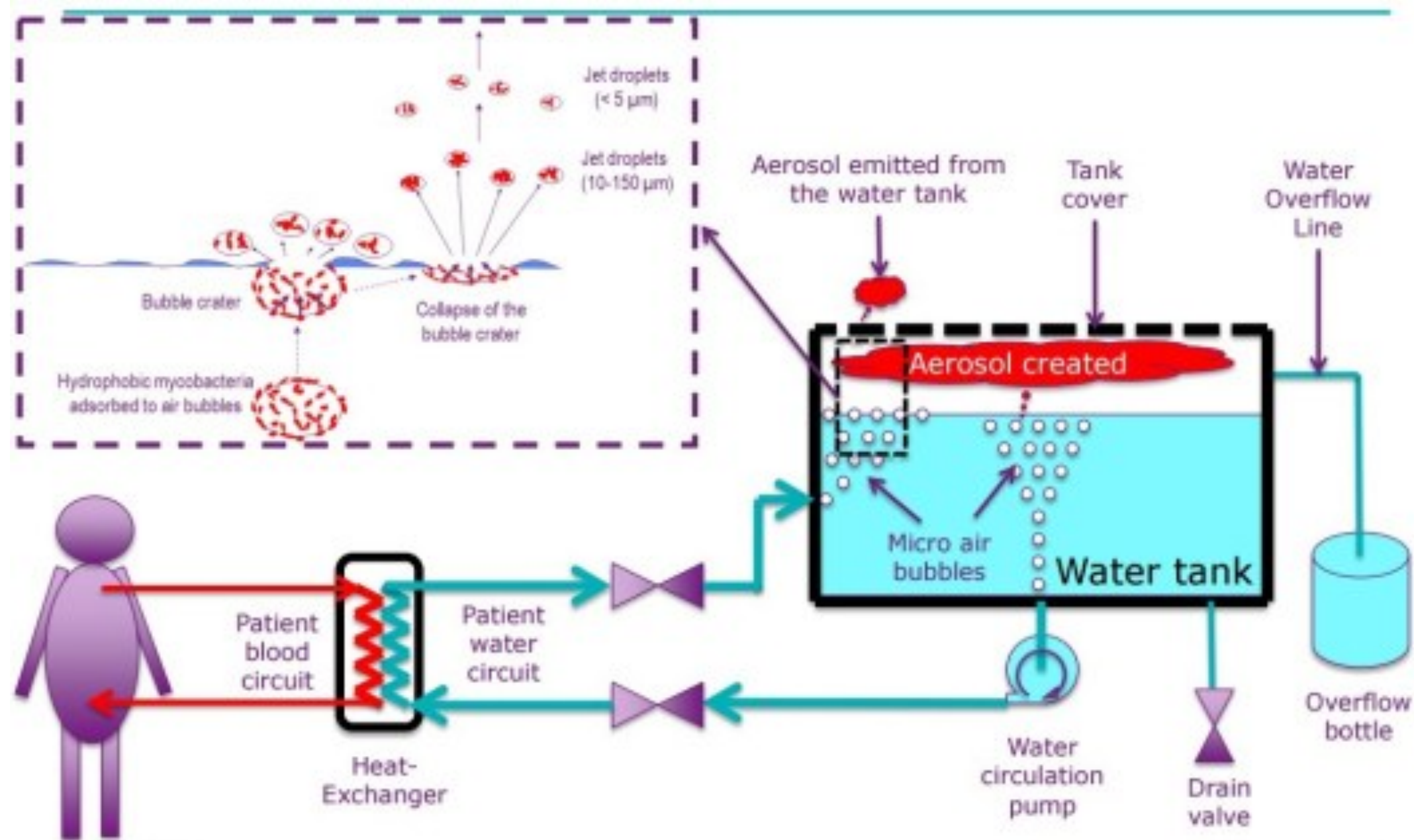
## Insidious Risk of Severe *Mycobacterium chimaera* Infection in Cardiac Surgery Patients

Meera Chand,<sup>1,2,3\*</sup> Theresa Lamagni,<sup>1,4</sup> Katharina Kranzer,<sup>1</sup> Jessica Hedge,<sup>4</sup> Ginny Moore,<sup>1</sup> Simon Parks,<sup>1</sup> Samuel Collins,<sup>1</sup> Carlos del Ojo Elias,<sup>4</sup> Nada Ahmed,<sup>1</sup> Tim Brown,<sup>1</sup> E. Grace Smith,<sup>1,3</sup> Peter Hoffman,<sup>1</sup> Peter Kirwan,<sup>1</sup> Brendan Mason,<sup>5</sup> Alison Smith-Palmer,<sup>6</sup> Philip Veal,<sup>7</sup> Maeve K. Lalor,<sup>1</sup> Allan Bennett,<sup>1</sup> James Walker,<sup>1</sup> Alicia Yeap,<sup>1</sup> Antonio Isidro Carrion Martin,<sup>1,8</sup> Gayle Dolan,<sup>1,9</sup> Sonia Bhatt,<sup>1</sup> Andrew Skingsley,<sup>1</sup> André Charlett,<sup>1</sup> David Pearce,<sup>1</sup> Katherine Russell,<sup>1</sup> Simon Kendall,<sup>10,11</sup> Andrew A. Klein,<sup>12,13</sup> Stephen Robins,<sup>14</sup> Silke Schelenz,<sup>15</sup> William Newsholme,<sup>2</sup> Stephanie Thomas,<sup>16</sup> Tim Collyns,<sup>17</sup> Eleri Davies,<sup>5,18</sup> Jim McMenamin,<sup>6</sup> Lorraine Doherty,<sup>7</sup> Tim E. A. Peto,<sup>4</sup> Derrick Crook,<sup>1,4</sup> Maria Zambon,<sup>1,3</sup> and Nick Phin<sup>1</sup>

- Cohort study, pooled UK database and collected 18 cases as possible or probable *M. chimaera* infection
- Reports of incidence suggest **0.17-3 invasive infections per 1000 at risk procedures** or 0.39 cases per 10000 person years
- Time between surgery and presentation ranged 3-62 months.
- Time from presentation to first AFB cx sent was 85 days
- Spatial analyses showed heavy aerosolization of organism
- Aerodynamic analysis noted leaks in the sealing plates on the water tanks and holes close to the flow and return pipes. Sealing these leaks reduced particle counts to near baseline.
- Water sampling: 77% + for mycobacteria, 48% were *M. chimaera*
- Case fatality was 50%

# Transmission

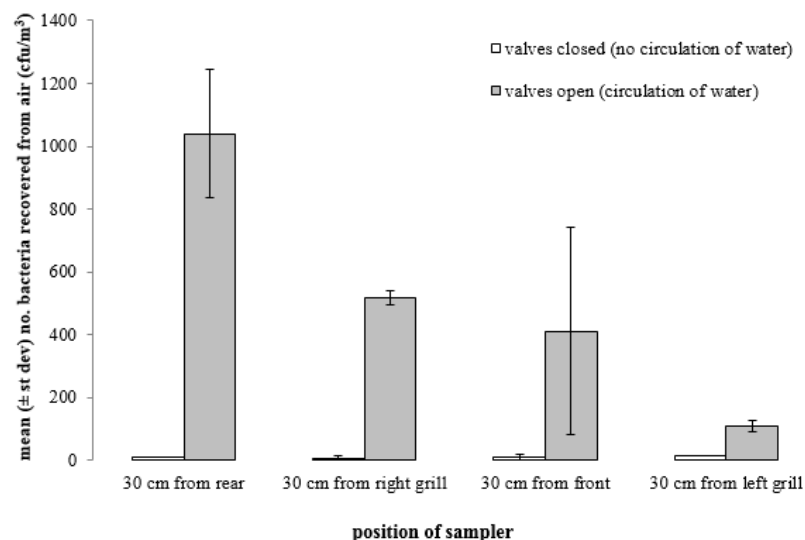




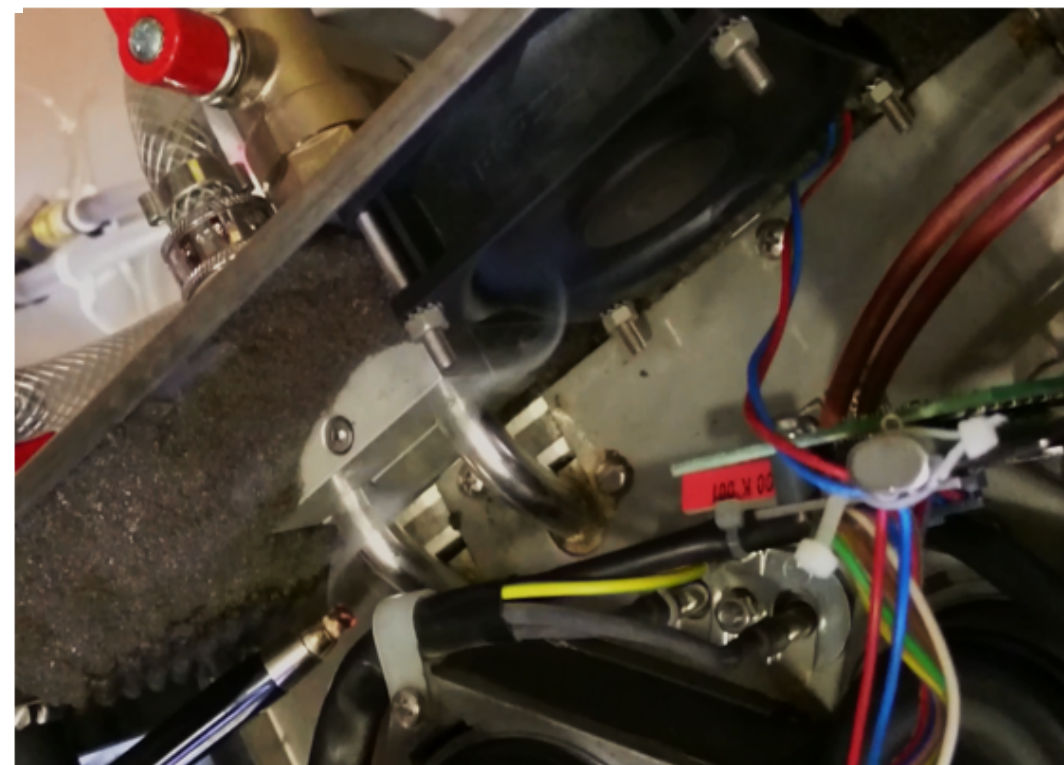


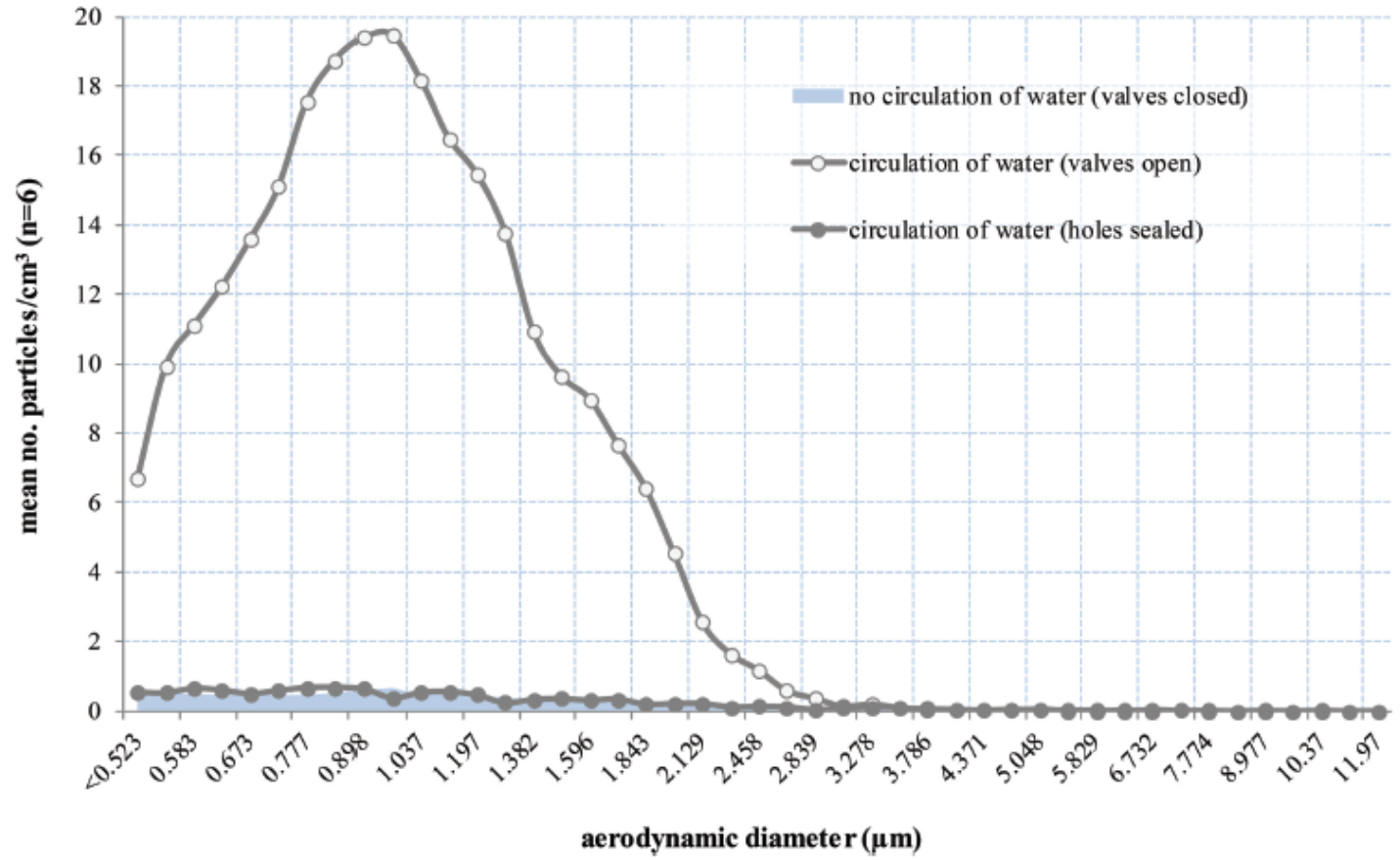
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**Supplementary Figure S8.** The mean number of bacteria released from the heater-cooler unit (HCU) with and without circulation of water. Air samples were taken using a cyclone air sampler (operating at 700 L/min) positioned at each side of the HCU.

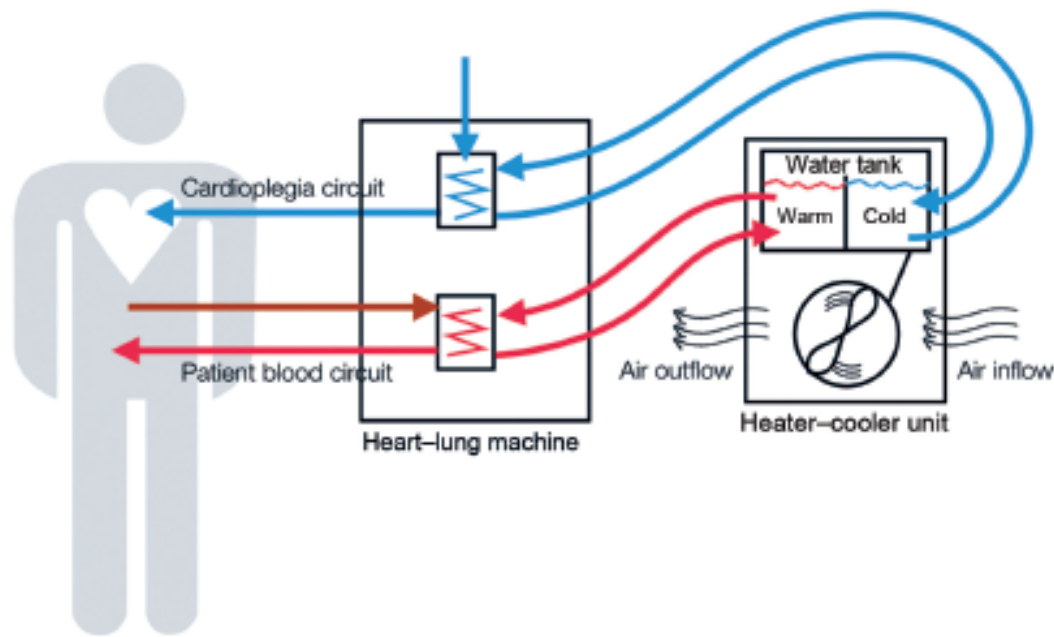




# Transmission of *Mycobacterium chimaera* from Heater–Cooler Units during Cardiac Surgery despite an Ultraclean Air Ventilation System

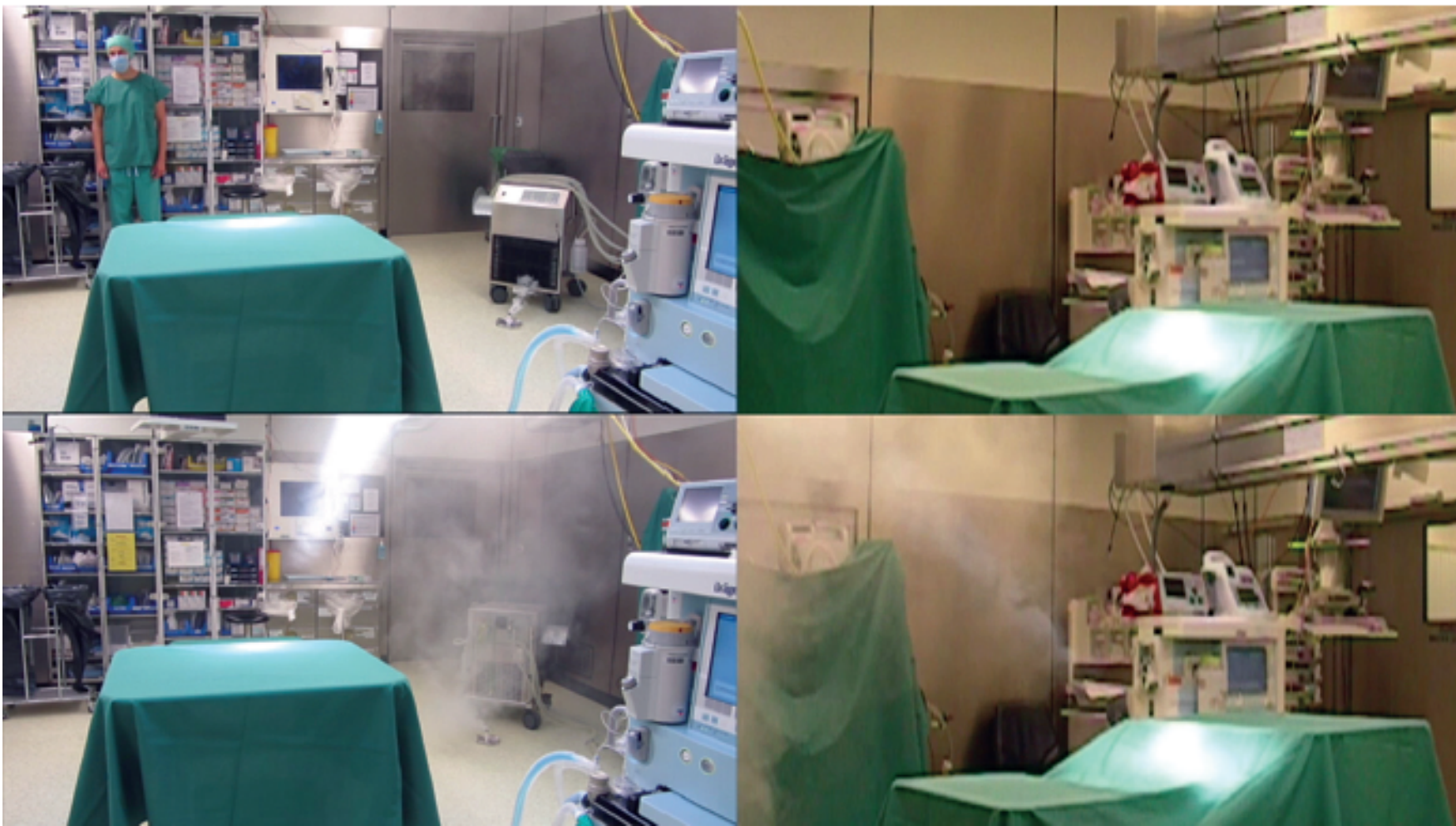
Rami Sommerstein, Christian Rüegg, Philipp Kohler, Guido Bloemberg, Stefan P. Kuster, Hugo Sax

1141511



- Experiments at University Hospital of Zurich, Switzerland
- Smoke experiments
  - Smoke reached surgical field by 10 s.
- Particle Experiments
  - Laser particle measurements demonstrated 26x increase in particle measurement over operative field when machine facing field and 2 m away.
- Sedimentation experiment
  - Middlebrook 7H11 agar plates placed 3, 4 and 5 m from exhaust on contaminated machine. Plates 3 and 5 m grew 2 and 1 CFU *M. chimaera*
- Challenges with Laminar flow in ORs





**Figure 2.** Video image captures showing effect of heater-cooler unit orientation on smoke dispersal in a cardiac surgery room and transmission of *Mycobacterium chimaera* during cardiac surgery despite an ultraclean air ventilation system (Video, <https://www.youtube.com/watch?v=YZ41aLoHrhQ>). The device was switched on and began to ventilate 10 s after the start of the video. Frames on the left show an overview including unit placement. Frames on the right provide a lateral view of the operating field under the laminar airflow. Simultaneously recorded videos in the upper 2 frames show the first scenario, in which the main ventilation exhaust was directed away from the operating field. Simultaneously recorded videos in the lower 2 frames show the second scenario, in which the main ventilation exhaust was directed toward the operating field.

• <https://www.youtube.com/watch?v=YZ41aLoHrhQ>

# How did it get there?

- July 2015-Bavarian Health and Food Safety Authority did on-site investigation at manufacturer including environmental sampling and isolated *M. chimaera* in 6 samples including from new machines.
- Strain typing from samples from authorities and manufacturer were nearly identical.

## SURVEILLANCE AND OUTBREAK REPORT

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

S Haller<sup>1</sup>, C Höller<sup>2</sup>, A Jacobshagen<sup>3</sup>, O Hamouda<sup>4</sup>, M Abu Sin<sup>1</sup>, DL Monnet<sup>4</sup>, D Plachouras<sup>4</sup>, T Eckmanns<sup>1</sup>

1. Department for Infectious Disease Epidemiology, Robert Koch Institute (RKI), Berlin, Germany

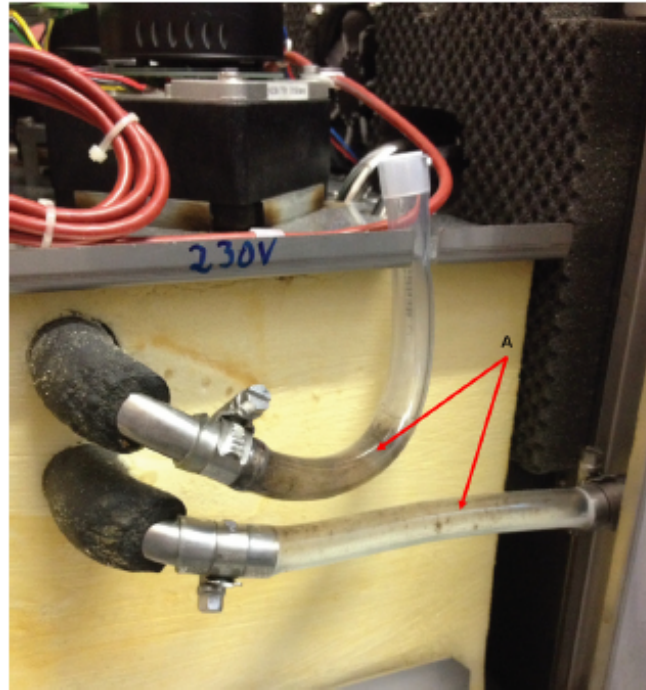
2. Bavarian Health and Food Safety Authority (LGL), Oberschleißheim, Germany

3. Federal Institute for Drugs and Medical Devices (BfArM), Bonn, Germany

4. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

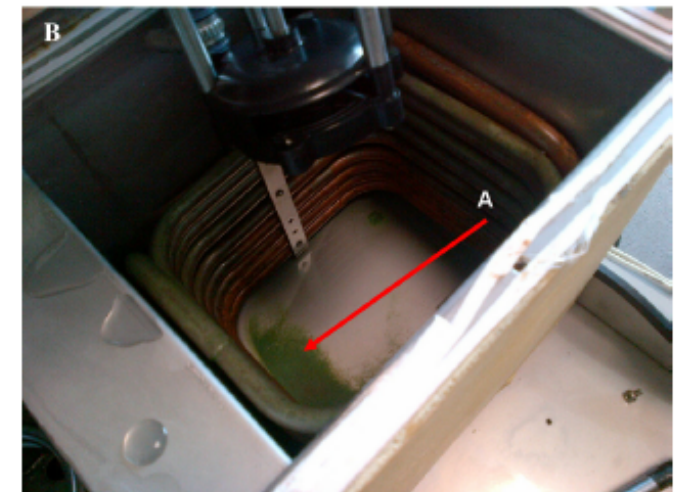


# Decontamination?

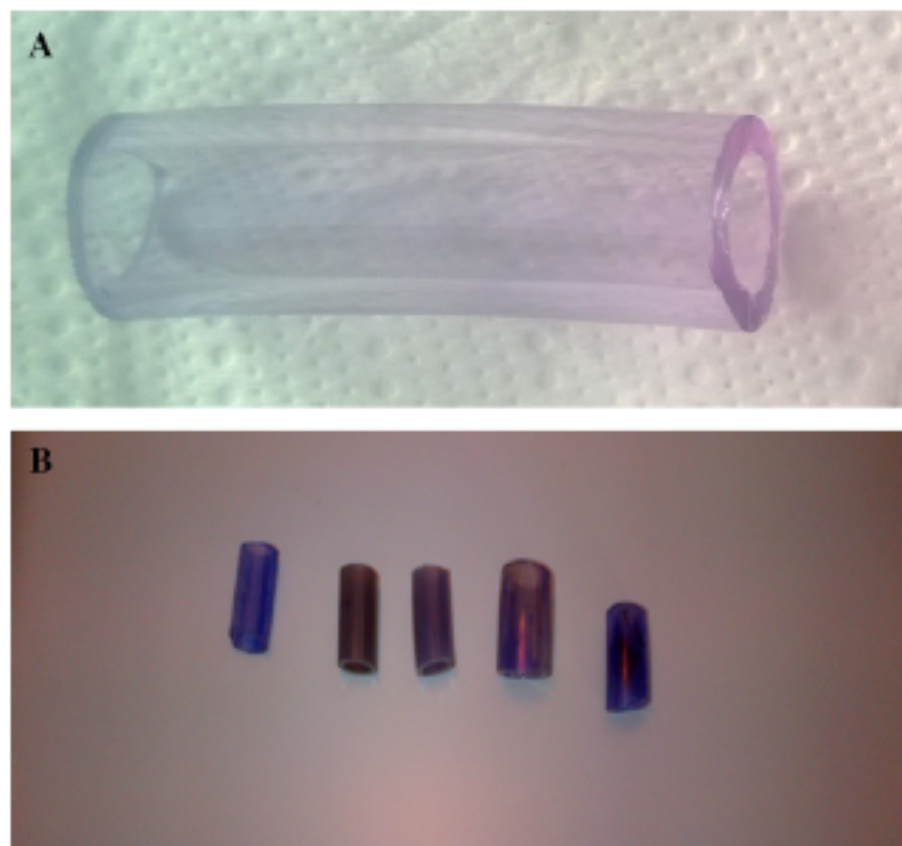


**Figure 1.** Overflow pipes in a Sorin heater-cooler unit. Arrows (A) highlight a 'dead leg' with visible biofilm.

(Figure 3). There were visible green particles in the HCU tank (likely copper particles; personal communication with the University of Birmingham), the significance of which is unclear at present (Figure 3B). After all the tubing within the HCU had been replaced, decontamination regimen 3 was undertaken. Two consecutive decontamination cycles with peracetic acid were undertaken, as before, on the first decontamination.



**Figure 3.** Tank in a heater-cooler unit. (A) Tank 1 and elements: visibly clean. (B) Tank 2 and elements: with visible chemicals, likely to be copper (arrow A).



**Figure 2.** Tubing cut from within the heater–cooler unit, stained with Crystal Violet to show the presence of biofilm. (A) Stained unused tubing. (B) Stained used biofouled tubing.

- Regimen 1: q2 week water removal, q5 day peroxide, q3 month bleach
- Regimen 2: q1 week water removal, q daily peroxide, q 1 week bleach
- Regimen 3 (+/- tubing replacement): qdaily water removal, q daily peroxide addition, q weekly decontamination with peracetic acid.

Decontamination regime	TVC	Environmental Gram negatives	<i>Pseudomonas</i> sp.	Fungi	<i>M. chimaera</i>
Decontamination regime 1	>300 CFU	+	+	+	+
Decontamination regime 2 (chlorine releasing agent)	>300 CFU	+	+	+	+
First decontamination*	100 CFU	+	-	-	-
Second decontamination* <sup>1</sup>	1 CFU	+	-	-	-
Weekly Counts	~1-300 CFU	+	+	+	+
Decontamination regime 3 (peracetic acid)	>300 CFU	+	+	+	+
First decontamination*	1-10 CFU	+	-	-	-
Second decontamination* <sup>1</sup>	0 CFU	-	-	-	-
Weekly Counts	~1-100 CFU	+	+ (0-5 CFU)	+ (0-30 CFU)	-
Current regime — decontamination regime 3 (tubing replaced)	0 CFU	-	-	-	-
First decontamination*	0 CFU	-	-	-	-
Second decontamination* <sup>1</sup>	0 CFU	-	-	-	-
Weekly Counts	0 CFU	-	-	-	-

Key. + = organisms present, - = no organisms present

Two consecutive decontamination cycles- \* first decontamination, \*<sup>1</sup> second decontamination.



# Other options?

- Turn the machine around?
- Jerry-rig some kind of a cover for the machine with vent to OR HEPA filter.
- Remove the machine from the OR and run tubing through holes in the wall?

- **Recommendations for the Use of Any Heater Cooler Device**
- On October 15, 2015, the FDA issued [Nontuberculous Mycobacterium Infections Associated with Heater-Cooler Devices – Safety Communication](#) to help reduce the risk of infection to patients. The recommendations include:
  - 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:

- If your facility uses 3T devices regardless of the date of manufacture, you should:
  - Immediately remove from service any heater-cooler devices, accessories, tubing, and connectors that have tested positive for *M. chimaera* or have been associated with known *M. chimaera* patient infections at your facility.
  - Use new accessories, tubing, and connectors to prevent recontamination when using a different manufacturer's or new 3T heater-cooler device.
  - Direct and channel the heater-cooler exhaust away from the patient, e.g., to the operating room exhaust vent.
  - Be aware that device contamination may also occur from other sources such as environmental contamination or device contact with contaminated accessories.
  - Be aware that testing of heater-cooler devices to identify units contaminated with *M. chimaera* presents technical challenges related to sample collection, the long culture time, and the high rate of false negative tests. Therefore, it is not recommended at this time.
- If your facility uses 3T devices manufactured prior to September 2014, you should also:
  - Strongly consider transitioning away from the use of these devices for open-chest cardiac surgery until the manufacturer has implemented strategies for these devices to mitigate the risks of patient infection.
    - Use of these devices should be limited to emergent and/or life-threatening situations if no other heater cooler devices are available.

	Make/model of heater-cooler unit (HCU)		
	Sorin 3T	Maquet HCU30	Maquet HCU40
<i>Water Samples</i>			
Number of hospitals sampled	10	3	2
Number of HCUs sampled	35	6	4
Number of HCUs contaminated with mycobacteria	27	3	4
Number of HCUs contaminated with <i>M. chimaera</i>	17	1	1
Number of contaminated cultures	1	2	0
<i>Air Samples</i>			
Number of hospitals sampled	7	2	2
Number of HCUs sampled	25	3	4
Number of HCUs associated with positive mycobacterial air samples	6	0	0
Number of HCUs associated with positive <i>M. chimaera</i> air samples	5	0	0
Number of contaminated cultures	1	1	1

# References

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- Garvey et al (2016), *Journal of Hosp. Inf*, 93, 229
- Sommerstein et al (2016), *EID*, 22, 1008
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- Schreiber, PW, and Sax, H. (2017), *COID*, 30, 388
- Haller, S. et al (2016), *Eurosurveillance*, 21 (17)
- 2016 webinar on *M. chimaera* on youtube.
- Iliad
- CDC, MMWR
- FDA