

Mycobacterium chimaera: under control or under water?



ECCMID 2018

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No relevant disclosures or COI



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Have you been involved in the global *M. chimaera* outbreak?

1. I have seen and treated cases of disseminated *M. chimaera* infections
2. My lab has experience with the subtyping of *M. avium* complex.
3. I was not involved. My hospital is not affected.
4. Positive cultures in my hospital, no cases so far.

Mycobacterium chimaera outbreak: under control?

Source of the outbreak

Pathogen transmission

Clonality/ Origin of the outbreak



Prolonged Outbreak of *Mycobacterium chimaera* Infection After Open-Chest Heart Surgery

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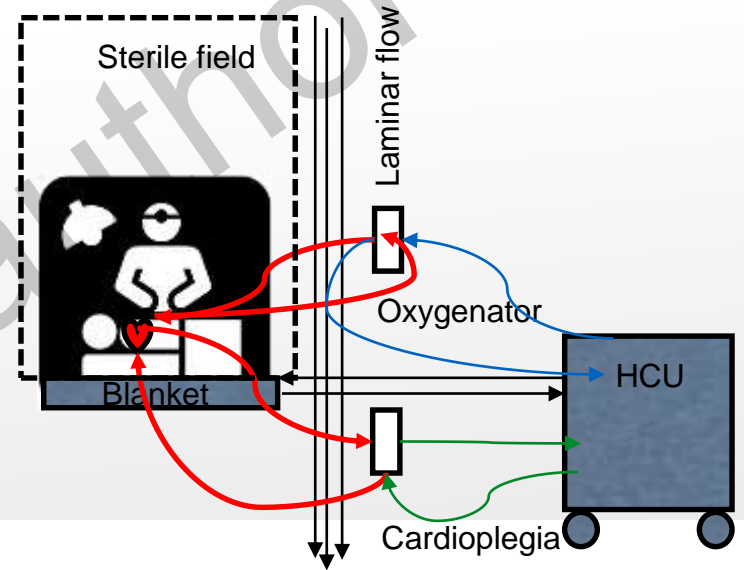
¹Division of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, ²Institute of Medical Microbiology, National Centre for Mycobacteria, University of Zurich, ³Institute of Surgical Pathology, and ⁴Division of Cardiac Surgery, University Hospital Zurich, Switzerland

Six heart surgery patients with disseminated *M. chimaera* infections
All patients had cardiac implants
Latency 1.7-3.6 years

Heater-cooler units (HCU) were contaminated with *M. chimaera*
Air samples from running HCU detected *M. chimaera*
Investigation of water, air and patient samples with RAPD-PCR

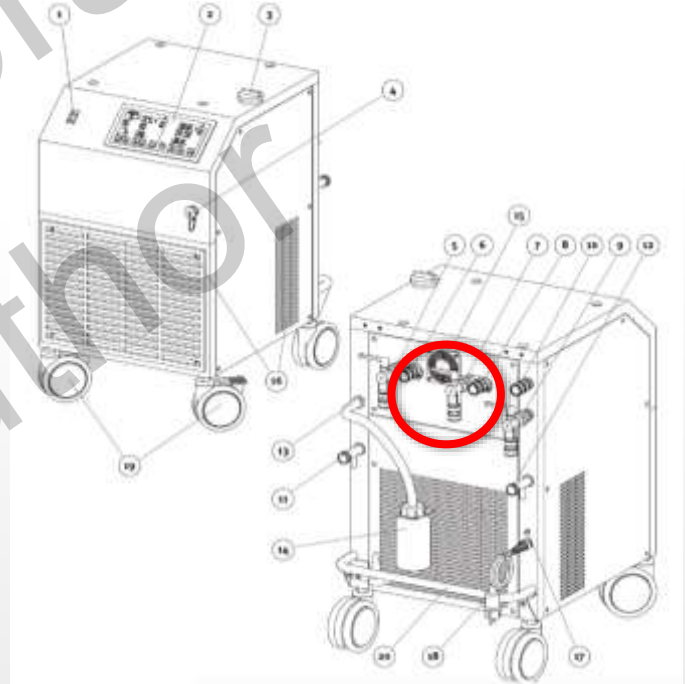
Heater Cooler Units (HCU)

- HCUs have three water circuits to warm/ cool patients; the cardioplegia circuit or the cardiac bypass circuit
- Key component of open cardiac procedures
- Implicated devices widely distributed:
 - Global outbreak



Heater Cooler Units (HCU) are not water- and airtight

- Water from HCU without direct patient contact
- Circuit is not air- or watertight (or watertight)



Why *M. chimaera*?

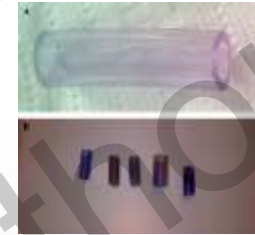
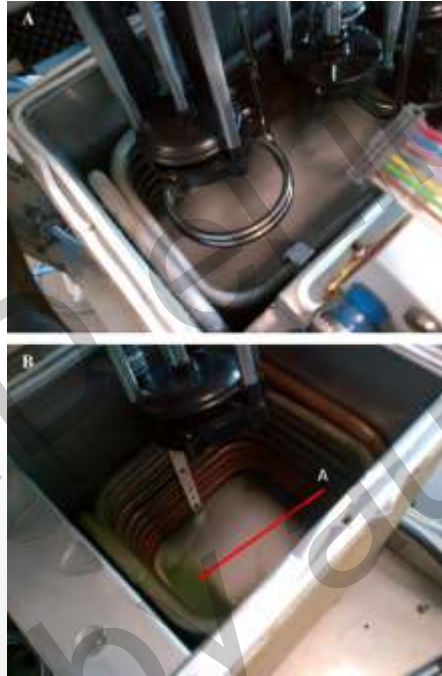
1. *M. chimaera* is resistant to heat and disinfectants
2. Biofilmformation by *M. chimaera* is the most likely cause.
3. *M. chimaera* is highly hydrophobic and well adapted for survival in water.
4. *M. chimaera* is well adapted to body temperature.

Origin of *Mycobacterium chimaera* in HCUs?



Stagnant water - optimal growth conditions for Mycobacteria

Mycobacterial biofilm formation in HCU as a problem



....we significantly reduced the microbial load of the water within the HCUs by removing the internal tubing soiled with biofilm followed by a weekly decontamination regimen with peracetic acid.

Ventilation fan aerosolizes contaminated water from the circuit



Figure 3. Use of a remote fan to maintain air flow path as it is extracted from the pump/leg assembly with the water bottle and sealing the heater water with air flow fan.



Airborne transmission of mycobacteria in the OR
Fan without contact to contaminated water!

Disturbance of laminar flow due to exhaust air of HCU

HCU fan facing away from operative field

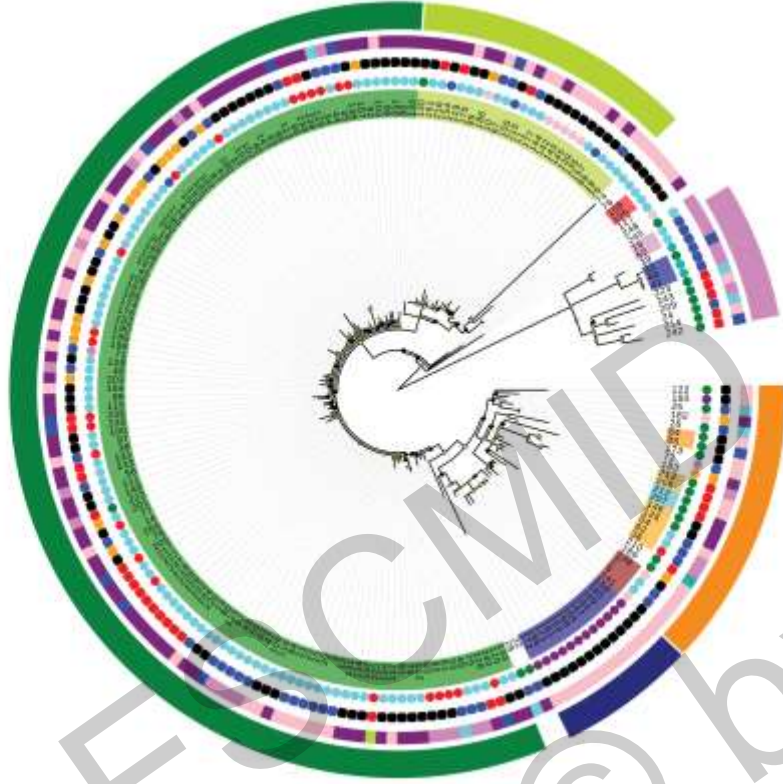


HCU fan facing operative field



erstein

Association of human cases with Stockert 3T HCU



<http://www.fda.gov/iceci/enforcementactions/warningletters/2015/ucm479684.htm>

Investigation reveals *M. chimaera* in factory-new HCDs and water from pump assembly area

Haller et al Eurosurveillance, 2016; Perkins KM et al. MMWR Morb Mortal Wkly Rep. 2016 Oct 14;65(40):1117-1118

Chand et al. Clin Infect Dis. 2017 Feb 1;64(3):335-342; Williamson D et al N Engl J Med 2017 Feb 9;376(6):600-602

Van Ingen et al. Lancet Infect Dis. 2017 Jul 12. pii: S1473-3099(17)30324-9



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Current global situation

Clinical cases



Australia	7
Belgium	0
Canada	5
China	2
CH	11
D	6
DK	0
NL	4
Italy	8
Ireland	4
Spain	3
USA	70
UK	30
Total	150

Medical Device Reporting: 86 patients
339 MDR reports (99 facilities, 5 HCU manufacturers)

April 21st, 2018 (Email count)
(To the best of my knowledge)



Bibliometric analysis of *M. chimaera* related articles



126 articles; 25 countries (USA 36.5%, F 9.76%, CH 7.69%, UK 7.05%, D 5.12%)

Who is thinking the *M. chimaera* outbreak is under control?

1. The source of the global epidemic is identified, but we are far away from having the outbreak «under control»
2. The outbreak is under control.
3. Some hospitals continue to use contaminated heater-cooler units, thus putting patients at risk.
4. Patients suffering from disseminated *M. chimaera* infections are «under water».

Mycobacterium chimaera patients are “under water”

Source of the outbreak

Pathogen transmission

Clonality/Origin of the outbreak

Patients with disseminated infections

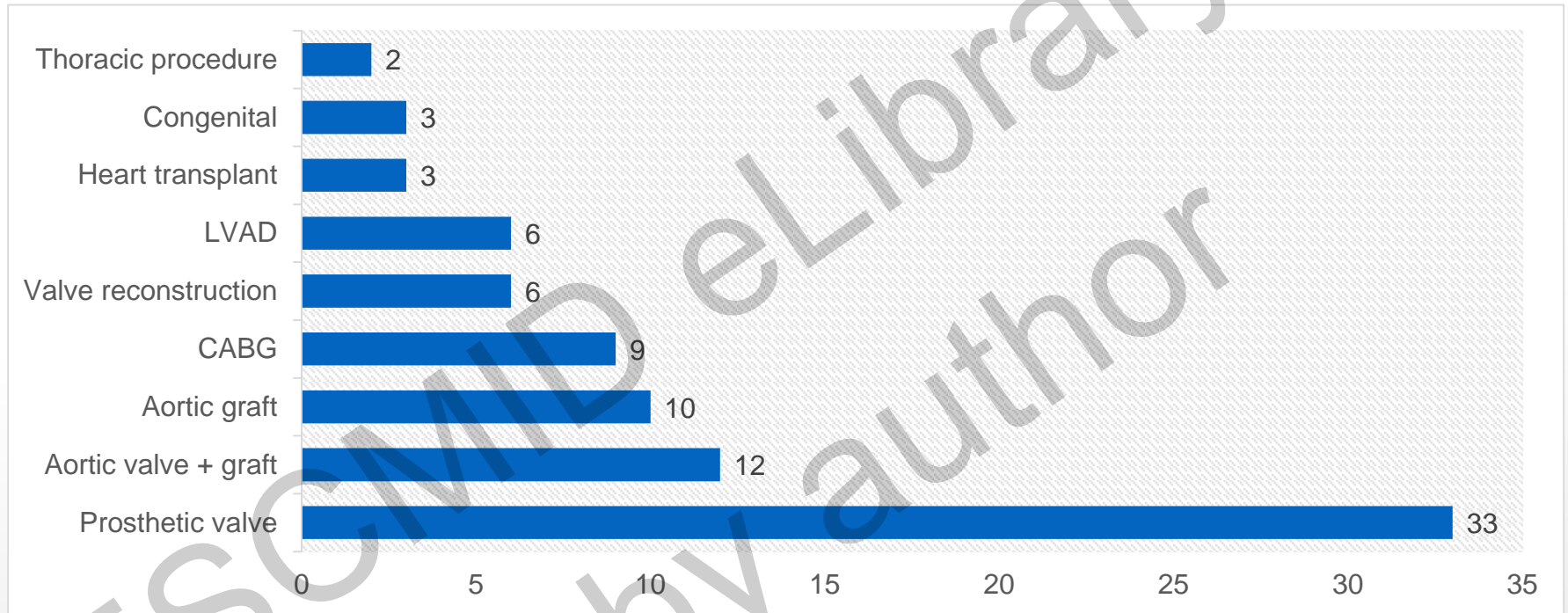


Published *M. chimaera* cases

Patient Characteristics	Results
Total number of cases, n (%)	84 (100)
Earliest sentinel surgery	2008
Male, n (%)	80 (95)
Age, y (median, IQR)	63 (19-73)
Prosthetic cardiovascular material n (%)	69 (84)
Duration from surgery to symptom onset in months, median months (range)	17 (1-72)
Duration from surgery to diagnosis in months (range)	1 month to 6 years
Crude mortality in published cases	37 (44)

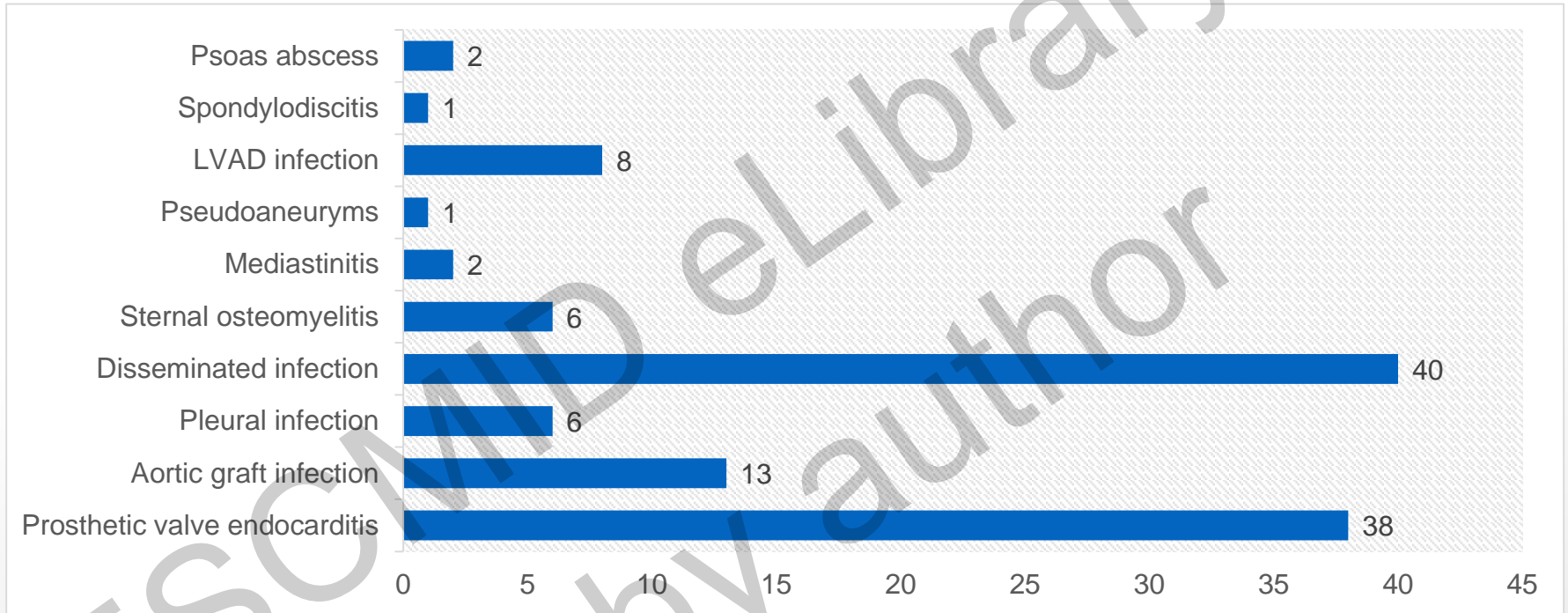
Kohler P, et al. *European Heart Journal* 2015;36:2745-53. Tan et al *Open Forum Infect Dis.* 2016 Jun 16;3(3):ofw131. Appenheimer AB et al. *Open Forum Infect Dis* 2016;3 (suppl 1), abstract 2392. Chand M, et al. *Clin Infect Dis* 2017;64:335-42. Hamad et al. *Ann Thorac Surg.* 2017 Jul;104(1):e43-e45. Yi Cai et al. *Can J Anesth* 2017; 64:513-516; Chiesi et al. *Infez Med.* 2017 Sep 1;25(3):267-269; O' Neill CR et al. *Open Forum Infect Dis.* 2018 Jan 24;5(2):ofy018. doi: 10.1093/ofid/ofy018. eCollection 2018 Feb. Asadi T et al. *J Thorac Cardiovasc Surg.* 2017 Dec 21. pii: S0022-5223(17)33001-5; Boeni C et al. *Retina.* 2017 Dec 4. doi: 10.1097; *Ophthalmology.* 2017 Feb;124(2):178-188. Balsam et al *J Card Surg* 2017;32:402-404

Surgical procedures: frequency of *M. chimaera* infections



Kohler P, et al. European Heart Journal 2015;36:2745-53. Tan et al Open Forum Infect Dis. 2016 Jun 16;3(3):ofw131. Appenheimer AB et al. Open Forum Infect Dis 2016;3 (suppl 1), abstract 2392. Chand M, et al. Clin Infect Dis 2017;64:335-42. Hamad et al. Ann Thorac Surg. 2017 Jul;104(1):e43-e45. Yi Cai et al. Can J Anesth 2017; 64:513-516; Chiesi et al. Infez Med. 2017 Sep 1;25(3):267-269; O' Neill CR et al. Open Forum Infect Dis. 2018 Jan 24;5(2):ofy018. doi: 10.1093/ofid/ofy018. eCollection 2018 Feb. Asadi T et al. J Thorac Cardiovasc Surg. 2017 Dec 21. pii: S0022-5223(17)33001-5; Boeni C et al. Retina. 2017 Dec 4. doi: 10.1097; Ophthalmology. 2017 Feb;124(2):178-188. Balsam et al J Card Surg 2017;32:402-404

Final diagnosis of *M. chimaera* infections



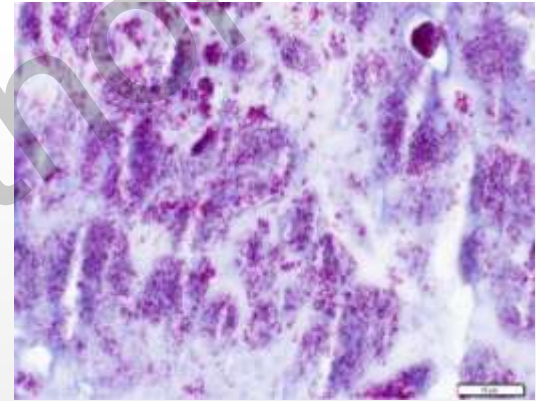
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M. chimaera treatment

Multiple drug treatment:

Macrolide, ethambutol, rifamycin+/- amikacin moxifloxacin, clofazimine

Removal of involved devices if possible



Acid fast stain from resected
composite aortic graft:
Culture: *M. chimaera*

Mycobacterium chimaera prevention measures?

1. I rely on the use of the cleaning and disinfection guidance by LivaNova
2. I rely on environmental air and water cultures.
3. I think that alle 3T HCU are contaminated and I either relocate them in front of the OR or I use a custom built encasing.
4. Separation of HCU from air volume is sufficient

Mycobacterium chimaera outbreak: under control?

Source of the outbreak

Pathogen transmission

Clonality/Origin of the outbreak

Patients with disseminated infections

Prevention measures



All 3T HCU have to be considered as contaminated

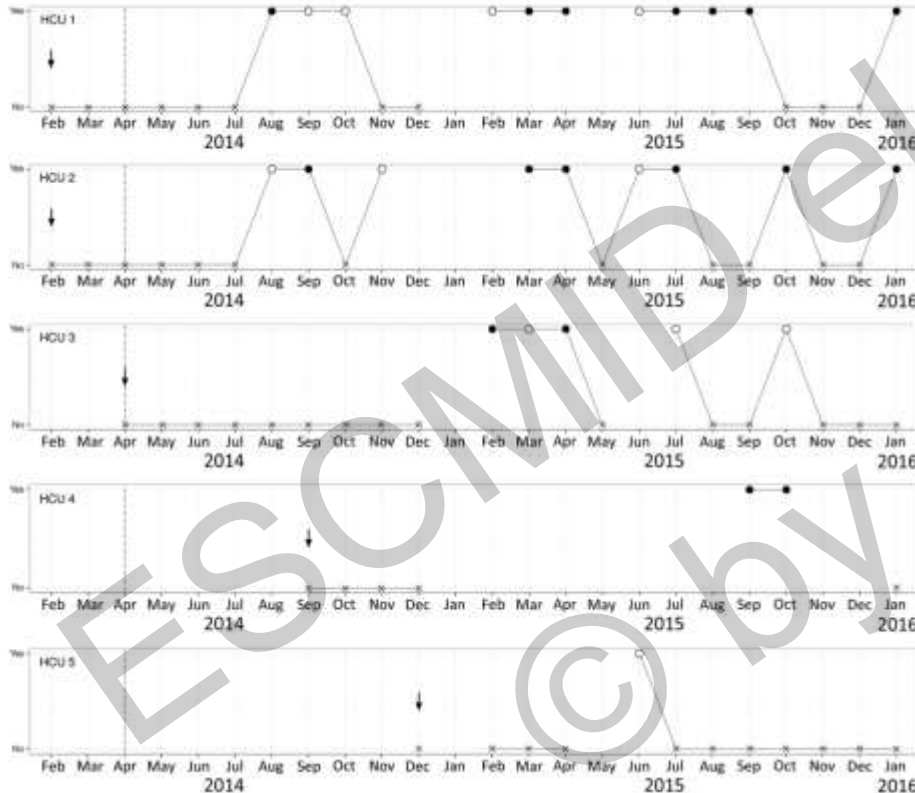


Institution	Mycobacterium species													Mycobacteria not detected	Total											
	<i>M. chimaera</i>	<i>M. indicus/praviae</i>	<i>M. abscessus complex</i>	<i>M. chelonae</i>	<i>M. chelonae/abscessus complex</i>	<i>M. goodii</i>	<i>M. lifium</i>	<i>M. goodii</i>	<i>M. goodii/abscessus complex</i>	<i>M. lifium</i>	<i>M. indicus/praviae</i>	<i>M. neoaurum</i>	<i>M. neoaurum</i>			<i>M. neoaurum</i>	<i>M. neoaurum</i>	<i>M. neoaurum</i>	<i>M. neoaurum</i>	<i>M. neoaurum</i>	<i>M. neoaurum</i>	<i>M. neoaurum</i>	<i>M. neoaurum</i>			
Hospital 1	17																							18	36	
Hospital 2																									24	24
Hospital 3	21																								33	54
Hospital 4																									32	33
Hospital 5																									11	11
Hospital 6																										30
Hospital 7	11																								2	2
Hospital 8																									2	2
Hospital 9	5	1																							19	22
Hospital 10	2	1																							3	14
Hospital 11	12																								9	21
Hospital 12	42			3	2			1																	5	238
Hospital 13	106	2	1	6	5	1	1	21	2																4	7
Rehabilitation Clinic																									1	411
Total	216	4	1	9	7	1	1	26	2	2	1	1	3	18	13	1									805	1111

August 2013-2016; 13/16 cardiac surgery institutions; 19.4% positive with *M. chimaera*

No standards for sampling frequency of HCU; Heterogeneous sampling frequency/ timeframe; Sampling based on voluntariness of the institutions; Cut off level of detection in water unknown. No information on placement of HCU and decontamination status!

Unsuccessful decontamination of HCUs – growth of mycobacteria after 174 days



Intensified in-house cleaning and disinfection procedure

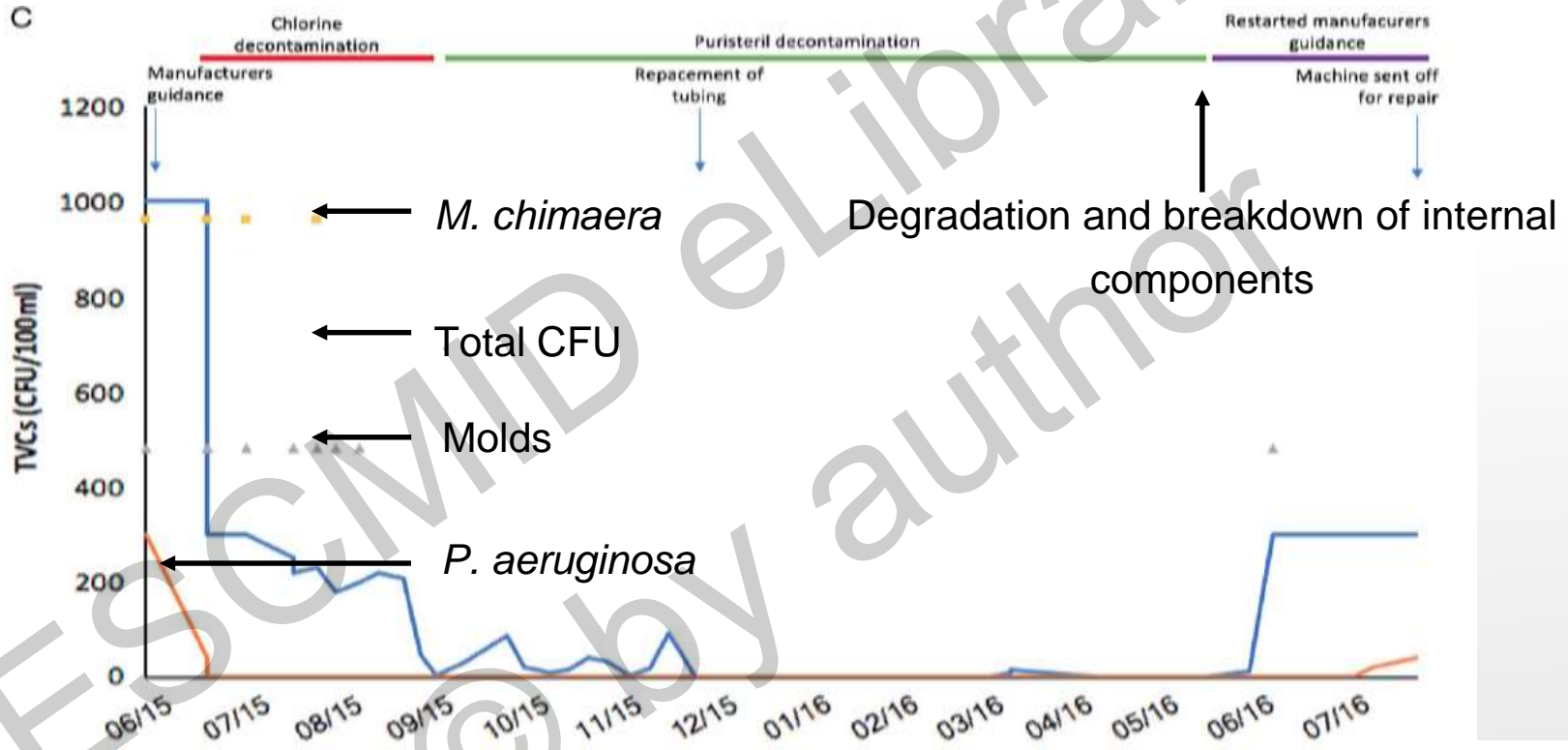
- Daily water changes
- Filtered tap water
- Peracetic acid + hydrogen peroxide in filled water tanks 2 weekly

Schreiber P et al, Emerg Infect Dis. 2016 Oct;22(10):1830-3

Garvey MI et al. J Hosp Infection 2016;93:229-34.

Gotting T et al. J Hosp Infection 2016;93:223-8.

Decontamination of HCU can lead to machine damage...



Separating HCUs from air volume of OR; other IC measures



Placement of HCUs outside the OR (airflow must be restrained from diffusion back in the OR; Production of air-tight housings; Ensure traceability of HCU use. Avoid crosscontamination by tubes

Device modification on the horizon?

Livanova PLC (NASDAQ:LIVN) (together with its subsidiaries as "LivaNova" or the "Company"), a market-leading medical technology company, today announced the implementation of a device modification to its existing 3T Heater-Cooler devices in Western Europe. During the past fiscal quarter, LivaNova successfully completed verification and validation processes, which allowed the Company to obtain CE Mark for its 3T Heater-Cooler device modification. It began implementing upgrades in Europe and implementation will extend to other regions as local regulatory approvals are received. The modification, which is being implemented at no cost to customers, includes the installation of an internal sealing and vacuum system on existing devices. This addresses regulatory actions and is designed to mitigate the potential for *Mycobacterium chimaera* (*M. chimaera*) contamination in open-heart surgery patients.

Internal sealing and vacuum system in existing devices....

Conclusions

- Global HCU related outbreak with *M. chimaera* ongoing (current extent unknown due to long incubation period)
- Clinical syndrome challenging and not specific (delayed presentation, high mortality rates; removal of devices necessary for cure)
- Hospitals/ Public health authorities (Patient and provider information, HCU management)

