

***M. chimaera* Infections Associated with Heater Cooler Units**
Prof. Michael Edmond, University of Iowa
A Webber Training Teleclass

***M. chimaera* Infections Associated with Heater Cooler Units**



Michael Edmond, MD, MPH, MPA

Chief Quality Officer

Clinical Professor of Infectious Diseases

UNIVERSITY OF IOWA
HOSPITALS & CLINICS

University of Iowa Health Care



Hosted by Bruce Gamage

Provincial Infection Control Network of British Columbia

www.webbertraining.com

January 26, 2017

M. chimaera

- Slow-growing mycobacterium belonging to the *M. avium* complex
- Established as a distinct species in 2004
- Requires molecular diagnostic testing for identification

2

Hosted by Bruce Gamage, PICNet BC
www.webbertraining.com

***M. chimaera* Infections Associated with Heater Cooler Units**
Prof. Michael Edmond, University of Iowa
A Webber Training Teleclass

Mycobacterium avium complex

Species	Associations
<i>M. avium</i> subsp. <i>hominissuis</i>	Opportunistic infections in pigs & immunosuppressed humans
<i>M. chimaera</i>	Pulmonary cavities, pulmonary abscess, chronic obstructive pulmonary disease, bronchiectasis, cystic fibrosis; pulmonary disease less virulent than <i>M. avium</i> and <i>M. intracellulare</i>
<i>M. intracellulare</i>	Enlarged lymph nodes in children; progressive pulmonary disease in elderly women
<i>M. colombiense</i>	Isolated from blood & sputum of HIV-infected patients in Colombia & from diseased lymph nodes in children
<i>M. arosiense</i>	Immunocompromised child with disseminated osteomyelitic lesions
<i>M. bouchedurhonense</i>	Isolated from patients with pulmonary disease
<i>M. marseillense</i>	
<i>M. timonense</i>	

Cayrou C et al. Microbiol 2010;156:687-94.

Boyle DP et al. Am J Resp Crit Care Med 2015;191:1310-7.

3

Epidemiology in a nutshell

- Common source outbreak:
 - LivaNova 3T HCUs were contaminated at the manufacturing facility in Germany and shipped to hospitals globally
- Extent unknown at this time
 - Very long incubation/discovery period (up to 6 years)
 - Diagnosis is difficult
 - Symptoms often nonlocalizing, nonspecific
 - Typically requires ABF blood cultures
 - Risk: if hospital detects a case, risk is 1/100 -1/1,000 (risk at U. of Iowa \geq 1/375)

4

***M. chimaera* Infections Associated with Heater Cooler Units**
Prof. Michael Edmond, University of Iowa
A Webber Training Teleclass

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

Hugo Sax,^{1,a} Guido Bloemberg,^{2,a} Barbara Hasse,^{1,a} Rami Sommerstein,¹ Philipp Kohler,¹ Yvonne Achermann,¹ Matthias Rössle,³ Volkmar Falk,⁴ Stefan P. Kuster,¹ Erik C. Böttger,^{2,b} and Rainer Weber^{1,b}

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

- Invasive *M. chimaera* infection in 6 patients
 - *M. chimaera* is one species of MAC
- All six patients had cardiac implants (2008-2012)
- Time from surgery to diagnosis: 1.7-3.6 years
- Manifestations: endocarditis, graft infections, bloodstream infections
- Investigation of water sources revealed:
 - Water in heater-cooler units (HCUs) grew *M chimaera*
 - Air samples grew outbreak strain when units ran

Clin Infect Dis 2015;61:67-75.

5

Heater-cooler units: contamination of crucial devices in cardiothoracic surgery

T. Götting^{a,*,} S. Klassen^a, D. Jonas^a, Ch. Benk^b, A. Serr^c, D. Wagner^d, W. Ebner^a

^aInfection Prevention and Hospital Epidemiology, University Medical Center Freiburg, Freiburg, Germany

^bUniversity Heart Center Freiburg – Bad Krozingen, Freiburg, Germany

^cDepartment of Medical Microbiology and Hygiene, University Medical Center Freiburg, Freiburg, Germany

^dCenter for Infectious Diseases and Travel Medicine and Center for Chronic Immunodeficiency, University Medical Center Freiburg, Freiburg, Germany

- Investigators in Freiberg, Germany confirmed:
 - No *M. chimaera* in hospital tap water
 - Presence of *M. chimaera* in 4/4 HCU water tanks
 - Presence of *M. chimaera* in the OR air when the HCUs were on in the OR, but none when HCUs were turned off
 - No *M. chimaera* detected in the OR air when the HCU was moved outside the OR and turned on

J Hosp Infect 2016;93:223-8.

6

Molecular epidemiology

- Comparison of the following *M. chimaera* strains via whole genome sequencing revealed the strains to be nearly identical (median 3 SNP differences) or similar (median 6 SNP differences):
 - Sorin 3T HCU isolates from Denmark (4)
 - Sorin 3T HCU isolates from England (8)
 - Sorin 3T HCU isolates from Iowa, Pennsylvania (9)
 - Patient isolates from Iowa, Pennsylvania (11)

Svensson E et al. Emerg Infect Dis 2017 (ebub ahead of print).

7

Scope of the problem

- LivaNova (formerly Sorin) 3T heater cooler in the US:
 - Used since 2006
 - 60% market share
 - Used in 200,000 surgeries US yearly

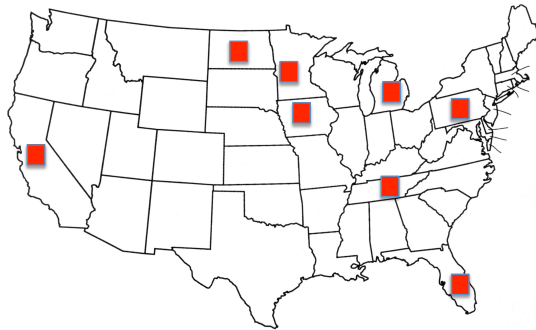
FDA.

LivaNova. December 2, 2016. <file:///C:/Users/mikee/Downloads/US%203T%20Customer%20Letter%20%20December%202016.pdf>

8

***M. chimaera* Infections Associated with Heater Cooler Units**
Prof. Michael Edmond, University of Iowa
A Webber Training Teleclass

HCU-associated *M. chimaera* cases



- Switzerland
- Germany
- Netherlands
- England
- Australia
- US
- Canada (Quebec)

9

Pathogenesis

- Almost all patients with serious infection have implants (valves, vascular grafts)
- High inoculum (long bypass time, direction of HCU exhaust, OR air handling) allows contamination of implant, leading to biofilm formation on an intravascular device, and subsequent dissemination
- Chronic granulomatous inflammatory response to near-continuous seeding of the bloodstream by a low virulence organism that is otherwise easily contained

Haller S et al. *Eurosurveillance* 2016;21:17.
van Ingen J. *ECCMID*, 4/16.

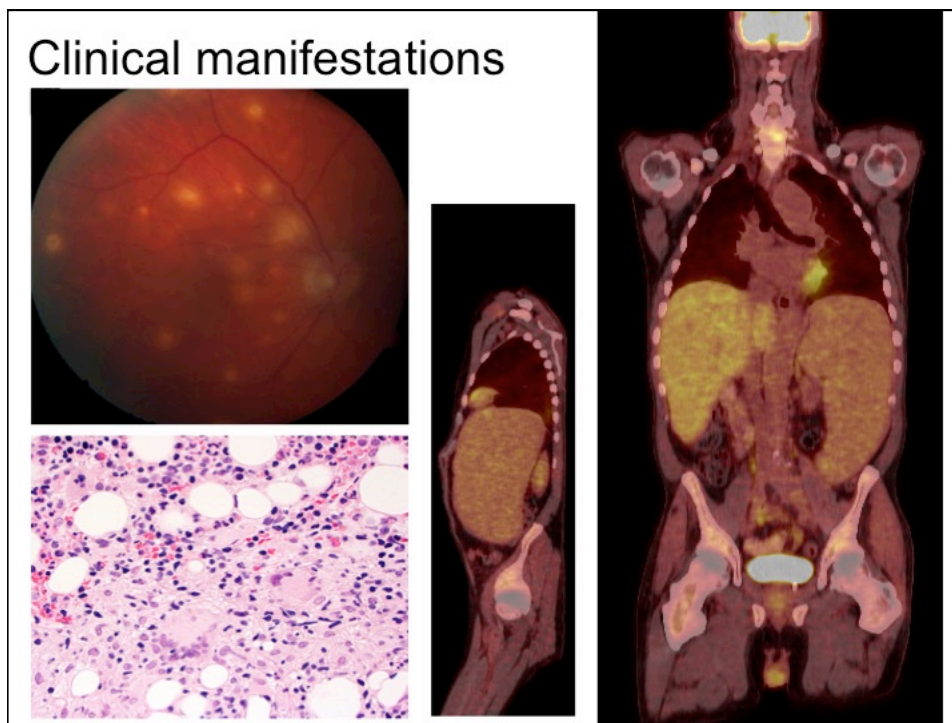
10

M. chimaera Infections Associated with Heater Cooler Units
Prof. Michael Edmond, University of Iowa
A Webber Training Teleclass

Clinical manifestations

- Surgical wound infection (soft tissue, osteomyelitis, mediastinitis, mediastinal abscess)
- Prosthetic valve endocarditis
- Vascular graft infection
- Disseminated infection
 - Splenomegaly
 - Arthritis
 - Osteomyelitis (spine, discitis)
 - Cytopenias (bone marrow involvement)
 - Chorioretinitis
 - Lung involvement
 - Hepatitis
 - Nephritis
 - Myocarditis
 - Elevated inflammatory markers

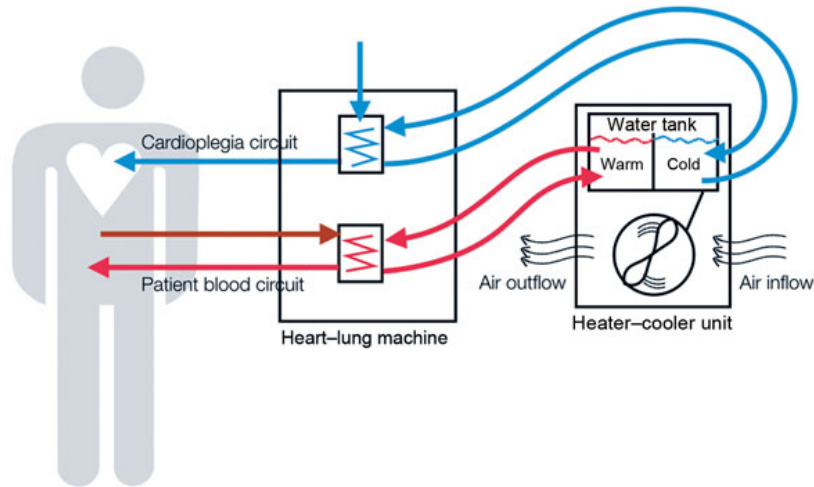
11



Hosted by Bruce Gamage, PICNet BC
www.webbertraining.com

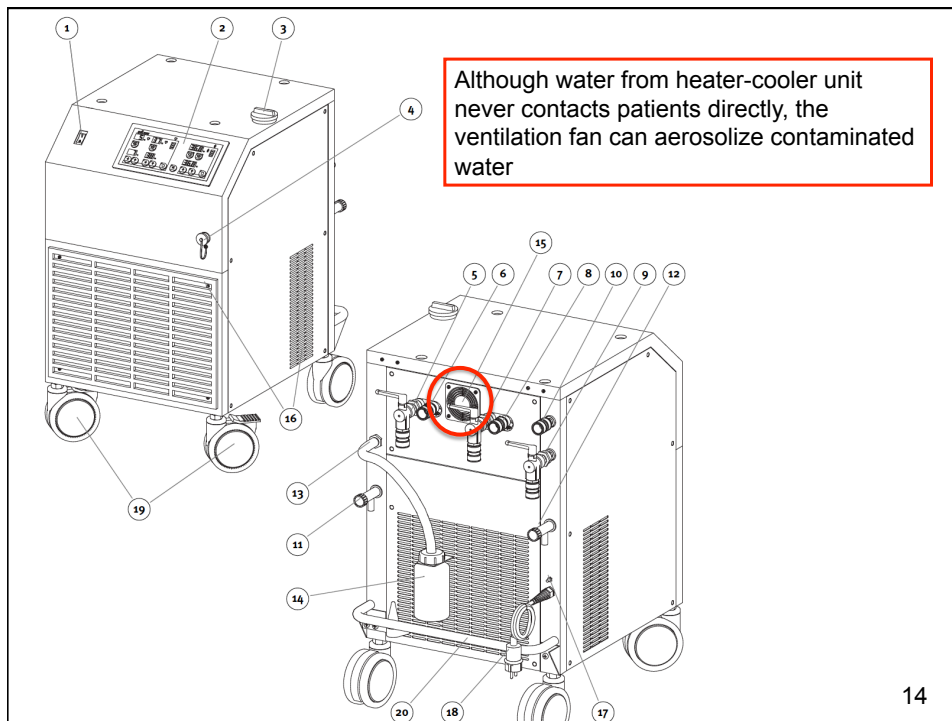
M. chimaera Infections Associated with Heater Cooler Units
Prof. Michael Edmond, University of Iowa
A Webber Training Teleclass

Heater cooler units



Sommerstein R et al. Emerg Infect Dis 2016;22:1008-13.

13

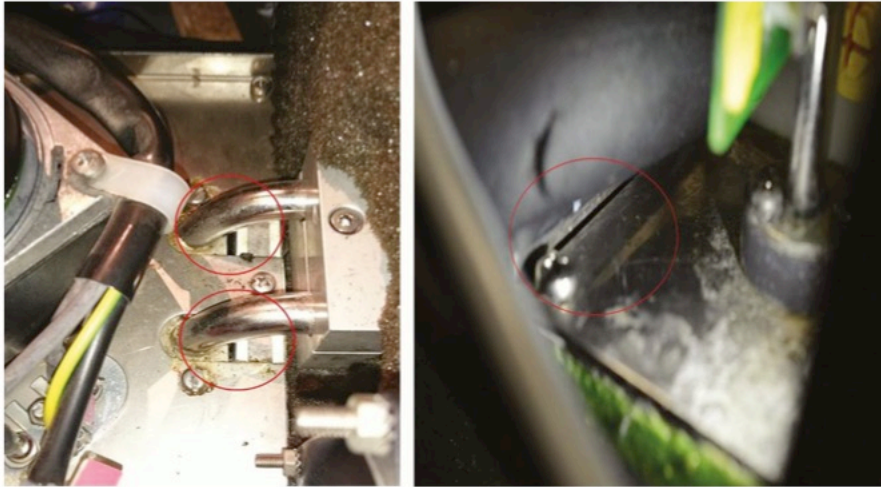


14

Hosted by Bruce Gamage, PICNet BC
www.webbertraining.com

M. chimaera Infections Associated with Heater Cooler Units
Prof. Michael Edmond, University of Iowa
A Webber Training Teleclass

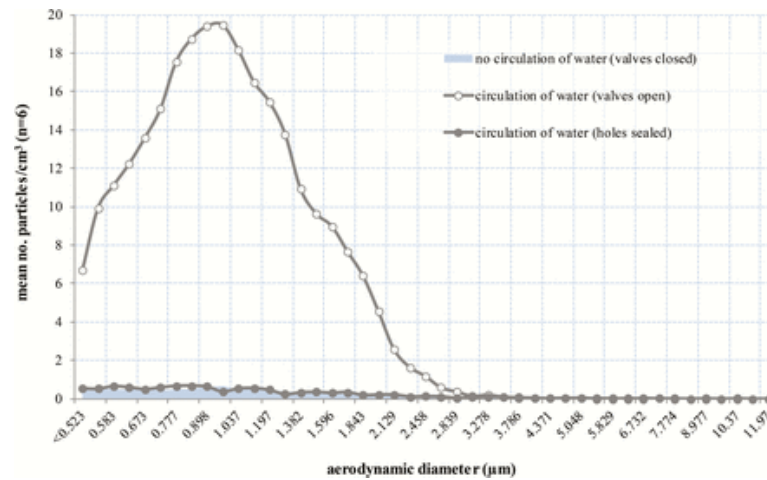
Source of bioaerosols



Chand M et al. Clin Infect Dis 2016 (epub ahead of print).

15

Source of bioaerosols

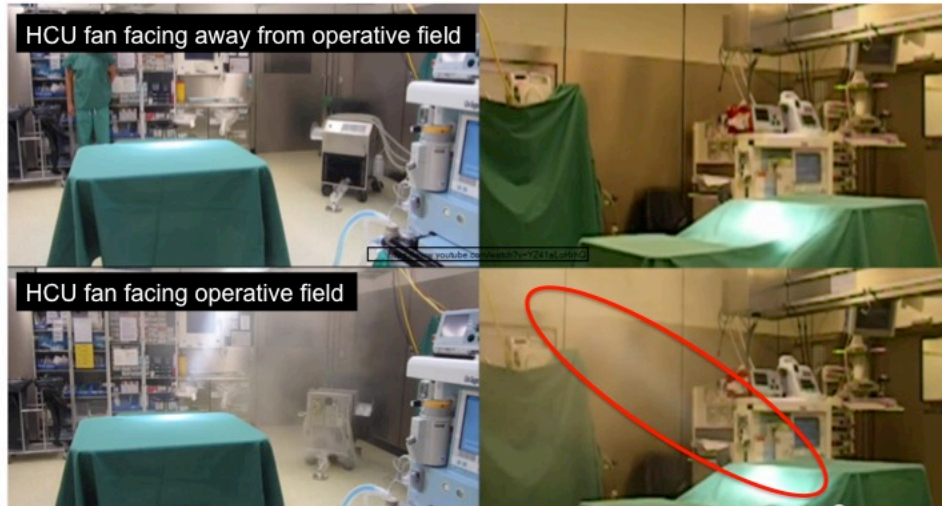


Chand M et al. Clin Infect Dis 2016 (epub ahead of print).

16

***M. chimaera* Infections Associated with Heater Cooler Units**
Prof. Michael Edmond, University of Iowa
A Webber Training Teleclass

Contamination of the operative field

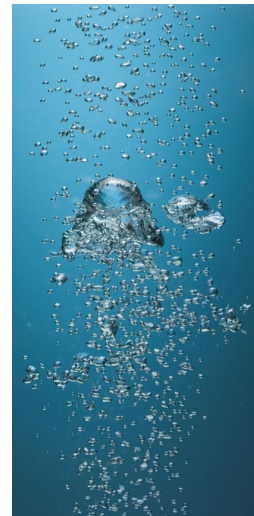


<https://www.youtube.com/watch?v=YZ41aLoHrhQ>
Sommerstein R et al. Emerg Infect Dis 2016;22:1008-13.

17

MAC: Perfect pathogen for HCUs

- Resistant to common disinfectants
 - Chlorine, chloramine, ozone
 - 1,000 times more resistant than industry standard for disinfection (*E. coli*): 2 hours vs. 5 seconds at 1 ppm chlorine
- Form thick biofilms, enhance resistance
 - 10,000 CFU/cm² in biofilm
- Lipid-rich hydrophobic barrier
 - Concentrate on surface of air bubbles that rise in water columns
 - Aerosolization occurs as bubbles reach surface
 - MAC concentration in ejected droplets is 1,000-10,000 X higher than in water



Taylor RH et al. Appl Environ Microbiol 2000;66:1702-5.
Steed KA et al. Appl Environ Microbiol 2006;72:4007-11.
Parker BC et al. Am Rev Respir Dis 1983;128:652-6.

18

Hosted by Bruce Gamage, PICNet BC
www.webbertraining.com

***M. chimaera* Infections Associated with Heater Cooler Units**
Prof. Michael Edmond, University of Iowa
A Webber Training Teleclass

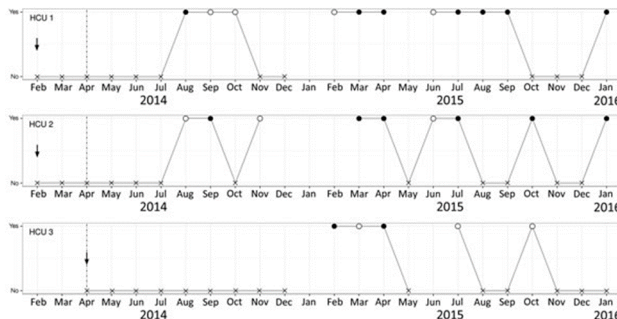


Garvey MI et al. J Hosp Infect 2016;93:229-34.

19

Inability to decontaminate HCUs

- Contamination of brand new, factory-direct units quickly detectable
- Multiple cycles of decontamination fail to eliminate *M chimaera* from HCUs



Decontamination protocol:

- Daily water changes w/ filtered water + 100 mL 3% H₂O₂
- Biweekly disinfection with sodium hypochlorite (or peracetic acid + H₂O₂)

Garvey MI et al. J Hosp Infection 2016;93:229-34.
 Gotting T et al. J Hosp Infection 2016;93:223-8.
 Schreiber PW et al. Emerg Infect Dis 2016;22:1830-3.

20

ECMO HCUs also contaminated

- *M. chimaera* has also been grown from HCUs used for ECMO
 - 7/10 HCUs in an ECMO center in Germany
 - Contaminated HCUs made by Medos, Novalung
 - These HCUs have a different design with an air-tight, closed system
 - Air sampling with contaminated machines running was negative
 - Hospital tap water negative for *M. chimaera*
 - 3/118 patients treated with ECMO since 2010 grew *M. chimaera* from respiratory secretions; not thought to be infected from the HCUs

Trudzinski FC et al. Eurosurv 2016;21:30398.

21

M. chimaera case series 4 US medical centers

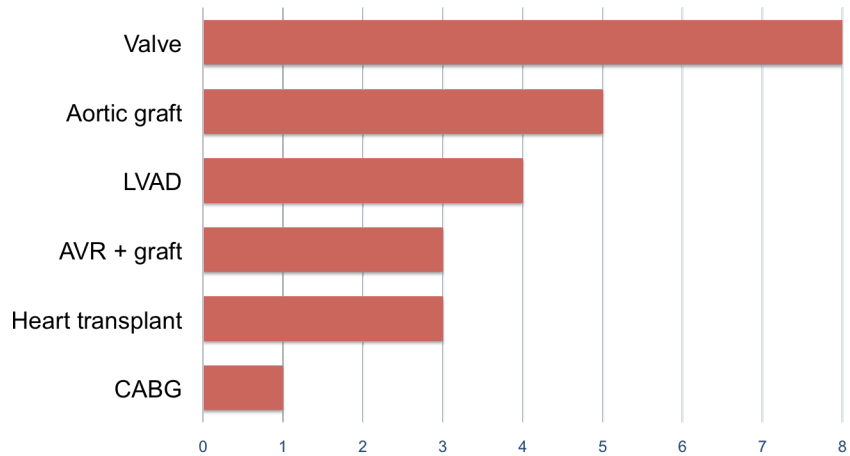
Patient Characteristics	Results
Total number of cases	24
Earliest sentinel surgery	2010
Male	87%
Age, y (mean, range)	60 (19-83)
Prosthetic cardiovascular material	83%
Duration from surgery to symptom onset in months, mean (range)	17 (1-72)

Appenheimer AB et al. IDWeek 2016, #2392, October 29, 2016.

22

***M. chimaera* Infections Associated with Heater Cooler Units**
Prof. Michael Edmond, University of Iowa
A Webber Training Teleclass

M. chimaera case series
Surgical procedure



Appenheimer AB et al. IDWeek 2016, #2392, October 29, 2016.

23

M. chimaera case series
Clinical presentation

Presumed source	N
Prosthetic valve	11
LVAD	6
Aortic graft	5
Sternal wound	2

Symptoms	%
Fatigue	100
Fever	70
Sweats	61
Cough	54
Dyspnea	50
Weight loss	50

- **Sites of dissemination:** liver, bone marrow, kidney, eye, thoracic and lumbar spine (osteomyelitis), pleural space, psoas muscle.
 - 13 patients had positive AFB blood cultures
- **Histopathology:** non-caseating granulomas, rarely AFB smear positive

Appenheimer AB et al. IDWeek 2016, #2392, October 29, 2016.

24

M. chimaera Infections Associated with Heater Cooler Units
Prof. Michael Edmond, University of Iowa
A Webber Training Teleclass

***M. chimaera* case series**

Outcomes

	Total patients	Deceased	Crude mortality
Antibiotics* + prosthetic material explantation	6	2	33%
Antibiotics* only	14	6	43%
No antibiotics	4	3	75%
Overall	24	11	46%

Duration of follow up for those with removal of prosthetic material is shorter than for those on medical treatment only (mean 16 vs 27 months).

*Most common regimen: macrolide + rifamycin + ethambutol +/- moxifloxacin +/- amikacin

Appenheimer AB et al. IDWeek 2016, #2392, October 29, 2016.

25

Control measures

- Use sterile or filtered water to fill HCUs
- Follow manufacturer's disinfection recommendations
- Ensure traceability of HCU usage
- Strict separation of HCU exhaust air from ORs
 - Move HCUs out of the OR; if not possible, the vents and fans of the HCU should face away from the patient

26

***M. chimaera* Infections Associated with Heater Cooler Units**
Prof. Michael Edmond, University of Iowa
A Webber Training Teleclass

Control measures:
Heater-cooler unit hose portal,
U. of Iowa



Hose portals constructed in all ORs where cardiopulmonary bypass is performed and all heater cooler units have been moved outside of ORs



Control measures:
Custom made stainless steel housing for
HCU's, U. of Zurich



Schreiber PW et al. Emerg Infect Dis 2016;22:1830-3.

28

Hosted by Bruce Gamage, PICNet BC
www.webbertraining.com

Environmental cultures

- FDA recommends considering environmental, air, and water cultures and monitoring if heater-cooler contamination is suspected <http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm466963.htm>
- Few labs have capability
- Negative predictive value is low
- Sequential testing demonstrates variability
- Safest strategy is to consider all LivaNova 3T HCU contaminated

29

Outbreak management

1. Determine risk: use of LivaNova T3 HCU in last 6 years?
2. Risk mitigation: separate bioaerosol from operative field
3. Case identification and notification:
 - Develop line list of potentially exposed cases (include standby case) over last 6 years
 - Notify potentially exposed patients
 - Notify referring MDs and internal consultants (ID, hem/onc, hepatology, ophthalmology)
 - Cross match list of patients with MAC isolated from blood, bone marrow or wounds in last 6 years against list of potentially exposed cases
 - Potentially exposed patients with consistent symptoms should have 2-3 AFB blood cultures obtained; if negative, consider bone marrow culture/histopathology
 - Report cases to the FDA via MedWatch

30

Challenges

- Case finding: Many pts receive follow-up care locally, not at the center where they had surgery
- Symptoms are very nonspecific (fever, fatigue, arthralgias/myalgias)
- Long incubation period
- Mycobacterial cultures are not routinely performed, but are required for diagnosis
- Very difficult to treat (multiple drug therapy, surgical removal of involved devices); unknown whether cure is possible

31

Take home messages

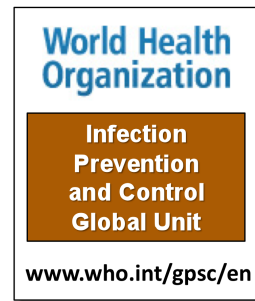
- Suspect *M. chimaera* infection in patients with history of cardiopulmonary bypass with any of the following syndromes:
 - Fever of unknown origin
 - Sarcoidosis
 - Vasculitis
 - Culture negative endocarditis
 - Culture-negative or treatment refractory sternal wound infection
- Most important control measure is to remove HCU from the OR

32

M. chimaera Infections Associated with Heater Cooler Units
Prof. Michael Edmond, University of Iowa
A Webber Training Teleclass

www.webbertraining.com/schedule1.php	
February 2, 2017	<p><i>(FREE Teleclass)</i> KNOWLEDGE GAP ABOUT EBOLA VIRUS DISEASE AMONG HEALTH WORKERS IN HOTSPOTS IN SUDAN Speaker: Musaab Mohamed Nour Abdelrahim Alfaki, Daoud Research Group and Charity Clinic, Sudan</p>
February 22, 2017	<p><i>(South Pacific Teleclass)</i> CATHETER-ASSOCIATED URINARY TRACT INFECTION PREVENTION IN THE CONTINUUM OF ACUTE CARE Speaker: Jan Gralton, Australian Commission on Safety and Quality in Healthcare</p>
February 23, 2017	<p>USING EXPERT PROCESS TO COMBAT CLOSTRIDIUM DIFFICILE INFECTIONS Speaker: Isabelle Guerreiro and Camille Achonu, Public Health Ontario, Canada</p>
February 28, 2017	<p><i>(European Teleclass)</i> THE ROLE OF DRY SURFACE CONTAMINATION IN HEALTHCARE INFECTION TRANSMISSION Speaker: Prof. Jon Otter, Imperial College Healthcare NHS Trust, London</p>
March 9, 2017	<p>EVALUATION OF INFECTION CONTROL TRAINING Speaker: Martin Kiernan, University of West London</p>
March 16, 2017	<p><i>(FREE Teleclass)</i> HOW TO BECOME CIC CERTIFIED WITHOUT BECOMING CERTIFIABLE</p>

Thanks to Teleclass Education
PATRON SPONSORS



Hosted by Bruce Gamage, PICNet BC
www.webbertraining.com