**M. chimaera**

- Slow-growing mycobacterium belonging to the *M. avium* complex
- Established as a distinct species in 2004
- Requires molecular diagnostic testing for identification
**M. chimaera Infections Associated with Heater Cooler Units**
*Prof. Michael Edmond, University of Iowa*
*A Webber Training Teleclass*

### Mycobacterium avium complex

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


### 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 > 1/375)
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


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

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)


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.
HCU-associated *M. chimaera* cases

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

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

van Ingen J. ECCMID, 4/16.
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
Although water from heater-cooler unit never contacts patients directly, the ventilation fan can aerosolize contaminated water.

Source of bioaerosols

Contamination of the operative field

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

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

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


---

*M. chimaera* case series

4 US medical centers

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

Appenheimer AB et al. IDWeek 2016, #2392, October 29, 2016.
M. chimaera case series

Surgical procedure

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

M. chimaera case series

Clinical presentation

<table>
<thead>
<tr>
<th>Presumed source</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosthetic valve</td>
<td>11</td>
</tr>
<tr>
<td>LVAD</td>
<td>6</td>
</tr>
<tr>
<td>Aortic graft</td>
<td>5</td>
</tr>
<tr>
<td>Sternal wound</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>100</td>
</tr>
<tr>
<td>Fever</td>
<td>70</td>
</tr>
<tr>
<td>Sweats</td>
<td>61</td>
</tr>
<tr>
<td>Cough</td>
<td>54</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>50</td>
</tr>
<tr>
<td>Weight loss</td>
<td>50</td>
</tr>
</tbody>
</table>

- **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.
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M. chimaera case series

Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Total patients</th>
<th>Deceased</th>
<th>Crude mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics* + prosthetic material</td>
<td>6</td>
<td>2</td>
<td>33%</td>
</tr>
<tr>
<td>explantation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics only</td>
<td>14</td>
<td>6</td>
<td>43%</td>
</tr>
<tr>
<td>No antibiotics</td>
<td>4</td>
<td>3</td>
<td>75%</td>
</tr>
<tr>
<td>Overall</td>
<td>24</td>
<td>11</td>
<td>46%</td>
</tr>
</tbody>
</table>

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.

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

Hosted by Bruce Gamage, PICNet BC  
www.webbertraining.com
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 HCUs, U. of Zurich

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](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 HCUs contaminated

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
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

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 HCUs from the OR
# M. chimaera Infections Associated with Heater Cooler Units

Prof. Michael Edmond, University of Iowa

A Webber Training Teleclass

<table>
<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>February 2, 2017</td>
<td>(FREE Teleclass) KNOWLEDGE GAP ABOUT EBOLA VIRUS DISEASE AMONG HEALTH WORKERS IN HOTSPOTS IN SUDAN</td>
<td>Musaab Mohamed Nour Abdelrahim Alfaki, Daoud Research Group and Charity Clinic, Sudan</td>
</tr>
<tr>
<td>February 22, 2017</td>
<td>(South Pacific Teleclass) CATHETER-ASSOCIATED URINARY TRACT INFECTION PREVENTION IN THE CONTINUUM OF ACUTE CARE</td>
<td>Jan Granton, Australian Commission on Safety and Quality in Healthcare</td>
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<tr>
<td>February 23, 2017</td>
<td>USING EXPERT PROCESS TO COMBAT CLOSTRIDIUM DIFFICILE INFECTIONS</td>
<td>Isabelle Guerreiro and Camille Achonu, Public Health Ontario, Canada</td>
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<tr>
<td>February 26, 2017</td>
<td>(European Teleclass) THE ROLE OF DRY SURFACE CONTAMINATION IN HEALTHCARE INFECTION TRANSMISSION</td>
<td>Prof. Jon Otter, Imperial College Healthcare NHS Trust, London</td>
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<tr>
<td>March 9, 2017</td>
<td>EVALUATION OF INFECTION CONTROL TRAINING</td>
<td>Martin Kieman, University of West London</td>
</tr>
<tr>
<td>March 16, 2017</td>
<td>(FREE Teleclass) HOW TO BECOME CIC CERTIFIED WITHOUT BECOMING CERTIFIABLE</td>
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