An Update on *Mycobacterium Chimaera* and Cardiac Surgery Infections Due to Contaminated Sorin 3T Heater-Cooler Units

**Presenter:**

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Disclosures

• None

Utilization Message

• As you view this presentation, consider the following important points regarding testing:
  • How is the test going to be used in your practice?
  • When should the tests be used?
  • How will results impact patient management?
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Objectives

- Discuss the global outbreak of *M. chimaera* infections following cardiac surgery
- Describe current knowledge about the heater-cooler units implicated as the cause of the outbreak
- Examine laboratory diagnostics for identification for detection, identification and susceptibility testing of *M. chimaera*

First Report of Cases¹

- In 2015, a group from Zurich, Switzerland reported a series of cases involving 6 patients with prosthetic valve endocarditis or vascular graft infections due to *Mycobacterium chimaera*
- First case dated back to surgery performed in 2012; reported latency of infection was 1.5 -3.6 years after surgery
- *M. chimaera* was cultured from blood, cardiac tissue and other surgical specimens for all cases
- *M. chimaera* was also cultured from heater-cooler units used for cardiac bypass during surgery and from air samples in the surgical suite

A Global Outbreak

- Since the first report, >100 cases of *M. chimaera* infection have been reported in Europe, the United States and Australia
- All cases are reported from patients who have previously undergone cardiothoracic surgery
- Cases involve the use of Sorin 3T heater-cooler units (HCU); also known as the LivaNova Stockert 3T HCU, manufactured in Germany
- >250,000 cardiothoracic surgical procedures annually in the United States alone raising concern that the cases detected so far are only the beginning a larger problem

What is a Heater-Cooler Unit and How is it Used in Cardiac Surgery?

- Used during major heart surgery when a heart-lung bypass machine is needed
- No direct contact with the patient but it contains 2 water tanks and tubing that through indirect thermal transfer are used to warm the blood and cool the cardioplegia solution used to slow/stop the heart

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Outbreak Investigation

- NTMs are environmental organisms frequently found in soil and water sources;
- NTMs are responsible for numerous reports of device-associated and post-surgical infections and outbreaks; found in hospital and household water sources; often resistant to disinfection.
- *M. chimaera* has been found in water from Sorin 3T HCUs used in cardiac surgeries around the world.
- *M. chimaera* isolates have been recovered from new, unused Sorin 3T HCUs and from water samples at the manufacturing site implicating the manufacturing site as the source of the microbial contamination.
- Sorin 3T HCUs account for approximately 60% of HCU units used in cardiac surgery in the U.S.

What Happened?
Smoke Testing of Airflow in Surgical Suite During HCU Operation

HCU exhaust directed away from operating field

HCU exhaust directed toward operating field
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What is Being Done?

• On June 1, 2016 the FDA advised hospitals to “determine a method for patient follow-up and establish patient surveillance in case of potential exposure”

• On October 13, 2016 the CDC said that “hospitals are advised to notify patients who underwent open surgery involving a Stockert 3T heater-cooler unit that the device was potentially contaminated, possibly putting patients at risk for a life threatening infection”.

Patient Notification

• At Mayo Clinic, >17,000 patients who underwent cardiac surgery at any of our sites (MN, FL, AZ, WI) within the past 5 years were notified of the recently discovered risk.

• Nurse and physician resources were made available to patients and their physicians who may have questions or concerns.

• The risk of infection appears to be low (1:100 to 1:1000) according to early reports from the CDC (https://www.cdc.gov/hai/outbreaks/heater-cooler.html)

• Patients may not experience any symptoms for months to years after the surgery (range 3 months to 5 years, median 18 months)
Clinical Presentation

Most common
- Cardiac manifestations
  - Endocarditis
  - Vascular graft infection
  - Mycotic aneurysm
- Surgical site infection
  - Mediastinitis
  - Sternal wound infection
- Abscess
- Bacteremia
- Other (osteomyelitis, ocular infections, granulomatous disease mimicking sarcoid, etc)

General symptoms are nonspecific
- Fever
- Night sweats
- Weight loss
- Fatigue
- Muscle aches
- Shortness of breath

Not necessary to test asymptomatic patients just because they have had cardiac surgery

Preventative Measures with the HCUs?

- The exact site(s) of contamination within the HCUs has not been well-defined
- Decontamination with a variety of agents has been successful in the short-term but fails to completely eradicate the organism
- Biofilm formation has been suggested
- Strict adherence to the manufacturer’s decontamination protocols and replacement of internal tubing/refurbishment has been recommended
- Reliable decontamination remains difficult

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Alternative Strategies

- Use of HCU from other manufacturers
- Positioning of the Sorin 3T outside of the operating suite and/or facing away from the surgical field has been demonstrated to reduce particle counts and disruption of the surgical air curtain (requires some construction)

M. chimaera

- Nontuberculous mycobacterium
- Member of the *Mycobacterium avium* complex
- Known as a genetic variant called “MAC-A” until Tortoli described it as a separate species in 2004
- *M. chimaera* was the name selected since a chimera in Greek mythology is a mixture of 3 different animals and *M. chimaera* is a genetic mix between different MAC strains
**M. avium Complex Species Members**

- *M. avium* subsp. *avium*
- *M. intracellulare*
  also
  - *M. avium* subsp. *silvaticum*
  - *M. avium* subsp. *paratuberculosis*
  - *M. avium* subsp. *hominissuis* (non-validated subsp.)
- *M. arosiense*
- *M. bouchedurhonense*
- *M. chimaera*
- *M. colombiense*
- *M. marseillense* (caution – do not confuse with *M. massiliense*)
- *M. paraintracellulare*
- *M. timonense*
- *M. vulneris*
- *M. yongonense*

**Laboratory Diagnostics for *M. chimaera***

- Slowly growing, non-pigmented, acid-fast mycobacterium
- Direct detection methods from patient specimens are not available in most clinical laboratories
- Acid-fast smear and mycobacterial culture recommended followed by identification to the species level for positive cultures
- Not all isolates of *M. chimaera* are clinically significant
  - MAC often isolated from respiratory specimens
  - MAC in respiratory specimens can be a pathogen, a commensal or a contaminant
  - in our experience, approximately one-third of MAC isolates from respiratory specimens can be further identified as *M. chimaera*
Common Questions for the Lab

- What type of specimen should I submit?
  - It depends on the clinical presentation
  - Consult your local ID specialist for help
  - Common samples: blood, purulent drainage (no swabs please!), tissue

- Should we do environmental testing on the HCU unit? Should we perform air sampling in the surgical suites?
  - Probably not
  - Consult your local Infection Control specialist
  - Literature has already firmly established that Sorin 3T HCUs manufactured prior to September, 2014 are likely to be contaminated with *M. chimaera*
  - Negative environmental cultures do not rule out *M. chimaera* contamination and do not negate the need to consider *M. chimaera* infection in patients with prior cardiac surgery and the appropriate clinical presentation
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Identification of *M. chimaera* from Culture Isolates

- Hologic/GenProbe AccuProbes for *M. avium* complex and for *M. intracellulare* will be positive but cannot identify to the species level
- Hain GenoType NTM-DR LiPA can differentiate *M. chimaera* from other MAC members
- MALDI-TOF mass spectrometry standard libraries cannot distinguish between *M. intracellulare* and *M. chimaera*
  - Software-based algorithm has been recently reported
- Sequencing of the 16S gene yields a single nucleotide mismatch with *M. intracellulare* at position 403; alternate targets are hsp65 and ITS.

Mycobacterial Blood Cultures for *M. chimaera*

- Yield from performing multiple blood cultures is unknown at present; general recommendation is to collect 1 to 3 blood cultures per patient
- Consult Microbiology Lab if large numbers of blood cultures will be collected to avoid rapidly exceeding available capacity
  - Mycobacterial blood cultures require prolonged incubation times
Susceptibility Pattern for *M. chimaera*

- AST should always be performed on clinically significant isolates
- Use CLSI-recommended panel for slowing growing mycobacteria
- *M. chimaera* is generally susceptible to clarithromycin
- No CLSI interpretive breakpoints for drugs other than clarithromycin; amikacin breakpoints coming soon
- Combination therapy with clarithromycin, rifabutin and ethambutol has been used; amikacin often added for first 3 months;
- ATS/IDSA guidelines - a minimum of 12 months of therapy for disseminated MAC disease; little data on cardiac implants infected with MAC so optimum therapy/duration of therapy is evolving

Summary

- *M. chimaera* is a NTM involved in a global outbreak event caused by use of Sorin 3T HCUs in cardiac surgery
  - Patient notification of possible exposure should follow CDC and FDA guidance
- CDC website is a good site for the most up-to-date information on the outbreak and they provide a toolkit to assist with patient notification
  - (https://www.cdc.gov/hai/outbreaks/heater-cooler.html)
- *M. chimaera* is a member of the *M. avium* complex; identification to the species level and AST should be performed by qualified laboratories for clinically significant isolates from patients with prior cardiac surgery
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References


Questions or requests…
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