



M. chimaera Infections After Exposure to Sorin 3T Heater-Cooler Devices during Open Chest Surgery: What Clinicians Need to Know

Webinar
October 14, 2016



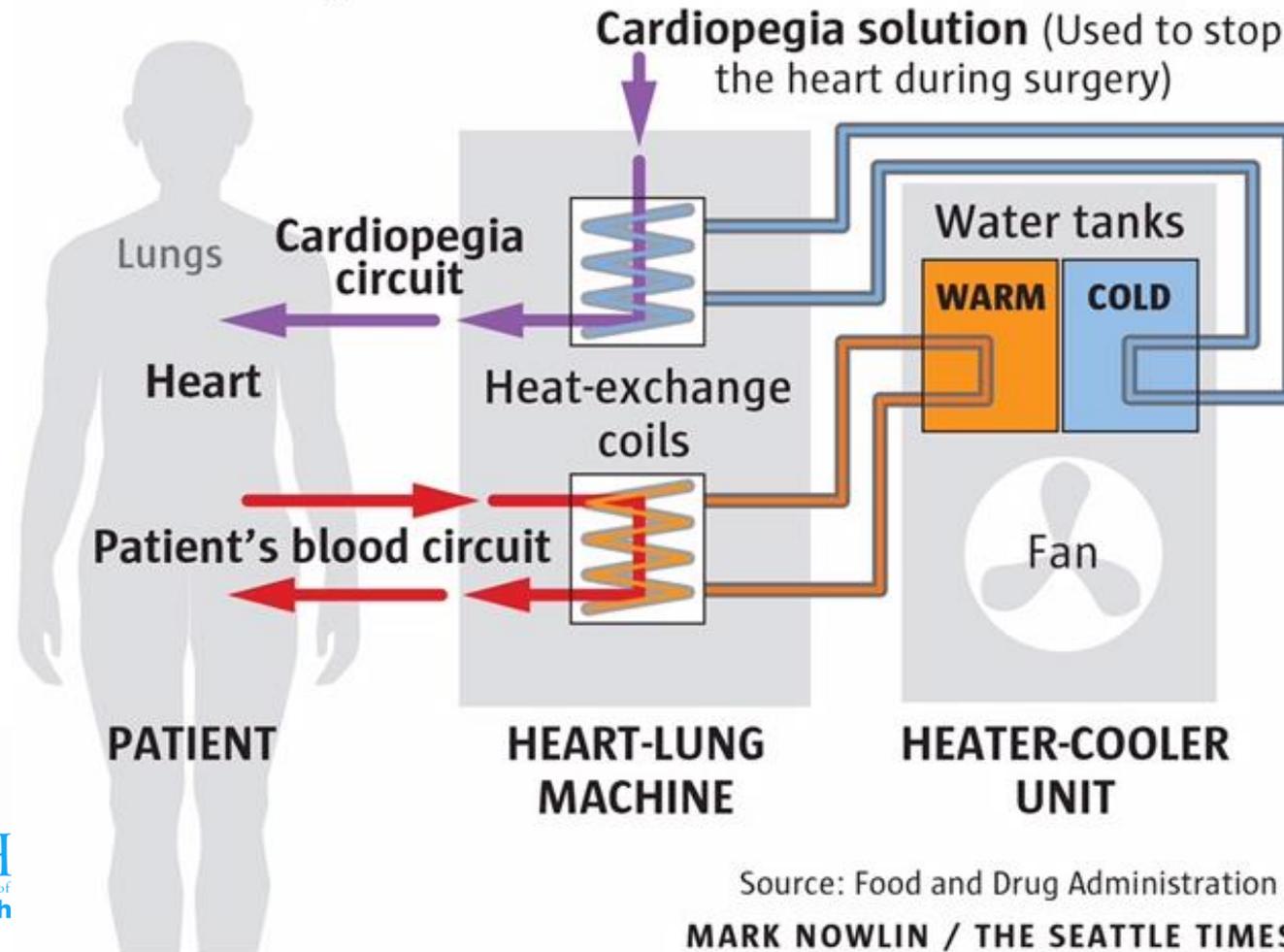
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Objectives

1. Alert the clinical community (these infections will not be identified if clinicians do not suspect *M. chimaera* as a possible source of infection)
2. Describe patient presentations and infection manifestations
3. Review laboratory testing and referral to reference laboratory for confirmation
4. Provide update on investigation and recommendations for mitigating further exposure risk

Heater-cooler devices

Heater-cooler units are used to regulate blood temperature during heart surgery. Federal health officials on Thursday warned that some devices have the potential to spread life-threatening infections.



Background

- Invasive infections due slow-growing *Mycobacterium chimaera* identified in patients in Europe and U.S.
 - CDPH aware of 2 CA cases
- Occur after open-chest bypass surgery using a heater-cooler device, the LivaNova Sorin Stockert 3T (Sorin 3T)
- Molecular typing highly suggestive of point-source outbreak due to device contamination during manufacturing
- Biofilm formation difficult (if not impossible) to eradicate
- Device fan can aerosolize *M. chimaera*, breach laminar flow, and contaminate sterile field

M. chimaera Infections Present Multiple Challenges for Clinicians

- Clinical presentations are non-specific, varied, and occur after long latency
- Diagnosis requires specific stains and cultures
- Most clinical laboratories cannot distinguish *M. chimaera* from *Mycobacterium avium* complex (MAC), nor perform drug susceptibility testing
- Treatment of *M. chimaera* infection is complex and prolonged, and guided by drug susceptibility testing results

Considerations for Identification and Diagnostic Evaluation



Case Summary: 17 U.S. and European *M. chimaera* Infections

- Median patient age, 62 years (range, 1–76)
- Gender, 16 (94%) male
- Surgery dates, 2008–2014
- Prosthetic implant, 16 (94%)
- Surgery type
 - Aortic valve replacement, 7
 - Aortic root and arch replacement, 3
 - Mitral valve reconstruction, 3
 - Aortic valve and arch replacement, 1
 - Aortic aneurysm repair, 1
 - Heart transplant, 1
 - Coronary artery bypass graft, 1



Kohler, Eur Heart J, 2015
Haller, Euro Surveill, 2016
Diekema, CDC Webinar, Aug 2016

Case Summary: 17 U.S. and European *M. chimaera* Infections (continued)

- Median time to diagnosis after open chest surgery, 26 months (range, 5–60 months)
- Common presenting symptoms (among 10 patients)
 - Fever, 8
 - Shortness of breath, 7
 - Weight loss, 7
 - Fatigue, 7
- Common presenting findings (among 10 patients)
 - Pancytopenia, 10
 - Elevated C-reactive protein, lactate dehydrogenase, transaminases, creatinine, 10
 - Splenomegaly, 8



Kohler, Eur Heart J, 2015
Haller, Euro Surveill, 2016
Diekema, CDC Webinar, Aug 2016

Case Summary: 17 U.S. and European *M. chimaera* Infections (continued)

- Common sites of infection (among 14 patients)
 - Cardiac
 - Prosthetic valve endocarditis, 7
 - Paravalvular abscess, 3
 - Prosthetic vascular graft infection, 2
 - Extracardiac
 - Osteomyelitis – sternum, distant site (wrist)
 - Vertebral osteomyelitis/discitis
 - Sternal wound infection with retrosternal abscess
 - Soft tissue infection at site of saphenous vein graft removal

Case Summary: 17 U.S. and European *M. chimaera* Infections (continued)

- Positive *M. chimaera* culture sites (among 13 patients)
 - Blood, 10
 - Cardiac tissue, 7
 - Bone marrow, 3
 - Bone, 4
 - Soft tissue, 2
- Histopathology with granulomatous inflammation (among 10 patients)
 - Liver, 3
 - Kidney, 2
 - Brain, 2

Some patients had multiple positive culture sites

Case Summary: 17 U.S. and European *M. chimaera* Infections (continued)

- Death attributed to *M. chimaera* infection, 6 of 17 (35%)
- Complications (among 10 patients)
 - Cardiosurgical re-intervention, 8
 - Breakthrough infection, 6



Kohler, Eur Heart J, 2015
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Diekema, CDC Webinar, Aug 2016

Diagnosis of *M. chimaera* Infection Requires Index of Suspicion

- Specific mycobacterial stains (i.e., acid fast bacillus (AFB)) and cultures are necessary
 - Typically obtained only when recognized risk factors (e.g., immunocompromised) present
 - Prior exposure to heater-cooler device in otherwise immunocompetent patient only recently described as a risk factor
- Not obtaining appropriate cultures at presentation can result in missed or delayed diagnosis, delayed therapy, and poor outcomes

Obtain AFB Stains and Cultures for Patients with Prior Exposure to Sorin 3T Device

Presenting symptoms:

- Recurrent or persistent fever of unknown etiology
- Night sweats
- Weight loss
- Fatigue
- Muscle aches
- Pain, redness, heat or pus around a surgical incision

Clinical manifestations:

- Prosthetic valve endocarditis
- Prosthetic vascular graft infection
- Sternotomy wound infection
- Mediastinitis or other deep organ space infection or abscess
- Disseminated infection, including embolic and immunologic manifestations (e.g., splenomegaly, cytopenias, osteomyelitis, chorioretinitis, hepatitis, nephritis)



Consider consultation with Infectious Disease specialist

Widespread Clinician Awareness Needed

- Identifying *M. chimaera* infections in patients with prior exposure to Sorin 3T device requires appropriate clinical suspicion
- Follow-up care for patients after open chest surgery often distant from cardiothoracic surgeon and hospital where surgery performed
- Late-onset, non-specific symptoms might prompt patients to seek care from primary care providers or primary cardiologists
- Infectious disease specialists might be consulted for evaluation of fever of unknown etiology

Laboratory Considerations



Mycobacterium avium Complex (MAC)

Includes *M. chimaera*

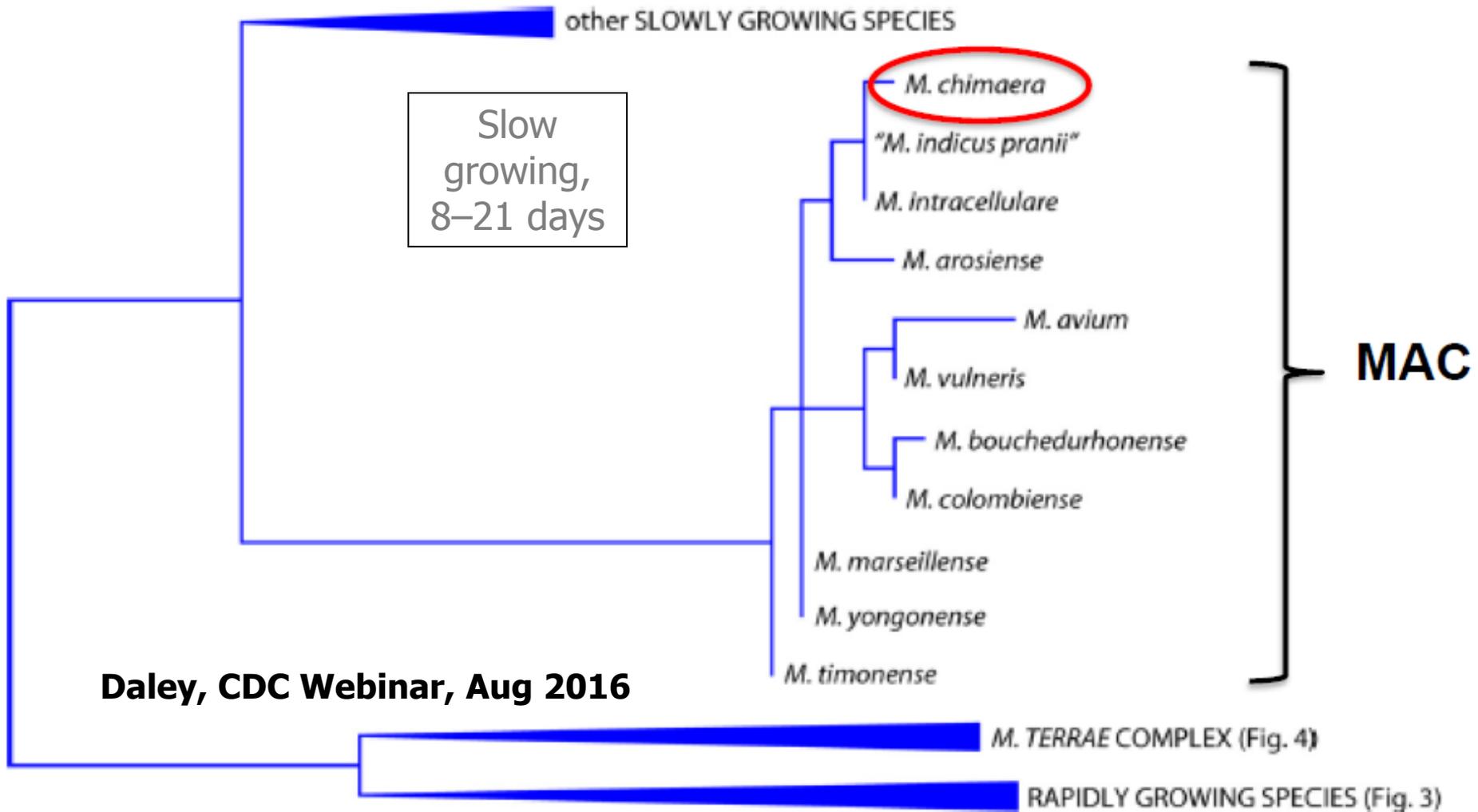


FIG 5 Phylogenetic tree, based on the 16S rRNA gene, for the species belonging to the *M. avium* complex.

Most Clinical Laboratories Cannot Distinguish *M. chimaera* from MAC

- MAC isolates from patients suspected to have *M. chimaera* infection should be submitted to a mycobacterial referral laboratory for identification and drug susceptibility testing
- Recommended: Mycobacteriology Laboratory at National Jewish Health
 - Requisition form may be accessed online
https://www.nationaljewish.org/getattachment/professionals/clinical-services/diagnostics/adx/ordering-tests/requisitions/ADxForm_Mycobacteriology_Form-new.pdf.aspx
 - Indicate in special instructions field that patient isolate is associated with exposure to Sorin 3T device

Treatment Considerations



Treatment of *M. chimaera* Infection is Complex and Prolonged

- Treatment duration undefined – prolonged, many months
- Multidrug regimen, may include injectable agent (e.g. amikacin)
- Choice of regimen guided by whether isolate is susceptible or resistant to macrolide antibiotics (e.g., azithromycin)
- Drug susceptibility testing for non-tuberculous mycobacteria (including MAC or *M. chimaera*) not typically available at clinical laboratories
 - MAC isolates from patients suspected to have *M. chimaera* infection should be submitted to a mycobacterial referral laboratory

M. chimaera Treatment is Difficult

Due to

- Delays in presentation and diagnosis result in widespread, disseminated infection
- Endovascular infection involving prosthetic materials
- Largely bacteriostatic drugs
- Low serum drug concentrations
- Patient co-morbidities

Consider expert consultation for
clinical management and treatment



Hospital Considerations



Recommendations for Clinician Outreach

- Notify clinicians who might evaluate patients in the years after cardiac surgery
 - Cardiothoracic surgeons
 - Cardiologists
 - Infectious disease physicians
 - Internal medicine physicians
 - Primary care physicians
 - Other clinicians
- Educate clinicians about the risk of infection associated with Sorin 3T heater-cooler devices manufactured before September 2014 (*date corrected after audio recording*)



Recommendations for Patient Identification

- Perform “look-back” of patient records who had open chest cardiac surgery with implicated Sorin 3T device
 - Review microbiology laboratory database for positive nontuberculous mycobacterium (e.g., MAC) in invasive samples, e.g., blood, pus, tissue biopsy, or implanted prosthetic material
 - Consider histopathology review to identify granulomatous disease (e.g. sarcoidosis)
- Consider use of electronic medical record system to alert or prompt clinicians to order AFB cultures in symptomatic patients who had cardiac bypass surgery in past 5 years
- Consider prospective surveillance strategies



Recommendations for Patient Notification

- Alert patients of infection risk due to potentially contaminated Sorin 3T heater-cooler device
 - Send notification by mail
 - Include letters that patients can present to their medical providers
- See CDC notification toolkit for sample patient and provider notification letters



Recommendations for All Heater-Cooler Devices

- Strictly adhere to manufacturer's maintenance, cleaning and disinfection instructions
- Use only sterile or filtered water (0.22 microns) – no tap water
- Immediately remove from service heater-cooler devices that show discoloration or cloudiness in fluid lines/circuits that may indicate bacterial growth
- Immediately remove from service any heater-cooler device, accessories, tubing, connectors that test positive or have been associated with patient infection
- Culturing device not recommended due to challenges with sample collection, long culture time, high false-negative rate



Note: Only select recommendations summarized here. For complete list of FDA recommendations, see

FDA Safety Alerts, Oct 15, 2015, & Oct 13, 2016

Recommendations for Sorin 3T Heater-Cooler Devices Manufactured Prior to September 2014

NEW

- Strongly consider transitioning away from use of these devices for open chest cardiac surgery
- Use of these devices should be limited to emergent and/or life-threatening situations if no other heater-cooler devices are available
- Testing of these heater-cooler devices to identify if contaminated with *M. chimaera* presents technical challenges (*see previous slide*) and is not recommended at this time



For complete updated FDA Sorin 3T recommendations, see

FDA Safety Alert, Oct 13, 2016

Summary

- Clinician awareness and index of suspicion for *M. chimaera* infections are critical to ensure patient identification and appropriate diagnostic testing (i.e., AFB stains and cultures)
- MAC isolates from patients suspected to have *M. chimaera* infection should be submitted to mycobacterial referral laboratory for species identification and drug susceptibility testing
- Expert consultation should be considered for clinical management and treatment guidance
- Current CDC and FDA recommendations should be implemented to notify clinicians and patients, and minimize further infection risk associated with heater-cooler devices

Providers must notify public health of *M. chimaera* infections

For more information, see our CDPH HAI Program webpage
"*M. chimaera* Infections Associated with Heater-Cooler Devices"

www.cdph.ca.gov/HAI

Or contact us

HAIProgram@cdph.ca.gov

Thank you

