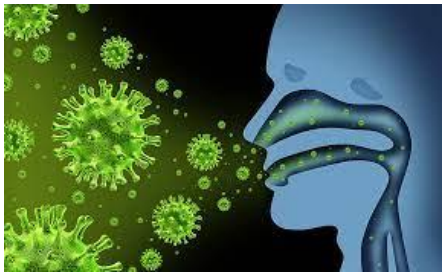


Sent on behalf of William Isenberg, M.D., Ph.D, Chief Medical & Quality Officer, Sutter Health, and Jeffrey Silvers, M.D., Medical Director of Pharmacy and Infection Control, Sutter Health

Emerging Infections Newsletter for Clinicians

July 6, 2023

Written by Dr. Silvers with contributions from Dr. Joan Etzell (Lab), Lisa Rieg (Pharmacy), and Gordon Sproul (Pharmacy). Please use Google Chrome for the best experience.

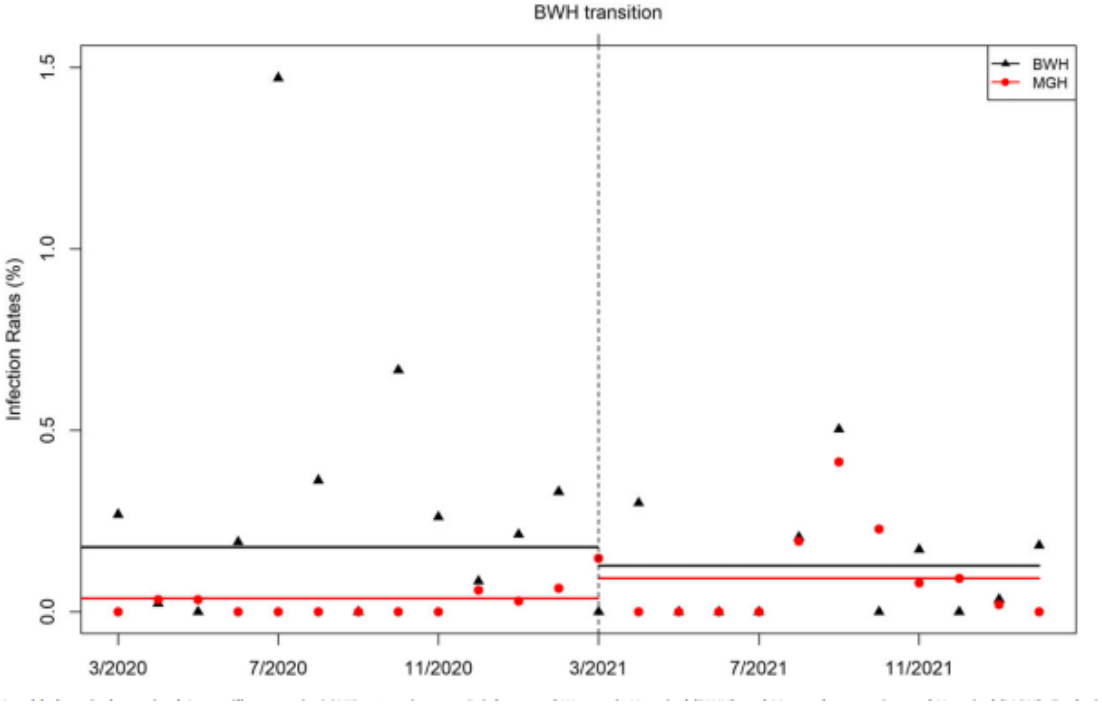
Topics

1. Aspergillus and COVID
    a. Does a negative pressure room increase the risk?
2. Candida auris
    a. Is this the first pathogen identified secondary to global warming?
    b. High risk of nosocomial transmission even with an infection control bundle
    c. Treatment with an echinocandin can lead to pan-resistant organisms
    d. Identification in coastal wetlands
3. Vaccines update
    a. RSV
    b. Influenza
    c. Mpox
4. Share the newsletter

Aspergillus and COVID-19

- Invasive fungal infections are a significant complication in critically ill patients with COVID-19. Aspergillus, Mucorales and Candida (including *C. auris*) are the most common groups reported.
- Nature in August 2022 published a review of the epidemiology, underlying co-morbidities, host immune response, effects of treatments including corticosteroids and immunomodulatory treatment, and diagnostic limitations.
- Infection Control and Hospital Epidemiology June 2023 published an observational, retrospective, single-variable, population-based study looking at the risk of hospital-acquired Aspergillus in patients with COVID-19 in the two major academic hospitals in Massachusetts (MGH and BWH).
    - Utilization of airborne-infection isolation rooms (AIIR) was the variable.
    - Otherwise, these two facilities shared and followed identical infection control practices.
    - MGH prioritized airborne-infection isolation rooms (AIIR) for patients with COVID-19 undergoing aerosol-generating procedures (AGP).

- BWH modified pressures in multiple wards to create AIIR for all patients with COVID-19.
- March-August 2020, 96% COVID-19 patient-days at BWH were in AIIR. During that time only 22% of that patient population were in AIIR at MGH.
- March 2021, BWH changed to follow MGH and only use an AIIR for an AGP.
- The graph below shows the mean incidence rates before and after the BWH transition (solid lines). The mean incidence rates before the transition showed a wide divergence which narrowed after BWH limited usage of an AIIR.



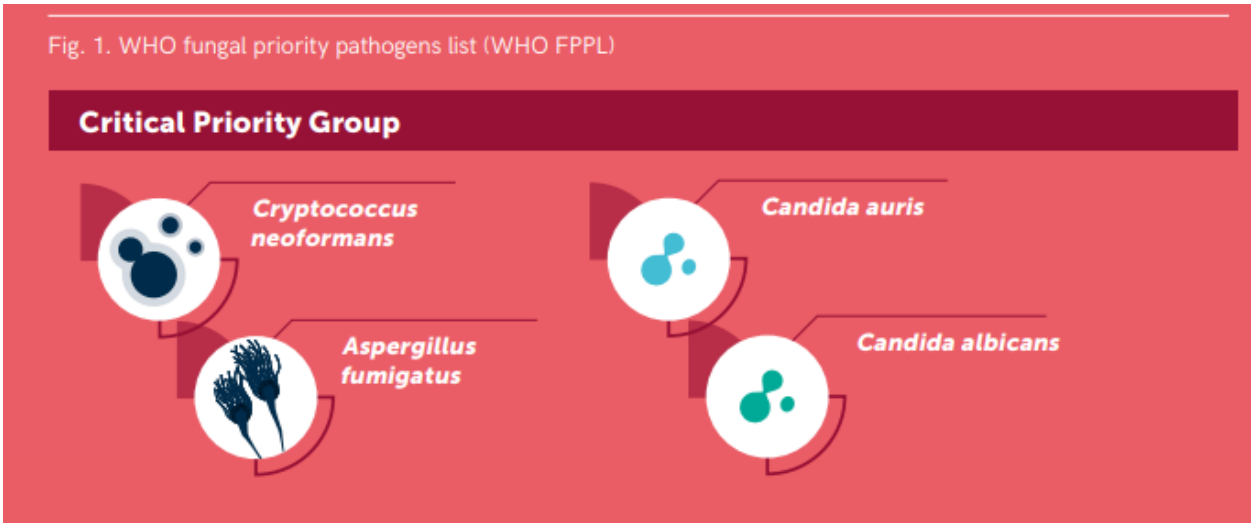
- This article raises the question of whether the AIIR increases the risk of Aspergillus in patients with COVID-19.
- Although this situation presented an unusual opportunity to look at a single variable (AIIR usage) and the impact on the incidence of identifying pulmonary Aspergillus in patients with COVID-19, there are many issues with this study.
  - The AIIR at BWH were modified AIIR, adapted for the pandemic. Further details are not provided.
  - No air sampling was performed to measure spore levels
  - Evaluation for Aspergillus was dependent on the providers.
  - This was a population-based study that does not look at how long individual patients were in an AIIR or any associations with treatment.
  - When BWH limited usage of AIIR to AGP, their mean incidence decreased but simultaneously the mean incidence at MGH increased.
  - The actual number of hospital-acquired Aspergillus cases was low and small differences would not be detected.
  - No information about construction during that time interval.

- **Take-Home Aspergillus, COVID-19 and AIIR**
  - Although there was only a single infection-prevention variable between the two hospitals in this study, there is inadequate information to rule out other unidentified, confounding variables.
  - The article assumes that modified wards where every room was converted to an AIIR have the same risk as standard approved AIIR.

- Small numbers of cases and provider-dependent testing could result in a Type II error.

Candida auris

- *Candida auris* is a multidrug resistant, highly transmissible, rapidly emerging, nosocomial pathogen. It joins *Aspergillus fumigatus*, *Cryptococcus neoformans* and *Candida albicans* as one of the four critical-priority, fungal pathogens listed by the WHO in their report published October 2022.



- The emergence of *C. auris* as a human pathogen is very recent. The oldest identified isolate dates to 1996.
- No other strains were identified searching through the historic *Candida* collection. Beginning in 2012, there has been a rapid emergence of *C. auris* as a human pathogen.
- It is believed to have started in a different ecologic niche, which remained unidentified until 2021, resulting from global warming.
- The high level of azole (fluconazole and multiple others) resistance in *C. auris* is thought to be related to widespread human medicinal and agricultural use starting in the late 1970s.
- Environment International published an article in 2015 discussing that wastewater treatment plants are only partially effective at removing azoles.
- Although the first cases of *C. auris* were reported in the United States by the CDC in 2016, it was already identified in at least four different states at that time.
- Only four years later (2020), the CDC reported three patients in New York with pan-resistant *C. auris* (defined as resistant to fluconazole, amphotericin B, and echinocandins).
- Examples of echinocandins include caspofungin, micafungin and anidulafungin. No nosocomial transmission was identified from those three isolates. They did not have an epidemiological link, but they all developed resistance to echinocandins during prolonged echinocandin treatment and they all had clade 1.
- This clade (South Asian clade) is known to exhibit increased antifungal resistance compared to the other 3 *C. auris* clades.
- In 2021, the CDC reported nosocomial transmission of pan-resistant and echinocandin-resistant *C. auris* in Texas and the District of Columbia. Prior to that report, echinocandin-resistant *C. auris* comprised only about 1% of tested isolates.

- The development of resistance to echinocandins was thought to be due to mutations in the FKS gene.

- Eurosurveillance in April 2023 published a retrospective report from Italy of over 500 cases at a single, tertiary-care facility from July 2019 through December 2022. This was predominantly during the COVID-19 pandemic. Spread within the facility continued despite a comprehensive infection control bundle. Of 483 colonized patients, 85 (17.6%) developed candidemia.
  - A total of 60 isolates were further characterized. These isolates were all from clade 1, were from the same subclade 1c, had an identifiable genetic signature for the hospital outbreak strain and were resistant to amphotericin B and fluconazole.
  - Two patients on chronic echinocandin medications for *C. auris* developed candidemia on treatment. They had less than five single nucleotide polymorphism (SNP) substitutions, but both had a single nucleotide polymorphism in the FKS gene.
    - The FKS substitution was different between the two resistant isolates suggesting that resistance developed from antifungal treatment pressure and emerged independently.
- How and why *C. auris* had four different clades initially found in geographically diverse areas of the world is still unknown. In general, fungi typically grow at lower temperatures and do not survive as well at the higher human body temperature. *C. auris* is more thermotolerant than other Candida species.
- The first environmental isolate of *C. auris* was reported from coastal wetlands in India in 2021. The journal mBio published commentary about how these environmental isolates support the global-warming-emergence hypothesis.
  - Environmental *C. auris* adapted to growth in warmer, more humid environments enabling transmission and pathogenicity in humans.
  - This would be considered the first identified, human pathogen that developed secondary to global warming.

- **Take-Home on Candida auris**
  - *Candida auris* is one of the four critical priority fungal pathogens listed by the WHO.
  - Most strains are resistant to azoles, and many are resistant to amphotericin. The majority are sensitive to echinocandins.
  - It is believed to have emerged because of global warming with high azole-resistance from human medicinal and agricultural use.
  - Nosocomial transmission is a very large risk with this organism and about 17% of patients colonized while in a hospital will develop candidemia.
  - The barrier to development of resistance to echinocandins is low.
  - Studies are showing the development of a mutation in the FKS gene while being treated with an echinocandin. This can result in a pan-resistant organism.
  - Antimicrobial stewardship is critical to ensure that patients infected with C. auris are treated for the minimal amount of time to eradicate the infection.
  - Echinocandins should not be part of an attempt at decolonization.
  - *C. auris* has now been identified in the coastal wetlands in India. This supports the theory that *C. auris* has emerged because of global warming.

Vaccines Update

- Between June 21-June 23, the CDC's Advisory Committee of Immunization Practices (ACIP) proposed updated recommendations for new and existing vaccines classes. Updates notable to Emerging Infections include the following:
  - **RSV (Older Adults):**
    - Adults 60 years of age and older may receive a single dose of RSV vaccine (Arexvy®, GSK or Abrysvo®, Pfizer) using shared clinical decision-making.

        - ✓ This is a weaker guidance compared to the prior proposal in February which was for routine administration recommended for adults 65 years and older.
        - ✓ Clinical trials were underpowered to show efficacy against RSV hospitalization, in adults 75 years of age and older, and in frail adults.
        - ✓ Efficacy of both RSV vaccines declined midway through a second RSV season, raising concerns about vaccine durability.
    - **Influenza:**
        - All 2023-2024 seasonal influenza vaccine will include an updated A H1N1 strain based on inter-seasonal data.
        - People with a history of egg allergy no longer need to receive their flu vaccine in a supervised medical setting.
            - ✓ In a limited CDC data set, there were no deaths, anaphylaxis or hospitalizations among 1,591 people receiving a seasonal inactivated influenza vaccine and 1,129 receiving live, attenuated, influenza vaccine for persons with egg allergy from 2017-2022.
    - **Mpox:**
        - Since the U.S outbreak, Jynneos vaccine efficacy has ranged from 36% to 75% for one dose received and 66% to 89% for two doses received.
            - ✓ As a result, the CDC is still not recommending Jynneos boosters for any populations.
            - ✓ The two-dose series provided enough protection during the prior outbreak and a 3rd dose has led to increased local site reactions in most patients.
    - **COVID-19:**
        - The COVID-19 Vaccines Workgroup discussed whether the vaccine schedule for children ages 2-4 years could be simplified to a single annual dose of updated COVID-19 vaccine.
            - ✓ Children ages 6 – 23 months have increased COVID-19 hospitalization rates.
            - ✓ Hospitalization rates in children ages 2 – 4 years appear to be similar to children 5 – 17 years based on March 2020 - May 2023 data.
            - ✓ Decision before new monovalent vaccine released.

- **Take Home on Vaccines and ACIP Recommendations:**
    - RSV vaccines for persons 60 and older will be available in the fall based on shared clinical decision-making.
    - People with egg-allergy may receive any flu vaccine (egg-based or non-egg based) that is otherwise appropriate for their age and health status.
    - A two-dose Jynneos vaccine series is still recommended for at-risk populations
    - Updated COVID-19 vaccine recommendations for children 2-4 years of age are anticipated in the Fall.

Share the Newsletter

Anyone who would like to be added to the Emerging Infections newsletter should send a request to bryan.gardner@sutterhealth.org

This communication is intended for clinicians caring for Sutter patients. If you have questions, please reach out to us at clinicians@sutterhealth.org.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