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## Infection Control Challenges of Infrequent and Rare Fungal Pathogens: Lessons from Disseminated *Fusarium* and *Kodamaea ohmeri* Infections

*To the Editor*—Infrequent and rare fungal infections represent special challenges with respect to infection prevention and control. The epidemiology of many of these infections is not well understood with regard to environmental reservoirs, modes of transmission, and ways to detect them. Because of their relative rarity, laboratory diagnosis of these potential pathogens is challenging. Specific identification requires expertise because most diagnoses of fungi, especially those that are filamentous, are morphology based and nonautomated.

Antifungal susceptibility testing of these rare pathogens is challenging because reliable methodology and antifungal breakpoints are often not readily available. Quality-assured diagnosis requires confirmation of rare species in reference laboratories, posing problems with regard to transportation of microbiologically hazardous culture isolates. In addition, reference laboratory facilities are not available in all regions and countries, and sometimes international collaboration and shipment of materials are required for confirmation of diagnosis. Here, we relate 3 cases of unusual fungal infections to illustrate these points.

A 4-year-old male child with acute lymphoblastic leukemia and receiving chemotherapy developed blackish necrotic lesions on the back and forehead in September 2011. Histopathology from a lesion showed acutely angled branching fungal hyphae in the dermis, and *Fusarium solani* was isolated on culture. Antifungal susceptibility showed the following minimum inhibitory concentrations (MICs): amphotericin B 2 µg/mL, voriconazole 8 µg/mL, itraconazole 16 µg/m, posaconazole 16 µg/mL. The patient initially responded to antifungal therapy but had a relapse of similar skin lesions. He eventually responded to a combination of liposomal amphotericin B, which was given for 31 days (1 to 2.7 mg/kg/day, intravenously [IV]), and voriconazole for 71 days at 10 mg/kg/day, orally. The child survived and is well on follow-up (3 years).

A 22-year-old male with aplastic anemia underwent a haplo-identical stem cell transplantation from a brother in August 2013. He developed multiple erythematous papular skin lesions 18 days post transplantation and cellulitis of right big toe. A blood culture from the central line grew filamentous fungus after 4 days of incubation, identified as *Fusarium* spp. Antifungal susceptibility showed the following MICs: amphotericin B-1 µg/mL, voriconazole 4 µg/mL, itraconazole >16 µg/mL. The patient had acute graft rejection, hemorrhagic cystitis. He was treated with liposomal amphotericin B for 26 days (3 mg/kg/day, IV), voriconazole for 29 days (200 mg, orally, twice daily), and caspofungin for 10 days (50 mg/day, IV). The patient died in September 2013.

A 75-year man with total colectomy developed *Klebsiella* bacteremia on postoperative day 5, which initially responded to a course of meropenem and colistin. Antibiotics were changed to piperacillin-tazobactam, ciprofloxacin, and doxycycline when *Ralstonia pickettii* and *Elizabethkingia meningoseptica* were isolated from central-line tip on different occasions. Because the patient remained febrile, repeat blood cultures were taken, which grew *Kodamaea ohmeri* on several occasions while the patient was on fluconazole and then on caspofungin. Fungaemia persisted despite changing the central line. Treatment with conventional amphotericin B (IV) for 2 weeks cleared the fungus. The patient was discharged in stable condition.

*Fusarium* is a hyaline hyphomycetes fungus that may cause localized infections, such as keratitis and onychomycosis, and disseminated infections in immunocompromised hosts.<sup>1,2</sup> The natural habitat of *Fusarium* is said to be plants and soil.<sup>1</sup>

Outbreaks of infections, such as keratitis due to contaminated lens solution, have been reported, as has the isolation of this fungus in hospital water systems.<sup>3–6</sup> Unlike infection in a normal host, fusariosis in immunocompromised patients is typically invasive and disseminated.<sup>1,2</sup> Disseminated fusariosis has high mortality rates.<sup>1</sup> Predictors of poor outcome have been identified in various studies as persistent neutropenia and recent corticosteroid therapy.<sup>1</sup> There is no consensus on optimal management of fusariosis. Antifungals alone or in combination, together with other measures such as surgical intervention or colony-stimulating growth factors, have been used to treat such infections.<sup>1</sup>

*Kodamaea (Pichia) ohmeri*, an uncommon fungus and formerly considered a contaminant, has recently been reported to cause fungemia, endocarditis, funguria, and peritonitis in immunocompromised patients.<sup>7–9</sup> This yeast, previously known as *Pichia ohmeri*, is commonly used in the food industry for its fermentation properties in pickles.<sup>8</sup> Misidentification of this fungus as a *Candida* species is not unusual unless specific molecular methods are used (ie, DNA sequencing or matrix-assisted laser desorption/ionization-time of flight [MALDI-TOF]).<sup>9,10</sup>

Prevention of infections due to rare fungi such as *Fusarium* and *Kodamaea* requires a multipronged strategy that includes the following elements: (1) attention to thorough environmental cleaning and disinfection, (2) surveillance of fungal infections through air and water microbiology especially in transplant units, (3) a high index of clinical suspicion especially in early phases when infections may still be localized (eg, onychomycosis in a case outlined above), (4) appropriate selection of prophylactic anti-fungal agents (eg, posaconazole in stem cell transplant recipients and voriconazole in patients with acute myeloblastic leukemia), (5) early diagnosis and appropriate empirical therapy in clinically suspected infections, and (6) availability of adequate laboratory diagnostic infrastructure for early recognition of these organisms in environmental and clinical samples. Furthermore, liaison with reference laboratories and specialists experienced in diagnosis and management of these infections is critical for optimizing outcome. In the cases outlined here, the *Fusarium* species were initially identified in the care-giving hospital by a laboratory technologist experienced in fungal diagnosis. *Kodamaea* was identified in the same center using the VITEK2 system (bio-Merieux, Durham, NC). The fungal identifications were confirmed by India's national reference laboratory for fungal infections, a World Health Organization Collaborating Center for Mycology. The cost of treatment, the need for prolonged intravenous antifungal therapy, the cost of prolonged hospital stay, and the cost of monitoring patients for optimal response, as well as side effects of treatment are major challenges on the path toward a successful outcome.

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## The Importance of Chemical Solutions Used for Cleaning Stainless Steel Surgical Instruments in the Central Sterile Supply Department

*To the Editor*—The sterilization process can only be effective if cleaning and disinfection are adequate. Surgical instrument cleaning is usually performed by manual cleaning followed by mechanical cleaning. After surgery, primary cleaning of an instrument takes place in the user area, and secondary cleaning is conducted in the Central Sterile Supply Department (CSSD) holding room for soiled items. In our 167-bed oncology center in eastern India, we use multienzyme solutions for manual cleaning, rust inhibitor for rust removal, and acidic and alkaline solutions for mechanical cleaning.<sup>1</sup> After instruments are presented to the CSSD for disinfection, they are sorted into wire-mesh baskets and soaked in neutral enzymatic solution for at least 10 minutes to remove gross blood from the instrument's surface and from hollow orifices. This enzymatic cleaning solution dissolves proteins by breaking the amino acid bonds, and the blood or tissue can then be easily removed from the instrument with normal water. According to the manufacturer's recommendation, the solution concentration of this cleaner is 5 mL per liter of water (minimum), and the solution is considered active for not more than 3 hours after it is originally mixed. A good-quality enzymatic solution should have some surfactant when used in hard water. In our experience, manual cleaning solutions should be transparent when mixed with water to reduce the chance of instruments being missed or forgotten.<sup>2</sup>

Pure stainless steel instruments never caught rust, but occasionally, due to poor water quality, various metallic reactions, or insufficient drying, superficial rusting may occur, which can be removed by using rust inhibitor. For this procedure, we use inorganic phosphorus (from phosphoric acid) at a concentration of 10 mL per liter of water (minimum) as a rust removal solution. The contact time with the solution must be properly maintained to protect the passive layer of the stainless steel surface. This solution is used in an ultrasonic bath (Soniclean PS 3000, Australia) with lukewarm water, and brushing is not required.<sup>1</sup>

The mechanical washing process requires different quantities of solution during the prewashing and intermediate washing steps. Every TIVA 700 (Steelco, Italy) washer/disinfector (W/D) has two pumps through which the solution is added according to predetermined concentration levels. In our institution, we use both alkaline and acidic solutions in our mechanical mixing system. Here, an alkaline solution (ie, a

phosphate) is used to remove organic substances and an acidic solution (ie, phosphoric acid) is used as a neutralizer, though phosphoric acid can also remove inorganic substances from the water, if they are present. The ratio of alkaline solution to acidic solution is 2:1 (4 mL:2 mL) per liter of water. In this system, low-foam enzymatic solution or alkaline with enzymatic solution can be used as a cleaning agent in the W/D.<sup>1</sup>

However, both systems exert some adverse effects on the instruments. If the ratio of the acidic to the alkaline solution (pH) is not maintained properly because of a faulty mixing pump, then black corrosion can occur on the instrument surface, which is difficult to remove.<sup>4</sup> Likewise, if the enzymatic solution creates foam during mechanical washing, then proper cleaning can be impaired due to bubble formation. Also, if the temperature of the water is >40°C, then the properties of enzyme break down, resulting in insufficient cleaning. Moreover, the quality of enzyme solutions and their preservatives can also hamper cleaning efficacy.

Cleaning performance can be monitored by using proper testing devices such as adenosine triphosphate (ATP) or soil testing. The ATP test (ie, a molecule test) is performed by swabbing the instrument after disinfection. The ATP reacts with the luciferase enzyme and emits light; the light intensity is then captured using a luminometer, and the level of contamination is determined according to a scale provided by the manufacturer. The amount of light produced is directly proportional to the amount of ATP present in the sample and, thus, to the quanta of organic matter contamination.

The soil indicator is composed of protein, fat and carbohydrate. The protein can coagulate when heat treatment starts (ie, a boiled egg). In the W/D there are three steps: pre-wash, intermediate wash, and thermal wash. In pre-wash, the temperature does not rise above 20 °C and so protein never coagulates. In intermediate wash, the temperature rises up to 40 °C and so protein only starts to coagulate. However, in thermal wash, the temperature rises between 40 °C and 90 °C and protein can easily coagulate and tightly adhere to the surface of the instrument. This soil indicator should be passed (by color change) before the final thermal wash step inside the W/D, or the color will never change due to protein coagulation.

Currently, various cleaning solutions have been introduced. Cleaning solutions must be optimized according to the potential contamination on the instruments and compatibility with the steel content. To avoid hazards, quality certificates and material safety data sheets are crucially important for every cleaning solution. Each solution should have proper certification by the original instrument manufacturers for use on the specific instrument being disinfected.

In our hospital, cleaning efficacy is monitored in every cycle using soil tests in the W/D. In our experience, soil tests rarely fail. However, failure may occur due to high total dissolved solids in the water or due to overloading surgical instruments in the mesh baskets.

The total cost of solution as a consumable is Rs. 809,947.12 (US\$13,499.11) per year, which represents 4.19% of the total