pediatric emergency physicians considered that the development of clinical decision rules in children less than 36 months of age with fever without source (FWS) was their top clinical priority.

Extensive efforts have been made for decades to find clinical signs and biologic markers that could predict severe bacterial infection (SBI) in infants with FWS. The combination of a clinical score associated with a normal white blood cell (WBC) count and a normal urinanalysis have been used to rule out SBI in infants for many years. More recently, acute phase reactant proteins such as C-reactive protein (CRP) and procalcitonin, alone or in combination, have been investigated and shown to be superior to WBC count to rule out or rule in SBI. Luaces-Cubells et al in the accompanying article compared different markers of infection in a large cohort of 868 children 36 months of age and younger with FWS. Fifteen (1.7%) presented with an invasive bacterial infection. As in numerous studies, results showed that procalcitonin at a cutoff level of 0.9 ng/mL was the best predictor of SBI with a positive and negative likelihood ratio (LR) of 9.13 and 0.15, respectively, compared with CRP (cutoff level 80 mg/L, positive LR 6.45, negative LR 0.7) and WBC count (cutoff 15,000/mm^3, positive LR 1.62, negative LR 0.8). It is interesting to note that they analyzed a subset of 275 children in whom the duration of fever was less than 8 hours, a window giving the opportunity to treat the disease very early, a condition associated with a better outcome in sepsis, meningitis and pyelonephritis. In this situation, the sensitivity and specificity of procalcitonin was significantly superior to CRP with an area under the receiver operating characteristic curve of 0.97 (95% confidence interval: 0.94–0.99). This result is due to the favorable kinetics of procalcitonin that increases in blood by 3–6 hours after a bacterial challenge.

Compelling evidence in the literature, coming from different settings and multiple countries, emphasizes the better characteristics of procalcitonin and CRP, or the combination of both, compared with the WBC count and with clinical signs in the prediction of SBI. It is time now to build and validate appropriate clinical decision rules including these markers in the management of infants with FWS. Subsequently, impact studies will need to demonstrate that such strategies can be implemented in practice, can improve the quality of care and are cost-effective. At the end of this process, new guidelines should be prepared by expert pediatric care providers.

PSEUDOMONAS AERUGINOSA OUTBREAK IN A PEDIATRIC ONCOLOGY CARE UNIT CAUSED BY AN ERRANT WATER JET INTO CONTAMINATED SIPHONS

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Abstract: We analyzed an outbreak of invasive infections with an exotoxin U positive *Pseudomonas aeruginosa* strain within a pediatric oncology care unit. Environmental sampling and molecular characterization of the *Pseudomonas aeruginosa* strains led to identification of the outbreak source. An errant water jet into the sink within patient rooms was observed. Optimized outbreak management resulted in an abundance of further *Pseudomonas aeruginosa* infections within the pediatric oncology care unit.

Key Words: *Pseudomonas aeruginosa*, genotyping, catheter-related infections, pediatric oncology patients

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Infection with the aerobic, Gram-negative bacterium *Pseudomonas aeruginosa* (*P. aeruginosa*) occurs frequently in critically ill children such as preterm infants or patients with immunodeficiency.[1] Moist environments are a common reservoir for nosocomial *P. aeruginosa* strains and outbreaks.[2,3] Outbreak reports structured according to the outbreak reports and intervention studies of nosocomial infection guidelines,[4] which identify the index patient or the source of nosocomial infection are aimed to better understand the routes of transmission and to promote rapid typing strategies such as amplified fragment length polymorphism[5] to prevent the dissemination of these strains. Here, we report a small outbreak of blood stream infections (BSI) with *P. aeruginosa* within a pediatric oncology care unit (POCU) and its management.

MATERIALS AND METHODS

Study Design and Patients

A retrospective study was performed to analyze a cluster of 3 *P. aeruginosa* BSI within a POCU in July 2008. To assess the effectiveness of the outbreak management, the incidence of infections with *P. aeruginosa* in patients of the POCU was analyzed in the period between 2004 and 2010. All hematooncologic patients in the POCU who were undergoing immunosuppressive treatment received oral antibacterial and antifungal prophylaxis with trimethoprim-sulfamethoxazole and nystatin and, during neutropenia, oral colistin as well.

Setting

The POCU is composed of 2 single and 8 double bedrooms (Fig., Supplemental Digital Content 1, http://links.lww.com/INF/B102). The 2 single bedrooms are protective isolation rooms for patients undergoing stem cell transplantation. They are equipped with laminar flows for air purification, a separate bathroom and an anteroom with a handwashing station. Caps, masks, gloves and shoe covers as well as standardized hand-disinfection procedures are required both for staff and visitors before entering the patient's room. The 8 double rooms are equipped with high-efficiency particulate air filters and a private bathroom. Water taps are all equipped with Pall-Aquasafe filter systems (Pall Corporation, Port Washington, NY).

Ethical Statement

The approval of the ethical committee and individual written consent were not required because all data enclosed in this report were collected during the acute management of an outbreak of *P. aeruginosa* infections in a POCU.

Microbiologic Sampling

Specimen collection from patients and the environment and microbiologic cultures were performed according to DIN EN ISO/IEC 17025, as well as species identification and antimicrobial susceptibility

testing with the VitekII (bioMérieux, Nürtingen, Germany), using susceptibility breakpoints according to the CLSI 2007 standard. During the outbreak in July 2008, environmental samples were taken from all water outlets, siphons, disinfectant dispensers and glove dispensers within the POCU. Samples from drains were taken with sterile tips, and water samples from siphons were drawn using sterile tubings attached to sterile 10 ml syringes. All other samples were taken using contact agar plates. Follow-up samples were taken in January 2010.

Characterization of *P. aeruginosa* Isolates

All *P. aeruginosa* isolates revealing the same resistance pattern as the outbreak strain were genotyped by random amplified polymorphic DNA polymerase chain reaction (RAPD-PCR) and an single-nucleotide polymorphism–type *P. aeruginosa* microarray. The RAPD-PCR was performed by using primer 208 as described previously.[6] The relatedness of RAPD patterns was assessed by calculating the Dice coefficient (SD) using Quantity One 1-D Analysis software (Bio-Rad, Munich, Germany). RAPD patterns with an SD of ≤ 0.8 represent different clones and were assigned arbitrarily by independent numbers.[7] Microarray analysis was performed by a commercially available *P. aeruginosa* microarray (*P. aeruginosa* Array Tube, Clondiag Jena, Germany; distributed by Alere Technologies GmbH, Jena, Germany) following the protocol published previously.[8] Genotyping of *P. aeruginosa* was based on 13 single-nucleotide polymorphisms and 2 multiallelic loci (flagellin *fliC* and pyoverdine receptor *fpvA*) of the *P. aeruginosa* core genome. The descending signal from the 16 binary single-nucleotide polymorphism pattern (0 for negative hybridization signal and 1 for positive hybridization signal) was translated in a 4-digit hexadecimal code (eg, EC29).[8]

RESULTS

Clinical Course of *P. aeruginosa* Infections

During the outbreak in the second week of July 2008, 3 female patients suffered from BSI with *P. aeruginosa* showing an identical antibacterial susceptibility pattern (Table, Supplemental Digital Content 2, http://links.lww.com/INF/B103). Patient A, a 17-year-old girl who received induction therapy according to the acute lymphoblastic leukemia–Berlin-Frankfurt-Munster–2000 protocol for a pre–B cell acute lymphoblastic leukemia spent previously 40 consecutive days within isolation room 3 (Fig., Supplemental Digital Content 1, http://links.lww.com/INF/B102). Four days after discharge, she was readmitted (into room 3) with fever and neutropenia. Despite initiation of cefuroxime therapy the patient deteriorated, developed pneumonia, ecthyma gangrenosum and a painful swelling of the region of the port-a-cath within the following 48 hours. Therefore, the antibiotic regimen was changed to piperacillin/ tazobactam plus tobramycin, and the central venous access device (CVAD) was explanted after a positive blood culture for *P. aeruginosa* was received. Two days later, a 4-year-old girl undergoing radiotherapy for a relapsed medulloblastoma (patient B) and a 5-year-old girl undergoing maintenance chemotherapy for a parameningeal embryonal rhabdomyosarcoma (patient C) were admitted with sepsis and neutropenia. In addition, patient C had a painful swelling above the port-a-cath; patient B had no skin alteration surrounding the Broviak catheter. Both patients had already been hospitalized 1 week before the outbreak (patient B was in room 5 and patient C in room 8). Unsuccessful conservative management and receipt of a positive blood culture for *P. aeruginosa* on day 3 after hospital admission led to immediate CVAD explantation in both patients. After 10 days of intravenous antibiotic treatment with ceftazidime (patient B) and piperacillin/ tazobactam (patient C), both patients could be discharged.

Environmental Investigations and Retrospective Study

Outbreak management included environmental investigations with observation of medical and nursing practices as well as environmental microbiologic sampling. There were no remarkable personnel alterations before the outbreak. Neither the storage of the CVAD equipment within the intervention room and the nursing station (Fig., Supplemental Digital Content 1, http://links.lww.com/INF/B102) nor the nursing practices and handling of the CVAD with aseptic techniques according to a well-established standard were altered previously. Smears from the inner part of the siphons of rooms 3, 6 and 10 as well as water samples of the standing water of the siphons in rooms 4, 5, 6, 8, 9 and of the intervention room and the nursing station were contaminated with *P. aeruginosa*. Inspection of the POCU revealed that water taps focused the water jet directly into the sink.

During the 4 years before the outbreak, there were in average 20 positive blood cultures sampled per year from febrile neutropenic patients within the POCU. Fourteen blood cultures per year were positive for Gram-positive organisms, 9 for *Staphylococcus* spp. and 6 for Gram-negative organisms (Table 1). In the year of the outbreak, a total of 17 positive blood cultures (14 Gram-positive and 3 Gram-negative) were recorded in the POCU (Table 1).

Microbiologic Investigation and Characterization of the Causative *P. aeruginosa* Strains

The 3 patient-derived *P. aeruginosa* isolates were characterized by the susceptibility to aminoglycosides, fluoroquinolones, ceftazidime, piperacillin and carbapenems. This resistance phenotype was shared by environmental *P. aeruginosa* isolates from patient rooms 4, 5, 6, 8 as well as the nursing station (Table, Supplemental Digital Content 2, http://links.lww.com/INF/B103). To further analyze the possible epidemiologic connection between the patient-derived and environmental *P. aeruginosa* isolates, we selected all strains revealing an antimicrobial susceptibility pattern similar to that of the outbreak strains for further genotyping by RAPD-PCR and *P. aeruginosa* microarray analysis. This procedure identified the clonal identity of the 3 patient strains and the environmental strains from patient rooms 5 and 8. It is interesting to note that patient B previously stayed within room 5 and patient C within room 8. The patient isolates as well as the *P. aeruginosa* isolates from siphon water of patient rooms 5 and 8 were typed as RAPD-PCR type 1, microarray type EC29 and exotoxin U positive (Table, Supplemental Digital Content 2, http://links.lww.com/INF/B103 and Table, Supplemental Digital Content 3, http://links.lww.com/INF/B104).

Outbreak Management

New, longer water taps at a horizontal angle of 110 degrees, supplied again with Pall-Aquasafe filter systems, were installed in the entire POCU to avoid direct water flow into the sink. The siphons of the anterooms in isolation rooms 2 and 3 were additionally replaced by BIOREC Medical Hygiene Siphons (BIOREC Dr. Schluttig, Lauta, Germany), which allow continuous physical disinfection (heat and ultraviolet) and electromechanical cleansing of the siphons' inner wall. Moreover, patients and staff were obliged to rinse the water taps with running hot water preceding every water use.

In control samples taken 18 months after the outbreak, *P. aeruginosa* clone EC29 was still detectable in 5 siphons within rooms 1, 5, 9 and 10 and the nursing station. But there was no further colonization of the siphons within the isolation rooms of the unit where the BIOREC Medical Hygiene Siphons were installed (data not shown). In the 2 years after the outbreak no further infections with *P. aeruginosa* occurred (Table 1).

TABLE 1. Bacteria Identified From Positive Blood Cultures Before (2004–2007), During (2008) and After (2008–2010) the Outbreak

	Time Interval of Assessment		
Positive Blood Cultures	Preoutbreak Interval	Outbreak Year (2008)	Postoutbreak Interval
Total number per year	20	17	22
Gram-positive bacteria	14	14*	16
Staphylococcus spp.†	9	6	8
Gram-negative bacteria	6	3	6
P. aeruginosa	0‡	3	0

*Eight of these samples were positive for *Enterococcus* spII> and were derived from 1 patient during 2 consecutive hospitalizations for neutropenia.

†No methicillin-resistant *Staphylococcus aureus* was identified among the staphylococcal isolates; >80% were coagulase-negative staphylococci.

‡One of 81 positive blood cultures between 2004 and August 2008 was positive for *Pseudomonas fluorescens*.

DISCUSSION

P. Aeruginosa, and in particular, multidrug-resistant strains frequently cause severe hospital-acquired infections especially among immunocompromised hosts. To minimize the risk of nosocomial spread and to better understand infection routes and dynamics of transmission, prompt and profound investigation of outbreaks is required. Due to its minimal nutritional requirements, *P. aerguinosa* is able to cause outbreaks via contamination of cleaning equipment,[9] disinfectant-soap dispensers[2] and medical devices such as flexible bronchoscopes[10,11] or mouth swabs.[12] The spread of *P. aeruginosa* due to contaminated water taps is the most common source,[13] but can be effectively prevented by the installation and accurate use of antibacterial filters.[14]

In this article, we described a small outbreak in a POCU with a *P. aeruginosa* exotoxin U clone that was present in 2 of the siphons within the patient rooms. The installation of very short water taps may have led to the formation of contaminated aerosols by focusing the water jet directly into the sink. Thus, contaminated aerosols may have emerged from the siphon at every water use. Patients could have acquired infection with the outbreak clone due to inhalation of contaminated aerosols (patients B and C), via smear infection with water drops directly from the water tap (patients B and C) or through horizontal transmission from contaminated persons such as staff or family members (patient A). This may have resulted in colonization and subsequent invasive infections in the immunocompromised hosts. It is conceivable that the *P. aeruginosa* outbreak strain has only been recently "acquired" in the POCU, because no BSI with *P. aeruginosa* occurred in the POCU between 2004 and 2007. After the implementation of the outbreak interventions, no further case of invasive *P. aeruginosa* infection was observed. It is remarkable that *P. aeruginosa* persisted in the siphons of the regular patient rooms within the POCU.

Microbiologic characterization of the *P. aeruginosa* outbreak clone revealed the presence of *exoU* gene. Exotoxin U, a potent toxin acting as intracellular phospholipase[15] that causes rapid necrotic death in many cell types, is associated with enhanced virulence and worse clinical outcomes. *ExoU* expressing strains are frequently responsible for hospital-acquired pneumonia.[16] Genotypic profiling and determination of virulence factors of outbreak strains in combination with analyzing the distinct clinical course of infections might lead to a better understanding of the pathogenicity of *P. aeruginosa* and may help to identify the source of infection. A combination of these measures may also serve as an additional tool for efficient therapeutic and outbreak management.

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VIRAL COINFECTION IN CHILDREN LESS THAN FIVE YEARS OLD WITH INVASIVE PNEUMOCOCCAL DISEASE

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Abstract: Seventy-one patients <5 years of age who were hospitalized with invasive pneumococcal disease were studied in the period between August 2008 and December 2009. The purpose was to determine the proportion of episodes that were coinfected with respiratory virus. Viral coinfection was common (44/71; 62%), with rhinovirus and influenza virus being the most frequently detected. Highly invasive serotypes (1, 5, 7F,