Although we were unable to culture *S. marcescens* from any products, based on the strength of the epidemiological data and molecular results, we concluded that the outbreak of *S. marcescens* bacteremia was most likely associated with contaminated prefilled heparin flushes. Prefilled heparin syringes were a common product shared by all cases at our institution, and this was also the only product shared by other institutions. Additionally, none of the cases were in the neonates or adult patient populations, which have limited use of prefilled heparin flushes at the concentrations used in pediatric patients. Although *S. marcescens* was not found in any cultures from any prefilled heparin flushes, *Bacillus* spp were identified from several different lots, suggesting a problem with sterility during manufacturing.[2,8]

In conclusion, our experience highlights key features of a successful epidemiologic outbreak investigation including rapid identification and reporting to public health of a suspected outbreak, investigation of all inpatient and outpatient clusters of bacteremia by infection preventionists, the essential role of molecular typing, and timely communication via a pediatric national network listserv. Furthermore, this investigation underscores the importance of pursuing product-associated outbreaks supported by strong epidemiologic data despite the lack of culture-proven product contamination.

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A phylogenetic study of *Elizabethkingia anophelis* bloodstream isolates obtained from inpatients at a single medical center

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To the Editor—Elizabethkingia anophelis is a rapidly emerging nosocomial pathogen reported to cause bacteremia in immune-compromised elderly people and neonates.[1,2] The unknown pathogenesis and unclear resistance mechanism of *E. anophelis* and their phenotypic similarity to *E. meningoseptica* mislead and complicate the infection management of this pathogen, resulting in treatment failure. Inherent resistance to multiple classes of drugs and absence of an antibiotic sensitivity profile standard for this bacterium makes empirical treatment nearly impossible. *Elizabethkingia anophelis* bacteremia has recently been considered clinically significant, leading to high morbidity and mortality that has been mistakenly attributed to *E. meningoseptica* because of their phenotypic similarity.[2] Molecular epidemiological analyses of recent *Elizabethkingia* bacteremia infections and outbreaks have been conducted in United States, Singapore, China, and Korea. These outbreaks were predominated by *E. anopheles*.[3–6] This finding warrants the implementation of molecular typing for an accurate diagnosis to guide appropriate antibiotic regimen instead of relying solely on conventional phenotypic identification with a compact automated VITEK-2 system, which uses a factory default database and lacks timely amendments.[3,5]

In the first report of an outbreak in a tertiary healthcare center of Eastern India, the clinical and molecular epidemiology of 9 bacteremia episodes during 2 months of surveillance from August to September 2017 were identified as *E. meningoseptica* by the VITEK-2 system. These findings were genetically validated by species-specific markers, such as lipid-A disaccharide synthase

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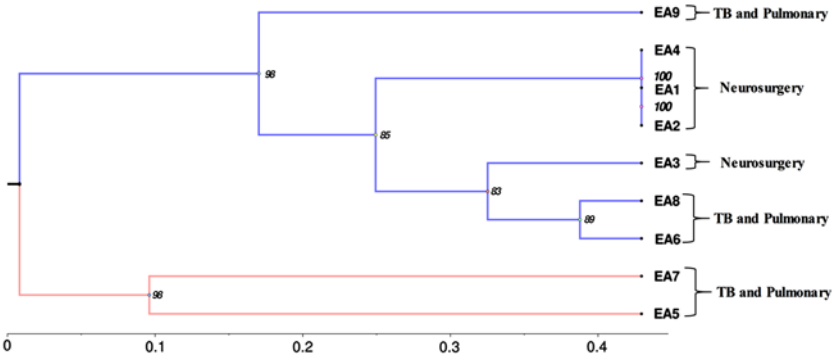

Fig. 1. The phylogenetic tree was developed using REP and (GTG)5 PCR. We observed close clustering among 9 isolates as they relate to the same in-patient department (as labeled): EA1 and EA2 with EA4; EA6 with EA8; and EA5 with EA7. A phylogenetic tree was constructed based on Jaccard similarity coefficient. Hierarchical clustering was performed by hclust function (R Core Team stats 3.5.3) using the unweighted pair group method with arithmetic mean (UPGMA) method, and the tree was cut into an optimal number of clusters along with bootstrapping 1,000 times (Pvclust version 2.0).

gene for *E. anophelis* and sodium-proton antiporter for *E. meningoseptica*,[5] and 16s rRNA gene sequencing. An antibiotic susceptibility study was conducted using the VITEK-2 compact automated system (BioMerieux) with the GN-AST-N280 card. Sensitivity was interpreted according to Clinical Laboratory Standards Institute (CLSI) guidelines (2013).[7] The clonal relatedness among 9 isolates was investigated using repetitive-element polymerase chain reaction (rep-PCR) and (GTG)5 PCR according to the method described by Adiguzel et al.[8]

Nonrepeated *Elizabethkingia* spp (EA1-9) were isolated from 9 inpatients, and we analyzed the demographic data, clinical characteristics, and outcomes for these cases (Table S1 online). In these 9 cases, *Elizabethkingia* bacteremia prevailed mostly among elderly people (n=8; median age 52 years), but 1 patient was a 2-year-old child. The male: female ratio among these patients was 7:2 (Table S1 online). Overall, 5 *Elizabethkingia* isolates were obtained from blood; the rest were obtained from tracheal aspiration (n = 3) and cerebrospinal fluid (n = 1). All of these patients were reported as having hospital-acquired, clinically significant bacteremia, with a high mortality rate (33.3%). Of these 9 patients, 3 died within 1 month of their hospital stay despite treatment with antibiotics (eg, quinolones, penicillin, cephalosporins, carbapenems, etc, either alone or in combination) due to several associated complications: pneumonia, lower respiratory infection, meningitis, acute kidney injury, and metabolic encephalopathy, etc.

These isolates showed resistance to different groups of antibiotics with varying percentages ranging from ~80% to 100% (Table S2 online). However, the highest susceptibility was found against tigecycline and piperacillin-tazobactam, which corroborates the previous reports[3,4,9] except isolate EA1, which matched a single study from China.[6] The resistance profile against levofloxacin was analogous to isolates identified in Korea and Wisconsin.[3,4] However, the alteration of the antibiotic resistance profile depends generally on different types of stress on different sources of *Elizabethkingia* isolates.[6]

All 9 isolates were identified as *E. meningoseptica* by the VITEK-2 compact automated system. Because the identification of *Elizabethkingia* spp has been reported to be misleading using the VITEK 2 and MALDI-TOF MS systems,[2] these samples were subjected to genotypic validation. However, upgrading the VITEK-2 system with better antibiotic sensitivity profiles, updating the CLSI guidelines, and expanding the database for MALDI-TOF mass spectra of *E. anophelis* will improve their proper identification. All 9 *Elizabethkingia* spp showed amplification of lipid-A disaccharide synthase gene, a species-specific primer of *E. anopheles*, and were further confirmed to be *E. anophelis* by 16s rRNA gene sequence analysis (GenBank accession no: MH121154-MH121158, MN038050-MN0380053). Rep PCR- and (GTG)5 PCR–based phylogenetic analysis of 9 isolates revealed a close clustering of EA1 and EA2 with EA4; EA6 with EA8; and EA5 with EA7. These findings explain the considerable clonal similarity among *E. anophelis* isolates belonging to the same in-patient departments (Fig. 1).

This study is the first molecular epidemiological report on a bacteremia outbreak of India with prevalence of *E. anophelis* bacteria establishing *E. meningoseptica* to be the more remote cause of bacteremia infection. However, future prospective studies with population-based data over longer surveillance periods should be performed to determine the prevalence and incidence of *E. anophelis* bacteremia. A repeated molecular epidemiological study should be employed for accurate diagnosis and appropriate treatment regimen.

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Impact of neutropenia on central venous catheter–related bloodstream infections in patients with hematological malignancies at the time of central venous catheter insertion: A matched-pair analysis

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To the Editor—Central venous catheter (CVC)–related bloodstream infections (CRBSIs) are potentially preventable complications associated with high morbidity, especially in patients with hematological malignancies.[1] Neutropenia is one of the most important risk factors for CRBSI[1,2] because of insufficient immune control of the patient's microbial flora or pathogens when absolute neutrophil counts (ANC) are <500/μL.[3,4] Neutropenia as a risk factor for CRBSI is only well defined for the time of CRBSI onset.[5,6] So far, no reliable data are available that address the impact of neutropenia on CRBSI at the time of CVC insertion. This impact is of special interest for hematology patients because CVCs are often inserted during neutropenia either due to the underlying malignancy, like acute myeloid leukemia (AML), or after application of chemotherapy. In addition, CVC reinsertions after CVC removal due to CRBSI are also common, especially during long-lasting neutropenia, for example, after remission-inducing chemotherapy in AML patients or after conditioning therapies before hematopoietic stem-cell transplantation (HSCT). Therefore, we aimed to investigate the impact of neutropenia on subsequent CRBSI at the time of insertion of short-term, nontunneled CVCs in adult patients with hematological malignancies.

We analyzed data from the prospective multicenter SECRECY study (German Clinical Trial Register, no. DRKS00006551), a CRBSI registry conducted in 6 German hematology and oncology centers, including the aforementioned group of high-risk patients receiving AML induction or HSCT. Inclusion criteria encompassed short-term, nontunneled jugular and subclavian vein CVCs with ≥1 day in situ, and CRBSI was classified according to the 2012 Infectious Diseases Working Party (AGIHO) of the German Society for Hematology and Medical Oncology (DGHO) CRBSI definition.[2] Only CRBSIs classified as definite or probable were considered. Hence, we identified 2,368 patients with a total follow-up of 37,932 CVC days. In 2,158 cases (91.1%), the underlying diseases were hematological malignancies. Among them, we identified 406 cases (17.1%) with neutropenia defined as ANC <500/μL or white blood cell counts <1,000/μL at the time of CVC insertion. Of 406 cases, 400 could be matched for age, sex, underlying disease, site of CVC insertion, use of chlorhexidine-coated CVC dressings, use of chlorhexidine-, antimicrobial- or silver sulfadiazine-coated CVCs, and complications during CVC insertion.

The median age of the patients was 59 years, and 60.3% were male (Table 1). Approximately 75% of CVCs were inserted in patients suffering from acute leukemia, and almost all CVCs were placed in the jugular vein (388 of 400, 97.0%). In a minority of patients, coated CVCs were inserted (23 of 400, 5.8%), whereas in half of the cases chlorhexidine-coated CVC dressings were used (196 of 400, 49.0%). Known high-risk CVC features (ie, male sex, complicated CVC insertion, diagnosis of AML, multiple myeloma, or non-Hodgkin lymphoma[7]) were present in half of the patients (203 of 400, 50.8%). The median CVC time in situ was nonsignificantly shorter in CVCs inserted during neutropenia compared to CVCs in nonneutropenic patients (14 vs 18 days; $P = .39$). We found no differences in CRBSI rates comparing neutropenic to nonneutropenic patients (45 of 400 [11.3%] vs 50 of 400 [12.5%]; $P = .66$). However, median time to CRBSI diagnosis was shorter in patients who received the CVC in neutropenia

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