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EDITORIAL COMMENTARY

Fecal ESBL Screening: Are We Ready for This Information?

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(See the Major Article by Karanika et al on pages 310–8.)

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Over the past several years, infections with extended-spectrum beta-lactamase (ESBL)–producing *Enterobacteriaceae* (ESBL-PE) have become an increasing concern in US healthcare settings, with an estimated 140 000 hospital-acquired ESBL-PE infections occurring each year [1]. Infections with these highly resistant bacteria are associated with higher observed mortality rates as well as hospital costs compared with infections with less-resistant organisms [1, 2]. Given the rising prevalence of these dangerous and costly ESBL-PE infections, a better understanding of the risk factors for their development is necessary to determine appropriate reduction and prevention strategies in hospital settings.

One suggested risk factor for the development of ESBL-PE infection is gut colonization with these organisms. In this issue of *Clinical Infectious Diseases,* Karanika, Karantanos, and colleagues [3] describe a retrospective metaanalysis of 66 studies that they performed in order to estimate the prevalence of ESBL-PE colonization in healthy individuals, with a focus on identifying risk factors for colonization. The authors report a global prevalence of ESBL-PE fecal colonization of 14%, with significantly higher rates in parts of Africa, East Asia, and India [3]. Additional important risk factors identified for colonization included international travel and recent antibiotic use [3]. To date, this manuscript represents the largest analysis of the prevalence of ESBL-PE colonization and its associated risk factors. The authors' conclusions provide important insights into the phenomenon of rising gram-negative resistance and raise further questions about the potential role of infection control and antimicrobial stewardship to thwart the spread of multidrug-resistant bacteria.

This study underscores several issues pertaining to ESBL-PE colonization and its potential sequelae. First, is ESBL-PE colonization a real risk factor for subsequent infection? Prior studies do indeed suggest a true association between colonization with resistant organisms and the development of infection [4–6]. For example, nasal colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) is associated with an increased risk of MRSA infection [5]. Few studies have linked the role of ESBL-PE fecal colonization with the development of infection. A recent cohort study performed by Cornejo-Juarez and colleagues [7] in patients with hematologic malignancies revealed that patients with fecal ESBL-PE colonization were 3.5 times more likely to develop ESBL-PE bacteremia compared with those not colonized. Although mortality was similar among ESBL-PE colonized and noncolonized individuals, the presence of fecal ESBL-PE was associated with longer hospitalizations, a reduced time to death, and higher hospital costs [7]. These findings contrast a similar study performed by Arnan and colleagues [8] in which no correlation was identified between ESBL-PE fecal colonization and infection in a neutropenic population. To our knowledge, no study has been performed to investigate an association between ESBL-PE fecal colonization and infection in nonhematologic patient populations. As the implementation of infection control practices can be costly and time consuming, a better understanding of the predictive value of ESBL-PE colonization to infection with these organisms is needed before standardized screening protocols can be considered.

Second, we need to ascertain the utility of screening procedures in the prevention of transmission. Most hospitals use active surveillance programs to identify multidrug-resistant organisms (MDROs) such as MRSA and vancomycin-resistant *Enterococcus* (VRE) in certain high-risk patient populations. However, outcomes that evaluate the utility of these programs remain mixed, with some studies showing a clear reduction in MDRO transmission and others showing no benefit from these initiatives [9, 10]. Less is known regarding the utility of active surveillance screening for ESBL-PE colonization, although a few studies have started to address this question. Troche and colleagues [11] reported a significant reduction in ESBL-PE transmission in a surgical intensive care unit through the use of active surveillance cultures and selective gut decolonization, while Gardam and colleagues [12] found no benefit to

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routine screening. Given these conflicting results, larger studies are required before active ESBL-PE surveillance can be recommended. Given the costs and logistics of active surveillance screening and isolation precautions, a more targeted research focus using these initiatives in the highest risk populations such as the critically ill, immunosuppressed, and those with significant antibiotic exposure may increase the potential value of these protocols. Most important is emphasis of appropriate hand hygiene as the most effective intervention to reduce MDRO transmission [13].

Karanika, Karantanos, and colleagues provide further evidence of the link between international travel and the development of ESBL-PE colonization in healthy individuals [3]. As active surveillance screening is often performed for other MDRO organisms in high-risk groups, these results raise the question of whether fecal screening for ESBL-PE colonization should be performed in patients with a history of travel, specifically to areas with high ESBL prevalence. The global sites that constitute a high prevalence rate would need to be identified as well as how other potential risk factors including duration of travel and travel-related antibiotic use inform the decision to screen [14]. The timing of screening from date of high-risk travel would also need to be considered as ESBL-PE colonization can persist for up to 1 year [15].

Finally, treatment options for ESBL-PE–colonized patients are unknown. Given the high prevalence of fecal ESBL-PE reported by Karanika, Karantanos, and colleagues, the role of decolonization as a way to reduce transmission and infection is an intriguing concept. Multiple decolonization strategies have been studied with regard to MRSA and VRE colonization. Overall, the results have been disappointing, prompting the Centers for Disease Control and Prevention to discourage the use of decolonization protocols as part of routine care [16]. Several studies that evaluated the specific role of gut decolonization with poorly absorbable antibiotics such as colistin, rifaximin, polymixin, neomycin, and erythromycin for asymptomatic ESBL-PE carriage failed to show successful rate reductions following treatment [11, 17, 18]. These studies were limited by small sample sizes as well as variable decolonization regimens, making it difficult to draw significant conclusions regarding the utility of antibiotic decolonization for ESBL-PE carriage. More recently, fecal microbiota transplantation (FMT) has become an increasingly popular and effective treatment method for *Clostridium difficile* infection [19]. This concept of "resetting" the gut microbiome as a way to eradicate pathogenic gut bacteria provides a potential mechanism by which asymptomatic fecal colonization with MDRO organisms could be curtailed. A recent case report from Crum-Cianflone and colleagues [20] describes this phenomenon, with a significant reduction in MDRO colonization seen in a critically ill patient after FMT for recurrent *C. difficile* colitis. Other case reports reveal similar findings, demonstrating the potential role of FMT as a decolonization strategy; however, formal studies are needed to accurately measure the impact on ESBL-PE carriage [21].

In summary, the current findings of Karanika, Karantanos, and colleagues firmly establish the growing worldwide burden of ESBL-PE fecal colonization. Future questions to be addressed include the true impact of colonization on infection as well as the need for active surveillance screening given the controversial nature of this practice with other MDRO bacteria. Finally, the role of gut decolonization strategies or possibly FMT to limit transmission and infection represent intriguing potential therapeutic interventions. Most importantly, strict adherence to hand hygiene protocols should be emphasized in an attempt to reduce transmission.

Notes

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