From ESKAPE to ESCAPE, From KPC to CCC.

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Francesco G. De Rosa[#]*, Silvia Corcione*, Nicole Pagani*,

Giovanni Di Perri*

*Department of Medical Sciences, Infectious Diseases, University of Turin, Amedeo di Savoia Hospital; Corso Svizzera 164, 10139 Turin.

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Address for Correspondence:

Francesco G. De Rosa, MD [# Corresponding Author]

Associate Professor, Infectious Diseases

Department of Medical Sciences,

University of Turin, Italy

Ospedale Amedeo di Savoia

Corso Svizzera 164, 10149 Turin

tel. +39 011 4393979

fax. +39 011 4393996

Dear Editor,

Colonization and infection due to multidrug resistant (MDR) bacteria is nowadays an important issue in nosocomial and health-care associated infections, as reported by several surveillance systems [1-2]. The spread of MDR microorganisms has been linked to asymptomatic carriage by the hands of health-care workers, contamination of hospital environment, colonization of the bowel, use and duration of antibiotic treatments. We are currently facing new microbiological, infection control and clinical issues and the epidemiologic variations observed in the last years highlighted the need of a change from the initial proposed acronym "ESKAPE", where MDR *Klebsiella pneumoniae* was acknowledged, to "ESCAPE" where Enterobacteriaceae and *C. difficile* were included.

The gut microbiota regulates important physiological metabolic functions of the host and can be impaired during prolonged antibiotic treatments, becoming a significant reservoir of microorganisms with a nosocomial profile of antibiotic resistance. In *C. difficile* infections there is a clearly recognized causal role of a dysbiotic microbiota, suggesting that similar alterations may be favoring colonization by carbapenem-resistant *K. pneumoniae* (KPC-*Kp*) or an excessive intestinal growth by *Candida* spp., thus favoring *Candida* bloodstream infections. Indeed, there are reports of candidemia following *C. difficile* severe infections [3], and KPC-*Kp* bloodstream infections associated with candidemia [4]. Interestingly, in murine models of gastrointestinal candidiasis Cole et al. analyzed the impact of colonization of gastrointestinal mucosa, alterations of the normal integrity of the mucosal epithelium and impairment of mucosal immunity in the development of invasive candidiasis [5].

If these considerations are correct, the gastrointestinal tube is a well recognized key player as the main reservoir for human disease by *Candida* spp. and for epidemic dissemination of MDR

bacteria such as KPC-Kp and *C. difficile*. Accordingly, we propose that antimicrobial stewardship programs should start focusing on a "CCC" strategy, aiming at Carbapanemases-producing Enterobacteriacee, *C. difficile* and *Candida* spp.

Amongst Enterobacteriacee, carbapenemases are mainly seen in KPC-producing *K. pneumoniae*, with increasing data coming not only from critically ill and surgical patients but also from internal medicine wards [6]. The identification of patients colonized by KPC-*Kp* in different settings deserves a dedicated intervention and a major compliance of health-care workers to simple standard hygiene procedures, such as hand washing [7]. The European guidelines on infection control issues for Gram-negative bacteria highlight the scientific evidence available on prevention and isolation, including *C. difficile* [8].

The "CCC" acronym may help antimicrobial stewardship programs to focus on current issues and may guide physicians in remembering and acknowledging the importance of disturbances of the GI tract, including the collateral damage due to antibiotic treatment [9]. Timely identification of at-risk patients, early treatment in symptomatic patients, antibiotic de-escalation are urgently needed. Save the tube!

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