

General review

## Management of multidrug resistant bacterial endemic

### *Gestion de l'endémie des bactéries multi-résistantes*

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Received 2 June 2014; received in revised form 16 July 2014; accepted 16 July 2014

Available online 29 August 2014

#### Abstract

The fight against multi-drug resistant Gram-negative bacilli (MDRGNB), especially extended-spectrum  $\beta$ -lactamase producing Enterobacteriaceae, is about to be lost in our country. The emergence of new resistance mechanisms to carbapenems in these Enterobacteriaceae exposes patients to a risk of treatment failure without any other therapeutic options. This dramatic situation is paradoxical because we are well aware of the 2 major factors responsible for this situation: 1) MDRO cross-transmission, associated with a low compliance to standard precautions, especially hand hygiene, and 2) overexposure of patients to antibiotics. The implementation of a “search and isolate” policy, which was justified to control the spread of some MDRO that remained rare in the country, was not associated with a better adherence to standard precautions. The antibiotic policy and the measures implemented to control antibiotic consumptions have rarely been enforced and have shown inconsistent results. Notably, no significant decrease of antibiotic consumption has been observed. There is no excuse for these poor results, because some authors evaluating the effectiveness of programs for the control of MDRO have reported their positive effects on antimicrobial resistance without any detrimental effects. It is now urgent to deal with the 2 major factors by establishing an educational and persuasive program with quantified and opposable objectives. Firstly, we have to improve the observance of hand hygiene above 70%. Secondly, we have to define and reach a target for the reduction of antibiotic consumption both in community and in hospital settings.

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**Keywords:** Multi-drug resistant organisms; Hand hygiene; Antibiotics

#### Résumé

La lutte contre la diffusion des bactéries à Gram-négatif multi-résistantes (BMR), notamment les Entérobactéries productrices de  $\beta$ -lactamases à spectre élargi, est en train d'être perdue dans notre pays. L'émergence de nouveaux mécanismes de résistance aux carbapénèmes chez ces bactéries expose les patients à un risque d'impasse thérapeutique. Cela survient alors que nous connaissons les 2 principaux facteurs sur lesquels nous pourrions agir : maîtriser la transmission des BMR en augmentant l'observance de l'hygiène des mains et le respect des précautions standard, et réduire l'exposition des patients aux antibiotiques. La mise en place de mesures spécifiques, le dépistage et l'isolement, nécessaires pour prévenir la diffusion de certaines BMR encore rares dans notre pays, ne s'est pas accompagnée d'une amélioration des précautions standard. Concernant la politique de l'antibiothérapie, les mesures mises en place sont encore trop timides et notamment n'ont pas permis d'obtenir une réduction significative des consommations d'antibiotiques. Les maigres résultats observés ne sont pas excusables : plusieurs études ont démontré l'efficacité et la faisabilité des programmes de maîtrise des BMR, que ce soit en termes de bénéfice écologique mais aussi individuels pour les patients. Une approche éducative et persuasive ferme doit être menée de façon urgente sur ces deux fronts en fixant des objectifs chiffrés opposables : il s'agit à

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la fois d'augmenter l'observance à l'hygiène des mains avec un objectif d'observance de plus de 70 % mais aussi de fixer et atteindre un objectif quantitatif de réduction de la consommation des antibiotiques, que ce soit en ville ou à l'hôpital.

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*Mots clés* : Bactéries multi-résistantes ; Hygiène des mains ; Antibiotiques

We have experienced a paradoxical situation over the past decade. Even though the battle against the spread of methicillin-resistant *Staphylococcus aureus* (MRSA) has probably been won in our country, we are facing a continuous and inexorable increase in the incidence of extended-spectrum  $\beta$ -lactamase producing Enterobacteriaceae (ESBL-PE) [1,2]. The fight against the spread of ESBL-PE has been unsuccessful despite numerous recommendations and various consensus guidelines on infection control measures to be adopted. The most concerning recent data suggests that improving hand hygiene and including active surveillance and contact precautions do not help to control the spread of ESBL-PE [3]. It has also been increasingly acknowledged that overexposure of patients to antibiotics was a real issue in our country, and a major determinant of antibiotic resistance. Furthermore, campaigns designed to control and reduce antibiotic consumption have also failed to produce sustained results [4,5]. A lot of accumulated data could explain these results and should help us to think differently.

## 1. Why are ESBL-PE more difficult to control than MRSA?

Some microbiological and epidemiological differences between MRSA and ESBL-PE should be taken into account before any new proposals are made.

Firstly, the ecological reservoirs are different. *S. aureus* and Enterobacteriaceae are both human commensals but there is a major difference in the percentage of carriers among the population. Screening studies suggest that only 30% of the population carries *S. aureus* whereas 100% carry Enterobacteriaceae [6]. Enterobacteriaceae carriage outnumbers *S. aureus* carriage by 3 to 6 logs. Moreover, the mechanisms of resistance are quite different. ESBL-PE resistance to  $\beta$ -lactams and other antibiotics is associated with plasmidic resistance determinants that are easily transferred between species, whereas MRSA resistance is associated with a chromosomal non-transferable determinant. This suggests that the potential reservoir (i.e. number of carriers) can be significantly more important in case of ESBL-PE compared to MRSA, and could explain for a large part the current endemic situation.

Secondly, despite numerous attempts at establishing the role of antibiotic therapy as a trigger of MRSA carriage, this issue is still debated; whereas the role of antibiotics at the individual and collective level seems to play a major role in the carriage and spread of ESBL-PE [7], [8–11]. One of the most worrisome facts is that any class of antibiotic prescribed can be associated with a high risk of selection and thereby dissemination because of combined resistance of ESBL-PE to multiple antibiotic classes.

We currently have to face 2 major mechanisms of resistance in the community and in hospital: ESBL-PE and carbapenemase PE (CPE). The first seems to be endemic in many regions of France whereas the second has remained sporadic up to now [12,13]. Despite the epidemiological differences (i.e. endemic versus sporadic), the 2 resistance mechanisms can be controlled in the same way.

### 1.1. What have we learned from MRSA management?

Success in controlling the spread of (endemic) MRSA was related to the various actions undertaken during the last decade. These actions were based on a widely applied and multifaceted program including an intensive “search and isolate” policy and the promotion of hand hygiene. Identifying patients infected or colonized by MRSA through active screening in high risk units, putting patient presenting with MRSA infections or colonization on contact isolation, and improving hand hygiene seem to be important and sufficient to control the spread of MRSA [14]. Jarlier and al. recently reported the success in Parisian hospitals based on a bundle of measures aimed at decreasing cross-transmission including: single bedroom placement, promotion of hand hygiene, active surveillance in high-risk patients, quick notification of cases, and feedback [1].

### 1.2. What have we learned from ESBL-PE management?

The situation is quite different for ESBL-PE. A lot of data suggest that the measures proposed to control MRSA are not sufficient to control the endemic situation. We conducted a retrospective investigation to determine whether the consumption of alcohol-based hand rub (ABHR) used was correlated with the incidence of acquired nosocomial infection due to ESBL-PE; we suggested that both increase of ABHR consumption and adherence to hand hygiene (from 55.6% to 70.9%) were not associated with a decreased incidence of nosocomial acquired ESBL-PE [15]. More recently, the authors of studies on the transmission rates of ESBL-PE in hospitals and households suggested that household transmission outweighed nosocomial transmission [16]. Moreover, the estimated rate of spread of ESBL-PE was low in tertiary care university-affiliated hospitals with a high rate of compliance to standard precautions [17].

The authors of a recent study summarized our concerns [18]. They assessed, in a multicenter randomized study including 13 ICUS from 8 different European countries, the various measures implemented to decrease the colonization and transmission of antimicrobial-resistant bacteria. They suggested that improved hand hygiene (77% compliance rate) plus systematic

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