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Multidrug Resistant Bacteria in the Community: Trends and Lessons Learned

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Abstract

Multidrug resistant (MDR) bacteria are one of the most important current threats to public health. Typically, MDR bacteria are associated with nosocomial infections. However, some MDR bacteria have become quite prevalent causes of community-acquired infections. The spread of MDR bacteria into the community is a crucial development, and is associated with increased morbidity, mortality, healthcare costs and antibiotic use. Factors associated with community dissemination of MDR bacteria overlap but are distinct from those associated with nosocomial spread. Community-associated (CA) MDR bacteria have an antibiotic resistance phenotype that is stable in the absence of antibiotic pressure of the type normally observed in hospitals or nursing homes. An exception to this rule may be those CA-MDR bacteria, of which the prevalence is driven by the presence of antibiotics in the food chain. Additionally, the colonization of otherwise healthy hosts is a common characteristic of CA-MDR bacteria. However, subtle immune deficiencies may still be present in the subjects colonized with specific CA-MDR bacteria. Methicillin-resistant *S. aureus* (MRSA) is the most prevalent of CA-MDR bacteria. CA-MRSA also has the greatest impact on morbidity and mortality. The main threat on the horizon is represented by Enterobacteriaceae. The production of extended spectrum β-lactamases in Enterobacteriaceae encountered in the community is becoming increasingly prevalent. Of great concern is the potential for the acquisition of carbapenemase genes in CA-Enterobacteriaceae. Prevention of further community spread of MDR bacteria is of the utmost importance, and will require a multi-disciplinary approach involving all stakeholders.

Keywords

carbapenem resistant enterobacteriaceae; *Klebsiella pneumoniae*; readmission; transmission; tigecycline

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Introduction

Multidrug resistant (MDR) bacteria are well-recognized to be one of the most important current public health problems. The Infectious Diseases Society of America (IDSA) recognizes antimicrobial resistance as “one of the greatest threats to human health worldwide”[1]. Several issues underlie the critical danger that is posed by the rise of MDR bacteria. First and most importantly, outcomes in patients infected with MDR bacteria tend to be worse as compared to patients infected with more susceptible organisms[2, 3]. In this way, rising rates of antibacterial resistance have an impact on all aspects of modern medicine, and threaten to decrease the yield of many accomplishments such as cancer care, transplantation and surgical procedures[4]. Second, tremendous added costs are associated with these infections. In the US, associated annual additional costs of infections caused by resistant organisms as compared to susceptible organisms are estimated between $21 billion and $34 billion[1]. Third, the prevalence of specific MDR bacteria is closely linked to the use of broad spectrum antibiotics, both for empiric as well as for definitive therapy[5]. This increased use in turn leads to even higher rates of MDR bacteria, thus creating a vicious cycle.

Typically, MDR bacteria are associated with nosocomial infections. However, some MDR bacteria have become quite prevalent causes of community-acquired infections. This is an important development as community spread of MDR bacteria leads to a large increase of the population-at-risk, and subsequently an increase in the number of infections caused by MDR bacteria. In addition, when the incidence of a certain resistance pattern in bacteria causing community-acquired infections exceeds a specific threshold, broader spectrum antibacterials and/or combination antibacterial therapy are indicated for the empiric treatment of community-acquired infections. In this review, we will outline the trends in and epidemiology of community prevalence of various MDR bacteria.

Community-associated, health-care associated and nosocomial infections

Infections can be divided into community onset and nosocomial acquisition. The widely used cut-off to distinguish between these two categories is whether the onset of infection was within the first 48 hours of hospitalization (community-onset) or later (nosocomial). Limitations of this division include the arbitrary nature of the 48 hour time point, as well as the dependence on the timing of diagnosis. If cultures are performed earlier during hospitalization, more infections are likely to be labeled as community-onset.

The category of community-onset can then be further subdivided into community-acquired and healthcare-associated, based on work pioneered by Morin et al. and Friedman et al.[6, 7]. Generally, an infection is deemed to be healthcare-associated if a patient was hospitalized in an acute care hospital for two or more days within 90 days of the infection; resided in a nursing home or long-term care facility; received recent intravenous antibiotic therapy, chemotherapy, or wound care within the past 30 days of the current infection; or attended a hospital or hemodialysis clinic[8].

The remaining category includes those patients who have a community-onset infection, and who do not meet any of the above criteria for health-care associated infection. These infections are considered to be community-acquired. However, for the purposes of evaluating MDR bacteria in the community, these definitions may not tell the whole story. Patients tend to get infected with organisms with which they were previously colonized. Therefore, it is the timing of colonization, rather than the timing of diagnosis of infection that is crucially important to determine the origin of the MDR bacteria. Studies that have employed screening of non-infected individuals have addressed these questions for some MDR bacteria in certain populations.

Requirements for Transition from Nosocomial Pathogen to Community-Associated Pathogen

The commonality of risk factors of MDR organisms, as well as opportunistic organisms such *Clostridium difficile* and *Candida* species was described by Safdar and Maki[9]. Many studies have studied specific risk factors for MDR bacteria and for the most part have found overlapping sets of risk factors. Exposure to antibiotics is a risk factor which is almost always found in studies with sufficient power to evaluate this risk. The specific antibiotic class associated with the risk for developing a specific antimicrobial resistance pattern may vary. Often, a simple association between the use of a specific antibacterial and resistance to that antibiotic is described. For instance, tigecycline use in patients with carbapenem-resistant *Klebsiella pneumoniae* was found to subsequently lead to tigecycline resistance in the same bacteria of those same patients[10]. Specific types of epidemiologic studies (case-case-control studies) often needed to determine the true extent of the risk of use of an antibiotic contributing to resistance to itself[11, 12]. Sometimes, patterns are more complicated. As an example, the use of ceftriaxone use – but not other cephalosporin use – was associated with the incidence of bloodstream infections caused by vancomycin-resistant Enterococci (VRE)[13]. These examples are clear indications of the importance of antimicrobial stewardship at all levels – in hospitalized patients, in patients treated in the community, as well as non-medical antibiotic use – for the control of antimicrobial resistance.

Healthcare exposure is an additional key risk factor for MDR bacteria. The presence of indwelling medical devices such as urinary catheters, feeding tubes, endotracheal tubes, and vascular lines is also a commonly identified risk factor[9]. Other categories of risk factors for infection with or colonization by MDR bacteria includes immunosuppressed states such as solid organ or hematopoietic stem cell transplant recipients, as well as other comorbid conditions such as renal failure. The impact of these last two categories is often difficult to definitively establish as there is usually considerable overlap with the first three categories.

In order for MDR bacteria to become widespread in the community, these traditional risk factors and their implied role in the pathophysiology of colonization have to become of lesser importance. First, the MDR phenotype has to be stable in the absence of antibiotic pressure of the type normally observed in hospitals or nursing homes. The potential implications of this requirement include an ability to compete with wild-type, antibiotic-susceptible bacteria, as well as a genetic stability of genes conferring the antibiotic

resistance phenotype of interest. This means that resistance genes that are associated with a fitness cost to the organism are unlikely to become widespread in the community, unless compensatory genetic content is accumulated as well, or if resistance gene expression is fully inducible upon antibiotic exposure. Examples of such inducible genes are the erythromycin resistance methylase (*erm*) genes, which are found in mycobacteria and *Staphylococcus aureus*. The products of these genes are only made if the bacteria are exposed to specific antibiotic classes, leading to rapid phenotypic resistance to those antibiotics.

Furthermore, MDR bacteria that are successful in the community have to be able to persist without having to form biofilms on non-organic matter. This involves competition with other microbial flora in specific microbiome settings such as the skin, nares, mouth and gut. Of course, even in the absence of foreign material, biofilm formation remains an important component of bacterial persistence. Biofilm formation is an essential pathophysiologic component of periodontal infections, gastric infection with *Helicobacter pylori*, middle ear infection, urinary cystitis, and many other common infections[14]. MDR bacteria with the ability to form biofilms in the absence of foreign material will be more likely to become common in community settings.

In addition, community-associated MDR bacteria have to be able to coexist with the immune systems of otherwise healthy human hosts in the absence of obvious immunosuppression. Nonetheless, specific polymorphisms in immunity genes of the host may facilitate colonization of select bacteria. In persistent *S. aureus* nasal carriage, human host genetics were even postulated to be the predominant determinant[15].

In summary, it is clear that genetic content encoding for several distinct functions needs to be accumulated for a specific strain of MDR bacteria to become community-associated.

MRSA

Methicillin-resistant *S. aureus* (MRSA) is probably the best example of a prevalent and important MDR bacterium that has successfully transitioned from an almost exclusively nosocomial setting to being widespread in the community. The epidemiology of community-associated MRSA (CA-MRSA) has been extensively reviewed elsewhere[16, 17]. Here, we will give a brief overview of MRSA in the community as it may be predictive of the behavior of other MDR bacteria.

As early as 1982 an outbreak of CA-MRSA was reported in Detroit[18]. In this outbreak, more than half of patients were intravenous drug users, and the remaining patients had several comorbidities that put them at risk. Importantly, various different strains were found in this outbreak[18]. It was not until the early 1990's that more genuine CA-MRSA outbreaks began to be reported. These outbreaks occurred in populations without specific risk factors. The MRSA strains involved were generally monoclonal or oligoclonal and rather than being extensively multidrug resistant such as nosocomial MRSA strains at that time, these CA-MRSA strains were susceptible to many non-β-lactam antibiotics. In the early 2000's, a new strain of CA-MRSA – USA300 – became the predominant CA-MRSA in the United States,

effectively replacing the previous USA400 CA-MRSA strain[16]. This USA300 strain is characterized by the presence of the staphylococcal cassette chromosome mec (SCCmec) type IV as well as of genes encoding for Panton-Valentine leucocidin (PVL) toxins[19]. Households are an important reservoir for the USA300 strain. In a recent study that utilized whole genome sequencing data, USA300 MRSA was shown to persist in households between 2 and 8 years prior to admission of a symptomatic patient from that household, and to continue to persist for at least another year after that[20]. This and other evidence shows conclusively that this specific strain of MRSA has been able to become entrenched in a community setting in the absence of ongoing antibiotic pressure. In addition, specific strains of CA-MRSA have been shown to be associated with exposure to lifestock; so-called lifestock-associated (LA) MRSA. The ST398 LA-MRSA is predominantly found in Europe and America, whereas ST9 LA-MRSA is encountered in Asia[21].

Vancomycin-resistant Enterococci (VRE)

Vancomycin-resistant enterococci (VRE) emerged in the late 1980's, and became a common cause of nosocomial infections in the 1990's[22]. Studies in the 1990's did not detect the presence of vancomycin resistance in enterococci isolated from subjects without healthcare exposure in the United States[23, 24]. In contrast, in European studies from the same time period, VRE was detected in the stool of healthy volunteers[25]. In addition, VRE was commonly found in European food animals[26, 27]. The underlying reason for this difference between Europe and the United States is the use of avoparcin – a glycopeptide antibiotic – for the purpose of promoting growth in food animals. Avoparcin was never approved for use in the United States or Canada, but its use was widespread in Europe up to 1997[27]. After a ban on avoparcin in animal husbandry, rates of VRE in both animal samples, as well as in samples from human volunteers started to decrease[25, 27]. These important data illustrate the critical link between antibiotic use in the food industry and antimicrobial resistance rates in humans. It also indicates that it is never too late to make a change and that banning antimicrobials from our food chain may have an almost instantaneous positive – and cost-saving – effect.

Around 2000, community-associated VRE began to appear in the US. In a screening study of patients attending an ambulatory care clinic in Nashville, Tennessee, 3 patients tested positive for VRE out of 100 patients screened. One of these patients came in for her annual check-up and had no prior healthcare exposures[28]. Also, VRE was found in wastewater from a semi-closed agri-food system[29]. Nonetheless, VRE remains an uncommon pathogen in community-associated infections. In 289 patients with community-onset VRE, 85% of patients had been hospitalized, and 71% had antimicrobial exposure in the last 3 months, respectively[30]. In another study that included 81 patients with community-onset VRE bacteremia, 79% of patients had prior hospitalizations[31]. These data indicate that even in those patients where VRE is detected on admission or early during hospitalization, acquisition likely occurred in the healthcare setting. This acquisition was driven by traditional risk factors of antimicrobial exposure, healthcare exposure, chronic illness, indwelling devices, malignancies and immunosuppression[30, 31].

The discrepancy between the community spread of MRSA and VRE is notable, as both *S. aureus* and enterococci are common human colonizers. However, overall colonization with enterococci is much more universal than with *S. aureus*, and *S. aureus* is not truly a commensal. Apparently – in contrast to MRSA – high prevalence of current strains of VRE in the community requires either an ongoing incoming supply of VRE into the shared community gut microbiome through the food chain, or a high level of antibiotic pressure. Fitness cost of maintaining a vancomycin resistant phenotype would be an intuitive explanation for the relative lack of true community-associated VRE infections. However, the fitness cost of vancomycin resistance appears to be minimal for enterococci, especially in the context of inducible resistance[32, 33]. A recent study suggests that pheromone-mediated killing of VRE may account for why vancomycin-susceptible commensal enterococci outcompete VRE in the human gut[34]. In this study, the prototype multidrug-resistant clinical isolate strain *E. faecalis* V583 was killed by human fecal flora, whereas commensal antibiotic-susceptible *E. faecalis* was able to survive in the presence of flora. The killing effect was traced to pheromone production by commensal *E. faecalis* strains[34].

Carbapenem-resistant *Acinetobacter baumannii* (CRAB)

Acinetobacter baumannii infections are commonly encountered in hospitalized patients, especially in the intensive care[35]. However, community-associated *A. baumannii* infections have been well-described especially in (sub-) tropical climates, including Asia and Australia[36]. These are generally associated with pharyngeal carriage and are linked to alcohol abuse and smoking[36]. These are serious infections and the attributable mortality in 80 patients with bacteremia and/or pneumonia from various case series was reported at 56%[36]. Community reservoirs for *A. baumannii* include environmental sources such as soil and vegetables, as well as human and animal skin and throat carriage. Furthermore, *A. baumannii* has also been recovered from human lice[37].

A. baumannii is intrinsically resistant to several antibiotic classes. In addition, carbapenem resistance may occur through acquisition of carbapenemases such as IMP-like carbapenemases and/or oxacillinases (OXA)[38]. The rate of carbapenem resistance in clinical isolates of *A. baumannii* rose sharply from 9% to 40% between 1995 and 2004 in the US[35]. More recent studies suggest that this rate has remained around 40%[39, 40]. In contrast, the rate of carbapenem resistance in *Acinetobacter* infections isolated from community-dwelling patients has remained around 4%[39]. Similarly, resistance to carbapenems was detected in only one out of 23 community-dwelling volunteers who had *A. baumannii* isolated from their hands[41]. In an Australian study on 36 patients with community-onset bacteremic *Acinetobacter* pneumonia, all tested isolates were susceptible to carbapenems[42]. A more worrisome report from China described 32 patients with community-acquired pneumonia caused by *A. baumannii*. Three and 6 isolates were non-susceptible to meropenem and imipenem, respectively. In addition, $bla_{\text{OXA-23}}$ found in 12 of 15 tested isolates, some of which tested susceptible to both meropenem and imipenem[43]. Of note, 87% of patients with MDR *A. baumannii* had a “hospitalization history”, suggesting that these did not truly represent community-associated infections[43].

In summary, community-associated CRAB appears to remain uncommon, likely reflecting the natural habitats of *Acinetobacter* species, and the differences between true community strains found to cause infections in Asia and Australia and hospital-associated strains. Of concern is the potential for acquisition of carbapenemases by such a community strain, especially in high antibiotic use areas in Asia.

Multi-drug resistant Pseudomonas aeruginosa

P. aeruginosa is a common cause of nosocomial infections, including bloodstream infections and pneumonia. It prefers moist environments and can be found in a large variety of places in the hospital, including sink traps and aerators, various equipment such as scopes and respiratory gear and contaminated solutions[44]. In addition, *P. aeruginosa* may be present on fresh fruits and vegetables as well as on the fingernails of healthcare providers[44].

Similar to *A. baumannii*, *P. aeruginosa* is intrinsically resistant to many antibiotic classes. Furthermore, additional acquired antibiotic resistance arises relatively easily and quickly after antibiotic exposure. Some patients have chronic biofilm-mediated pseudomonal colonization; patients with cystic fibrosis (CF) are an important example[45]. In these patients, repeated antibiotic courses are the rule, as is the subsequent development of MDR strains. While these patients are often community-dwelling, these infections are clearly healthcare-associated. Nonetheless, spread of MDR isolates between patients with CF has been well described and is an important infection control risk[46].

True community-associated infections with MDR *P. aeruginosa* fortunately remain very uncommon[47, 48]. In a cohort of 60 patients with community-acquired bloodstream infections with *P. aeruginosa*, 100% of isolates were meropenem susceptible, and 95% were susceptible to piperacillin/tazobactam and ceftazidime[49]. A case report from Turkey describes a young man without healthcare exposure who presented with a pyogenic liver abscess caused by a *P. aeruginosa* strain that was only susceptible to imipenem, amikacin, and colistin [50].

Enterobacteriaceae that produce extended spectrum β-lactamases

Enterobacteriaceae are very common causes of community-associated infections, including urinary tract infections and bacteremia. Unfortunately – in contrast to the situation described above with *P. aeruginosa* and *A. baumannii* – there is widespread resistance in community-associated enterobacteriaceae isolates mediated by extended spectrum β-lactamases (ESBL) [51]. This is a global phenomenon and involves patients of all ages including pediatric populations. In a multicenter, prospective US study over a one year period in 2009–2010, 4% of E. coli community-onset isolates were ESBL producers[52]. The majority reflected urinary tract infections such as cystitis or pyelonephritis. The most common ESBL encountered were of the CTX-M group (91%), the remaining ESBLs were either SHV (8%) or CMY-2 (1%). Most isolates (54%) belonged to the ST131 clonal group[52]. *E. coli* ST131 is a globally disseminated MDR clone, and is characterized by resistance to fluoroquinolones in addition to production of CTX-M type ESBL[53].

In Asia, the Middle East, South America and some parts of Europe, community-onset infection with ESBL-producing *E. coli* is extraordinarily frequent. Lower prevalence regions include North America, some parts of Northern Europe, Australia and New Zealand. Specific risk factors for community-onset ESBL-producing *E. coli* infections have been found in these low prevalence regions. Reported risk factors from a Chicago-based study for ESBL-producing *E. coli* included travel to India (OR 14.4), increasing age (OR 1.04 per year), and prior use of ciprofloxacin (OR 3.92)[54]. In a German survey-based study, risk factors for ESBL-positive *E.coli* colonization included an Asian language being the primary language spoken in the household (OR 13.4) and frequent pork consumption (OR 3.5)[55]. A population-based study in London also suggested South-Asian ethnicity and older age as risk factors for ESBL-positive *E. coli* bacteriuria[56]. A study performed in Australia and New Zealand also found that birth on the Indian subcontinent or travel to SouthEast Asia, China, India, Africa or the Middle East were risk factors for community-onset third generation cephalosporin resistant *E. coli* infections[57].

A significant problem in Asia is disseminated infection with hypervirulent *Klebsiella pneumoniae* strains. These “hypermucoviscous” strains have a propensity to cause community-onset pyogenic liver abscess and sometimes metastatic infections, including meningitis[58]. While these strains were typically susceptible to multiple antibiotics, community-onset ESBL-producing strains are now well described and appear to be increasing[59].

Community-associated ESBL-producing enterobacteriaceae are of specific concern as treatment requires broad-spectrum antibiotics. Whether carbapenems are always indicated for severe infections caused by ESBL-producing organisms remains controversial. Retrospective studies suggest that carbapenem treatment is either superior or equivalent to treatment with alternatives such as piperacillin/tazobactam[60, 61]. Nevertheless, most clinicians consider a carbapenem the drug of choice for serious infections caused by ESBL-producing enterobacteriaceae. Therefore, widespread infections from the community with these organisms is likely to lead to a dramatic increase in empiric carbapenem use. A randomized controlled trial is ongoing to address the question of comparative efficacy of piperacillin-tazobactam vs. meropenem to treat bloodstream infections caused by ceftriaxone non-susceptible *E. coli* and *Klebsiella* sp., and has enrolled more than 100 patients at the time of writing (MERINO trial, NCT02176122).

Carbapenemase-producing Enterobacteriaceae

Carbapenem-resistant enterobacteriaceae (CRE) represent an immediate public health threat that requires urgent and aggressive action[1, 62]. CRE are resistant to most antibiotics and clinical outcomes after CRE infections are generally poor[63–68]. While less frequent than carbapenem-resistant *Klebsiella pneumoniae* (CRKP), carbapenem resistant *E. coli* (CREC) constitute an important subset of CRE, and are on the rise globally and outbreaks have been reported in the US[69, 70]. To date, most CRE infections in the United States and Europe are health-care associated, with patients from long term care facilities at especially high risk[71]. Although data from Asia are somewhat sparse, carbapenemases have been found in bacteria recovered from drinking water in India and in food-producing animals in China[72, 73]. This

raises the spectre of huge numbers of people in these large countries being colonized with CRE. Clinical reports of the consequences of this are awaited.

Given the rapid global spread of ESBL-producing *E. coli* ST131, the obvious concern is for this highly successful clone to acquire a carbapenemase. Indeed, several reports of carbapenemase-producing E. coli ST131 have been published[74–76]. In a study from India, ST131 clinical isolates were compared to non-ST131 clinical isolates. Overall 20% of clinical isolates were positive for metallo-β-lactamases such as $bla_{\text{NDM-1,}}$ which was evenly distributed between ST131 and non-ST131 *E. coli*[75]. As the epidemiology of ESBL is estimated to be about 10 years ahead of that of the carbapenemases, it is likely that community-associated carbapenem-resistant ST131 *E. coli* will become a major threat in the near future.

Prevention

Prevention of further spread of MDR bacteria in the community is one of the most urgent public health challenges. Unfortunately, national or even regional data on antibiotic susceptibilities are often limited. In addition, when these data are available in some form, the accompanying epidemiologic metadata is usually too restricted to determine which isolates are truly community-associated. Furthermore, clinical infections are generally the tip of the proverbial iceberg and once a signal is generated that is sufficient in amplitude to get the attention of policy-makers, subclinical spread has already occurred.

Any successful prevention strategy will have to consist of a multi-pronged approach and involve all stakeholders. In addition to human clinical antimicrobial stewardship, we need to remove antibiotics from the food chain. Furthermore, we need to limit the amount of xenobiotics such as quaternary ammonium compounds that reach the environment[77]. Another challenging step in limiting exposure of bacteria to antibiotics is the treatment of contaminated wastewater such as that generated by pharmaceutical factories and medical facilities. For instance, a study evaluated samples collected from a wastewater treatment plant in India that received water from 90 regional bulk drug manufacturers containing – amongst other compounds – higher concentrations of ciprofloxacin than are generally found in the blood of patients who are being treated with this agent. Bacteria recovered from this water were tested against 39 antibiotics. Approximately 30% of bacteria were resistant 29–32 antibiotics tested, and another ~20% were resistant to 33–36 antibiotics[78]. The magnitude of this effect, combined with the knowledge that soil-dwelling bacteria will pass on resistance genes to more clinically relevant bacteria, illustrates the importance of limiting this contamination[79].

Antimicrobial stewardship is developing rapidly as a hospital specialty. Stewardship teams often will combine strengths from Infectious Disease medical specialist and doctors of pharmacy to evaluate the appropriateness of choice and duration of antibiotic strategies[80]. However, most antibiotics are prescribed in ambulatory care and more attention is needed in this realm to really impact overall community antibiotic exposure[81]. This will not only require a paradigm shift in the behavior of prescribers, but also a cultural shift in the public on the risks and benefits of antibiotics. Rapid diagnostic testing to identify MDR bacteria

more quickly and thus limit the empiric use of unnecessarily broad antibiotics will be of great significance. Also, rapid testing to diagnose alternative, non-bacterial etiologies is important.

An important question is whether any interventions can address the issue of chronic colonization with MDR bacteria. Obviously, decolonizing these patients would decrease the risk of transmission. Also, the burden on the individual patient of this condition should not be underestimated. In many healthcare systems, patients with MRSA or CRE are “labeled” as carriers for life, resulting in the institution of isolation precautions whenever they are admitted to the hospital. This has multiple adverse effects and leads to decreased patient satisfaction[82]. For these reasons, decolonization is a theoretically attractive option. However, most decolonizing strategies involve the use of antibiotics. For MRSA decolonization, most strategies involve some combination of intranasal mupirocin with topical chlorhexidine[83]. This approach has been shown to be effective in decreasing infections after surgery[84]. However, the effect is generally short-lived and recurrence of colonization is the rule. For enteric bacteria, no good options are currently available. Various selective gut decontamination strategies have been described, but none have shown true promise. In addition, with growing knowledge of the role of the gut microbiome in the defense against MDR bacteria, it would seem counter-intuitive to give even more antibiotics. Modulating the gut microbiome either through probiotics or through fecal microbiota transplantation is a promising, but as of yet experimental method of decolonizing patients.

Summary

In conclusion, wide variability is observed in community spread of common nosocomial MDR pathogens. This variability is likely secondary to a number of factors that include the natural habitats of the bacteria, and the competition present in those niches. In addition, certain strains of bacteria appear to be much more able to maintain their MDR phenotype and spread throughout the community. This is most likely secondary to additional genetic content that compensates for the relative fitness cost of the expression of genes associated with antibacterial resistance. Community spread of MDR bacteria is an important public health threat that should be approached urgently and pro-actively.

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- Wide variability is observed in community spread of common nosocomial MDR pathogens.
- This variability is likely secondary to a number of factors that include the natural habitats of the bacteria, and the competition present in those niches.
- In addition, certain strains of bacteria appear to be much more able to maintain their MDR phenotype and spread throughout the community.
- This is most likely secondary to additional genetic content that compensates for the relative fitness cost of the expression of genes associated with antibacterial resistance.
- Community spread of MDR bacteria is an important public health threat that should be approached urgently and pro-actively.

Table 1

Multidrug resistant bacteria observed in the community.

MDR Phenotype	Epidemiologic setting of community-onset infections
MRSA	Household colonization; farm animal exposure (emerging)
VRE	Typically healthcare-associated
ESBL + *E. coli*	Endemic in Asia; in low-prevalence areas travel to Asia
CRE	Rare at present; emerging in India and China
CR-PA	Extremely rare
CR-AB	Extremely rare