Multidrug-Resistant Bacteria Among Patients Treated in Foreign Hospitals: Management Considerations During Medical Repatriation

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DOI: 10.1111/j.1708-8305.2012.00668.x

Background. The repatriation of patients from foreign hospitals can foster the emergence and spread of multidrug-resistant bacteria (MRB). We aimed to evaluate the incidence of MRB in patients treated in foreign hospitals and repatriated by international inter-hospital air transport in order to better manage these patients and adjust our procedures.

Methods. The records from all consecutive aeromedical evacuations and overseas repatriations carried out by Mondial Assistance France between December 2010 and November 2011 were reviewed for this study. Only inter-hospital transfers with inpatient destination of an acute care unit were considered. Patients were allocated to one of two groups: those identified as MRB carriers at their arrival in France and those who were not identified as such (either negative for MRB or not tested). Data were compared between the two groups.

Results. Analysis was performed on 223 patients: 16 patients (7%) were identified as MRB carriers. Compared with confirmed non-MRB patients, MRB carriers came more frequently from a high-risk unit (88% vs 59%, p = 0.05) and had a longer foreign hospital stay [13 (3–20) vs 8 (6–14) d, p = 0.01].

Conclusions. The occurrence of MRB among patients repatriated from foreign hospitals is noted in a significant minority of such individuals transferred back to their home country. The typical MRB patient was admitted to a high-risk unit in a foreign hospital prior to repatriation with longer foreign hospital admissions. The prospective identification of these patients prior to transport is difficult. While these factors are associated with MRB presence, their absence does not rule out highly resistant bacterial colonization. A systematic review of this important medical issue is warranted with the development of guidelines.

The repatriation of patients from foreign hospitals can foster the emergence and spread of multidrug-resistant bacteria (MRB) acquired in high-resistance prevalent areas.1,2 The ever-growing international tourism industry coupled with the repatriation of patients who become ill during their travel has enhanced this phenomenon.1 Studies systematically screening repatriates from foreign hospitals, however, are scarce and relatively out-dated.4,5 Recent case reports as well as limited epidemic occurrences involving MRB with extensive media coverage have forced French Health Authorities to consider the problem and develop a strategy aimed at the appropriate repatriation of these patients.6–9 Thus far, these efforts have been marginally effective. Further, the French Health Authorities have forced the hospitals to follow very strict mandatory guidelines when admitting patients from abroad; these hospitals have isolated these patients upon repatriation and admission followed by rapid attempts to detect MRB—in fact, the guidelines employed include travelers who have been hospitalized for more than 24 hours in a foreign country within the last year.10 While these measures aim to limit MRB exposure to the greater French population, they also dramatically complicate the procedure of repatriation of patients; hospitals are reluctant to offer admission to these individuals immediately after repatriation. Medical repatriation and evacuation services must deal with this new challenge. In this study, we attempted to evaluate the incidence of MRB occurrence among...
patients treated in foreign hospitals and repatriated by international inter-hospital air transport; obviously, the determination of the incidence of this important and complex medical issue will allow hospitals to better manage these patients and adjust admission procedures in an appropriate fashion.

Methods
This descriptive, retrospective study was carried out in Mondial Assistance France (MAF, French branch of Allianz Global Assistance Group), which provides worldwide medical assistance and aeromedical repatriations and evacuations. As previously described, the company has a medical coordination platform (MCP) in Paris with a number of physicians, including emergency physicians and critical care specialists. MAF has medical teams involved in the evacuations and repatriations; members of this team include emergency physicians, nurses, and nurse anesthetists. International transfers are performed using air ambulance aircraft or commercial airlines, depending on the severity and needs of the patient during the transfer. In most cases, the MAF MCP attempts to directly contact the physician in charge of the patient prior to transfer so as to obtain detailed and accurate medical information. If this contact cannot be established, the intervention of a local MAF agent, termed the medical correspondent, is required. The medical correspondent then provides a written medical report. The actual movement of the patient is determined entirely by the MAF MCP physician, including the decision to repatriate the patient, the time period in which to perform the repatriation, and the method of transfer. The identification of an accepting hospital and specific bed assignment is also the responsibility of the MAF MCP.

The records from all consecutive aeromedical evacuations and overseas repatriations executed by MAF from December 2010 to November 2011 were reviewed for this study by a single investigator, an MCP physician at MAF. All inter-hospital transfers from a foreign to a French hospital and escorted by one of the MAF teams were included. All admissions to a hospital in France were considered with the exception of long-term units, rehabilitation centers, and psychiatric units. The characteristics of the patient, conditions, treatments, type of unit in the foreign hospital, high-risk setting of initial hospital unit, time to repatriation, and modalities of the transfer were abstracted from the electronic medical record of MAF. Follow-up determinations were made, consisting of collection and review of the discharge summary from the French hospital. The Committee for Protection of Persons waived the requirement for patient’s consent; nonetheless, we determined that all study patients were not opposed to the use of their data for a scientific purpose. All the patients and provider identities were blinded in all aspects.

To more specifically describe the population, patients who clearly underwent MRB detection were allocated to one of two groups: those with MRB detected after testing at their arrival in the French hospital and those found to be negative for MRB. Data were expressed as mean ± SD, or median (interquartile range) and percentage of patients; these descriptive data were compared between the two groups. Statistical analysis was performed by non-parametric tests for quantitative data and a Fisher exact test for qualitative data. We used statistical package Stat-View 5 (Abacus Concept, Berkeley, CA, USA).

Results
Among 248 patients who met inclusion criteria, 7 patients were excluded because they were involved in armed conflicts with uncertain initial care in the foreign hospital. Demographic and other basic descriptive data were determined for the 241 patients. Mean age was 55 ± 21 years with 54% male gender. The primary diagnostic groups included trauma (40%), cardiac (15%), neurologic (12%), and respiratory (7%). Geographic locations are shown in Figure 1a and b, consisting of Europe (44%), North Africa (22%), sub-Saharan Africa (12%), and Asia (12%). During their stay in the foreign hospital, 85 patients presented with infectious syndromes (34%) and 86 received antibiotics (35%). One-hundred sixteen (48%) patients were admitted to a high-risk unit. The median stay before their international inter-facility transfer was 7 days with an interquartile range of 4 to 10 days.

Of the total included population, for 18 patients, the hospital into which the patient was admitted refused to collaborate. The remaining 223 patients represent the study population analyzed. When admitted in France, 16 patients were identified as having MRB colonization (7%). Of the 207 patients who were not positive for MRB, 32 patients were clearly determined as non-MRB carriers after appropriate testing. The characteristics of MRB carriers as compared with confirmed non-MRB patients are presented in Table 1. The duration of foreign hospital stay was significantly longer in MRB carriers as compared with confirmed non-MRB patients [13 (3–20) vs 8 (6–14) d, p = 0.01] and admission into a high-risk unit was more frequently observed.

Detailed data concerning the 16 MRB carriers are presented in Table 2. Ten different types of bacteria have been detected in MRB carriers. Methicillin-resistant Staphylococcus aureus (MRSA) and multidrug-resistant Acinetobacter baumannii (MDRAB) were the most frequent (in five and four patients, respectively). Six extended-spectrum β-lactamase (ESBL)-producing bacteria were found in another five patients. Among these ESBL-producing bacteria, two were identified as cephalosporinase-producing bacteria, three as non-carbapenemase producers, and one (patient #14) as having undefined anti-microbial resistance patterns.
Josseaume et al. (a) Origin of patients (total population). Data are \( n \) (number of patients in each country). 56 countries: Algeria, Andorra (And), Argentina, Armenia, Australia, Austria, Belgium (Bel), Benin, Bulgaria, Burkina, Cameroon, Canada, Chad, China, Congo, Croatia, Denmark, Djibouti, Dominican Republic (Rep Dom), Ecuador, Egypt, Gabon, Germany, Greece, Guinea, Hong Kong (HK), Hungary, India, Ireland, Israel, Italy, Japan, Kenya, Kuwait (Kow), Mali, Malta, Mauritius (Mau), Morocco, Nigeria, Norway, Poland, Portugal, Romania, Russia, Senegal, Serbia, Spain, Switzerland (Sui), Thailand, Tunisia, Turkey, United Arab Emirates, United Kingdom, United States, Uruguay, and Vietnam. Also three French overseas areas: Guadeloupe (Gua), La Réunion (La Reu), and Martinique (Mar). (b) Origin of patients—European countries. Data are \( n \) (number of patients in each country). 20 countries: Andorra (And), Austria, Belgium (Bel), Bulgaria, Croatia, Denmark, Germany, Greece, Hungary, Ireland, Italy, Malta, Norway, Poland, Portugal, Romania, Serbia, Spain, Switzerland (Sui), and United Kingdom.

Geographic locations of initial foreign hospitalization are depicted in Figure 2.

Lastly, only 18% of the study population analyzed for this investigation were clearly identified as having undergone isolation/rapid detection of MRB as recommended by the French Health Authorities.

Discussion

The results of this study demonstrate that colonization by MRB among repatriates from foreign hospitals is not infrequent wherever they are transferred from, with long stay in a high-risk unit in the foreign hospital before the international inter-facility transfer being more frequent in the case of MRB colonization. Another noteworthy finding is the relative low proportion of patients who in effect underwent MRB detection despite the existence of a specific directive issued by French Health Authorities; of course, some patients may have undergone this procedure without being identified as such.

We noted a higher occurrence rate of MRB colonization as compared with previous studies in which the incidence was low. These studies, however, used different recruitment strategies. Nonetheless, our
Table 1 Characteristics of multidrug-resistant bacteria (MRB) patients compared with confirmed non-MRB patients

<table>
<thead>
<tr>
<th>MRB patients</th>
<th>Confirmed non-MRB patients</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 16</td>
<td>N = 32</td>
<td></td>
</tr>
<tr>
<td>Duration of foreign hospital stay (d)</td>
<td>13 (3–20)</td>
<td>8 (6–14)</td>
</tr>
<tr>
<td>High-risk unit</td>
<td>14 (88%)</td>
<td>19 (59%)</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>11 (69%)</td>
<td>16 (50%)</td>
</tr>
<tr>
<td>Visiting family</td>
<td>8 (50%)</td>
<td>13 (41%)</td>
</tr>
</tbody>
</table>

Data are n (%) or median (interquartile), compared with a Fisher exact test and a Mann–Whitney U-test.

findings confirm that MRB colonization does occur in a significant minority of repatriated and admitted patients.

Among the 10 different types of bacteria that have been detected in MRB carriers reported in the present series, MRSA and MDRAB were the most frequent, which is consistent with previous studies.4,5 The geographic locations of MRB patients are also consistent with previous findings.4,5 Noteworthy, the recent French regulatory measures have been implemented in response to a limited epidemic of imported Klebsiella pneumoniae carbapenemase (KPC)-producing bacteria. The emergence of KPC-producing organisms is of particular concern and numerous epidemics involving them have been reported around the world and, more specifically, in Southern Europe12–14 although no KPC-producing organisms were found in this population. However, the mechanism of anti-microbial resistance was most often not fully known and as a consequence not analyzed here because specific testing was simply not performed in the patients admitted in French hospitals.

Because most of ESBL bacteria was detected by systematic swab and had no relation with the primary medical condition, our results strengthen the relevance of a systematic detection as requested by the French regulations.

The results support the contention that MRB spread originating from repatriates must be considered. When health authorities implemented the recent protective guidelines, the current process was implemented as a compromise, balancing the absolute need for such a system with the practical and logistical challenges involved.1

When these guidelines are followed, the identification of an accepting hospital and bed assignment process becomes very complicated for such evacuation/repatriation companies. Strict application of guidelines will probably delay the return of patients to the home country. The needs of the individual patient, however, at times exceed the capabilities of local facilities, necessitating urgent and/or emergent evacuation.15

Moreover, patients becoming ill or injured abroad may cause emotional distress to both the patient and the family, especially in case of mass casualty event, and the earliest repatriation is regarded as a priority.16 Nonetheless, do the needs of an individual patient outweigh the protection of larger segments of society? This question, along with the medical and logistical challenges faced in these considerations, describes the substantial difficulty faced by the medical team when evacuation/repatriation is required.

It is also noteworthy that we observed poor adherence to the French Health Authorities’ directive. Additional investigation of this poor adherence and consideration of more functional guidelines should be pursued. Outside France, previous programs have been developed, such as the “Search and Destroy” policy that has been conducted in North European countries and has demonstrated its efficacy in limiting MRSA spread.16 To our knowledge, this kind of regulatory measure is specific to France. For instance, the United States does not have current regulations on this topic. Very recently, the French Ministry of Health defined a procedure of identification/reporting of repatriated patients to health authorities; MAF follows this new procedure.17

Study Limitations

This study is a retrospective review issued from a single medical agency managing a selected French population. Further, patients meeting inclusion criteria during the study period were transported from only 54 countries. The number of cases who were identified as MRB-carriers is limited. Hence we did not attempt to identify independent risk criteria for MRB colonization. Some relevant information such as the origin of patients (French born, other native related, etc.) and any previous hospitalization within 1 year with prior acquisition of MRB are missing. This study is the initial step of a program we aim to establish both in a prospective fashion and from a multicenter perspective. Furthermore, our study design—retrospective with incomplete follow-up—likely underestimates the magnitude of this problem. Finally, we excluded patients who were transferred from an armed conflict setting; this exclusion likely affects the study population and our results.

It is also noteworthy that patients traveling to western countries to access advanced treatment unobtainable in their home country may also import MRB.1 There is also an increase of patients traveling from developed countries to other areas offering care at a lower cost, without delay, or with greater privacy for cosmetic and other procedures.18–22 Certainly, these two populations can also import MRB; we did not consider either group in our study.

Conclusion

The occurrence of MRB among patients repatriated from foreign hospitals is noted in a significant minority

### References

1. Very recently, the French Ministry of Health defined a procedure of identification/reporting of repatriated patients to health authorities; MAF follows this new procedure.17

### Table 1

**Characteristics of multidrug-resistant bacteria (MRB) patients compared with confirmed non-MRB patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MRB patients</th>
<th>Confirmed non-MRB patients</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of foreign hospital stay (d)</td>
<td>13 (3–20)</td>
<td>8 (6–14)</td>
<td>0.01</td>
</tr>
<tr>
<td>High-risk unit</td>
<td>14 (88%)</td>
<td>19 (59%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>11 (69%)</td>
<td>16 (50%)</td>
<td>0.35</td>
</tr>
<tr>
<td>Visiting family</td>
<td>8 (50%)</td>
<td>13 (41%)</td>
<td>0.55</td>
</tr>
</tbody>
</table>

Data are n (%) or median (interquartile), compared with a Fisher exact test and a Mann–Whitney U-test.

**Recommendations**

1. Health authorities should implement the recent protective guidelines to prevent MRB spread.
2. Patients meeting inclusion criteria during the study period should be transported from only 54 countries.
3. Relevant information such as the origin of patients and any previous hospitalization within 1 year with prior acquisition of MRB should be collected.
4. Patients who were transferred from an armed conflict setting should be excluded from the study.
5. The study design—retrospective with incomplete follow-up—likely underestimates the magnitude of the problem.
6. The needs of the individual patient should outweigh the protection of larger segments of society.

**Conclusion**

The occurrence of MRB among patients repatriated from foreign hospitals is noted in a significant minority.
### Table 2 Characteristics of multidrug-resistant bacteria (MRB) carrier patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Condition</th>
<th>Type of foreign hospitalization</th>
<th>Duration of hospitalization before repatriation (d)</th>
<th>Location</th>
<th>Modalities of repatriation</th>
<th>Type of hospitalization after repatriation</th>
<th>Germ</th>
<th>Site of detection</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67 Stroke</td>
<td>Medicine ward</td>
<td>10</td>
<td>Morocco</td>
<td>Stretcher on scheduled airlines</td>
<td>Medicine ward</td>
<td>Cephalosporinase-producing Enterobacteriaceae</td>
<td>Urine culture</td>
</tr>
<tr>
<td>2</td>
<td>64 Severe trauma</td>
<td>ICU</td>
<td>2</td>
<td>Tunisia</td>
<td>Air ambulance</td>
<td>ICU</td>
<td>MDRAB</td>
<td>Bronchoalveolar lavage</td>
</tr>
<tr>
<td>3</td>
<td>8 Third degree burn</td>
<td>ICU</td>
<td>1</td>
<td>Algeria</td>
<td>Air ambulance</td>
<td>ICU</td>
<td>MRSA</td>
<td>Nasal swab</td>
</tr>
<tr>
<td>4</td>
<td>65 Severe trauma</td>
<td>ICU</td>
<td>14</td>
<td>Spain</td>
<td>Air ambulance</td>
<td>Medicine ward</td>
<td>MDRAB</td>
<td>Rectal swab</td>
</tr>
<tr>
<td>5</td>
<td>67 Pulmonary embolism</td>
<td>ICU</td>
<td>14</td>
<td>Portugal</td>
<td>Air ambulance</td>
<td>ICU</td>
<td>QRE</td>
<td>Urine culture</td>
</tr>
<tr>
<td>6</td>
<td>62 Acute coronary syndrome with cardiac arrest</td>
<td>ICU</td>
<td>12</td>
<td>Spain</td>
<td>Air ambulance</td>
<td>ICU</td>
<td>MRSA</td>
<td>Bronchoalveolar lavage</td>
</tr>
<tr>
<td>7</td>
<td>18 Severe trauma</td>
<td>ICU</td>
<td>19</td>
<td>Tunisia</td>
<td>Air ambulance</td>
<td>ICU</td>
<td>ESBL-producing K pneumoniae + Proteus mirabilis cephalosporinase</td>
<td>Rectal swab</td>
</tr>
<tr>
<td>8</td>
<td>45 ARDS</td>
<td>ICU</td>
<td>26</td>
<td>Spain</td>
<td>Ground transportation</td>
<td>ICU</td>
<td>CRPA</td>
<td>Bronchoalveolar lavage</td>
</tr>
<tr>
<td>9</td>
<td>65 Sepsis shock</td>
<td>ICU</td>
<td>32</td>
<td>Thailand</td>
<td>Air ambulance</td>
<td>ICU</td>
<td>MRSA + ESBL</td>
<td>Skin swab</td>
</tr>
<tr>
<td>10</td>
<td>47 Severe trauma</td>
<td>ICU</td>
<td>3</td>
<td>Congo</td>
<td>Air ambulance</td>
<td>Medicine ward</td>
<td>VRE</td>
<td>Rectal swab</td>
</tr>
<tr>
<td>11</td>
<td>64 ARDS</td>
<td>Medicine ward</td>
<td>8</td>
<td>Thailand</td>
<td>Stretcher on scheduled airlines</td>
<td>ICU</td>
<td>ESBL Escherichia coli</td>
<td>Rectal swab</td>
</tr>
<tr>
<td>12</td>
<td>87 Gastro-enteritis</td>
<td>ICU</td>
<td>14</td>
<td>Uruguay</td>
<td>Stretcher on scheduled airlines</td>
<td>Medicine ward</td>
<td>MDRAB</td>
<td>Urine culture</td>
</tr>
<tr>
<td>13</td>
<td>29 Acute lower-limb ischemia</td>
<td>Medicine ward</td>
<td>2</td>
<td>Tunisia</td>
<td>Air ambulance</td>
<td>ICU</td>
<td>MDRAB</td>
<td>Skin swab</td>
</tr>
<tr>
<td>14</td>
<td>71 ARDS</td>
<td>ICU</td>
<td>43</td>
<td>Thailand</td>
<td>Air ambulance</td>
<td>ICU</td>
<td>ESBL-producing</td>
<td>Throat specimen</td>
</tr>
<tr>
<td>15</td>
<td>83 Severe trauma</td>
<td>Medicine ward</td>
<td>2</td>
<td>Morocco</td>
<td>Air ambulance</td>
<td>ICU</td>
<td>MRSA</td>
<td>Osteosynthesis equipment</td>
</tr>
<tr>
<td>16</td>
<td>68 Severe trauma</td>
<td>ICU</td>
<td>24</td>
<td>Portugal</td>
<td>Stretcher on scheduled airlines</td>
<td>Medicine ward</td>
<td>MRSA</td>
<td>Nasal swab</td>
</tr>
</tbody>
</table>

ARDS = acute respiratory distress syndrome; ICU = intensive care unit; MDRAB = multidrug-resistant *A. baumannii*; MRSA = methicillin-resistant *S. aureus*; QRE = quinolone-resistant Enterococcus; ESBL-producing *K pneumoniae* = extended-spectrum β-lactamase-producing *K pneumoniae*; CRPA = ceftazidime-resistant *Pseudomonas aeruginosa*; ESBL = extended-spectrum β-lactamase-producing Enterobacteriaceae; VRE = vancomycin-resistant Enterococcus; ESBL Escherichia coli = extended-spectrum β-lactamase-producing Escherichia coli.
of such individuals transferred back to their home country. The typical MRB patient was admitted to a high-risk unit in the foreign hospital prior to repatriation; in addition, longer foreign hospital admissions and antibiotic administration during the initial hospital admission were also seen more frequently in these MRB patients. While these factors are associated with MRB presence, their absence does not rule out highly resistant bacterial colonization. The prospective identification of these patients prior to transport is difficult yet extremely important to aid in the selection of the most appropriate transfer hospital location as well as the protection of the local population from MRB. Lastly, existing guidelines and system of consideration are not consistently applied; the impact of and reasons for this non-compliance are unknown. A systematic review of this important medical issue is warranted with the development of guidelines.

Declaration of Interests
The authors state they have no conflicts of interest to declare.

References