Typhoid fever, which is caused by *Salmonella enterica* serotype Typhi, is endemic to the developing world; there were an estimated 26.7 million cases in 2010 (1). The incidence of typhoid fever in sub-Saharan Africa was an estimated 725 cases/100,000 persons in 2010, despite a lack of incidence studies conducted in West and central Africa (1). Antimicrobial susceptibility data are also scarce for this part of Africa. This issue is problematic because treatment with appropriate antimicrobial drugs is essential for recovery in the context of the global emergence of multidrug resistance.

In the Indian subcontinent and Southeast Asia, the multidrug-resistant (MDR) *Salmonella* Typhi H58 clone, which was named after its haplotype (a combination of defined chromosomal single-nucleotide polymorphisms [SNPs]) (2,3), has spread rapidly and become endemic and predominant. During the 1990s, this clone acquired a large conjugative incHI1 pST2 plasmid encoding resistance to ampicillin, chloramphenicol, and co-trimoxazole (4,5); also in the 1990s, this MDR clone became resistant to quinolones and showed decreased susceptibility to ciprofloxacin because of point mutations in the chromosomal *gyrA* gene (2). The H58 clone has also spread to eastern Africa, where it has been the most prevalent haplotype (87%) in Kenya since the early 2000s (6).

During 1997–2011, high incidence of MDR *Salmonella* Typhi was reported in some countries near the Gulf of Guinea in Africa, including Nigeria (7), Ghana (8,9), Togo (10), and the Democratic Republic of the Congo (11). During 1999–2003, a British surveillance system reported a prevalence of 19% (49/261) for MDR *Salmonella* Typhi isolates among imported cases of typhoid fever acquired in Africa, particularly in Ghana (12). However, nothing is known about the genotypes of these isolates, including whether they belong to the spreading MDR H58 clone.

We report data for the occurrence, genotypes, and characterization of the resistance mechanisms of MDR *Salmonella* Typhi isolates. These isolates were obtained from the French National Reference Center for *Salmonella* (FNRC-Salm), Institut Pasteur (Paris, France), and Centre Pasteur du Cameroun (Yaoundé, Cameroon).

**The Study**

Almost all *Salmonella* Typhi strains referred to the FNRC-Salm. Most isolates were obtained from travelers or immigrants, most of whom were infected in Africa and Asia. In Cameroon, the Centre Pasteur du Cameroun collects *Salmonella* Typhi isolates from several hospitals in.

Antimicrobial susceptibility testing was performed according to the guidelines of the antibiogram committee of the French Society for Microbiology (http://www.sfm.asso.fr/nouvelles/general.php?pa = 2). Isolates were considered to be MDR if they were resistant to ≥2 of the following antimicrobial drugs: amoxicillin, co-trimoxazole (trimethoprim/sulfamethoxazole), chloramphenicol, or tetracyclines.

During 1996–2013, a total of 1,746 *Salmonella* Typhi isolates were collected through the French national surveillance system and subjected to antimicrobial susceptibility testing; 408 were acquired in sub-Saharan Africa (n = 237) and northern Africa (n = 171), and 55 (13.5%) of those acquired in Africa were MDR (Table). All but 1 of the MDR isolates were acquired in sub-Saharan Africa (Table). 

**Table**

<table>
<thead>
<tr>
<th>Geographic Region</th>
<th>Number of MDR Isolates</th>
<th>Percentage of MDR Isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>408</td>
<td>13.5%</td>
</tr>
<tr>
<td>Northern Africa</td>
<td>171</td>
<td>13.5%</td>
</tr>
<tr>
<td>Total</td>
<td>555</td>
<td>13.5%</td>
</tr>
</tbody>
</table>

Author affiliations: Institut Pasteur, Paris, France (M. Baltazar, E. Lepillet, M. Pardos de la Gandara, S. Le Hello, F.-X. Weill); Centre Pasteur du Cameroun, Yaoundé, Cameroon (A. Ngandjio, A. Nzouankeu, M.-C. Fonkoua); University of Melbourne, Melbourne, Victoria, Australia (K.E. Holt); Wellcome Trust Sanger Institute, Cambridge, UK (K.E. Holt, G. Dougan); Scientific Institute of Public Health, Brussels, Belgium (J.-M. Collard); Institut Pasteur de Bangui, Bangui, Central African Republic (R. Bercion)

DOI: http://dx.doi.org/10.3201/eid2104.141355
Lineage A consisted mostly of haplotype H56 isolates and more rarely H42 (which differs from H56 by 2 SNPs) and was found only in the western part of the Gulf of Guinea region. Lineage B consisted of haplotype H55 isolates and was found in the eastern and southern parts of the Gulf of Guinea region. Lineage C consisted of haplotype H77 isolates and was found only in Cameroon. All 3 lineages had distinctive CRISPR1 spacer contents. 

The 3 lineages contained a large (≈190 kb) conjugative MDR incHI1 pST2 plasmid that differed among lineages. Resistance to trimethoprim was encoded by different class 1 integron gene cassettes: dfrA15, dfrA7, and dfrA1 for incHI1 plasmids of lineages A, B, and C, respectively. All incHI1 plasmids from lineage A encoded resistance to chloramphenicol, and none of those from lineage C encoded such resistance. A second smaller (50-kb) MDR plasmid belonging to the incN incompatibility group (pST3 by plasmid multilocus sequence typing), was present mostly in lineage C isolates, but was also found in 1 lineage A isolate (02-1739) (online Technical Appendix).

**Conclusions**

Analysis of older isolates and previously published data (2) showed that susceptible *Salmonella* Typhi strains of haplotypes H42, H56, and H77 had already been identified in Senegal in 1962, Tunisia in 1969, and Cameroon in 1958, respectively. This finding suggests that the MDR isolates from lineages A and C are derived from local *Salmonella* Typhi populations in Africa, rather than being recently imported from other regions to which this bacterium is endemic. Haplotype H55 was previously restricted largely to the Indian subcontinent and eastern Africa (2); it was

**Table.** Characteristics of *Salmonella enterica* serotype Typhi isolates, France and Cameroon, 1996–2013*

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>France</td>
<td>345</td>
<td>266</td>
<td>627</td>
<td>508</td>
</tr>
<tr>
<td>No. isolates studied</td>
<td>86</td>
<td>64</td>
<td>155</td>
<td>103</td>
</tr>
<tr>
<td>No. (%) MDR†</td>
<td>0</td>
<td>7 (10.9)</td>
<td>25 (16.1)</td>
<td>23 (22.3)</td>
</tr>
<tr>
<td>Country of infection</td>
<td>Benin (3), Togo (2), Burkina-Faso (1), Cameroon (1)</td>
<td>Cameroon (7), Côte d’Ivoire (4), Burkina-Faso (3), Angola (2), Congo (1), Mali (1), Benin (1), Nigeria (1), Mauritania (1), Togo (1), Central African Republic (1), Guinea (1), not specified (1)</td>
<td>Côte d’Ivoire (7), Guinea (3), Burkina-Faso (3), Cameroon (2), Congo (1), Central African Republic (1), Niger (1), Mali (1), Nigeria (1), Chad (1), Togo (1), Algeria (1)</td>
<td></td>
</tr>
<tr>
<td>MDR isolates (no.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yaoundé, Cameroon</td>
<td>ND</td>
<td>61</td>
<td>75</td>
<td>49</td>
</tr>
<tr>
<td>No. isolates studied</td>
<td>ND</td>
<td>29 (47.5)</td>
<td>50 (86.6)</td>
<td>37 (75.5)</td>
</tr>
<tr>
<td>No. (%) MDR†</td>
<td></td>
<td></td>
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</table>

*MDR, multidrug resistant; ND, not determined.
†For isolates acquired in Africa.
detected in association with an incHI1 pST2 plasmid in India during the mid-1970s (5). Therefore, lineage B might have been imported into central Africa from eastern Africa/southern Asia.

A previous study also reported isolation of an MDR clone in the Democratic Republic of the Congo in 2004 that was resistant to quinolones, showed decreased susceptibility to ciprofloxacin, and belonged to the Asian H58 lineage (2). Because only a limited number of isolates from central Africa were tested in our study, studies of a larger collection of isolates might provide more information about bacterial genotypes/MDR plasmids circulating in central Africa.

Despite intrinsic limitations of a laboratory surveillance system for typhoid fever that is used mostly for travelers and immigrants and has the bias of preferential links caused by colonial history and choices of tourist destinations, we documented emergence of 3 MDR Salmonella Typhi lineages in the Gulf of Guinea area. Two lineages found in Guinea and Cameroon were local lineages that acquired MDR conjugative plasmids, either a large incHI1 pST2 plasmid or a smaller incN pST3 plasmid. The H58 lineage, which is currently predominant in Asia and eastern Africa, was not detected among MDR isolates from West and central Africa.

Acknowledgments
We thank all the corresponding laboratories of the FNRC-Salm network for participating in this study.
This study was supported by the Institut Pasteur, the Réseau International des Instituts Pasteur, the Institut de Veille Sanitaire, and the French Government Investissement d’Avenir Program (Integrative Biology of Emerging Infectious Diseases, Laboratory of Excellence, grant ANR-10-LABX-62-IBEID).

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References


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