Nature strikes back!
Patient 65 y old male

- Previously healthy
- Recently vacation in Egypt
- Signs of urinary tract infection the last couple of days
- Arrives at the ER hypotensive, tachycardia, fever (40.1 degrees Celsius), respiratory frequency 36 /minute
- WBC 18, CRP 163, Lactate 8.6
<table>
<thead>
<tr>
<th>Bakterie</th>
<th>Antal stammar (%) i Norge</th>
<th>Antal stammar (%) i Malmö</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>E. coli</strong></td>
<td>131 (31,0)</td>
<td>231 (26,4)</td>
</tr>
<tr>
<td><strong>S. pneumoniae</strong></td>
<td>69 (16,4)</td>
<td>46 (5,3)</td>
</tr>
<tr>
<td><strong>S. aureus</strong></td>
<td>59 (14,0)</td>
<td>110 (12,6)</td>
</tr>
<tr>
<td><strong>Klebsiella spp.</strong></td>
<td>29 (6,9)</td>
<td>54 (6,2)</td>
</tr>
<tr>
<td><strong>Enterokock spp.</strong></td>
<td>20 (4,7)</td>
<td>61 (7,0)</td>
</tr>
<tr>
<td><strong>S. pyogenes</strong></td>
<td>18 (4,3)</td>
<td>50 (5,7)</td>
</tr>
<tr>
<td><strong>Viridans streptokocker</strong></td>
<td>17 (4,0)</td>
<td>69 (7,9)</td>
</tr>
<tr>
<td><strong>P. mirabilis</strong></td>
<td>15 (3,6)</td>
<td>17 (1,9)</td>
</tr>
<tr>
<td><strong>P. aeruginosa</strong></td>
<td>9 (2,1)</td>
<td>21 (2,4)</td>
</tr>
<tr>
<td><strong>Neisseria spp.</strong></td>
<td>8 (1,9)</td>
<td>1</td>
</tr>
<tr>
<td><strong>S. agalactiae</strong></td>
<td>8 (1,9)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Enterobacter spp.</strong></td>
<td>7 (1,7)</td>
<td>47 (5,4)</td>
</tr>
<tr>
<td>Övrigt</td>
<td>32 (7,6)</td>
<td>165 (18,9)</td>
</tr>
</tbody>
</table>
Numerous studies have identified risk factors for acquirement and infection of Enterobacteriaceae with ESBL-production.
Duration of colonization with extended-spectrum beta-lactamase-producing Escherichia coli in patients with travellers’ diarrhoea

Johan Tham\textsuperscript{1}, Mats Walder\textsuperscript{2}, Eva Melander\textsuperscript{2,3} & Inga Odenholt\textsuperscript{1}

From the \textsuperscript{1}Infectious Diseases Unit, Department of Clinical Sciences, Lund University, Malmö, \textsuperscript{2}Medical Microbiology, Department of Laboratory Medicine, Lund University, Malmö, and \textsuperscript{3}Department of Infection Control, Laboratory Medicine, Skåne County, Sweden

Abstract

Background: Resistant Enterobacteriaceae have become a worldwide epidemic during the last decade and are a great threat to health care worldwide. International travel is a major risk factor for becoming colonized with extended-spectrum beta-lactamase (ESBL)-producing bacteria. Data on the persistence of colonization with ESBL-producing bacteria in the faecal flora are limited. Methods: A prospective cohort study was performed between October 2007 and October 2010. Fifty-three patients with faecal carriage of ESBL-producing Escherichia coli from a previous study of patients with travellers’ diarrhoea were included. Results: Forty-one of the patients had a complete follow-up. Ten of these patients (24\%) carried ESBL-producing E. coli at the first follow-up point (3–8 months), of whom 4 had a new ESBL strain. At the 3-year follow-up, patients carried ESBL (10\%), of whom 1 had 2 new ESBL strains. Conclusions: The long duration of ESBL carriage is worrisome. These carriers may be an important source of the spread of ESBLs in the population and this has implications for infection control measures. The current study confirms that patients with ESBL-producing E. coli should be isolated and that contact precautions with regards to ESBL should be taken for a minimum of 3 weeks after treatment.

Original Article

Extended-spectrum beta-lactamase-producing Escherichia coli in patients with

Johan Tham\textsuperscript{1}, Jonas Ahl\textsuperscript{2}

From the \textsuperscript{1}Infectious Diseases Unit, Department of Clinical Sciences, Lund University, Malmö, \textsuperscript{2}Medical Microbiology, Tumour and Cell Biology

H. Strömsholm
P. J. Edquist

Abstract

The identification of patients at risk of developing a serious infection caused by extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae is important. The prevalence of ESBL-producing E. coli in a group of patients with cancer in Sweden was studied. Patients with cancer were identified from the National Cancer Registry in Sweden and were matched to controls using the Swedish population register. ESBL-producing E. coli were isolated from 12.4% of the patients and 7.6% of the controls. The risk of carrying ESBL-producing E. coli was increased in patients with cancer compared with controls (OR 2.7; 95\% CI 1.4–5.1). The prevalence of ESBL-producing E. coli was higher in patients with cancer than in controls (14.5\% vs 7.2\%). The prevalence of ESBL-producing E. coli was higher in patients with cancer than in controls (14.5\% vs 7.2\%).
Extended-spectrum beta-lactamase-producing Escherichia coli in patients with travellers’ diarrhoea

242 patients with travellers’ diarrhoea

ESBL-screen
Medium selective for cephalosporin resistance (ChromID ESBL, BioMerieux)

Synergy testing
With disks containing ceftazidime and cefotaxime amoxicillin/clavulanic acid
Extended-spectrum beta-lactamase-producing Escherichia coli in patients with travellers’ diarrhoea
Extended-spectrum beta-lactamase-producing Escherichia coli in patients with travellers’ diarrhoea

242 Patients with travellers’ diarrhoea

ESBL-screening
Medium selective for Cephalosporine resistance (ChromID ESBL, BioMerieux)

Synergy testing
with disks containing ceftazidime and cefotaxime and amoxicillin/clavulanic acid

58 patients
ESBL-producing E.coli
Extended-spectrum beta-lactamase-producing Escherichia coli in patients with travellers’ diarrhoea

242 patients with travellers’ diarrhoea

30 female

58 patients with faecal carriage of ESBL-producing E.coli

28 Male

Median age 40 y

Range 7month-83 Y
Regions and countries involved in the study

Table II. Regions and countries involved in the study: Europe (Bosnia, Bulgaria, Denmark, UK, France, Germany, Greece, Hungary, Ireland, Italy, Kosovo, Romania, Spain, Turkey and Ukraine), Middle East (Kurdistan, Lebanon, Morocco, Iraq, Oman, Saudi Arabia, Syria and Tunisia), Africa (Gambia, Ghana, Guinea, Kenya, Tanzania and unspecified), Southeast Asia (Afghanistan, Australia, Bangladesh, Cambodia, China, Pakistan, Papua New Guinea, Philippines, Singapore and Tahiti), America (Argentina, Bolivia, Caribbean, Chile, Mexico and unspecified parts of America).

<table>
<thead>
<tr>
<th>Region</th>
<th>ESBL-positive (n)</th>
<th>ESBL-negative (n)</th>
<th>Total (n)</th>
<th>Proportion positive</th>
<th>95% CI</th>
<th>p-Value compared to Europe</th>
</tr>
</thead>
<tbody>
<tr>
<td>World</td>
<td>58</td>
<td>184</td>
<td>242</td>
<td>(58/242)=0.24</td>
<td>0.19–0.30</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>World excl. Europe and unspecified</td>
<td>50</td>
<td>88</td>
<td>138</td>
<td>(50/138)=0.36</td>
<td>0.29–0.45</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Europe excl. Sweden</td>
<td>2</td>
<td>61</td>
<td>63</td>
<td>(2/63)=0.03</td>
<td>0.004–0.11</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Egypt</td>
<td>19</td>
<td>19</td>
<td>38</td>
<td>(19/38)=0.50</td>
<td>0.33–0.67</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Thailand</td>
<td>8</td>
<td>28</td>
<td>36</td>
<td>(8/36)=0.22</td>
<td>0.10–0.39</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>India</td>
<td>11</td>
<td>3</td>
<td>14</td>
<td>(11/14)=0.79</td>
<td>0.49–0.95</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Middle East</td>
<td>4</td>
<td>6</td>
<td>10</td>
<td>(4/10)=0.40</td>
<td>0.12–0.74</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Southeast Asia incl. Australia</td>
<td>5</td>
<td>8</td>
<td>13</td>
<td>(5/13)=0.38</td>
<td>0.14–0.68</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Africa excl. Egypt</td>
<td>2</td>
<td>15</td>
<td>17</td>
<td>(2/17)=0.12</td>
<td>0.015–0.36</td>
<td>0.1965 (NS)</td>
</tr>
<tr>
<td>America incl. West Indies</td>
<td>1</td>
<td>9</td>
<td>10</td>
<td>(1/10)=0.10</td>
<td>0.0025–0.44</td>
<td>0.3615 (NS)</td>
</tr>
<tr>
<td>Unspecified</td>
<td>6</td>
<td>35</td>
<td>41</td>
<td>(6/42)=0.15</td>
<td>0.06–0.29</td>
<td>0.0550 (NS)</td>
</tr>
</tbody>
</table>

ESBL, extended-spectrum beta-lactamase; CI, confidence interval; NS, not significant.
Pathogens found in the stool samples. All of these isolates were ESBL-negative.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>ESBL-negative</th>
<th>ESBL-positive (E. coli)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campylobacter jejuni/coli</td>
<td>31</td>
<td>3</td>
<td>34</td>
</tr>
<tr>
<td>Salmonella enteritidis</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Salmonella group 04</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Salmonella group 07</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Salmonella group 08</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Salmonella senftenberg</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Shigella flexneri</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Shigella sonnei</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Shigella boydii</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>All pathogens (SSYC)</td>
<td>40</td>
<td>7</td>
<td>47</td>
</tr>
</tbody>
</table>

ESBL, extended-spectrum beta-lactamase.
## Antibiotic resistance

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Clinical E. coli isolates with ESBLs (%)</th>
<th>Study E. coli isolates with ESBLs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobramycin</td>
<td>42</td>
<td>54</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>62</td>
<td>68</td>
</tr>
<tr>
<td>Piperacillin–tazobactam</td>
<td>22</td>
<td>8</td>
</tr>
<tr>
<td>Mecillinam</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>80</td>
<td>91</td>
</tr>
<tr>
<td>Trimethoprim–sulfamethoxazole</td>
<td>87</td>
<td>75</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>8</td>
<td>5</td>
</tr>
</tbody>
</table>
Enzyme typing and rep PCR results

- 90% CTX-M group
- CTX-M 1 68% (The only group found in India)
- CTX-M 9 24%
- The others were TEM or SHV and some isolates both TEM and SHV
CTX-M typing and rep PCR results

- rep PCR fingerprint pattern:
  - the strains from the same geographical region displayed no genetic similarity
  - were also different from Swedish E. coli isolates studied earlier
Limitations

• Our patients were not cultured for ESBL-producing bacteria before going abroad
• Lack of other epidemiologic information
• Low number of patients with travellers’ diarrhoea from some parts of the world
Summary  Objectives: Extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli* have emerged as significant causes of community-onset disease. We sought to identify risk factors for acquiring community-onset ESBL-producing *E. coli*.

Methods: Prospective, population-based surveillance for ESBL-producing *E. coli* was performed in the Calgary Health Region (population 1.2 million), Canada during a two-year period.

Results: 247 patients were identified; 177 (72%; 7.6 per 100,000/year) were community acquired, and 70 (28%; 3.0 per 100,000/year) were healthcare associated. The acquisition risk increased with advancing age. Females were at higher risk as compared to males [relative risk (RR) 4.3; 95% confidence interval (CI), 3.1–6.1] as were urban as compared to rural residents (RR 2.2; 95% CI, 1.4–3.6). A number of co-morbidities increased risk (RR; 95% CI) including requirement for hemodialysis (56.3; 15.1–147.4), urinary incontinence (21.7; 15.0–30.9), cancer (11.1; 7.0–17.0), heart disease (6.5; 4.3–9.7), and diabetes (4.4; 2.6–7.1). Overseas travel overall increased the risk (5.7; 4.1–7.8) and was highest in travelers to India (145.6; 77.7–252.1), the Middle East (18.1; 8.1–35.2), and Africa (7.7; 2.8–17.2).
Foreign Travel Is a Major Risk Factor for Colonization with *Escherichia coli* Producing CTX-M-Type Extended-Spectrum β-Lactamases: a Prospective Study with Swedish Volunteers

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*Sections of Infectious Diseases¹ and Clinical Bacteriology,² Department of Medical Sciences, Uppsala University, Uppsala, Sweden

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Foreign travel has been suggested to be a risk factor for the acquisition of extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae*. To our knowledge, this has not previously been demonstrated in a prospective study. Healthy volunteers traveling outside Northern Europe were enrolled. Rectal swabs and data on potential travel-associated risk factors were collected before and after traveling. A total of 105 volunteers were enrolled. Four of them did not complete the study, and one participant carried ESBL-producing *Escherichia coli* before travel. Twenty-four of 100 participants with negative pretravel samples were colonized with ESBL-producing *Escherichia coli* after the trip. All strains produced CTX-M enzymes, mostly CTX-M-15, and some coproduced TEM or SHV enzymes. Coreistance to several antibiotic subclasses was common. Travel to India was associated with the highest risk for the acquisition of ESBLs (88%; *n* = 7). Gastroenteritis during the trip was an additional risk factor (*P* = 0.003). Five of 21 volunteers who completed the follow-up after 6 months had persistent colonization with ESBLs. This is the first prospective study demonstrating that international travel is a major risk factor for colonization with ESBL-producing *Enterobacteriaceae*. Considering the high acquisition rate of 24%, it is obvious that global efforts are needed to meet the emergence and spread of CTX-M enzymes and other antimicrobial resistances.

• Twenty-four of 100 participants with negative pretravel samples were colonized with ESBL-producing *Escherichia coli* after the trip

• All strains produced CTX-M enzymes, mostly CTX-M-15, and some coproduced TEM or SHV enzymes

• Coresistance to several antibiotic subclasses was common

• Gastroenteritis during the trip was an additional risk factor

• Five of 21 (24%) volunteers who completed the follow-up after 6 months had persistent colonization with ESBLs
Foreign travel is increasing
Duration of colonization with Extended-spectrum beta-lactamase producing Escherichia coli in patients with travellers’ diarrhoea

- 58 patients
- ESBL positive: 3-8 months
- 41 (76%) ESBL negative
- 13 (24%) ESBL positive
- 38 (90%) ESBL negative
- 4 (10%) ESBL positive
- 2 same strains (5%)
- 1 two new strains
- 1 missing data
Risk factors for infections with Extended-spectrum beta-lactamase producing Escherichia coli

218 Patients with E.coli infections

109 E.coli ESBL

stomach problems
urinary catheter, endoscopy
repeated urinary infections
stomach ulcer medicine
hospital stay, antibiotics
and foreign travel etc

Range
2-95 år
58 (53%)

109 "ordinary E.coli"

Median
65 år
53 (49%)

Range
2-65 år

2008
Jan-oct
Risk factors for infections with Extended-spectrum beta-lactamase producing Escherichia coli

Hospital stay (n=8)
> 1 month
P<0.01

Foreign travel (n=14)
Asia, Middle East
P=0.02
Colonization of Returning Travelers With CTX-M-Producing *Escherichia coli*

Gisele Peirano, PhD,† Kevin B. Laupland, MD,†‡§ Daniel B. Gregson, MD,†‡ and Johann D.D. Pitout, MD*†¶

*Division of Microbiology, Calgary Laboratory Services; †Department of Pathology and Laboratory Medicine; ‡Department of Medicine; §Department of Critical Care, and †Department of Microbiology and Infectious Diseases, University of Calgary, Calgary, Alberta, Canada

DOI: 10.1111/j.1708-8305.2011.00548.x

**Background.** We previously identified foreign travel as a risk factor for acquiring infections due to CTX-M (active on cefotaxime first isolated in Munich) producing *Escherichia coli*. The objective of this study was to assess the prevalence of extended-spectrum β-lactamase (ESBL)-producing *E.coli* among stool samples submitted from travelers as compared to non-travelers (a non-traveler had not been outside of Canada for at least 6 months before submitting a stool specimen).

**Methods.** Once a travel case was identified, the next stool from a non-traveler (not been outside of Canada for at least 6 months) was included and cultured on the chromID-ESBL selection media. Molecular characterization was done using polymerase chain reaction and sequencing for *blaCTX-M*, *blaTEM*, *blaSHV*, plasmid-mediated quinolone-resistant determinants, O25-ST131, phylogenetic groups, pulsed-field gel electrophoresis (PFGE), and multilocus sequencing typing.

**Results.** A total of 226 individuals were included; 195 (86%) were negative, and 31 (14%) were positive for ESBL-producing *E.coli*. Notably, travelers were 5.2 (95% CI 2.1–31.1) times more likely than non-travelers to have an ESBL-producing *E.coli* infection.
Colonization of Returning Travelers With CTX-M-Producing *Escherichia coli*

- stool samples submitted from travelers as compared to non-travelers
- travelers were 5.2 (95% CI 2.1–31.1) times more likely than non-travelers to have an ESBL-producing *E coli*

- Confirms that foreign travel, especially to the Indian subcontinent and Africa, represents a major risk for rectal colonization with CTX-M-producing *E coli* and contributed to the worldwide spread of these bacteria
Changes in serotype and resistance pattern of the intestinal Escherichia coli flora during travel. Results from a trial of mecillinam as a prophylactic against travellers' diarrhoea.

Stenderup J, Orskov I, Orskov F.

Abstract
The changes in the intestinal Escherichia coli flora during travel has been studied by serological methods. A group of 74 tourists visiting Egypt and the Far East were given mecillinam or placebo in a randomized double-blind study. In all but 3 participants, 2 in the placebo group and 1 in the mecillinam group, a complete change in the E. coli flora occurred after a few days, and changes continued to occur during the 25 days of travel. The percentage of multiresistant strains rose from 8% in the pretravel samples to 50-60% in the posttravel samples. Less than 5% of the pretravel E. coli strains were resistant to mecillinam, whereas in the posttravel samples 42.9% of the E. coli strains in the mecillinam group and 19.1% in the placebo group were resistant to mecillinam. Of the 30 mecillinam resistant E. coli strains from the diarrhoeal samples only 6 showed transferable mecillinam resistance.

PMID: 6318304 [PubMed - indexed for MEDLINE]
What about the patient?

- What shall we do?
- Which antibiotic should we choose?
Comparisons among the fully sequenced genomes of nonpathogenic and pathogenic strains have revealed an average genome size of approximately 5000 genes, but only approximately 2200 of these are shared among all *E. coli* strains. Most of the pathogens have larger genomes than do the nonpathogenic strains.[26,99] Furthermore, many of the genes that are not found in the nonpathogenic strain are specific to particular strains or pathotypes. It is estimated that the total “pangenome” of *E. coli* consists of more than 13,000 genes.[99]