
Nature strikes back!


ANDNINGSVÅRDEN
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DUM
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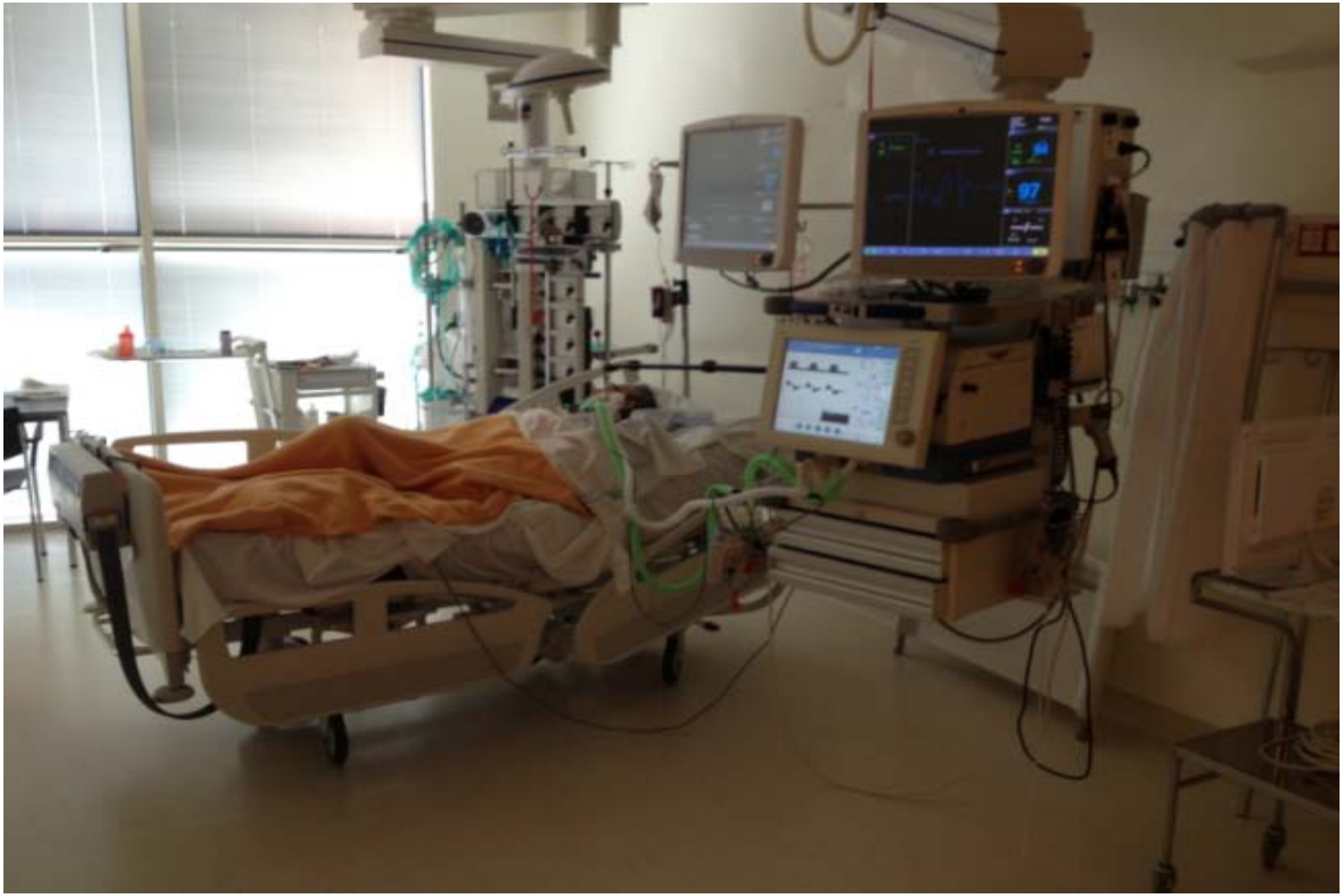
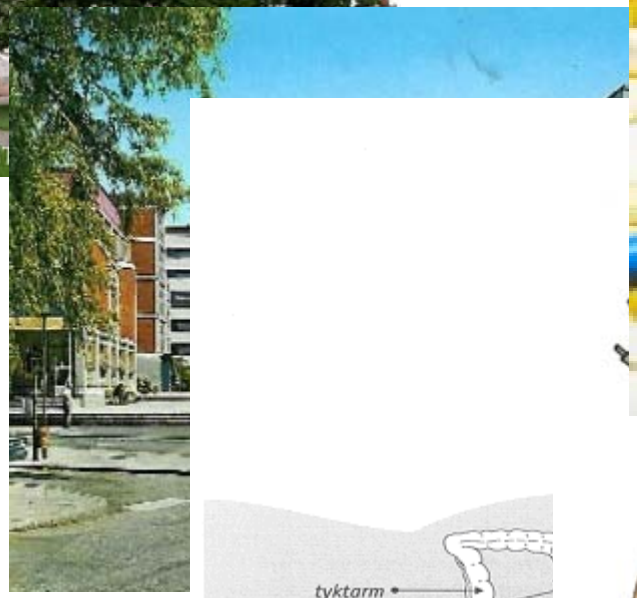
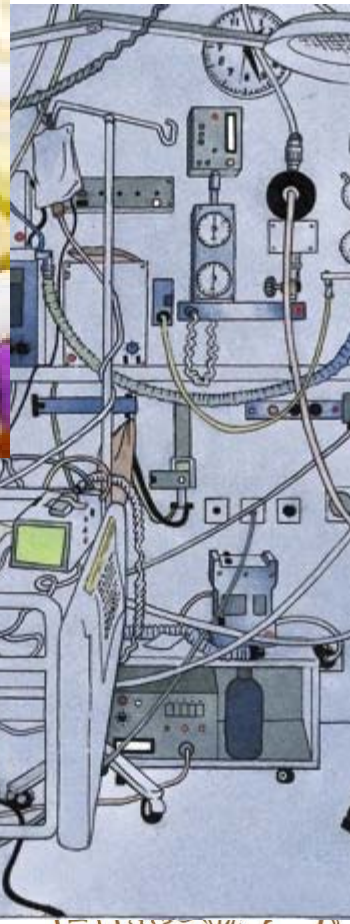
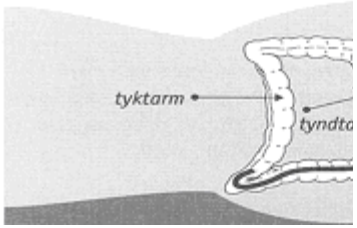


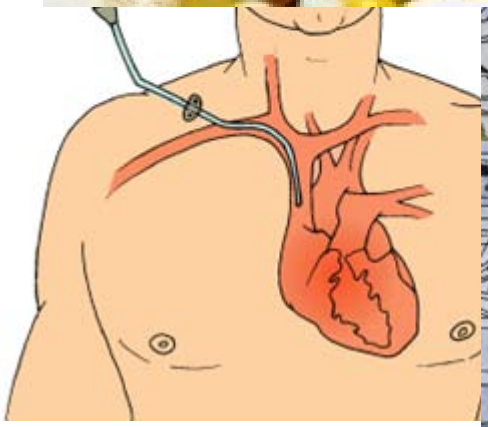
| Bakterie | Antal stammar (%) i Norge | Antal stammar (%) i Malmö |
|---|---|---|
| *E. coli* | 131 (31,0) | 231 (26,4) |
| *S. pneumoniae* | 69 (16,4) | 46 (5,3) |
| *S. aureus* | 59 (14,0) | 110 (12,6) |
| *Klebsiella spp.* | 29 (6,9) | 54 (6,2) |
| *Enterokock spp.* | 20 (4,7) | 61 (7,0) |
| *S. pyogenes* | 18 (4,3) | 50 (5,7) |
| *Viridans streptokocker* | 17 (4,0) | 69 (7,9) |
| *P. mirabilis* | 15 (3,6) | 17 (1,9) |
| *P. aeruginosa* | 9 (2,1) | 21 (2,4) |
| *Neisseria spp.* | 8 (1,9) | 1 |
| *S. agalactiae* | 8 (1,9) | 0 |
| *Enterobacter spp.* | 7 (1,7) | 47 (5,4) |
| Övrigt | 32 (7,6) | 165 (18,9) |

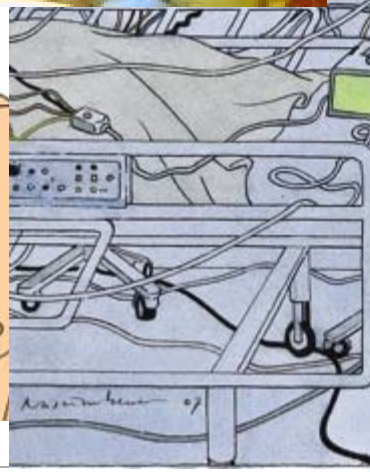
# Numerous studies ha s for acquirement and infe *aceae* duction







*Scandinavian Journal of Infectious Diseases*, 2010; 42: 275–280

ORIGINAL ARTICLE

**Extended-spectrum beta-lactamase-producing Escherichia coli in patients wit**

Eur J Clin Microbiol Infect Dis
DOI 10.1007/s10096-011-1202-5

ARTICLE

JOHAN THAM
JONAS AHL[1] &

*From the [1]Infectious*
*[2]Medical Microbiolog*
*Tumour and Cell Bio*

**Prevale**
**and in a**

**H. Ströndahl**
**P. J. Edquist**

**Abstract**
The identification of
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carriage of ESBL-pr
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**Introduction**

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producing Enterob

Correspondence: J. Tham
E-mail: johan.tham@med.

Received: 24 No
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**Abstract** The
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*Scandinavian Journal of Infectious Diseases*, 2012; Early Online, 1–5

ORIGINAL ARTICLE

# Duration of colonization with extended-spectrum beta-lactamase-producing Escherichia coli in patients with travellers' diarrhoea

JOHAN THAM[1], MATS WALDER[2], EVA MELANDER[2,3] & INGA ODENHOLT[1]

*From the [1]Infectious Diseases Unit, Department of Clinical Sciences, Lund University, Malmö, [2]Medical Microbiology, Department of Laboratory Medicine, Lund University, Malmö, and [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 t
to health care worldwide. International travel is a major risk factor for becoming colonized with extended-spectrum
lactamase (ESBL)-producing bacteria. Data on the persistence of colonization with ESBL-producing bacteria in the f
flora are limited. *Methods:* A prospective cohort study was performed between October 2007 and October 2010. Fifty-
patients with faecal carriage of ESBL-producing Escherichia coli from a previous study of patients with travellers' diarr
were included. *Results:* Forty-one of the patients had a complete follow-up. Ten of these patients (24%) carried ES
producing E. coli at the first follow-up point (3–8 months), of whom 4 had a new ESBL strain. At the 3-y follow-
patients carried ESBL (10%), of whom 1 had 2 new ESBL strains. *Conclusions:* The long duration of ESBL carria
worrisome. These carriers may be an important source of the spread of ESBLs in the population and this has implica

# Extended-spectrum beta-lactamase-producing Escherichia coli in patients with travellers' diarrhoea

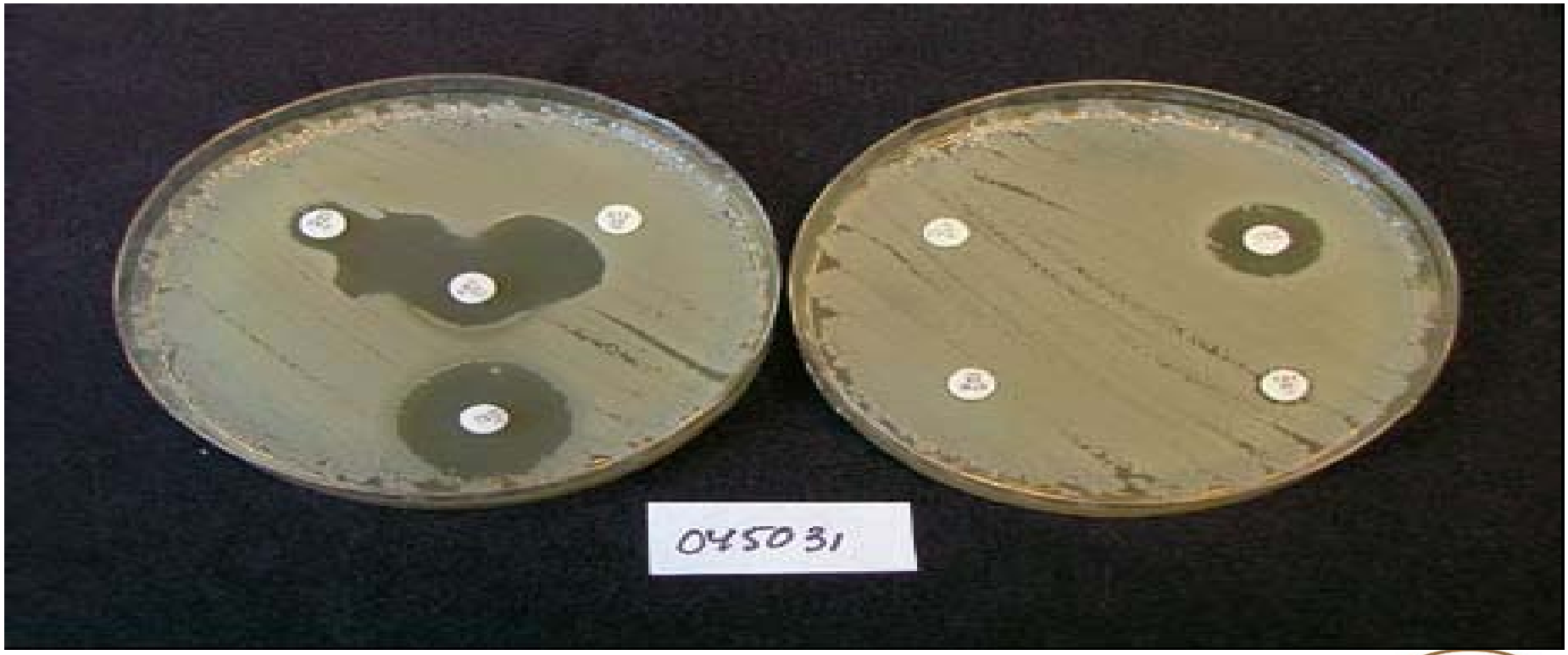
**242 patients with travellers' diarrhoea**

**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

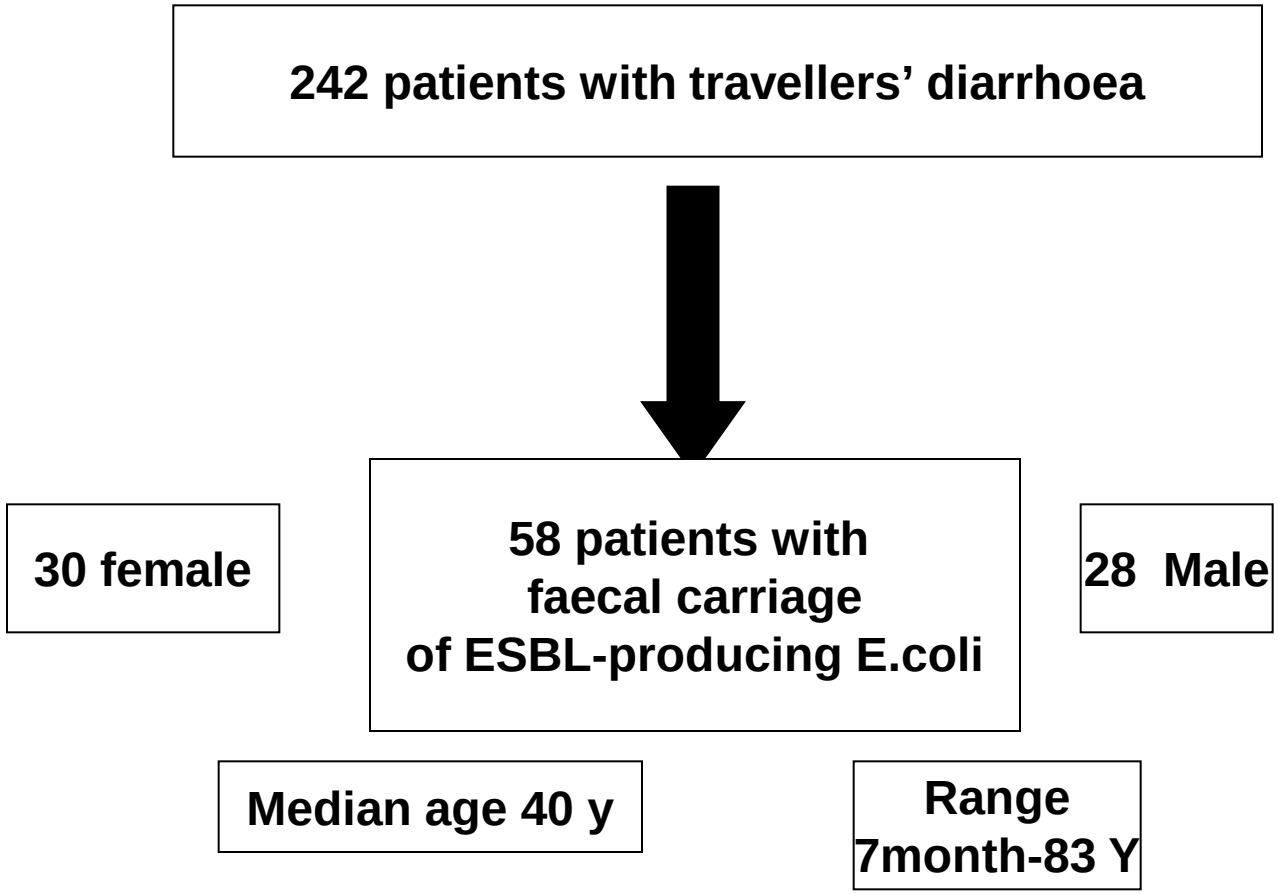
**242 Patients with travellers' diarrhoea**

**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



# 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).

| Region | ESBL-positive (*n*) | ESBL-negative (*n*) | Total (*n*) | Proportion positive | 95% CI | *p*-Value compared to Europe |
|---|---|---|---|---|---|---|
| World | 58 | 184 | 242 | (58/242)=0.24 | 0.19–0.30 | |
| World excl. Europe and unspecified | 50 | 88 | 138 | (50/138)=0.36 | 0.29–0.45 | <0.0001 |
| Europe excl. Sweden | 2 | 61 | 63 | (2/63)=0.03 | 0.004–0.11 | |
| Egypt | 19 | 19 | 38 | (19/38)=0.50 | 0.33–0.67 | <0.0001 |
| Thailand | 8 | 28 | 36 | (8/36)=0.22 | 0.10–0.39 | 0.0042 |
| India | 11 | 3 | 14 | (11/14)=0.79 | 0.49–0.95 | <0.0001 |
| Middle East | 4 | 6 | 10 | (4/10)=0.40 | 0.12–0.74 | 0.0025 |
| Southeast Asia incl. Australia | 5 | 8 | 13 | (5/13)=0.38 | 0.14–0.68 | 0.0012 |
| Africa excl. Egypt | 2 | 15 | 17 | (2/17)=0.12 | 0.015–0.36 | 0.1965 (NS) |
| America incl. West Indies | 1 | 9 | 10 | (1/10)=0.10 | 0.0025–0.44 | 0.3615 (NS) |
| Unspecified | 6 | 35 | 41 | (6/42)=0.15 | 0.06–0.29 | 0.0550 (NS) |

ESBL, extended-spectrum beta-lactamase; CI, confidence interval; NS, not significant.

# Pathogens found in the stool samples. All of these isolates were ESBL-negative

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

ESBL, extended-spectrum beta-lactamase.

# Antibiotic resistance

| Antibiotic | Clinical E. coli isolates with ESBLs (%) | Study E. coli isolates with ESBLs (%) |
|---|---|---|
| Tobramycin | 42 | 54 |
| Ciprofloxacin | 62 | 68 |
| Piperacillin–tazobactam | 22 | 8 |
| Mecillinam | 6 | 0 |
| Trimethoprim | 80 | 91 |
| Trimethoprim–sulfamethoxazole | 87 | 75 |
| Nitrofurantoin | 8 | 5 |

# 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

Journal of Infection (2008) 57, 441–448

**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).

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Available online 5 November 2008

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Sept. 2010, p. 3564–3568 Vol. 54, No. 9
0066-4804/10/$12.00 doi:10.1128/AAC.00220-10


# 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▽

Thomas Tängdén,[1]* Otto Cars,[1] Åsa Melhus,[2]† and Elisabeth Löwdin[1]†

*Sections of Infectious Diseases[1] and Clinical Bacteriology,[2] Department of Medical Sciences, Uppsala University, Uppsala, Sweden*

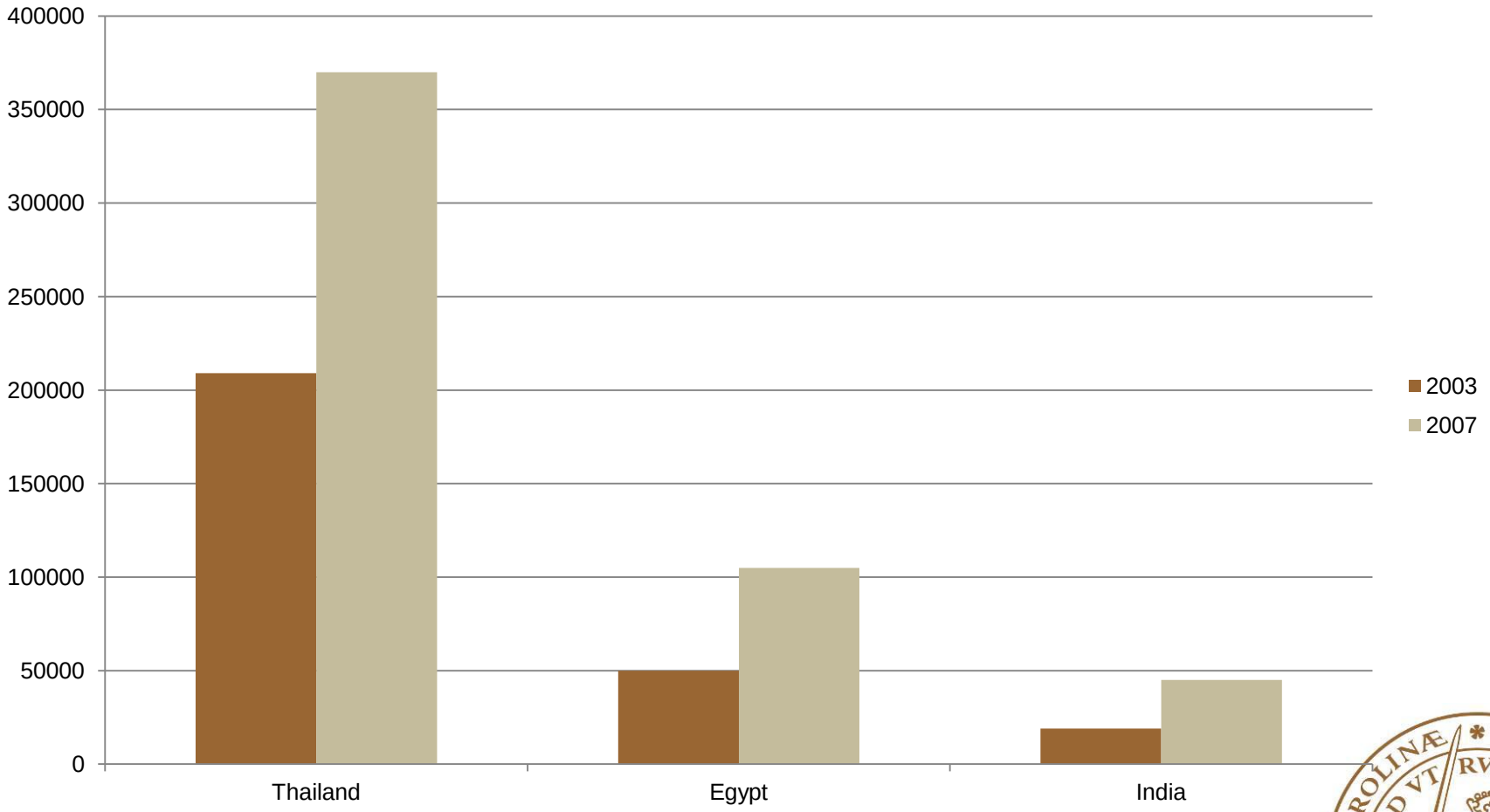
Received 15 February 2010/Returned for modification 17 April 2010/Accepted 8 June 2010

**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. Coresistance 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.**

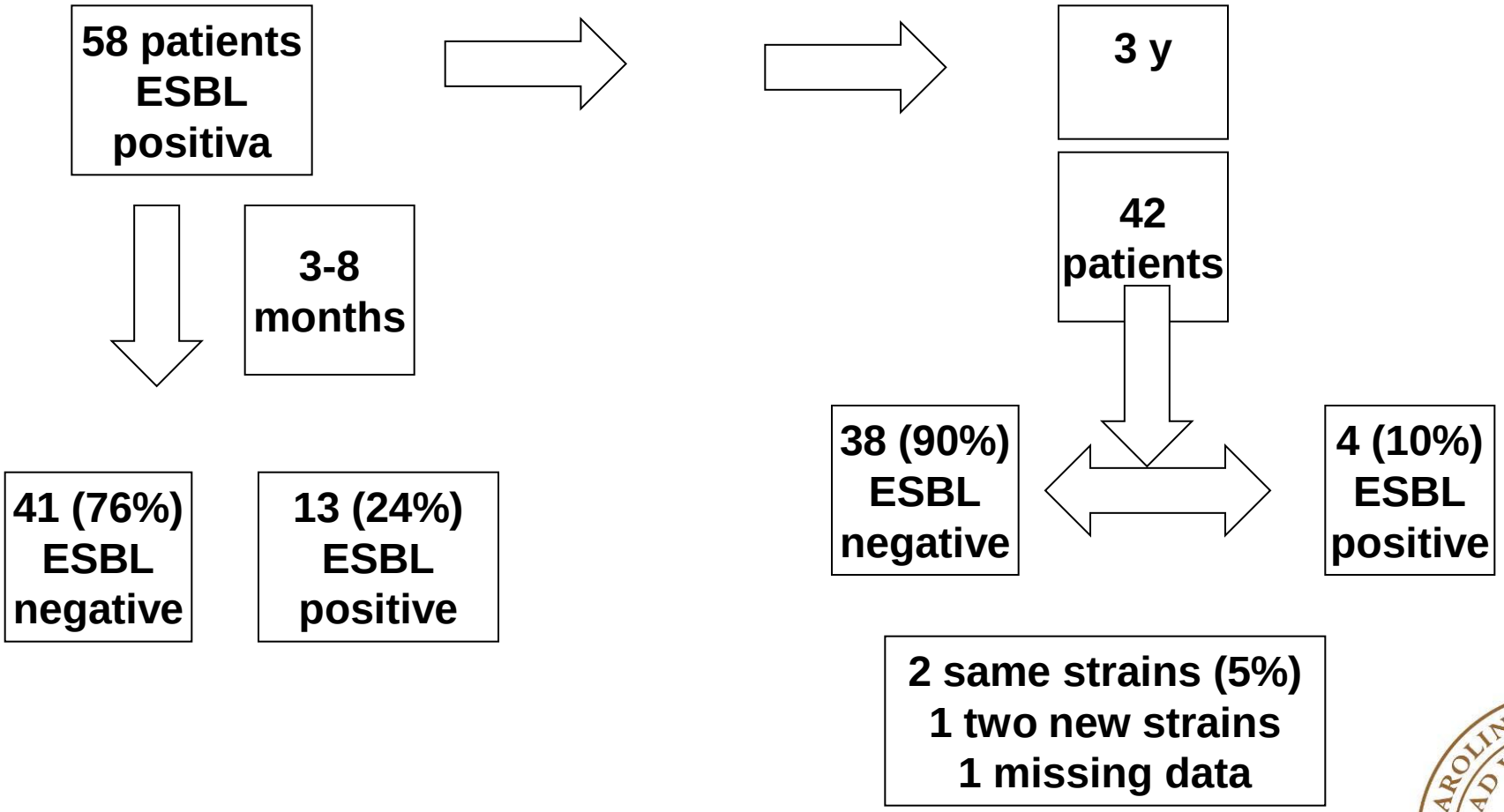
## Tängden et al (ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Sept. 2010, p. 3564–3568)

- **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**

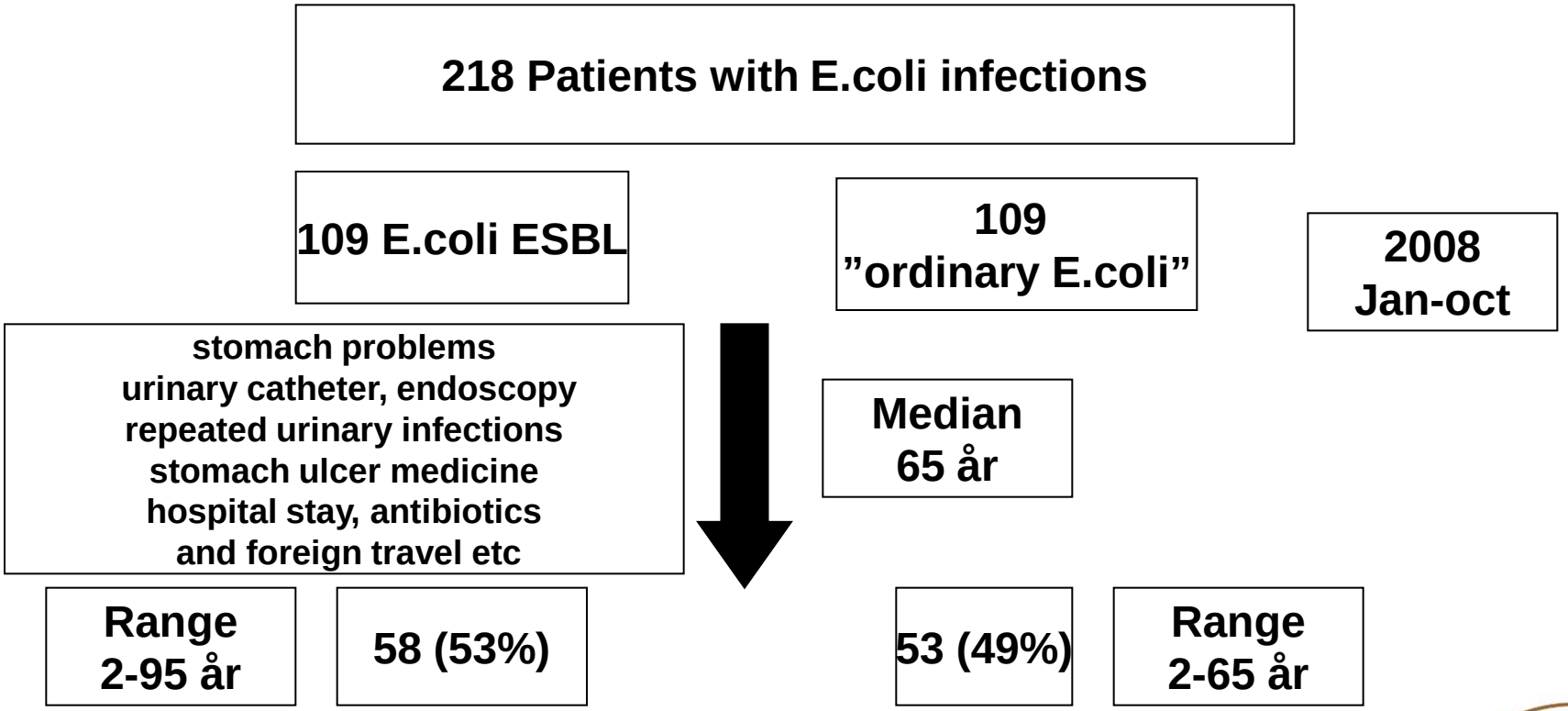
# Foreign travel is increasing



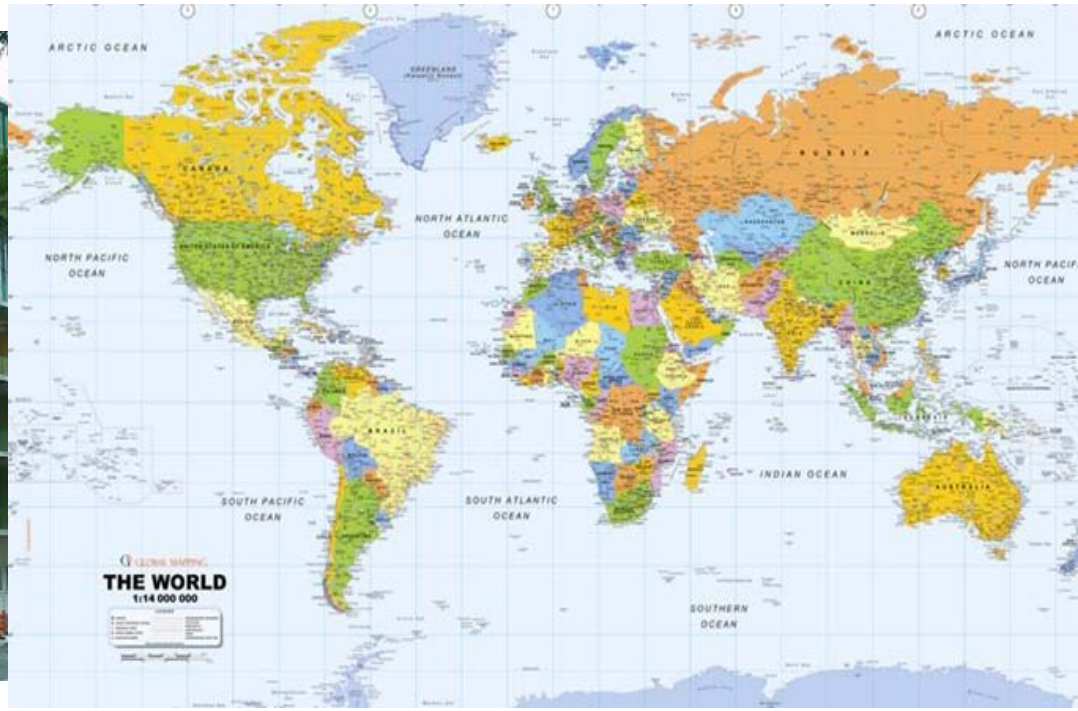
# Duration of colonization with Extended-spectrum beta-lactamase producing Escherichia coli in patients with travellers' diarrhoea



# Risk factors for infections with Extended-spectrum beta-lactamase producing Escherichia coli



# 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**

Ot

Journal of
TRAVEL MEDICINE



ORIGINAL ARTICLES

# 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 $bla_{\text{CTX-Ms}}$, $bla_{\text{TEMs}}$, $bla_{\text{SHVs}}$, 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*

# 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 theWorldwide spread of these bacteria

Scand J Infect Dis. 1983;15(4):367-73.

# 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.

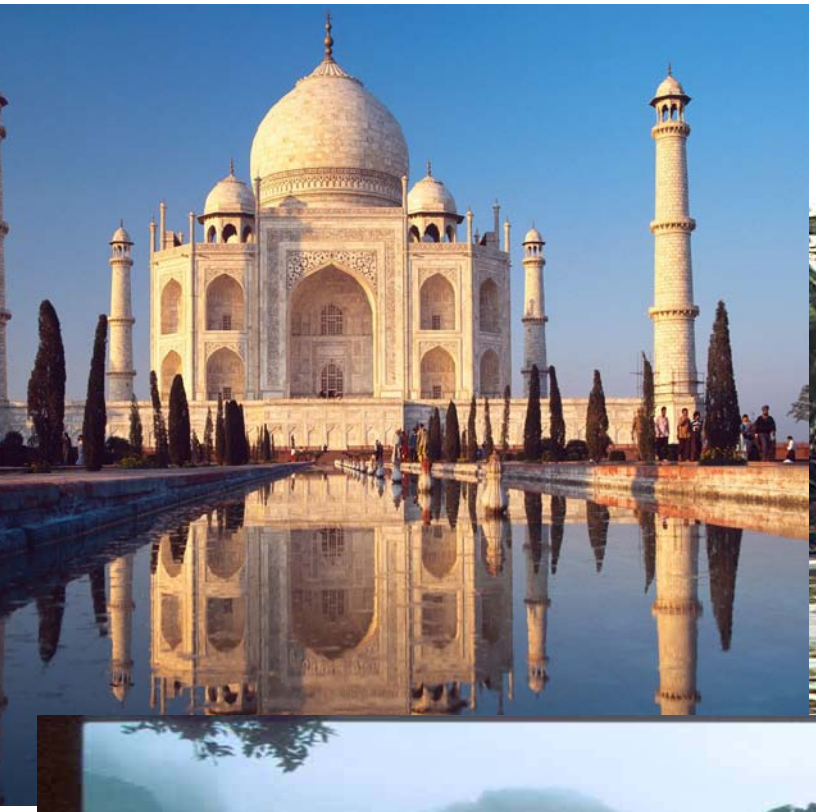
## Abstract

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?




SIGILL
AD VT RVMQVE
CAROLINÆ
ORVM


SIGILL
AD VT RVMQVE
CAROLINÆ
ORVM

- 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]