Evidence of household transfer of ESBL-/pAmpC-producing Enterobacteriaceae between humans and dogs – a pilot study

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Background: Extended-spectrum cephalosporin-resistant Enterobacteriaceae (ESCRE) are an increasing healthcare problem in both human and veterinary medicine. The spread of ESCRE is complex with multiple reservoirs and different transmission routes. The aim of this study was to investigate if ESCRE carriage in dogs is more prevalent in households with a known human carrier, compared to households where humans are known to be negative for ESCRE. Identical ESCRE strains in humans and dogs of the same household would suggest a possible spread between humans and dogs.

Methods: Twenty-two dog owners with a positive rectal culture for ESCRE each collected a rectal sample from their dog. In addition, a control group of 29 healthy dog owners with a documented negative rectal culture for ESCRE each sampled their household dog. Samples were cultivated for ESCRE using selective methods. In households where both humans and dogs carried ESCRE, isolates were further analysed for antimicrobial susceptibility by disc diffusion or microdilution and for genotype and genetic relatedness using molecular methods.

Results: In 2 of 22 households studied, identical ESCRE strains with respect to bacterial species, antibiogram, genotype, and MLVA type were found in humans and dogs. The ESCRE found in the two households were ESBL-producing *E. coli* with the resistance gene *bla*<sub>CTX-M-27</sub> and AmpC-producing *E. coli* with *bla*<sub>CMY-2-bla</sub>TEM-1. ESCRE were not found in dogs in the control group.

Conclusions: In households where humans are carrying ESCRE, identical strains were to a limited extent found also in household dogs, indicating a transfer between humans and dogs. In contrast, ESCRE were not found in dogs in households without human carriers.

Keywords: animal; human; antimicrobial resistance; Escherichia coli; cephalosporin

The prevalence of ESCRE in Swedish health care is low compared to many other countries, but the number of total human cases with such bacteria has increased by 9–33% annually since 2007, including asymptomatic carriers and ESCRE infections (4). Recent studies found a 5% prevalence of asymptomatic faecal ESCRE carriage in healthy Swedes (5) and a 3% prevalence of ESBL-producing *E. coli* in preschool children (6). Similar levels in healthy humans are reported from other European countries (7–10). In other parts of the world, notably Southeast Asia, the Eastern Mediterranean, and the Western Pacific, the prevalence of ESCRE in healthy humans is much higher (10). This is reflected in a high...
incidence of ESCRE carriage in travellers returning from high-prevalence areas to Sweden (11) or to other low-prevalence countries (7, 8).

ESCRE are found in food-producing animals worldwide and in meat thereof, potentially spreading from animals to humans through the food chain (1, 12). ESCRE are also found in healthy and diseased companion animals such as dogs (1, 13–19), and the potential zoonotic risk of this has been emphasized (20). The prevalence of ESCRE in dogs in Sweden is largely unknown, but in a recent study screening clinical urinary tract samples from dogs, ESCRE was found in less than 0.1% of 1,042 samples (21), and in a screening of 84 healthy dogs in 2012 only one carried ESCRE (22). Thus, clinical cases with ESCRE in dogs in Sweden are rare, but the number of confirmed cases has increased in the last years (4, 22, 23).

Risk factors for humans acquiring ESCRE are, for example, foreign travel, recent antibiotic treatment, and having/living with a family member treated for urinary tract infection caused by an ESCRE (24). Pet ownership is also reported to be a risk factor for ESCRE carriage (25). As for humans, dogs recently treated with antibiotics or dogs being kept in shelters or at breeders were identified to be at risk for being colonized with ESCRE (14, 15).

Humans and dogs are known to be able to share identical strains of Enterobacteriaceae, suggesting spread of bacteria between humans and dogs (26–29). Moreover, the same plasmids carrying genes coding for ESC resistance are found in ESCRE from humans and dogs and, thus, household dogs are potential reservoirs and may expose humans of the same household to ESCRE (13, 30, 31). However, little is known about the extent to which ESCRE are spread between humans and dogs in the same household.

The aim of this study was to investigate if ESCRE carriage in dogs is more prevalent in households with a known human carrier, compared to households where humans are known to be negative for ESCRE. Identical ESCRE strains in humans and dogs of the same household would suggest a possible spread between humans and dogs.

Materials and methods

Study group

The study group consisted of persons known to carry ESCRE in the intestinal flora. Inclusion criteria for entering the study group were positive for selective ESCRE screening from rectal/faecal swabs in the recent 3 months and at least one dog in the household. Persons in the study group were selected from patients receiving health care in the region of Skåne with a total population of 1,286,584 people (32). In an 18-month period between March 2014 and August 2015, 498 patients were positive for ESCRE in a selective cultivation of faeces at the Department of Clinical Microbiology, Skånes University Hospital. The samples had been taken from patients by caretakers all over Region Skåne, including primary, secondary, and tertiary health centres. Many of the patients were screened for ESCRE because of recent (within 6 months) hospitalization abroad. In Sweden, all patients who have received in-treatment health care abroad are screened for ESCRE by cultivation of faeces. In other patients, ESCRE were found in other cultivations, for example, urine sample, followed by a confirming cultivation from faeces.

All 498 patients with a positive selective ESCRE screening from rectal/faecal swabs were considered for inclusion in the study. Patients with ongoing prophylactic or therapeutic antibiotic treatment were excluded, as well as newborns receiving neonatal care. Patients considered for entering the study were contacted by telephone and asked for dog ownership, and if they would agree to participate in the study, collect a sample from their dog. Many patients could not be reached, for example, immigrants without contact information in the medical records.

After reviewing the medical chart and after the telephonic interview, 22 persons were enrolled in the study group. All were regarded healthy carriers of ESCRE in the intestinal tract, that is, no clinical infection with ESCRE was identified or suspected.

Enrolled persons were sent further information about the study and a formulary for informed consent to be returned to the investigator. In addition, they were sent materials and instructions on how to collect a rectal swab from one household dog. The rectal swab was sent by mail to the National Veterinary Institute (SVA), Uppsala, Sweden, for selective cultivation for ESCRE. In order to justify a temporal correlation for possible transfer of strains, the time between documented ESCRE carriage in a person until cultivation of the household dog was less than 3 months. If the dog was positive for ESCRE, other family members as well as other dogs of the household were sampled. Of the 22 persons enrolled in the study group, 20 returned the informed consent and provided rectal swabs from dogs. In addition, two persons from the control group (see below) that were positive for ESCRE on selective cultivation of a rectal swab were included in the study group.

A supplementary interview with questions regarding possible bacterial transmission between humans and dogs was conducted in households, where both dog and human were positive for ESCRE. In these households, four additional persons and two additional dogs were tested for ESCRE as described above.

Control group

The control group consisted of 31 healthy dog owners recruited from the area of Helsingborg and Uppsala.
None were treated with antibiotics within 2 weeks prior to sampling. Persons in the control group were sent the same information and instructions on how to sample one household dog as persons in the study group. In addition, they were instructed to collect a rectal swab from themselves. This sample was sent by mail to the Department of Clinical Microbiology, Skånes University Hospital, for selective cultivation for ESCRE. Persons in the control group also provided written consent to participate in the study. Two of the persons in the control group were positive for ESCRE on selective cultivation and were transferred to the study group.

Ethical approval
Ethical approval for the study was obtained from the regional ethical review board in Lund.

Selective cultivation for ESCRE
Samples from humans
Samples from humans were cultivated for ESCRE at Department of Clinical Microbiology, Skånes University Hospital, according to the routines of the hospital. Briefly, the sample material was plated on URI-Select four agar plates with vancomycin (BioRad) complemented with two antimicrobial susceptibility discs containing ceftazidime (10 μg/mL, Oxoid) and meropenem (10 μg/mL, Oxoid), respectively, and incubated at 37°C overnight. Sample material was also plated on the chromogenic agar plate ChromID ESBL (BioMerieux) and incubated as above. Colonies of presumptive ESCRE were subcultivated on horse blood agar (HBA) and typed to bacterial species using matrix-assisted laser desorption/ionization time of flight (MALDI-TOF).

Samples from dogs
Samples from dogs were cultivated at the National Veterinary Institute. Briefly, the sample material was plated on MacConkey agar plates supplemented with cefotaxime (1 mg/mL) and incubated at 37°C overnight. In parallel, the material was enriched in liquid MacConkey broth supplemented with cefotaxime (1 mg/L) and incubated as above. If no growth was recorded on the plates, 100 μL from the enrichment was plated on MacConkey agar plate supplemented with cefotaxime (1 mg/L) and incubated at 37°C overnight. Colonies of presumptive ESCRE were subcultivated on HBA and typed to bacterial species using MALDI-TOF.

Antimicrobial susceptibility testing
Isolates from humans
Presumptive ESCRE from humans were confirmed as ESBL or pAmpC producers by susceptibility testing. Briefly, isolates were grown on Mueller–Hinton agar plates complemented with the cepodoxime ESBL ID disc set (Mast Group Ltd). Isolates were also tested for susceptibility to imipenem, meropenem, gentamicin, tobramycin, amikacin, trimethoprim–sulfamethoxazole, tigecycline, cefotaxime, ceftazidime, and ciprofloxacin by disc diffusion using antibiotic-impregnated discs (Oxoid). Inhibition zone diameters were interpreted using the NordicAST (Nordic Committee on Antimicrobial Susceptibility Testing) breakpoints (www.nordicast.org). In addition, in households with dogs carrying ESCRE, human isolates were also tested for susceptibility by determination of minimum inhibitory concentration (MIC) by microdilution using Sensititre EUVSEC2 plates (Trek Diagnostic System Ltd) according to the standards of the Clinical and Laboratory Standards Institute (33). Antimicrobials tested were: cefotaxime, cefotaxime/clavulanic acid, ceftazidime, ceftazidime/clavulanic acid, cefepime, cefoxitin, temocillin, ertapenem, imipenem, and meropenem. MICs were interpreted using EUCAST (The European Committee on Antimicrobial Susceptibility Testing) epidemiological cutoff values (ECOFFs) (www.eucast.org/).

Isolates from dogs
Presumptive ESRCRE from dogs were phenotypically confirmed as ESBL or pAmpC producers by determination of MIC by broth microdilution using EUVSEC2 plates as above.

Genotyping and epidemiological typing of presumptive ESCRE
In households where ESCRE were found in both persons and dogs, the isolates were further characterised genotypically by PCR for specific resistance genes and by multilocus variable number of tandem repeats analysis (MLVA) to determine the relatedness between isolates from dogs and humans.

DNA extraction
Total DNA extraction was performed by suspending 1 μL of colony material in 200 μL of Tris–EDTA (pH 7.5). The suspension was heated to 95°C for 15 min and centrifuged for 3 min at 20,000 × g. The supernatant was isolated and kept at −20°C until analysis.

Characterisation of resistance genes
ESC-resistant isolates were characterized by PCR targeting the blaSHV, blaOXA, blaTEM, blaCTX-M group and pAmpC variants (MOX-1, MOX-2, CMY-1 to CMY-11, LAT-1 to LAT-4, BIL-1, DHA-1, DHA-2, ACC, MIR-1T, ACT-1, FOX1 to FOX5b) (34–36). The PCR amplicons were sequenced with in-house variants of published primers to determine the specific resistance gene variants (37–40).

MLVA
MLVA was performed according to Lobersli et al. (41). Ten previously described MLVA targets were analysed. Repeats were amplified using PCR and multiple fluorescently labelled primers. PCR products were separated by capillary electrophoresis in an ABI PRISM 3100 Genetic
Analyzer (Applied Biosystems). We divided the multiplex PCR reaction M2 into two (42), separating the CVN004 and CVN007 from the CVN001 and CV015 primers, running them as two separate multiplex PCR reactions.

Each peak was normalized and identified according to colour and size using the Peak Scanner Software 2 (Applied Biosystems). An allele number was assigned based on the fragment size.

Results

Twenty-two persons confirmed to carry ESCRE from 22 households were included in the study group (Table 1). Of these, 20 carried ESBL-producing *Escherichia coli*. One of these persons also carried ESBL-producing *Klebsiella pneumonia*. Two persons carried pAmpC-producing *E. coli* and ESBL-producing *K. pneumonia*. The age of the persons ranged from 1 to 82 years. Of the 22 households with persons carrying ESCRE, 2 households (9%) had dogs that tested positive for ESCRE (Table 1). In each of these households, two additional persons were screened for ESCRE but all four were negative (Table 1). In the control group, none of the 29 dog owners or their dogs were positive for ESCRE.

**Patient number 1 of household number 1**

Patient 1, a 1-year-old child, belonged to a family of two adults, the child, and two dogs. All were screened for ESCRE. The child and one of the dogs carried the same ESBL-producing *E. coli* strain as determined by MLVA. The other family members, both adults, and the second dog had negative cultures. The antibiogram showed that both *E. coli* strains were resistant to cefotaxime, ceftazidime, and cefepime. The β-lactamase gene *bla*<sub>CTX-M-27</sub> was found in both isolates.

### Table 1. Results of selective cultivation for ESCRE of faecal/rectal swabs from 26 humans and 24 dogs from 22 households in the study group

| Household | Human* | Birth year | Species/type | Genes             | Dog   | Species/type | Genes             |
|-----------|--------|------------|--------------|-------------------|-------|--------------|-------------------|
| 1         | a      | 2013       | *E. coli* ESBL | *bla*<sub>CTX-M-27</sub> | a     | *E. coli* ESBL | *bla*<sub>CTX-M-27</sub> |
|           | b      | 1981       | Not found    |                   | b     | Not found    |                   |
|           | c      | 1983       | Not found    |                   | c     | Not found    |                   |
| 2         | a      | 2013       | *E. coli* pAmpC | *bla*<sub>CMY-2</sub>, *bla*<sub>TEM-1</sub> | a     | *E. coli* pAmpC | *bla*<sub>CMY-2</sub>, *bla*<sub>TEM-1</sub> |
|           | b      | 2009       | Not found    |                   | b     | Not found    |                   |
|           | c      | 1976       | Not found    |                   | c     | Not found    |                   |
| 3         | a      | 1942       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 4         | a      | 1962       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 5         | a      | 1988       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 6         | a      | 1992       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 7         | a      | 1973       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 8         | a      | 1944       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 9         | a      | 2013       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 10        | a      | 1943       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 11        | a      | 1948       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 12        | a      | 1993       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 13        | a      | 1958       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 14        | a      | 1947       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 15        | a      | 1974       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 16        | a      | 1954       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 17        | a      | 1932       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 18        | a      | 1966       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 19        | a      | 1939       | *K. pneumonia* ESBL | Not determined    | a     | Not found    |                   |
| 20        | a      | 1955       | *E. coli* ESBL/*K. pneumonia* ESBL | Not determined | a     | Not found    |                   |
| 21        | a      | 1943       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |
| 22        | a      | 1959       | *E. coli* ESBL | Not determined    | a     | Not found    |                   |

In two households, four additional persons were tested. “*a*” signifies the person initially enrolled in the study group, ‘*b* and *c*’ signify additional persons or dogs tested for ESCRE in a household.
Patient number 2 of household number 2

Patient 2, a 2-year-old child, belonged to a family of two adults, the child, an older sibling aged 5, and two dogs. Three humans and two dogs were screened for ESCRE. One adult declined sampling. The 2-year-old child and both dogs were found to have faecal flora containing pAmpC-producing E. coli, whereas the other family members had negative cultures for ESCRE. The pAmpC-producing E. coli isolated from the child and from one of the dogs were determined to be identical by MLV A. The other dog had a similar but not identical pAmpC-producing E. coli as determined by MLV A. The E. coli strains were resistant to cefotaxime, ceftazidime, cefepime, and cefoxitin. The β-lactamase genes blaTEM1 and blaCMY2 were found in all three isolates.

In interviews made with the adults in households 1 and 2, the adults reported that they had witnessed sharing of food and cutlery between toddlers and dogs.

Discussion

In this study, identical ESCRE strains with respect to bacterial species, antibiogram, genotype, and MLVA type were found in humans and dogs in 2 of the 22 households studied. This indicates that household transmission of ESCRE between humans and dogs occurs. Similar studies investigating household spread of non-ESBL/pAmpC-producing E. coli show that dogs and humans share identical clones (26–29, 43), but to our knowledge, this is the first report describing sharing of identical ESCRE strains between humans and dogs of the same household.

The potential risk of sharing ESCRE strains between dogs and humans within a household depends on the extent of such sharing. In our study, sharing occurred in about 10% of the households. This is of the same magnitude as in a study where 10% of 60 dog–human pairs shared E. coli of similar PFGE types (43). A higher extent of sharing was found in a longitudinal study, where the same AFLP types of E. coli were found in humans and dogs on at least one occasion over a 6-month period in four of eight studied households (29). Similarly, a higher extent of sharing was found in a study of 48 households, where the same E. coli clones were found in 17% of pet–human pairs (28). The extent of sharing was, however, higher (31%) between human pairs in that study. In agreement, in another study sharing of ESBL-producing E. coli and K. pneumoniae between humans of the same household was 23 and 25%, respectively (44). These latter studies indicate that humans carrying ESCRE probably are more likely to share the bacteria with other household members than with dogs.

This pilot study could not conclude on the initial transmission route of ESCRE, whether from humans to dogs or vice versa. However, since dogs were negative for ESCRE in the majority of households in the study group, the person carrying ESCRE most likely contracted the bacteria from another source than the household dog. Persons in the study group predominantly carried ESBL-producing E. coli and only one carried a pAmpC-producing strain. This is in accordance with the proportions of ESCRE types notified in human health care in Sweden, where the vast majority of isolates are ESBL producers and about 5% pAmpC producers (45). Interestingly, E. coli with the resistance gene blaCTX-M-27, which was found in humans and dogs in household 1, has hitherto been documented only five times in dogs in Sweden comprising 7% of the 74 confirmed ESCRE isolates in dogs up to 2014 (4). The blaCTX-M-27 gene is, however, a more common finding in human health care (4, 45). In contrast, E. coli with the gene blaCMY-2 is the single most common type found in clinical infections in dogs in Sweden comprising 34% of confirmed ESCRE isolates up to 2014 (4), but only 5–6% of human cases (4, 45). Moreover, E. coli with the gene blaCMY-2 are commonly found in raw dog food diets that accordingly could be a source of such bacteria for dogs (46). However, the impact on carriage of such bacteria by dogs is not known.

In our study, only children below 3 years of age were colonized with the same ESCRE as the household dog during the 3-month study period. This suggests that toddlers and dogs of the same household have closer contact and thus may transfer bacteria between each other. Children are less aware of the hygiene aspects of living close to a dog, and in both household 1 and 2, the toddlers petted, kissed, and shared food with the dogs. This could facilitate spreading of ESCRE between dogs and persons in a household.

The major shortcoming of the present study is the small number of households included; thus, no statistical evaluation was possible. Future studies need to include larger number of households in order to make statistically reliable analysis. Another shortcoming is that dogs were sampled only on one occasion, which could have underestimated the extent of ESCRE carriage. Also, a part of the control group was recruited from another area (Uppsala) than the study group. This could have led to an underestimation of ESCRE carriage in dogs in households without persons carrying ESCRE. However, given the conceivably low carriage rate of ESCRE in healthy dogs (23), it is unlikely that this influenced the conclusions of the study. Also, for practical reasons different methods were used to screen human and dog samples for ESCRE. Both methods are well established and entail selective culture for ESBL- and pAmpC-producing Enterobacteriaceae, but the relative sensitivity of the two methods was not evaluated. Tentatively, a lower sensitivity of the method used in samples from dogs could result in an underestimation of the extent of sharing of strains.
In conclusion, this study shows that in households where humans are carrying ESCRE, identical strains were to a limited extent found also in household dogs, indicating transfer between humans and dogs. In contrast, ESCRE was not found in dogs in households without human carriers. The objective of this study was to study the sharing of ESCRE in households where humans were the identified carriers, focusing on transfer from human to dogs. It would, however, be equally relevant to study sharing of ESCRE, where dogs are the primary identified carriers of ESCRE.

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Conflict of interest and funding

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References

1. Ewers C, Bethe A, Semmler T, Guenther S, Wieler LH. Extended-spectrum β-lactamase-producing and AmpC-producing Escherichia coli from livestock and companion animals, and their putative impact on public health: a global perspective. Clin Microbiol Infect 2012; 187: 646–55.
2. Rubin JE, Ptout JD. Extended-spectrum β-lactamase, carbapenemase and AmpC producing Enterobacteriaceae in companion animals. Vet Microbiol 2014; 170: 10–18.
3. Machado E, Coque TM, Canton R, Sousa JC, Peixe L. Commensal Enterobacteriaceae as reservoirs of extended-spectrum β-lactamases, integrons, and sul genes in Portugal. Front Microbiol 2013; 4: 80.
4. SWEDRES-SV ARM. Consumption of antimicrobials and occurrence of antimicrobial resistance in Sweden. Solna; 2013. Available from: http://www.sva.se/en/antibiotics/svarm-reports [cited 14 January 2016].
5. Egerviørn M, Rosengren Å, Englund S, Börjesson S, Löfmark S, Ny S, et al. ESBL-bildande E. coli i vår omgivning – livsmedel som spridningsväg till människa. (In Swedish with English summary). Stockholm; 2014. Available from: http://www.sva.se/antibiotika/anmalningspliktig-resistens/esbl/antibiotikaresistens-i-livsmedel-och-var-omgivning [cited 14 January 2016].
6. Kaarre J, Molin Y, Olsen B, Melhus A. Prevalence of extended-spectrum β-lactamase-producing Enterobacteriaceae in healthy Swedish preschool children. Acta Paediatr 2013; 102: 655–60.
7. Kuenzli E, Jaeger VK, Frei R, Neumayr A, DeCrom S, Haller S, et al. High colonization rates of extended-spectrum beta-lactamase (ESBL)-producing Escherichia coli in Swiss travellers to South Asia – a prospective observational multicentre cohort study looking at epidemiology, microbiology and risk factors. BMC Infect Dis 2014; 14: 528.
8. Reuland EA, Al Naiemi N, Kaiser AM, Heck M, Kluytmans JA, Savelkoul PH, et al. Prevalence and risk factors for carriage of ESBL-producing Enterobacteriaceae in Amsterdam. J Antimicrob Chemother 2016; 71: 1076–1082. doi: http://dx.doi.org/10.1093/jac/dkv441
9. van Hoek AH, Schouls L, van Santen MG, Florijn A, de Greeff SC, van Duijkeren E. Molecular characteristics of extended-spectrum cephalosporin-resistant Enterobacteriaceae from humans in the community. PLoS One 2015; 106: e0129085.
10. Woerther PL, Burdet C, Chachaty E, Andremont A. Trends in human fecal carriage of extended-spectrum beta-lactamases in the community: toward the globalization of CTX-M. Clin Microbiol Rev 2013; 264: 744–58.
11. Tangden T, Cars O, Melhus A, Lowdin E. Foreign travel is a major risk factor for colonization with Escherichia coli producing CTX-M-type extended-spectrum beta-lactamases: a prospective study with Swedish volunteers. Antimicrob Agents Chemother 2010; 549: 3564–8.
12. Leverstein-van Hall MA, Dierikx CM, Cohen Stuart J, Voets GM, van den Munckhof MP, van Essen-Zandbergen A, et al. Dutch pets, retail chicken meat and poultry share the same ESBL genes, plasmids and strains. Clin Microbiol Infect 2011; 176: 873–80.
13. Damborg M, Mørsing MK, Petersen T, Bortolaia V, Guardabassi L. CTX-M-1 and CTX-M-15-producing Escherichia coli in dog faeces from public gardens. Acta Vet Scand 2015; 571: 83.
14. Rocha-Gracia RC, Cortes-Cortes G, Lozano-Zarain P, Bello F, Martinez-Laguna Y, Torres C. Fecal Escherichia coli isolates from healthy dogs harbour CTX-M-15 and CMY-2 beta-lactamases. Vet J 2015; 2033: 315–19.
15. Belas A, Salazar AS, Gama LT, Couto N, Pomba C. Risk factors for faecal colonisation with Escherichia coli producing extended-spectrum and plasmid-mediated AmpC beta-lactamases in dogs. Vet Rec 2014; 1758: 202.
16. Wedley AL, Maddox TW, Westgarth C, Coyne KP, Pinchbeck GL, Williams NJ, et al. Prevalence of antimicrobial-resistant Escherichia coli in dogs in a cross-sectional, community-based study. Vet Rec 2011; 16813: 354.
17. Gandolfi-Decristophoris P, Petrini O, Ruggeri-Bernardi N, Schelling E. Extended-spectrum beta-lactamase-producing Enterobacteriaceae in healthy companion animals living in nursing homes and in the community. Am J Infect Control 2013; 419: 831–5.
18. Hordijk J, Schoormans A, Kwakernaak M, Duim B, Broens E, Dierikx C, et al. High prevalence of fecal carriage of extended-spectrum beta-lactamase/AmpC-producing Enterobacteriaceae in cats and dogs. Front Microbiol 2013; 4: 242.
19. O’Keefe A, Hutton TA, Schifferli DM, Rankin SC. First detection of CTX-M and SHV extended-spectrum beta-lactamases in Escherichia coli urinary tract isolates from dogs and cats in the United States. Antimicrob Agents Chemother 2010; 548: 3489–92.
20. Ewers C, Grobbel M, Bethe A, Wieler LH, Guenther S. Extended-spectrum beta-lactamases-producing gram-negative bacteria in companion animals: action is clearly warranted! Berl Munch Tierarztl Wochenschr 2011; 124: 94–101.
21. Windahl U, Holst B, Nyman A, Gronlund U, Bengtsson B. Characterisation of bacterial growth and antimicrobial susceptibility patterns in canine urinary tract infections. BMC Vet Res 2014; 101: 217.
22. SWEDRES-SVARM. Use of antimicrobials and occurrence of antimicrobial resistance in Sweden. Solna; 2013. Available from: http://www.sva.se/en/antibiotics/svarm-reports [cited 14 January 2016].
23. SWEDRES-SVARM. Use of antimicrobials and occurrence of antimicrobial resistance in Sweden. Solna; 2012. Available from: http://www.sva.se/en/antibiotics/svarm-reports [cited 14 January 2016].
24. Rodriguez-Bano J, Lopez-Cerero L, Navarro MD, Diaz de Alba P, Pascual A. Faecal carriage of extended-spectrum beta-lactamase-producing Escherichia coli: prevalence, risk factors and molecular epidemiology. J Antimicrob Chemother 2008; 625: 1142–9.

25. Meyer E, Gastmeier P, Kola A, Schwab F. Pet animals and Escherichia coli. J Infect Dis 2012; 206: 685–7.

26. Johnson JR, Clabots C. Sharing of virulent Escherichia coli clones among household members of a woman with acute cystitis. Clin Infect Dis 2006; 4310: e101

27. Damborg P, Nielsen SS, Guardabassi L. Characterization and sequence analysis of extended-spectrum- β-lactamase-encoding genes from Escherichia coli, Klebsiella pneumoniae, and Proteus mirabilis isolates collected during tigecycline phase 3 clinical trials. Antimicrob Agents Chemother 2009; 532: 465–75.

28. Johnson JR, Owens K, Gajewski A, Clabots C. Escherichia coli colonization patterns among human household members and pets, with attention to acute urinary tract infection. J Infect Dis 2008; 1972: 218–24.

29. Damborg P, Nielsen SS, Guardabassi L. Escherichia coli shedding patterns in humans and dogs: insights into within-household transmission of phylotypes associated with urinary tract infections. Epidemiol Infect 2009; 13710: 1457–64.

30. Bogaerts P, Huang TD, Bouchahrouf W, Bauraing W, Bauraing C, Berhin C, El Garch F, et al. Characterization of ESBL- and AmpC-producing Enterobacteriaceae from diseased companion animals in Europe. Microb Drug Resist 2015; 216: 643–50.

31. Schaufler K, Bethe A, Lubke-Becker A, Ewers C, Kohn B, Wieler LH, et al. Putative connection between zoonotic multi-resistant extended-spectrum beta-lactamase (ESBL)-producing Escherichia coli in dog faeces from a veterinary campus and clinical isolates from dogs. Infect Ecol Epidemiol 2015; 5: 25334, doi: http://dx.doi.org/10.3402/iee.v5.25334

32. Statistics Sweden. Folkmängd i landskapen den 31 december 2014. Available from: http://www.scb.se/sv_/Hitta-statistik/Statistik-efter-amne/Befolkning/Befolkningens-sammansattning/Befolkningstastistik/25788/25795/Helarsstatistik—ForsAMLandskap-och-stad/389798/# [cited 31 December 2014].

33. CLSI (2013). Performance standards for antimicrobial disk and dilution susceptibility tests for bacteria isolated from animal; Approved standards – fourth edition. CLSI document VET01-A4. Wayne, PA: Clinical and Laboratory Standards Institute.

34. Fang H, Ataker F, Hedin G, Dornbusch K. Molecular epidemiology of extended-spectrum beta-lactamases among Escherichia coli isolates collected in a Swedish hospital and its associated health care facilities from 2001 to 2006. J Clin Microbiol 2008; 462: 707–12.

35. Perez-Perez FJ, Hanson ND. Detection of plasmid-mediated AmpC beta-lactamase genes in clinical isolates by using multiplex PCR. J Clin Microbiol 2002; 406: 2153–62.

36. Woodford N, Fagan EJ, Ellington MJ. Multiplex PCR for rapid detection of genes encoding CTX-M extended-spectrum (beta)-lactamases. J Antimicrob Chemother 2006; 571: 154–5.

37. Alvarez M, Tran JH, Chow N, Jacoby GA. Epidemiology of conjugal plasmid-mediated AmpC beta-lactamases in the United States. Antimicrob Agents Chemother 2004; 482: 533–7.

38. Jones CH, Tuckman M, Keeney D, Ruzin A, Bradford PA. Characterization and sequence analysis of extended-spectrum-beta-lactamase-encoding genes from Escherichia coli, Klebsiella pneumoniae, and Proteus mirabilis isolates collected during tigecycline phase 3 clinical trials. Antimicrob Agents Chemother 2009; 532: 465–75.

39. Roche C, Boo TW, Walsh F, Crowley B. Detection and molecular characterisation of plasmidic AmpC beta-lactamases in Klebsiella pneumoniae isolates from a tertiary-care hospital in Dublin, Ireland. Clin Microbiol Infect 2008; 146: 616–18.

40. Sundsfjord A, Simonsen GS, Haldorsen BC, Haaheim H, Hjelmevoll SO, Littauer P, et al. Genetic methods for detection of antimicrobial resistance. APMIS 2004; 112: 815–37.

41. Lobersli I, Haugum K, Lindstedt BA. Rapid and high resolution genotyping of all Escherichia coli serotypes using 10 genomic repeat-containing loci. J Microbiol Methods 2012; 881: 134–9.

42. Lindstedt BA, Brandal LT, Aas L, Vardund T, Kapperud G. Study of polymorphic variable-number of tandem repeats loci in the ECOR collection and in a set of pathogenic Escherichia coli and Shigella isolates for use in a genotyping assay. J Microbiol Methods 2007; 691: 197–205.

43. Stenske KA, Bemis DA, Gillespie BE, D’Souza DH, Oliver SP, Draughon FA, et al. Comparison of clonal relatedness and antimicrobial susceptibility of fecal Escherichia coli from healthy dogs and their owners. Am J Vet Res 2009; 709: 1108–16.

44. Hilty M, Betsch BY, Bogli-Stuber K, Heiniger N, Stadler M, Kuffer M, et al. Transmission dynamics of extended-spectrum beta-lactamase-producing Enterobacteriaceae in the tertiary care hospital and the household setting. Clin Infect Dis 2012; 557: 967–75.

45. Brolund A, Edquist PJ, Makitalo B, Olsson-Liljequist B, Soderblom T, Wisell KT, et al. Epidemiology of extended-spectrum beta-lactamase-producing Escherichia coli in Sweden 2007–2011. Clin Microbiol Infect 2014; 206: O344–52.

46. Nilsson O. Hygiene quality and presence of ESBL-producing Escherichia coli in raw food diets for dogs. Infect Ecol Epidemiol 2015; 5: 28758, doi: http://dx.doi.org/10.3402/iee.v5.28758