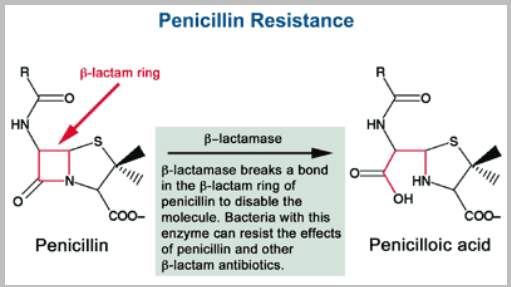
Institute for Microbiology and Epizootics

Freie Universität Berlin

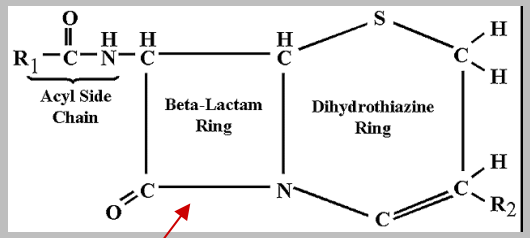
Extended-spectrum- β-lactamase (ESBL)-producing *Enterobacteriaceae* in companion animals: what does the future hold for us?

Christa Ewers, Ivonne Stamm, Peter A. Kopp, Lothar H. Wieler, Sebastian Guenther

ESBL: Extended spectrum beta lactamases



Hydrolysis of penicillins, cephalosporins (1st, 2nd, 3rd generation) and aztreonam



http://www.wiley.com

SHV

Sulf-Hydryl-Variabel

CTX

Cefotaximase

TEM

Temoneira

KPC

K. pneumoniae carbapenemase

OXA

Oxacillinase

PER, VEB, CMY, NDM-1, etc..... www.lahey.org/studies

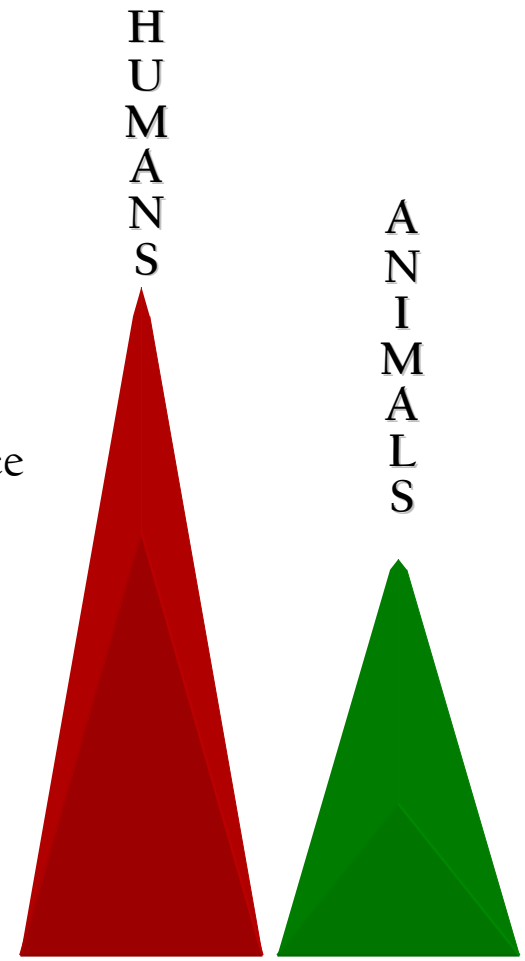
ESBL timeline

- 1964 Introduction of 1st generation cephalosporins
- 1980 Introduction of 3rd generation cephalosporins
- 1983 First detection of ESBL in Germany
- 1985 First report on nosocomial outbreaks in France
- 1998 First report on ESBL in companion animals
- 2000 First report on ESBL in lifestock

.....increasing prevalence of ESBLs

.....ongoing change of the face of ESBL types

.....occurence of emerging clones



Presence and type of ESBL in companion animals

Consecutively collected clinical isolates, routinely tested for antimicrobial resistance, were screened for the production of ESBLs

BACTERIAL SPECIES	Number	Time
Escherichia coli	14827	April 2008
Klebsiella/Raoultella spp.	1664	
Enterobacter/Pantoea spp.	1631	
Citrobacter spp.	82	
Serratia spp.	305	
Salmonella Serovare	478	March 2010

Pictures: www.idt-biologika.de

Results

- Percentage of ESBL producing isolates among clincial *Enterobacteriaceae* spp. from animals between 2 and 10% depending on the species

- *E. coli* ESBL showed a relative equal distributions in different animal hosts

- High rates of *E. coli* ESBL implicated in wound infections

- Identical genetic resistance determinants are present in human and animal samples

-MLST analysis of approx. 300 *E. coli* isolates revealed about 80 different sequence types (ST), few of them being prominent

- Identical STs are observed in strains of human and animal origin

-Human pandemic O25b-ST131 is also present in companion animals

E. coli O25b:H4-B2-ST131-CTX-M-15

J Antimicrob Chemother 2010
doi:10.1093/jac/dkp496
Advance publication 12 January 2010

Detection of pandemic B2-O25-ST131 *Escherichia coli* harbouring the CTX-M-9 extended-spectrum β-lactamase type in a feral urban brown rat (*Rattus norvegicus*)

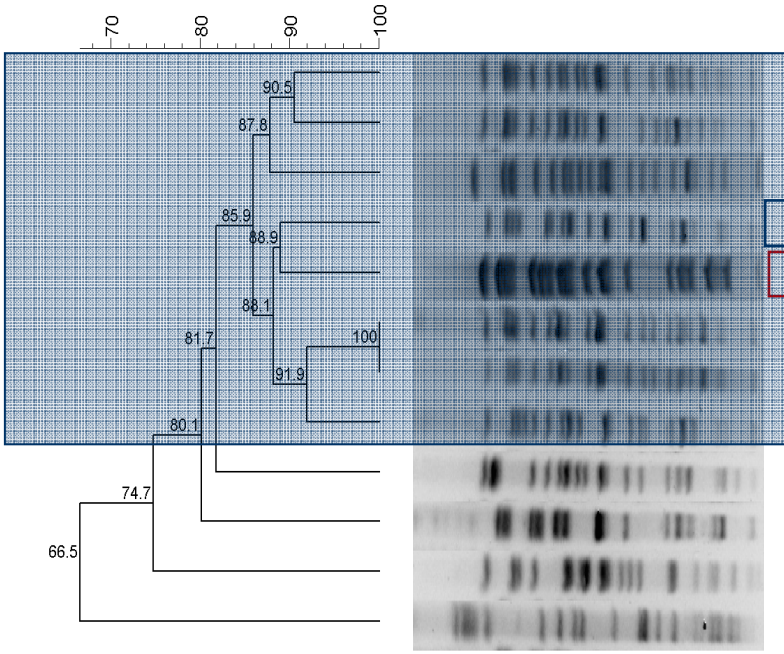
Sebastian Guenther[1]*, Mirjam Grobbel[1], Janine Beutlich[2], Beatriz Guerra[2], Rainer G. Ulrich[3], Lothar H. Wieler[1] and Christa Ewers[1]

J Antimicrob Chemother 2010; **65**: 651–660
doi:10.1093/jac/dkq004 Advance publication 29 January 2010

Journal of Antimicrobial Chemotherapy

Emergence of human pandemic O25:H4-ST131 CTX-M-15 extended-spectrum-β-lactamase-producing *Escherichia coli* among companion animals

Christa Ewers[1]*, Mirjam Grobbel[2], Ivonne Stamm[3], Peter A. Kopp[3], Ines Diehl[1], Torsten Semmler[1], Angelika Fruth[4], Janine Beutlich[5], Beatriz Guerra[5], Lothar H. Wieler[1] and Sebastian Guenther[1]



IMT17433	Dog	UTI	Germany	CTX-M-15
IMT17898	Dog	UTI	Spain	CTX-M-15
IMT19336	Dog	Resp. tract infection	Germany	CTX-M-15
IMT19205	Rat	None	Germany	CTX-M-9
E467	Human	UTI	Germany	CTX-M-15
IMT18570	Dog	UTI	Netherlands	CTX-M-15
IMT18572	Dog	UTI	France	CTX-M-15
IMT18582	Dog	Wound infection	Denmark	CTX-M-15
IMT17530	Dog	UTI	Denmark	CTX-M-15
IMT18342	Dog	UTI	Germany	CTX-M-15
IMT12556	Dog	UTI	Germany	SHV
IMT18354	Horse	Eye inflammation	Germany	CTX-M-15

E. coli D-Ont:H45-ST648-CTX-M-15 Animal vs. Human

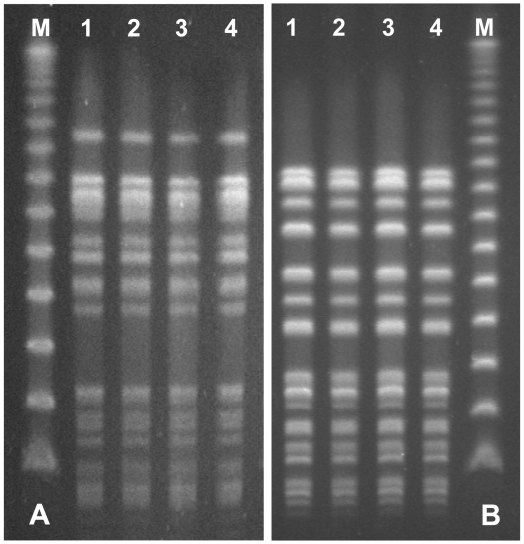
environmental microbiology reports

Environmental Microbiology Reports (2010) doi:10.1111/j.1758-2229.2010.00148.x

CTX-M-15-type extended-spectrum beta-lactamases-producing *Escherichia coli* from wild birds in Germany

Sebastian Guenther,[1]* Mirjam Grobbel,[1] Janine Beutlich,[2] Astrid Bethe,[1] Nicole D. Friedrich,[3] Andreas Goedecke,[4] Antina Lübke-Becker,[1] Beatriz Guerra,[2] Lothar H. Wieler[1] and Christa Ewers[1]

[1]*Institut für Mikrobiologie und Tierseuchen, Fachbereich Veterinärmedizin, Freie Universität Berlin, Germany.*
[2]*Federal Institute for Risk assessment (BfR), Department of Biological Safety, National Reference Laboratory for Antimicrobial Resistance (NRL-AR), Berlin, Germany.*
[3]*Justus von Liebig Universität, Fachbereich Veterinärmedizin, Gießen, Germany.*
[4]*ProRing e.V., Schenkenberg, Germany.*

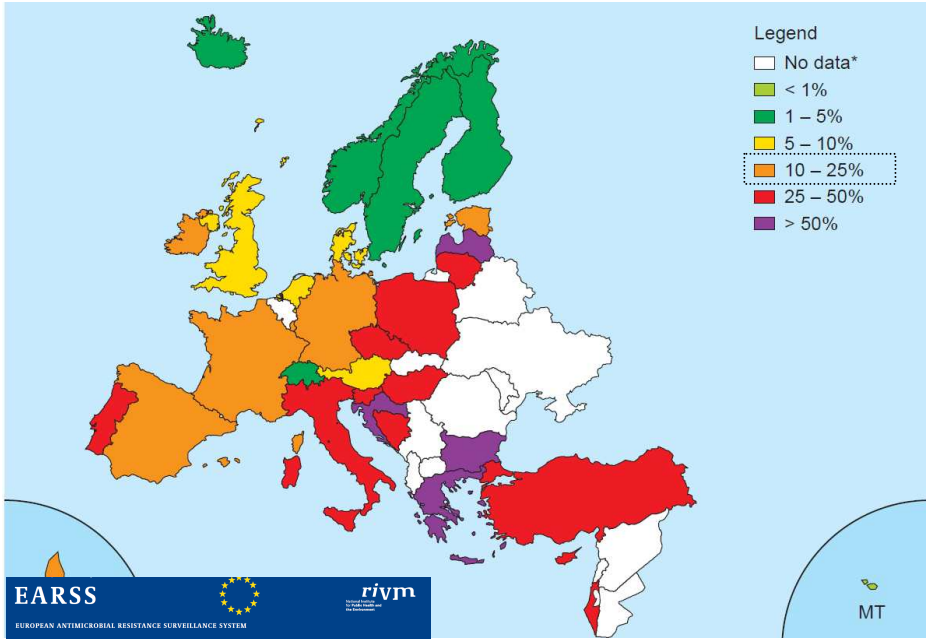


- ST648 recently detected in wild avian hosts in also present in human clinical samples

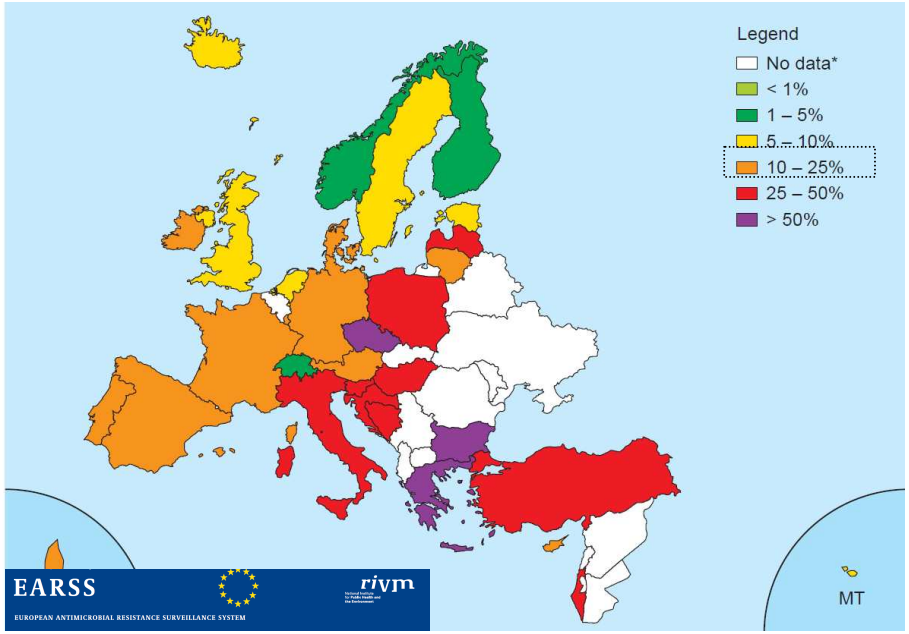
Klebsiella pneumoniae ssp. pneumoniae

- Second most frequent cause of gram-negative blood stream infections in humans
- High mortality rates due to therapeutic failures

Proportion of *K. pneumoniae* isolates resistant to 3rd gen. cephalosporins in humans (2008)



Proportion of *K. pneumoniae* isolates resistant to fluoroquinolones in humans (2008)



Journal of Antimicrobial Chemotherapy (2008) **62**, 978–985
doi:10.1093/jac/dkn287
Advance Access publication 30 July 2008

JAC

Expansion and countrywide dissemination of ST11, ST15 and ST147 ciprofloxacin-resistant CTX-M-15-type β-lactamase-producing *Klebsiella pneumoniae* epidemic clones in Hungary in 2005—the new 'MRSAs'?

Molecular epidemiology of Hungarian CTX-M-15-producing klebsiellae

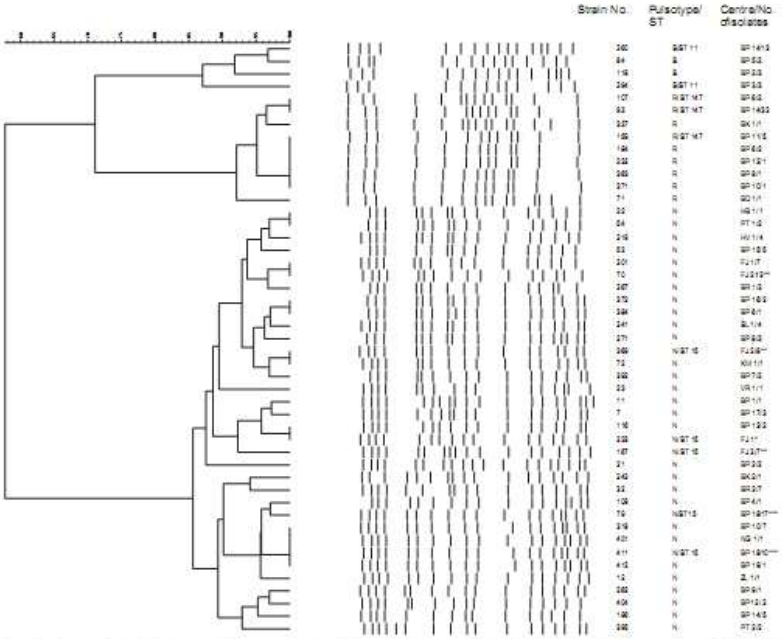


Figure 2. Cluster analysis of 196 *K. pneumoniae* macrorestriction profiles from 35 centres and STs of selected isolates. *Prototype isolate of HEC from 2003. **Isolates from April and October 2005 from the outbreak in the FI2 centre. ***Isolates from April and August 2005 from the outbreak in the BP18 centre.

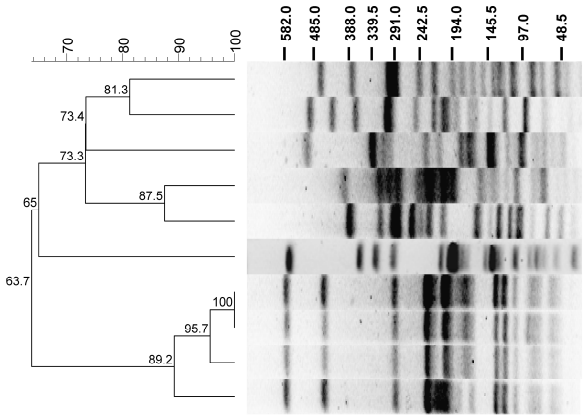
ESBL positive strains among *K. pneumoniae* from different hosts and diseases

- High rates of *K. pneumoniae* ESBL in wound infections

- STs dominant in human medicine are also present in companion animals

- Clonal spread of ESBL-positive *K. pneumoniae* isolates among companion animals in Europe

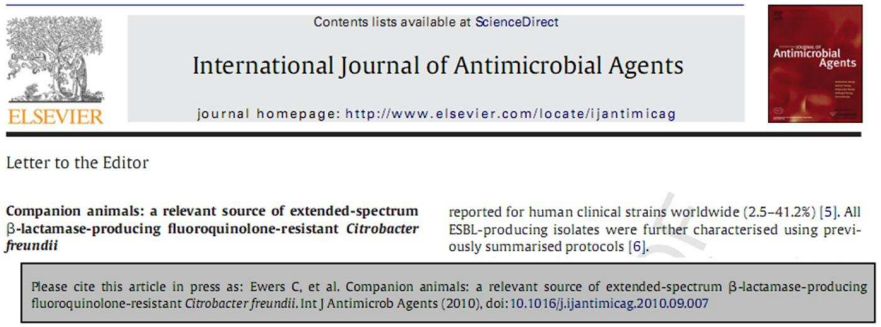
ESBL producing *Citrobacter freundii* in companion animals



Strain	Host species	Region	ESBL type	Integron cassette type
VB950066	Dog	Schleswig Holstein	CTX-M-1	*aadA2*
VB994305.2	Cat	Baden Wuerttemberg	SHV-12	*sul1*
VB984587.1	Degu	Schleswig Holstein	SHV-12	*aadA2*
IMT16288	Tawny owl	Hesse	SHV-12	*sul1*
VB918293	Derbyan parakeet	Northrhine-Westphalia	SHV-12	*aadA2*
VB962564.2	Cat	Lower Saxony	SHV-12	*aadA2*
VB972435*	Horse	Schleswig Holstein	CTX-M-1	*dfrA12-orfF-aadA2*
VB967320*	Horse	Schleswig Holstein	CTX-M-1	*dfrA12-orfF-aadA2*
VB967518*	Horse	Schleswig Holstein	CTX-M-1	*sul1*
VB993616.2*	Horse	Schleswig Holstein	CTX-M-1	*dfrA12-orfF-aadA2*

Fig. 1 Dendrogram showing the relationship of ESBL-producing *Citrobacter freundii* (n=10) strains based on XbaI-generated PFGE profiles.
*** These isolates originate from samples of four individual horses from two nearby veterinary clinics (clinic 1: VB972435 , VB967320 , and VB967518 ; clinic 2: VB993616.2).**

- Frequent isolation of clinical, ESBL-producing, fluroquinolone-resistant *C. freundii* from companion animals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Letter to the Editor

Companion animals: a relevant source of extended-spectrum β-lactamase-producing fluoroquinolone-resistant *Citrobacter freundii*

reported for human clinical strains worldwide (2.5–41.2%) [5]. All ESBL-producing isolates were further characterised using previously summarised protocols [6].

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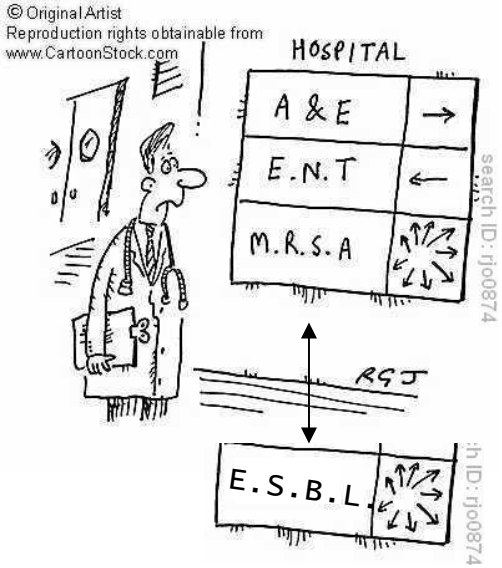
Summary and Conclusions

- ESBL in companion animals: it´s time to react!
  - new putative infection cycles demand for novel surveillance programs
  - consequent basic hygiene in veterinary clinics („standard precautions“)
  - prudent use of antibiotics („Antimicrobial Guidelines“)



- Montoring of multiresistant bacteria
- Data exchange with human medicine („One Health“)

FU Berlin
Mirjam Grobbel
Astrid Bethe
Petra Krienke
Ines Diehl
Birgit Lauzat
Torsten Semmler

BfR
Dr. B. Guerra
Charité
Prof. P. Gastmeier
PD Dr. A. Kola
RKI
Dr. A. Fruth
Dr. Y. Pfeiffer

Vet Med Labor GmbH
Ivonne Stamm
Peter Kopp