

**L'évolution de l'exposition aux antibiotiques
et l'évolution de l'antibiorésistance : un lien
simple à démontrer ?
Dans le domaine animal**

Sanders P

Laboratoire de Fougères

Inférence Biologique

- Etudes expérimentales
- Etudes descriptives
 - Association entre usage et résistance aux antibiotiques
- Etudes étiologiques
 - Effet dose ou durée
 - Réversibilité de l'effet

Etude expérimentale

Low or High Doses of Cefquinome Targeting Low or High Bacterial Inocula Cure *Klebsiella pneumoniae* Lung Infections but Differentially Impact the Levels of Antibiotic Resistance in Fecal Flora

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Rat
Flore intestinale
5 mg/kg/j/4 j
50 mg/kg/j/4 j

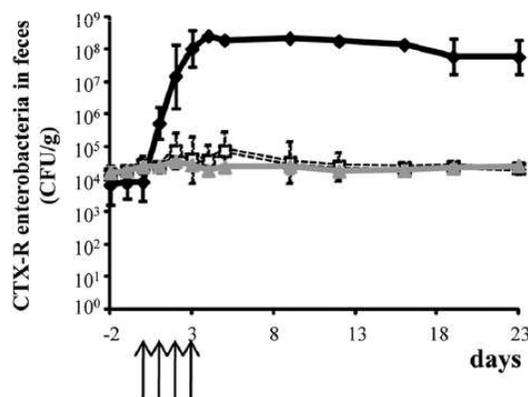


FIG 2 Impact of the different cefquinome dosage regimens on cefotaxime-resistant *Enterobacteriaceae* in the fecal flora of rats before, during, and after treatment. ◆, Patent-phase-adjusted dose (50 mg/kg of body weight); □, prepatent-phase-adjusted dose (5 mg/kg); △, control untreated group. Data are means ± standard deviations (SDs). The arrows indicate the days of antibiotic administration.

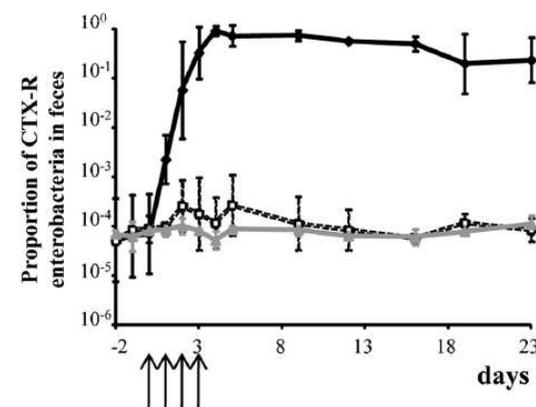


FIG 3 Impact of the different cefquinome dosage regimens on the proportion of cefotaxime-resistant *Enterobacteriaceae* in the fecal flora of rats before, during, and after treatment. ◆, Patent-phase-adjusted dose (50 mg/kg); □, prepatent-phase-adjusted dose (5 mg/kg); △, control untreated group. Data are means ± SDs. The arrows indicate the days of antibiotic administration.

Etudes expérimentales

- Etudes PK/PD & Résistance
 - Sélection de bactéries résistantes au site d'infection
 - Sélection de bactéries résistantes dans le microbiote intestinal
 - Notion de dose et de fenêtre de sélection
 - 1 Antibiotique x 1 espèce bactérienne
 - Problème :
 - Diversité des espèces bactériennes

Etude descriptive

Impact of Third-Generation-Cephalosporin Administration in Hatcheries on Fecal *Escherichia coli* Antimicrobial Resistance in Broilers and Layers

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- Injection in ovo
 - Ceftiofur, 0,1 mg à 18 j d'incubation
 - Associé au vaccin de Marek
 - 30 **lots** de poulets de chair
 - 15 Traités et 15 non traités
 - Suivi sur 77 jours
- Injection sous cutanée
 - Ceftiofur, 0,1 mg à 1 j
 - 22 **lots** de futures pondeuses (12 traités, et 10 non traités)
 - Suivi sur 220 jours

Lot	N° Prélèvement	N°E. coli	N° E coli résistant C3G	N bla _{CTX-M}	N°blaCMY-2	N° bla _{TEM}
Poulets Traités	66	330	116 (35 %)	85	27	26
Poulets non traités	71	349	39 (11 %)	22	11	7
Pondeuses traitées	45	224	104 (46 %)	81	17	8
Pondeuses non traitées	39	192	42 (22 %)	20	16	1

Baron et al, AAC 2014

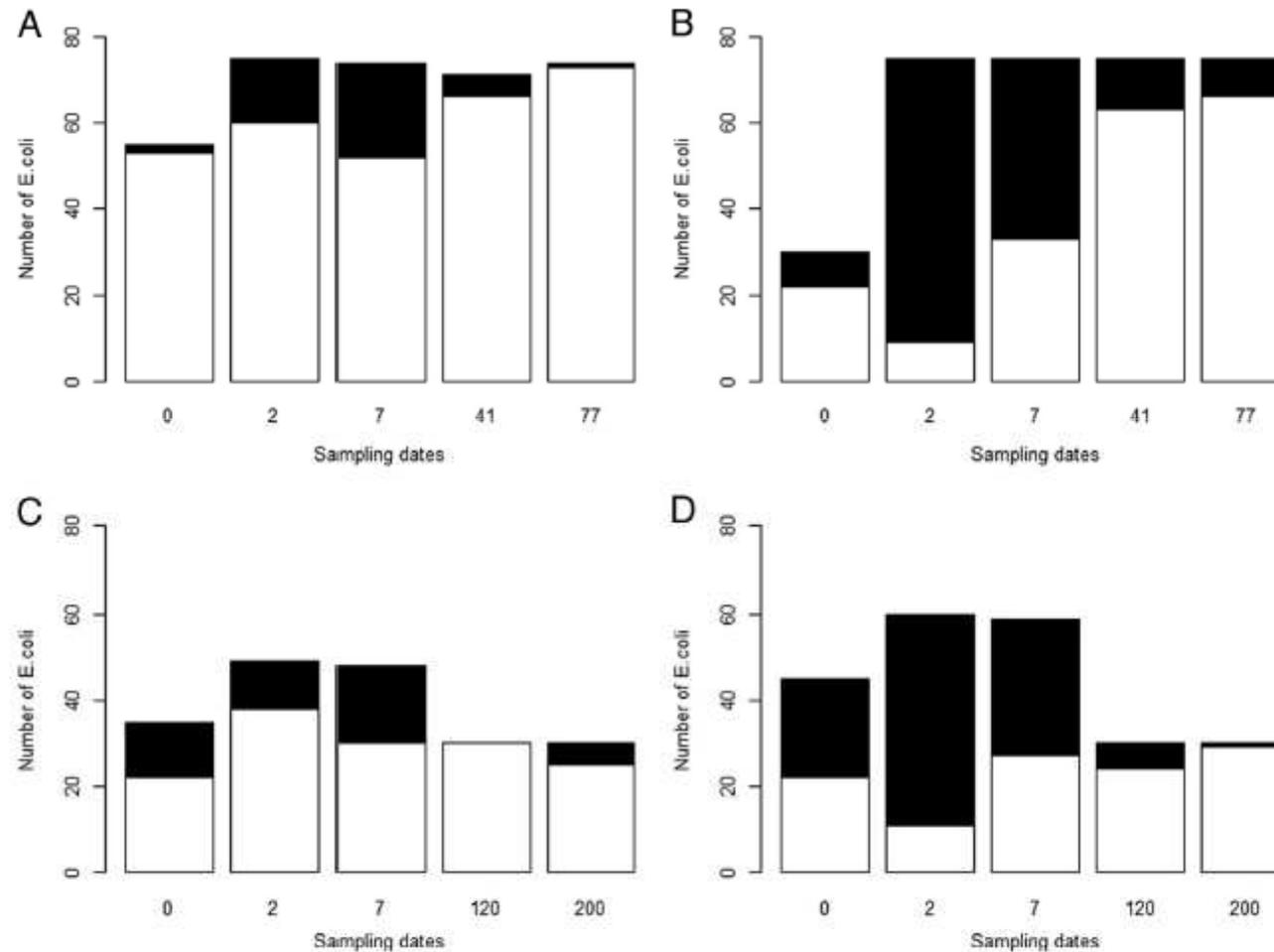
Non Traités

Traités

**Poulets
*In ovo***

Non traités

Traités



**Pondeuses
Sous cutanée**

FIG 1 Numbers of 3GC-resistant *E. coli* (black) or 3GC-susceptible *E. coli* (white) strains in samples from broiler flocks without *in ovo* ceftiofur treatment (A), with *in ovo* ceftiofur treatment (B), from future laying hen flocks without (C) and with (D) subcutaneous injection of ceftiofur in 1-day-old chicks.

Etude descriptive

J Antimicrob Chemother 2012; 67: 582–588
doi:10.1093/jac/dkr507 Advance Access publication 29 December 2011

Journal of
Antimicrobial
Chemotherapy

Elevages
16 19

Prevalence of extended-spectrum cephalosporinase (ESC)-producing *Escherichia coli* in Danish slaughter pigs and retail meat identified by selective enrichment and association with cephalosporin usage

Yvonne Agersø^{1*}, Frank M. Aarestrup¹, Karl Pedersen², Anne Mette Seyfarth², Tina Struve³
and Henrik Hasman¹

- Programme de surveillance à l'abattoir
- Recherche *E. coli*
 - sur milieu sélectif (1 mg/L Ceftriaxone) après enrichissement (1 mg/L ceftriaxone)
- Données usage antibiotique (C3G C4G)
 - VetStat

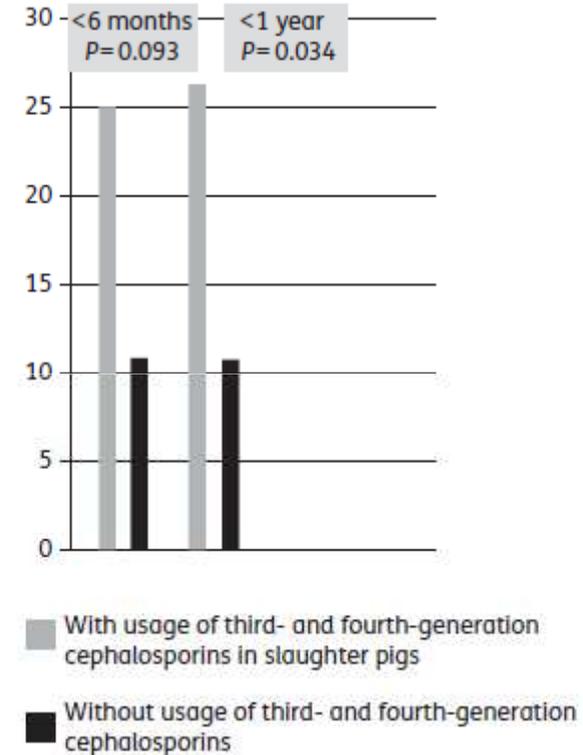


Figure 4. Correlation between consumption of third- and fourth-generation cephalosporins for slaughter pigs in the farms prior to sampling and the presence of ESC-producing *E. coli* in pigs at slaughter. <6 months, third- or fourth-generation cephalosporin consumption for slaughter pigs at least once in the 6 months prior to sampling. <1 year, third- or fourth-generation cephalosporin consumption for slaughter pigs at least once in the 12 months prior to sampling. The y-axis represents the percentage of farms positive for ESC *E. coli*.

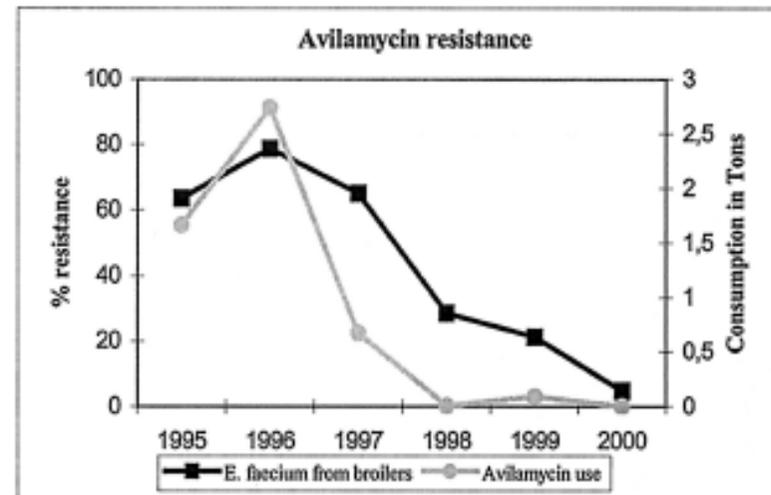
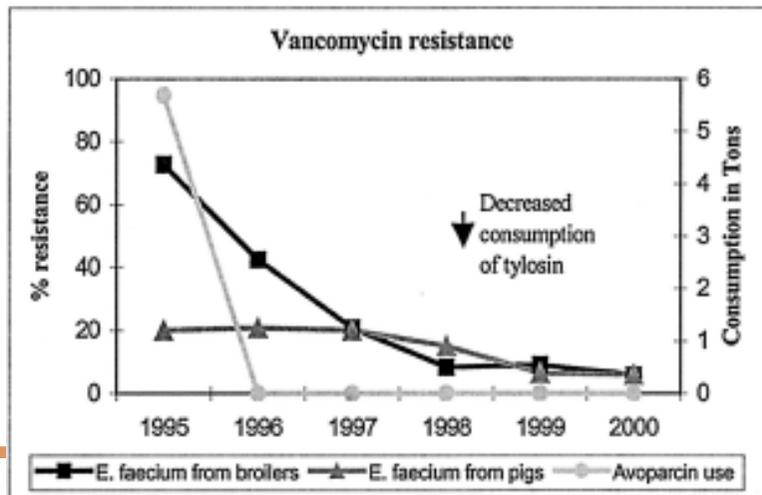
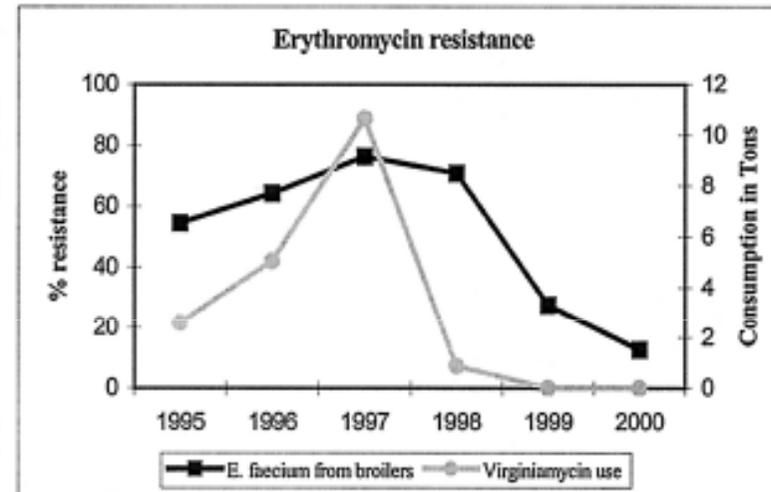
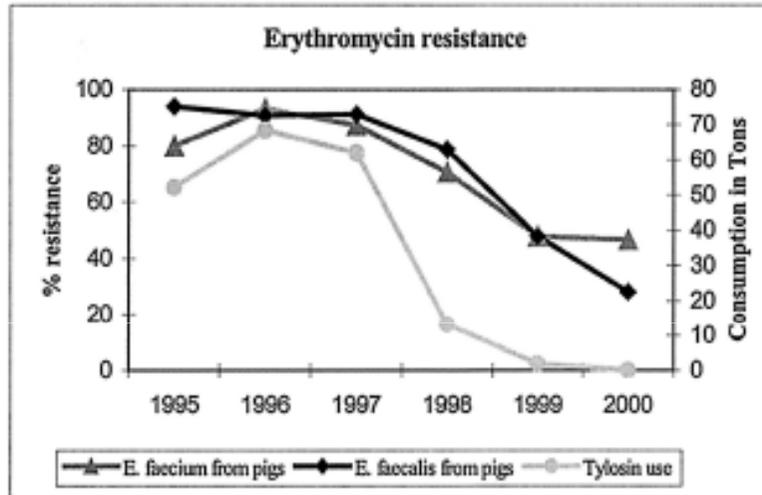
Etude étiologique

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, July 2001, p. 2054–2059
0066-4804/01/\$04.00+0 DOI: 10.1128/AAC.45.7.2054-2059.2001
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Effect of Abolishment of the Use of Antimicrobial Agents for Growth Promotion on Occurrence of Antimicrobial Resistance in Fecal Enterococci from Food Animals in Denmark

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Ceftiofur Resistance in *Salmonella enterica* Serovar Heidelberg from Chicken Meat and Humans, Canada

Lucie Dutil, Rebecca Irwin, Rita Finley, Lai King Ng, Brent Avery, Patrick Boerlin, Anne-Marie Bourgault, Linda Cole, Danielle Daignault, Andrea Desruisseau, Walter Demczuk, Linda Hoang, Greg B. Horsman, Johanne Ismail, Frances Jamieson, Anne Maki, Ana Pacagnella, and Dylan R. Pillai

- Programme Canadien de surveillance de la résistance (CIPARS)
 - *Salmonella* heidelberg
 - Viande
 - Cas humain
- Arrêt volontaire de l'usage du ceftiofur *in ovo* puis réintroduction partielle

Etude étiologique

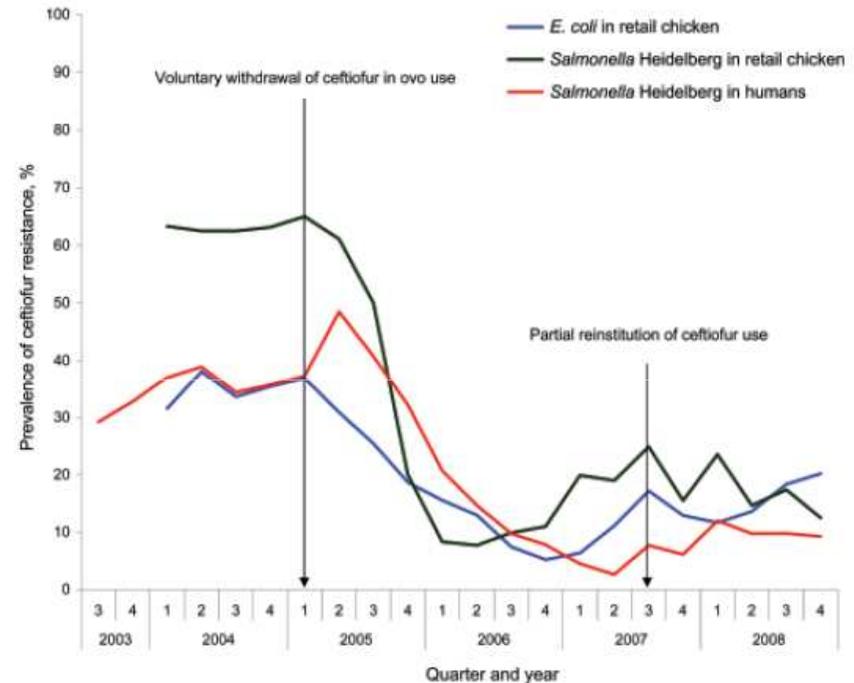
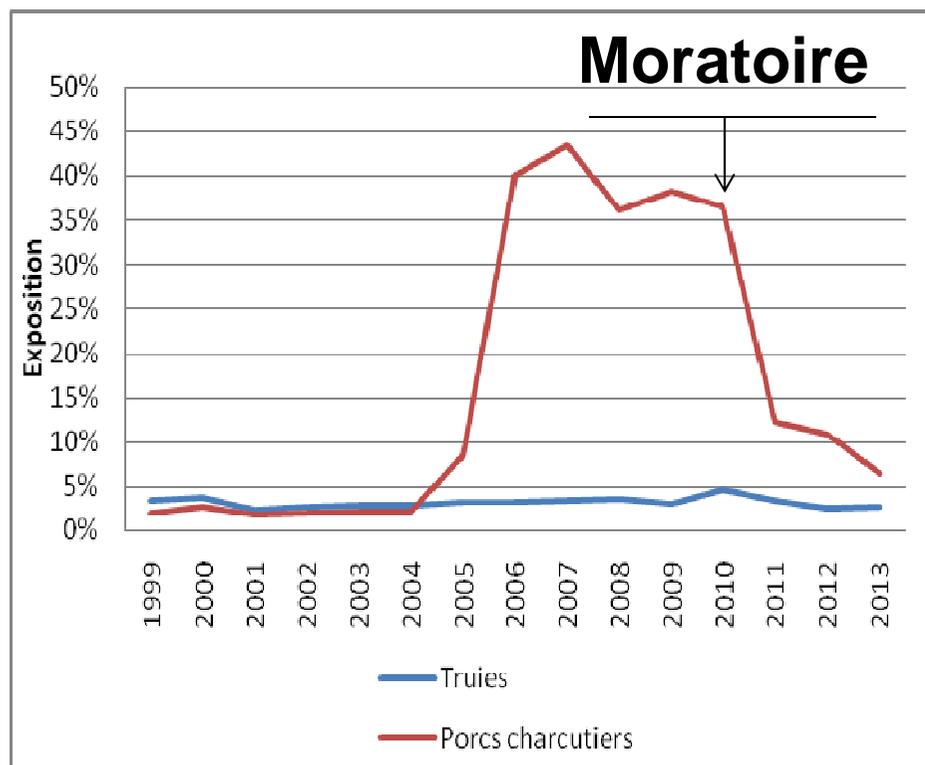
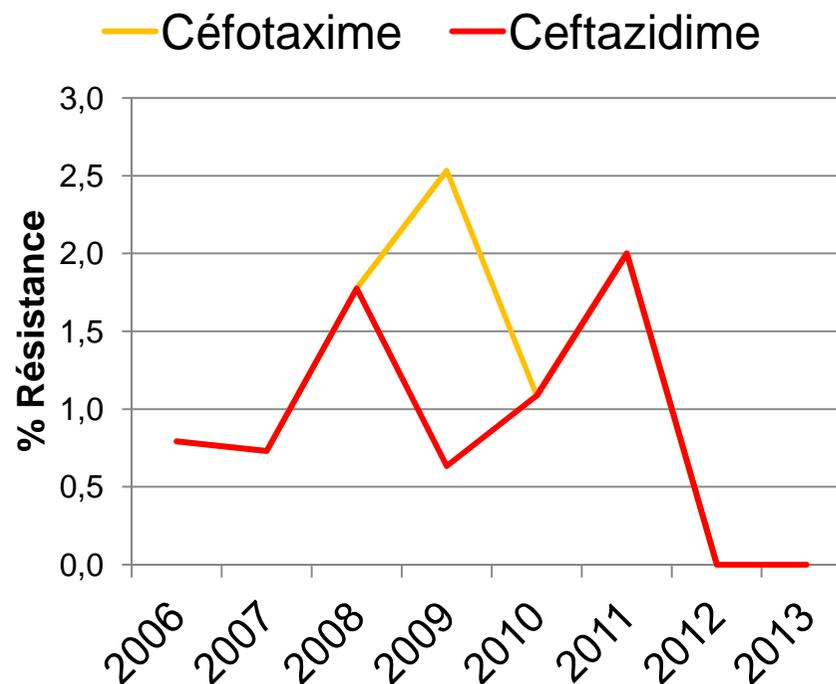


Figure 2. Prevalence of ceftiofur resistance (moving average of the current quarter and the previous 2 quarters) among retail chicken *Escherichia coli*, and retail chicken and human clinical *Salmonella enterica* serovar Heidelberg isolates during 2003–2008 in Québec, Canada.

- Utilisation C3G / C4G Porc



- E. coli / Porc / Plan Abattoir



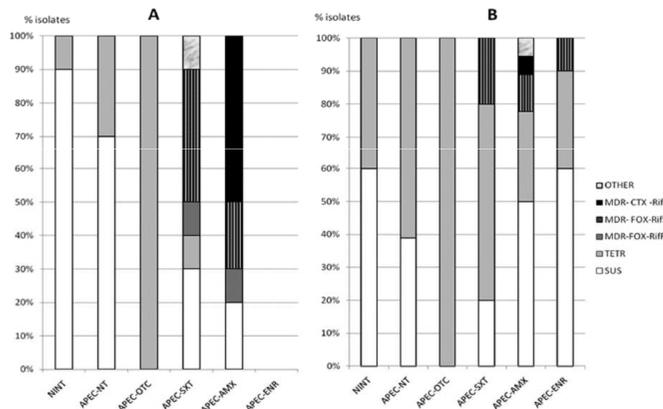
Mais ce n'est pas si simple !

SCIENTIFIC
REPORTS



Resistance Gene Transfer during Treatments for Experimental Avian Colibacillosis

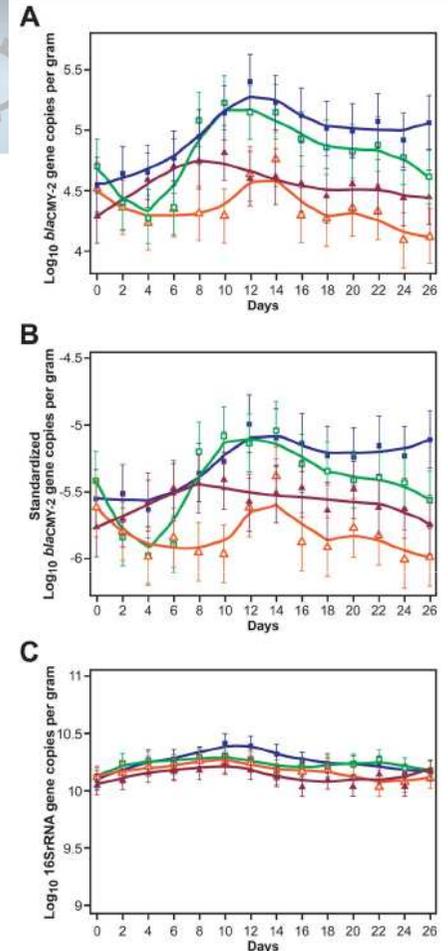
Alexandra Dheilly,* Laëtitia Le Devendec, Gwenaëlle Mourand, Axelle Bouder,* Eric Jouy, and Isabelle Kempf
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OPEN Impact of treatment strategies on cephalosporin and tetracycline resistance gene quantities in the bovine fecal metagenome

SUBJECT AREAS:
MOLECULAR BIOLOGY
MICROBIAL ECOLOGY

Multi résistance Différents traitements



Contents lists available at ScienceDirect

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journal homepage: www.elsevier.com/locate/vetmic



In vivo spread of macrolide-lincosamide-streptogramin B (MLS_B) resistance—A model study in chickens

D. Marosevic, D. Cervinkova, H. Vlkova, P. Videnska, V. Babak, Z. Jaglic*

Veterinary Research Institute, Brno, Czech Republic





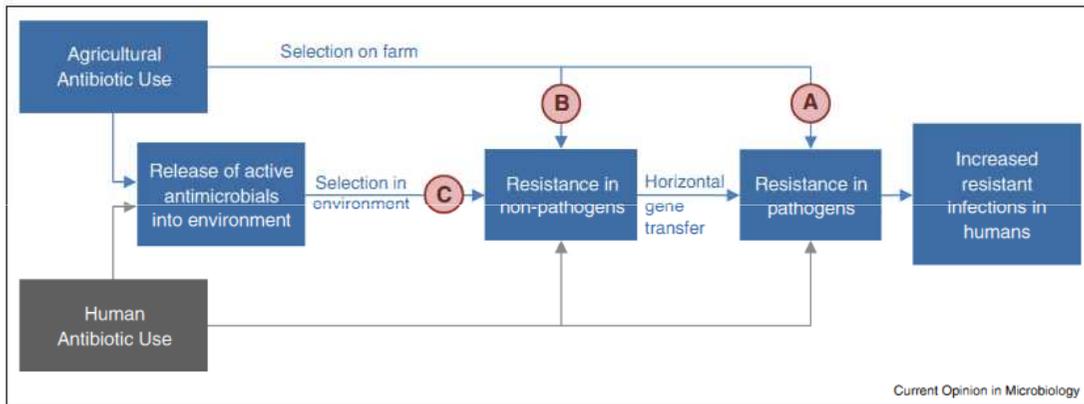
ELSEVIER

Human health impacts of antibiotic use in agriculture: A push for improved causal inference

Randall S Singer^{1,2} and Jessica Williams-Nguyen^{1,3}

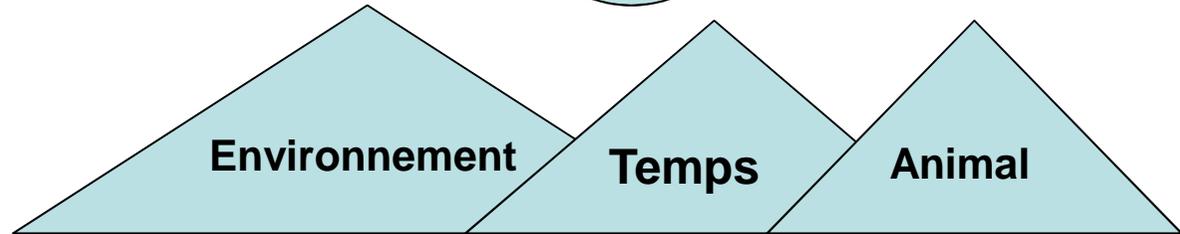
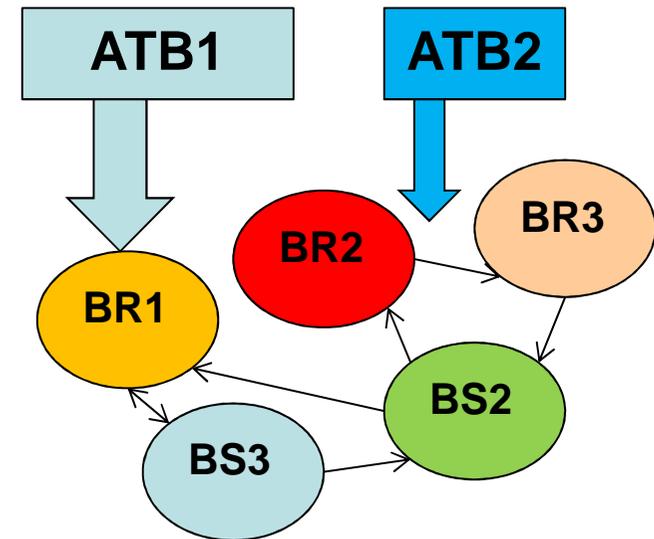


Figure 1



Conceptual model of the ways in which agricultural antibiotic use (AAU) can cause increased resistant infections in humans. In Scenario A, AAU leads to an increase in resistant pathogens which are then transmitted to humans via the food chain or the environment. In Scenario B, AAU selects for resistance in non-pathogens which then transfer resistance genes to pathogens leading to more resistant infections in humans. In Scenario C, active antimicrobial compounds are released into the environment where selection occurs predominantly in non-pathogens, and resistance is transferred horizontally to pathogens as in B. Human antibiotic use is shown for reference but not discussed.

Biocide, métaux



Conclusion

- Evolution de l'exposition aux antibiotiques et l'évolution de la résistance, un lien simple à démontrer chez l'animal.
 - Etudes expérimentales (PK/PD)
 - Des études descriptives au niveau de l'élevage
 - Des dispositifs de surveillance de l'usage et de la résistance aux antibiotiques
 - Après introduction récente de molécules ou un retrait, un lien peut être étudié et démontré
- Mais de nombreux autres facteurs (autres antibiotiques, voie de transmission, biosécurité) sont à prendre en compte et influent sur l'évolution globale.