

Portage des bactéries multi-résistantes chez les éleveurs et chez leurs animaux

Dr E. PIEDNOIR
Médecin Infectiologue
Pharmacien Hygiéniste



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Une problématique



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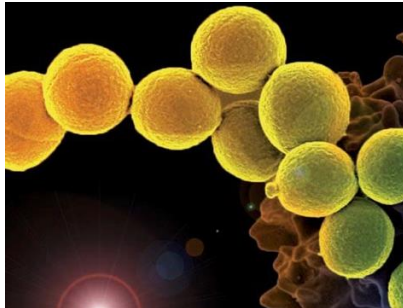




Etudes sur 2 grands types de Bactéries Multi-résistantes Problématiques en médecine humaine

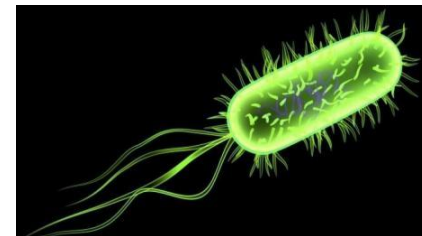
Staphylococcus aureus
Méthicillino-Résistant

SARM

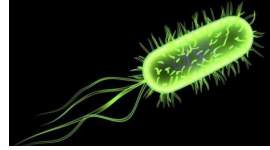


Escherichia coli
B-Lactamase Spectre Etendu

E-BLSE



E-BLSE : ou en est-on ?



Un premier exemple

Dahms C *et al.* Occurrence of ESBL-Producing *Escherichia coli* in Livestock and Farm Workers in Mecklenburg-Western Pomerania, Germany. PLoS One. 2015 Nov 25;10:e0143326.

Population :

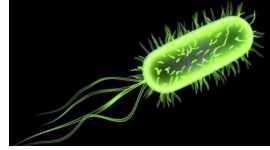
- Eleveurs : 73 de 23 exploitations différentes (écouvillonnages inguinaux)
- Animaux : 34 fermes (17 élevages de porcs, 11 de bovins et 6 avicoles) ont été analysées (selles.)

Méthode : typage par MLST et des gènes codant pour les BLSE

Résultats :

- Eleveurs : 5/73 (**6,8%**) des travailleurs (3 de fermes bovines et 2 d'élevages porcins) porteurs d'EBLSE
- Animaux : **70%** des élevages (15 porcins, 6 bovins et 3 avicoles) porteur d'EBLSE.

E-BLSE : Chez l'animal....ou en est-on ?



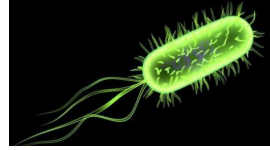
5 Eleveurs
EBLSE +

24 / 36
Fermes +

1 : génotype
identique H/A

2 : gène de Rce
identique,
profil MLST ≠

E-BLSE : ou en est-on ?



Un premier exemple

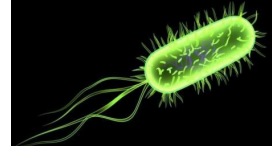
Forte prévalence de la résistance aux C3G

Lien montré Homme – Animal démontré

MAIS

Probablement sous estimé : prélèvement inguinaux non recommandés pour un dépistage d'entérobactéries (sensibilité moyenne)

E-BLSE : ou en est-on ?



Une étude grande échelle

Dohmen W et al. Carriage of extended-spectrum β -lactamases in pig farmers is associated with occurrence in pigs. Clin Microbiol Infect. 2015 ;21:917-23.

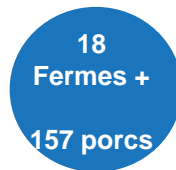
Fermes : 5 prélèvements de poussières + 5 animaux

Eleveurs : 1 prélèvement de selles + écouvillonnage nasal

BLSE

Fermes : 40, 2388 porcs (écouvillonnage rectal) : 18 fermes + (45%)

Eleveurs : 142 (Selles) : 6% positifs dans 6 fermes différentes



Lien avec la durée de l'exposition

SARM : ou en est-on ?



Deux exemples français

Armand-Lefevre L *et al.* Clonal comparison of *Staphylococcus aureus* isolates from healthy pig farmers, human controls, and pigs. *Emerg Infect Dis.* 2005 ;11(5):711-4.

Aubry-Damon H *et al.* Antimicrobial resistance in commensal flora of pig farmers. *Emerg Infect Dis.* 2004;10(5):873-9

Fréquence de portage de SARM :
éleveurs (≈ 10 %) >> non éleveurs (≈ population générale)

Clonal Comparison of *Staphylococcus aureus* Isolates from Healthy Pig Farmers, Human Controls, and Pigs

Laurence Armand-Lefevre,* Raymond Ruimy,* and Antoine Andremonn†

Pig farming is a risk factor for increased nasal *Staphylococcus aureus* colonization. Using sequence typing and phylogenetic comparisons, we showed that over-colonization of farmers was caused by a few bacterial strains that were not present in nonfarmers but often caused swine infections. This finding suggests a high rate of strain exchange between pigs and farmers.

Pig farmers work in close contact with animals that are given heavy loads of antimicrobial agents and therefore are highly colonized by resistant bacteria (1). The transfer of resistant bacteria from farm animals to farmers has been demonstrated in several instances (2,3). In a recent comparison of pig farmers and nonfarming controls, farmers were at a significantly greater risk for colonization by resistant commensal bacteria, including fecal enterobacteria and enterococci, and nasal *Staphylococcus aureus* colonization farmers, in whom it rose controls (4). The latter published cross-section among study participants (5). However in the pre, the sources and origin of resistance in farmers recently developed testing (MLST) (available characteristics of these

The Study
The *S. aureus* strains studied included 44 nasal isolates

*Groupe Hospitalier Bichat-Claude Bernard, Paris, France

from healthy pig farmers and 21 from healthy nonfarmer controls (i.e., bank or insurance workers). These participants all had been part of the population included in a previously published epidemiologic study in which the resistance rates in commensal bacteria from healthy pig farmers were compared with the rates in controls matched for age, sex, and county of residence (4). This population was disseminated over 7 French departments, chosen because they were the leading areas of porcine production. A department is a French administrative territory roughly the size of a British or American county. Each pig farmer worked on a different pig farm. We also studied 14 *S. aureus* isolates from the following types of swine infections: cutaneous, for isolates CA-1, CA-2, CA-6, F-9, and F-10; urinary, for isolates CA-3, CA-5, F-8, F-9, IV-11, IV-13, and IV-14; blood, for IV-12; and bone for CA-4. Isolates were collected from 1996 to 2002 in 4 of the 7 departments in which the pig farmers were working and were kindly provided by state veterinary laboratories. All strains had been identified with conventional techniques, and their susceptibility to antimicrobial agents had been determined by the disk-diffusion technique (available from www.afim.asso.fr).

S. aureus strains were lysed with 30 µg/mL lysothapsin, which was incubated for 10 min at 37°C, and DNA was extracted by using MagNA Pure LC automaton (Roche, Mannheim, Germany), as recommended by the manufacturer. DNA concentrations were measured by optical density, and extracts were diluted to obtain concentrations of 50 ng/µL. DNA for amplification.

The presence of *mecA* and *mecC* genes was determined

Antimicrobial Resistance in Commensal Flora of Pig Farmers

Hélène Aubry-Damon,* Karine Grenet,† Penda Sall-Ndiaye,‡ Didier Che,† Eugenio Cordeiro,* Marie-Elisabeth Bougnoux,† Emma Rigaud,‡ Yann Le Strat,† Véronique Lemanissier,‡ Laurence Armand-Lefevre,† Didier Delzescaux,§ Jean-Claude Desenclos,‡ Michel Liénard,‡ and Antoine Andremonn†

We assessed the quantitative contribution of pig farming to antimicrobial resistance in the commensal flora of pig farmers by comparing 113 healthy pig farmers from the major French porcine production areas to 113 nonfarmers, each matched for sex, age, and county of residence. All reported that they had not taken antimicrobial agents within the previous month. Throat, nasal, and fecal swabs were screened for resistant microorganisms on agar containing selected antimicrobial agents. Nasopharyngeal carriage of *Staphylococcus aureus* was significantly more frequent in pig farmers, as was macrolide resistance of *S. aureus* from carriers. Nongroupable streptococci from the throat were more resistant to the penicillins in pig farmers. The intestinal isolation of enterococci resistant to erythromycin or vancomycin was not significantly higher in pig farmers in contrast to that of enterobacteria resistant to nalidixic acid, chloramphenicol, tetracycline, and streptomycin. Prevalence of resistance in transorbital fecal enterobacteria

ria that can then contaminate the food and, in turn, humans (9,10). Farmers are more likely to acquire enteric antimicrobial-resistant bacteria from food-producing animals, even if not treated with antimicrobials agents themselves (11-14). However, this link has never been quantitatively assessed. Antimicrobial resistance in nasal and pharyngeal commensal strains might possibly be affected in the same manner, and this hypothesis has also not been investigated. We thus designed an exposed-observer epidemiologic study to determine the association between contact with animals in pig-raising farms and isolation of antimicrobial-resistant nasal, pharyngeal, and intestinal commensal microorganisms.

Methods

Industrial animal farming is also associated with large-scale antimicrobial use (8), which leads to a high level of colonization of animals with antimicrobial-resistant bacteria.

Study Design
A health insurance system-related services. We included group and nonfarmers (in insurance services) as size was calculated absence of antimicrobial reach residents (15) to detect, of a 10% would be found with a Pig farmers were chosen, exclusively pig farmers (1-84 pigs) and contacted during the yearly MSA preventive medicine visits to obtain permission for participation. One pig farmer per farm was randomly selected to fill a panel of 20 in each of the seven major French porcine production areas.

Study Population
One nonfarmer control, matched for sex, age, and county of residence, was selected for each pig farmer and approached similarly. Nonfarmers were not living or working on a farm, in a slaughterhouse, or in the pharmaceutical

*National Institute for Public Health, Saint-Maurice, France; †Bichat Hospital, Assistance Publique, Paris, France; ‡National Mutualité Sociale Agricole, Bagnères, France; §National Federation of Cattle and Pig Raisers, Paris, France; and ‡Antrobre Hospital, Assistance Publique, Paris, France



SARM : ou en est-on ?



Une belle étude

Mroczkowska A *et al.* Livestock-associated *Staphylococcus aureus* on Polish pig farms. PLoS One. 2017 ;12(2):e0170745.

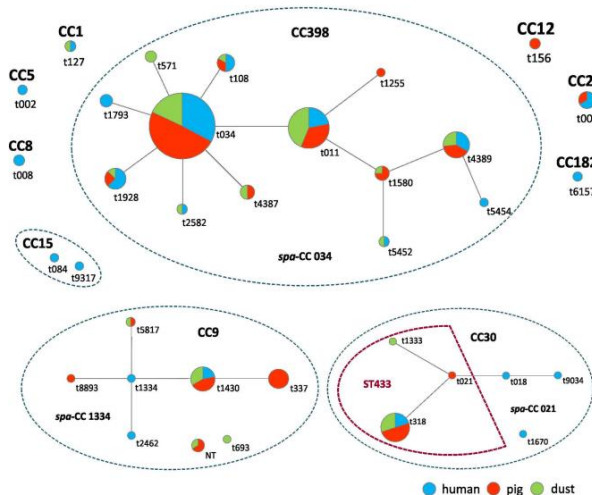
Population :

- Eleveurs : 123
- Animaux : 123 fermes

Méthode : typage par MLST et des gènes codant pour les BLSE

Résultats :

- Eleveurs : 18/123 (**14,7%**) des fermes SAMR + ont au moins un éleveur SAMR +
- Animaux : 26/123 (**21,1%**) des élevages SARM +.



72 isolats de SARM dont la majorité appartiennent à la lignée génétique ST 398
Tant pour les hommes, les porcs et la poussière

SARM : ou en est-on ?



Une belle étude

Mroczkowska A *et al.* Livestock-associated *Staphylococcus aureus* on Polish pig farms. PLoS One. 2017 ;12(2):e0170745.

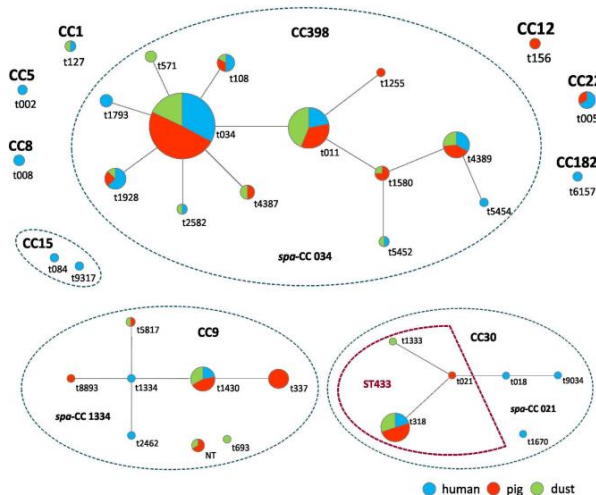
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SARM : ou en est-on ?



Ce clone ST 398

Physiopathologie

Souche de colonisation dans un premier temps

Responsable d'infections cutanéomuqueuses et pulmonaires +++

- - - Fréquent : infections invasives de type bactériémie, endocardite.....

- 1^{ères} souches isolées aux Pays-Bas chez le porc dès février 2003 (Van Loo et al. 2007) et aussi en France à la même période chez l'homme (Armand-Lefevre et al. 2005).
- Le portage humain d'un tel clone a été statistiquement corrélé au réservoir animal (porc, bovin) et à la profession d'éleveurs et ce clone était responsable de plus de 20 % des infections rapportées chez l'homme aux Pays-Bas.
- Détection aux Pays-Bas
 - en 2003 : 0%
 - en 2007 : 33%
 - > 50 en 2010

Phénotype de résistance

Souvent Tetracycline-R
Aminosides +/- touchés



E-BLSE/SARM : ... ou en est-on ?



Une étude mixte : SARM et EBLSE

Fischer J *et al.* Simultaneous occurrence of MRSA and ESBL-producing Enterobacteriaceae on pig farms and in nasal and stool samples from farmers. *Vet Microbiol.* 2017 Feb;200:107-113.

Fermes : 5 prélèvements poussières + 5 animaux

Eleveurs : 1 prélèvement de selles + écouvillonnage nasal

SARM

96 % (49/51) Fermes

84,7 % (72/85) Eleveurs

72
Eleveurs
SARM +

49
Fermes +

71
génotypes
identiques
H/A-E

E-BLSE

61 % (31/51) Fermes

6,0 % (5/85) Eleveurs

5
Eleveurs
EBLSE +

31
Fermes +

1 génotype
identique
H/A-E

4 gènes de
Rce
identiques

Chez l'animal....ou en est-on ?



Une étude mixte

Fischer J *et al.* Simultaneous occurrence of MRSA and ESBL-producing Enterobacteriaceae on pig farms and in nasal and stool samples from farmers. *Vet Microbiol.* 2017 Feb;200:107-113.

Fermes : 30/51 (58,8%) ont au moins un prélèvement positif et à SARM et à E-BLSE

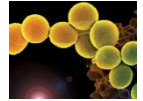
Eleveurs : 4/85 (4,70 %) étaient positifs pour le portage de SARM et E-BLSE

Et les poussières dans tout cela ?



AIR/ CONTACT DIRECT

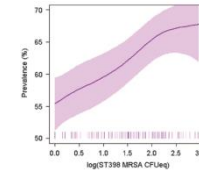
Bos M *et al.* Transmission through air as a possible route of exposure for MRSA. J Expo Sci Environ Epidemiol. 2016 ;26(3):263-9



Mesure de l'exposition au SARM via les poussières des éleveurs

Forte association entre exposition aux poussières dans les élevages animaux sur le portage nasal de SARM chez les éleveurs (+++ si exposition >20h hebdomadaire)

Prévalence de portage en lien avec le niveau de contamination



Dohmen W *et al.* Air exposure as a possible route for ESBL in pig farmers. Environ Res. 2017 May;155:359-364.

131 personnes, 32 fermes, 192 porcs
2 campagnes de prélèvement à 1 an d'intervalle
Recherche gène CTX-M-1 chez *E.coli* EBLSE

Prévalence : **3,6 %** chez les hommes

Prévalence : **35 %** chez les porcs

Poussière : **26 %**



Portage chez l'homme associé à (analyse univariée) :

- durée de l'exposition (x 1,03 / 10 h)
- présence de porcs porteurs (x 7,4)
- présence dans les poussières (x3,5 ; p=limite)

En population générale ?



Prévalence en milieu communautaire (France)

SAMR : 2-3 %

E-BLSE : 5-10 %



Conclusion



SARM >> BLSE

Modes de transmission : Contact >> Air

Exposition : durée de travail

Prévention ??

Finalement lien éleveurs-animaux établis mais lien épidémiologique de la diffusion de ces souches/plasmides avec la population générale peu clair

Merci de votre attention