# Temporal increase of resistance in *E. coli* after penicillin-treatment of pigs

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Presented at Society for Veterinary Epidemiology and Preventive Medicine, Annual Conference 2018, 21. – 23. March, Tallinn, Estonia

## Introduction

Development of antibiotic resistance in *E. coli* from pigs treated with antimicrobials has been little investigated with regard to the whole life cycle of the pigs to date. Hence, the aim of this study was to evaluate the **effect of time interval between treatment and sampling on the probability of resistance detection in *E. coli* from focal pigs** in German pig production. In the present evaluation, we concentrate on the use of penicillins.

## Material & Methods

- Longitudinal study between 2014 and 2016
- 406 focal pigs: ca. 7 per each of 2 dams from 29 German breeding herds
- Followed from birth to end of fattening through their production chains
- All antimicrobial treatments documented (Fig. 1)
- Fecal samples collected with rectal swabs 5 times during pigs' life (Fig. 2)
- *E. coli* isolated and susceptibility to ampicillin (and 13 other agents) tested using broth microdilution
- Descriptive evaluation
- Logistic analysis, binary resistance outcome, input factors time interval and production stage, hierarchical data structure (pigs nested in dams nested in herds) and repeated measurements per pig (proc glimmix in SAS 9.4)

## Results

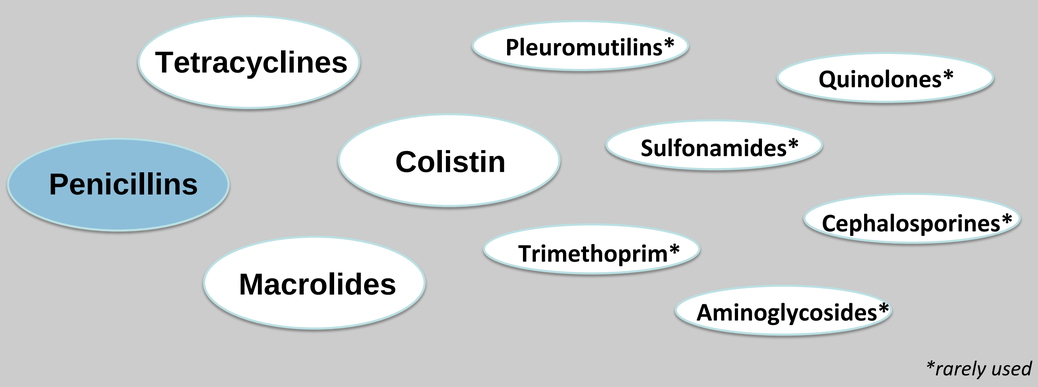


**Figure 1: What kind of antimicrobials received the 406 focal pigs in their life?**

Different antimicrobial classes were applied to the focal pigs (Fig. 1). **Penicillins were given to 92 focal pigs from 7 herds at the suckling or weaning stage.** In 5 of these 7 herds, further antimicrobials were applied to the focal pigs: tetracyclines, aminoglycosides or colistin at weaning, fattening or finishing stage. Potential effects of antimicrobials other than penicillins were not considered in the present evaluation.


**Figure 2: Scheme of fecal sampling times (5x) during life cycle of the focal pigs and at the dam around farrowing (1x)**

Fecal samples were collected from the focal pigs repeatedly during their life (Fig. 2): 1x in suckling, 1x in weaner, 3x in fatting stage and from their dams 1x around farrowing time.

### Descriptive

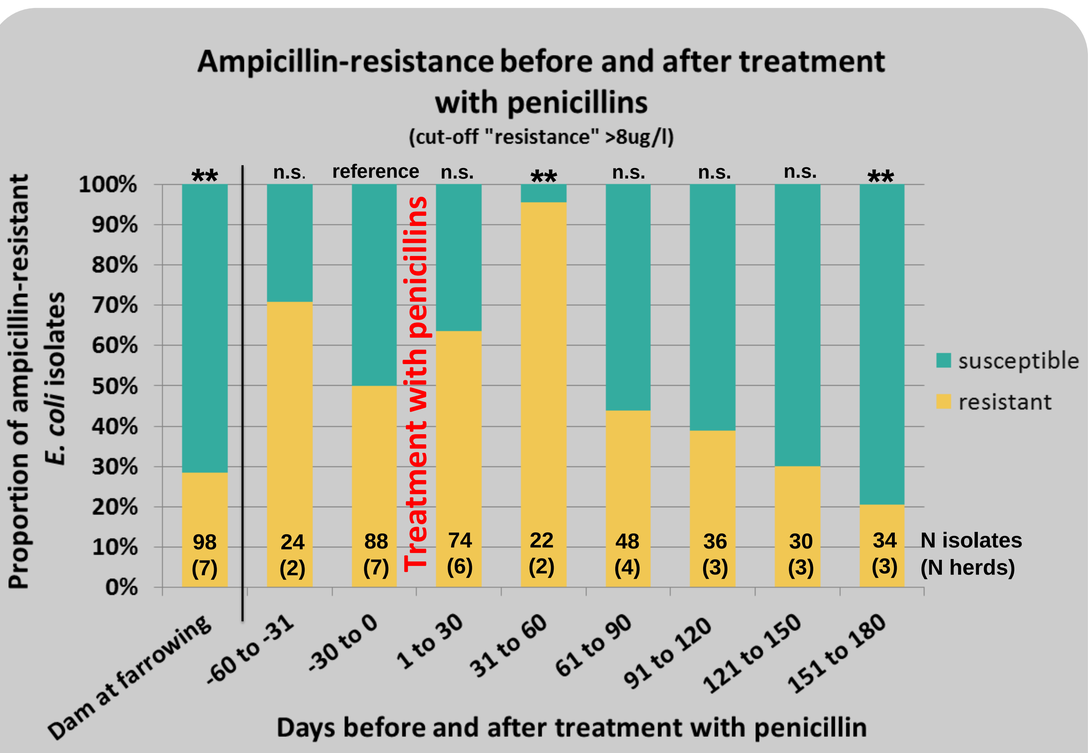


**Figure 3: Proportion of ampicillin-resistant *E.coli* from pigs over time**; difference of proportions per 30-days-steps was tested relative to the reference-proportion in the interval previous to treatment (** = $p < 0.01$, n.s. = $p > 0.05$ in univariate analysis)

Relative to the point of time of penicillin-treatment per pig, the resistance patterns were mapped in steps of 30-days (Fig. 3). Prior to the treatment, resistances in *E. coli* isolated from the pigs were already high. Compared to the time before the treatment, the risk for ampicillin-resistance was significantly higher 31 to 60 days after the treatment. Thereafter (151 to 180 days after treatment) the risk decreased to significantly lower proportions according to the univariate analysis.
When adjusting the statistics for the clustering of dams and herds there was no significant change of resistance between time intervals anymore.

### Analytical

**Table 1: Risk of ampicillin-resistance before and after penicillin treatment** (454 *E. coli*, logistic analysis, type III: time variable p = 0.1355, df = 28, estimated total variation was 6.3 of which herd explained 32% and dam 16%)

| Estimates | Number of days relative to the point of time of treatment | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Dam at farrow-ing | -60 to -31 | -30 to 0 | 1 to 30 | 31 to 60 | 61 to 90 | 91 to 120 | 121 to 150 | 151 to 180 |
| Odds ratio | 0.2 | 2.2 | 1 | 2.0 | 22.5 | 0.7 | 0.4 | 0.3 | 0.2 |
| Lower limit | 0.0 | 0.1 | 1 | 0.3 | 0.7 | 0.1 | 0.0 | 0.0 | 0.0 |
| Upper limit | 1.3 | 38.0 | 1 | 14.9 | 760.5 | 6.1 | 5.2 | 4.3 | 2.7 |

## Conclusion & Outlook

- Treatment with penicillins was followed by a transient increase of risk for resistance (0 to 60 days after treatment) and the risk decreased thereafter
- Herd and dam explained most of the variation
- Testing more than one isolate per sample and using a bigger sample size would increase statistical power and highlight the resistance effect
- Treatments of other pigs in the barn or treatment of the focal pigs with other antimicrobials may have biased the results
- Results suggest a higher risk period of at least 60 days after treatment with penicillins – however, further investigation is needed
- Next, we intent to evaluate potential effects of the other antimicrobials

### Acknowledgements

Thanks to farmers in Bavaria and North Rhine-Westphalia for participating in the study. Special thanks to Bavarian Animal Health Services (Dr. Rostalski, Dr. Gangl) and the animal health service of agricultural chamber of North Rhine-Westphalia (Dr. Harlizius) for data and sample collection, processing and lab analysis.

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