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Published in:

Veterinary Record

Published: 01/06/2018

Document Version:

Final Published version, also known as Publisher's PDF, Publisher's Final version or Version of Record

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Publication record in CityU Scholars:

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Published version (DOI):

[10.1136/VR.104421](https://doi.org/10.1136/VR.104421)

Publication details:

Gerber, P. F., Macleod, A., & Opriessnig, T. (2018). Erysipelothrix rhusiopathiae serotype 15 associated with recurring pig erysipelas outbreaks. *Veterinary Record*, 182(22). <https://doi.org/10.1136/VR.104421>

Citing this paper

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Erysipelothrix rhusiopathiae serotype 15 associated with recurring pig erysipelas outbreaks

Priscilla F Gerber,^{1,2} Alasdair MacLeod,³ Tanja Opriessnig^{1,4}

Erysipelothrix rhusiopathiae is the causative agent of pig erysipelas and can be associated with sporadic cases or larger outbreaks of septicaemia with characteristic skin lesions or chronic polyarthritis.¹ Within the genus *Erysipelothrix*, at least 6 species (*Erysipelothrix rhusiopathiae*, *Erysipelothrix tonsillarum*, *Erysipelothrix* species strain 1, *Erysipelothrix* species strain 2, *Erysipelothrix* species strain 3 and *Erysipelothrix inopinata*) and 28 serotypes (1a, 1b, 2–26 and N) have been recognised.¹ *E rhusiopathiae* serotypes 1 and 2 are frequently isolated from clinically affected pigs, although other *E rhusiopathiae* serotypes have been sporadically associated with clinical disease.^{1,2} While there is no experimental evidence that *Erysipelothrix* species other than *E rhusiopathiae* cause disease in pigs,³ certain *Erysipelothrix* species strains have been isolated from clinical cases^{4,5} and from condemned carcasses in abattoirs.^{2,6}

Pig erysipelas is generally seen in adults and grow-finish pigs after the decline of maternal antibodies.¹ Humoural immunity is considered most important for disease prevention and vaccines containing live or inactivated *E rhusiopathiae* serotype 1 or 2 isolates are commonly used.⁷ In the UK, there are two *E rhusiopathiae* bacterins available commercially based on serotype 2 or serotypes 1 and 2.⁸

In recent years, the incidence of *E rhusiopathiae* infection in pigs appears to have increased worldwide^{2,9–11}

and is also increasing in European poultry production systems.¹² This study summarises the findings associated with chronic *E rhusiopathiae* infection in a commercial wean-finish pig herd in the UK (farm A) that received piglets from an *E rhusiopathiae* vaccinated high health breeding herd free of porcine reproductive and respiratory syndrome virus (PRRSV) and *Mycoplasma hyopneumoniae* as monitored by serological testing in three-month intervals. Specifically, the breeding farm used a commercial *E rhusiopathiae* serotype 2-based bacterin (Porcillis Ery, Intervet UK) which was administered to gilts twice before first service and to sows once at each weaning.

Farm A, a continuous flow farm with routine PCV2 vaccination at 4 weeks of age (Ingelvac CircoFLEX, Boehringer Ingelheim), experienced clinical signs of pig erysipelas of pigs aged 18–22 weeks from February 2015 through August 2016 characterised by delayed growth and a high incidence of lameness and ear discolourations (Fig 1). Morbidity was approximately 8–12 per cent during this time.

A total of 10 animals with representative clinical signs observed in different age groups in farm A were selected by the veterinarian and euthanased for postmortem examination as specified below. Three 18-week-old pigs that were in the hospital pen due to losing body condition showed interstitial pneumonia, valvular endocarditis with dilated hearts and enlarged joints with turbid fluid at necropsy. Four 22-week-old pigs, from a pen with severe lameness in 8 per cent of the pigs, showed turbid joint liquid in several articulations but had no cardiac lesions. *E rhusiopathiae* was isolated on several occasions from the spleen, heart and joint swabs from the affected animals aged 18–22 weeks in farm A (Fig 1). Additionally, three small pigs aged 6–10 weeks showed necrotic colitis without pulmonary or heart lesions, and *Salmonella enterica* serovar Typhimurium was isolated from caecum swabs from these animals. This finding was unrelated to the *E rhusiopathiae* cases described in the pigs aged 18–22 weeks. The S

Veterinary Record (2018)

doi: 10.1136/vr.104421

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Provenance and peer review Not commissioned; externally peer reviewed.

Received March 17, 2017

Revised February 13, 2018

Accepted February 20, 2018

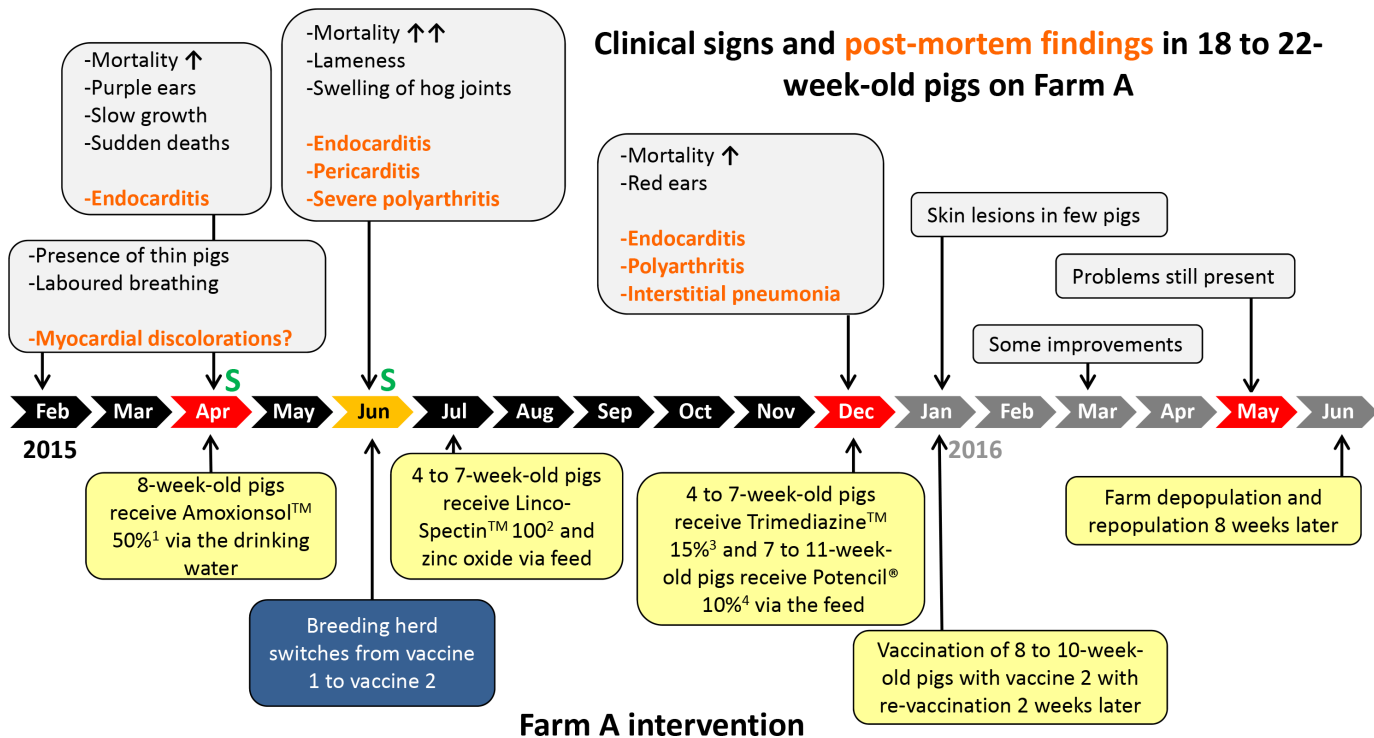


FIG 1: Timeline of the *E rhusiopathiae* infection dynamics, including clinical signs, postmortem findings and intervention strategies on farm A. *E rhusiopathiae* serotype 15 was isolated in April and December 2015 and in May 2016 (red-coloured chevrons), an untypable *E rhusiopathiae* was isolated in June 2015 from pigs aged 18–22 (orange-coloured chevron) and *S* Typhimurium was isolated in April and June 2015 from pigs aged 6–10 weeks (green S). Vaccine 1 contains an *E rhusiopathiae* serotype 2 stain (Porcillus Ery, Intervet UK) and vaccine 2 contains serotype 1 and 2 strains (Erysend Parvo, Hipra, Spain). ¹Vetoquinol, active ingredient amoxicillin. ²Zoetis, active ingredients lincomycin and spectinomycin. ³Vetoquinol, active ingredients sulfadiazine and trimethoprim. ⁴Elanco, active ingredient phenoxymethyl penicillin potassium.

Typhimurium could have contributed to an overall immunocompromised condition of the pig herd.

The *E rhusiopathiae* isolates were serotyped as previously described.² Serotype 15 was identified on three different occasions (Fig 1). After initial onset of clinical signs, medicated feed containing 44 ppm lincomycin, 44 ppm spectinomycin and 1250–2500 ppm zinc oxide was administered to the farm A pigs aged 4–7 weeks. In addition, amoxicillin was administered via the drinking water at eight weeks of age. At the same time, the breeding herd moved to a different vaccine supplier/vaccine product and now used a commercial *E rhusiopathiae* serotypes 1 and 2-based bacterin (Erysend Parvo, Hipra, Spain) in gilts and sows according to the manufacturer’s instructions. Because of lack of clinical improvement, 14-week-old farm A pigs started to be medicated with penicillin via feed at a concentration of 200 ppm in December 2015 (Fig 1). Skin lesions typical of pig erysipelas were first observed in January 2016 in a few pigs at which time off-label vaccination with Erysend was initiated in pigs aged 8–10 weeks with revaccination 2 weeks later. However, no obvious impact of the intervention strategies was observed.

In December 2015, 25 serum samples were collected from poor-doing farm A pigs aged 6–22 weeks. Ten serum samples were obtained from farm B pigs aged 17–22 weeks in March 2016 for comparison purposes. Serum samples were tested for the presence of antibodies against *E rhusiopathiae* surface protective antigen (Spa) A by an *in-house* fluorescent microsphere immunoassay.¹³ The positive cut-off was established at a mean

fluorescence intensity value of 1800. On the clinically affected farm A, seropositive animals were first detected at 14 weeks of age and the mean anti-*E rhusiopathiae* antibody levels increased with age, being higher in pigs aged 18–22 weeks (Fig 2). In contrast, healthy pigs from farm B aged 17–20 weeks, which received piglets from the same breeding herd as farm A and operated in an all-in-all-out system, were negative for anti-*E rhusiopathiae* antibodies (Fig 2).

The recurring *E rhusiopathiae* outbreaks on vaccinated farm A could indicate issues with vaccine handling and administration or vaccine failure. *E rhusiopathiae* strains express Spa, classified in SpaA or SpaB based

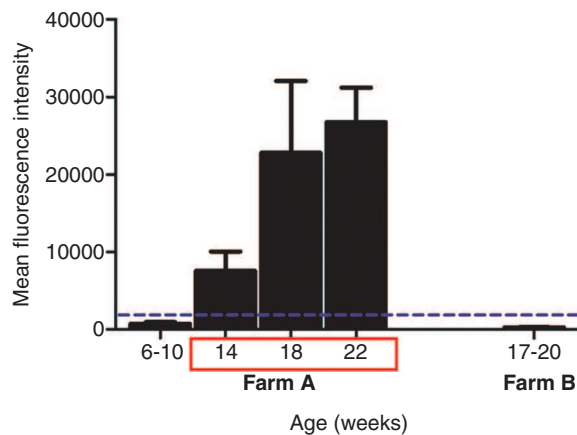


Fig 2: Antibodies against *E rhusiopathiae* SpaA were measured in serum samples obtained in December 2016 before implementation of *E rhusiopathiae* vaccination in growing pigs, from pigs of different ages from the clinically affected farm A and the unaffected farm B. Clinical signs were seen in pigs between 14 and 22 weeks of age and included discoloration of the ears and lameness (red box). The dashed line indicates the assay cut-off.

on phylogenetic analysis, which are associated with protection.¹⁴ In mouse challenge studies, recombinant Spa protected against virulent *E rhusiopathiae* strains containing the homologous Spa but protection varied against strains possessing a heterologous Spa.^{14 15} Serotypes 1 and 2 (present in vaccines) and serotype 15 (field isolate) all contain SpaA (data not shown) and cross-protection should have occurred. Vaccination with *E rhusiopathiae* serotype 2 provided protection against serotype 15 challenge in mice and pigs.¹⁶ Recent studies have also shown that commercially available vaccines protected mice and pigs against challenge with highly pathogenic serotype 1a and untypeable strains containing mutations in the *spa* region.¹¹ However, most cross-protection studies evaluate only short-term protection and acute erysipelas and the conclusions may not always be applicable for long-term protection and/or chronic erysipelas.¹⁷ The breeding herd was vaccinated against *E rhusiopathiae* on a regular basis. A change of the vaccine type/supplier had no effect on the clinical outcomes in farm A pigs.

As clinical signs on farm A were only seen after 12–14 weeks of age, from January 2016 onwards the pigs were vaccinated at 8–10 weeks of age using an inactivated vaccine and revaccinated two weeks later. This two-dose off-label vaccination protocol however also failed to provide protection under the high-infectious pressure conditions. Alternatively, vaccine handling and administration issues could have occurred. As seroconversion due to vaccination or natural infection cannot be differentiated and antibody responses after vaccination were not assessed, the reason for the lack of clinical improvement after implementation of vaccination in the growing pigs in farm A is unknown. It has been shown that, in the presence of *E rhusiopathiae* passively derived antibodies, pigs vaccinated with a live *E rhusiopathiae* vaccine at 8–10 weeks of age had improved antibody responses compared with pigs vaccinated at six weeks.¹⁸ In piglets without passively derived antibodies, seroconversion occurred regardless of the age at vaccination.¹⁸ Passively derived antibodies could potentially have decreased the efficacy of the inactivated vaccine used in farm A, although piglets aged 6–10 weeks were seronegative before implementing the vaccination programme (Fig 2) and the breeding herd vaccination protocol remained unchanged. Furthermore, seroconversion against *E rhusiopathiae* was seen at 14 weeks of age in farm A (Fig 2), suggesting active infection or recirculation at 12–13 weeks of age.¹³

Antimicrobial therapy can also impact the host immune system.¹⁹ Specifically, after *E rhusiopathiae* vaccination and compared with an untreated control group, the antibody response was lower in pigs receiving intramuscular doses of ceftiofur, doxycycline and tiamulin and higher in pigs treated intramuscularly with amoxicillin or tulathromycin.¹⁹ The effects of lincomycin and spectinomycin administered in farm A on the response

to *E rhusiopathiae* vaccination are unknown. In addition, pathogens such as PRRSV and PCV2 may also impair the immune system, interfere with vaccinations and contribute to bacterial infections. Serum samples from affected animals tested negative for the presence of antibodies against PRRSV (IDEXX PRRS X3 Ab test; IDEXX Laboratories) in March 2015. In December 2015, PCV2 DNA²⁰ was identified in one of 25 serum samples. Combining these results suggests that PRRSV and PCV2 were unlikely to have contributed to the persistence of the outbreak.

On farm A, *E rhusiopathiae* infection persisted after multiple antimicrobial treatments and vaccination of the growing pigs. Clinical signs associated with the *E rhusiopathiae* serotype 15 infection consisted of lameness of various degrees and slow growth with presence of stunted pigs. Macroscopic lesions were limited to joints and the heart. Classical skin lesions¹ were only observed in few pigs approximately 10 months after the initial problems had started. The reasons for the lack of improvement after implementing or changing antimicrobial treatments and vaccinations are unknown, but the high stocking rate and poor hygiene in the continuous flow of pigs likely contributed. Because of the inability to control the clinical disease signs, farm A was depopulated in July 2016, washed, disinfected, left empty for eight weeks and then repopulated with implementation of an All-In/All-Out production system. Clinical signs consistent with pig erysipelas were not observed after repopulation. Appropriate medication and vaccination protocols may be inefficient to control chronic erysipelas under high-infectious pressure settings.

Funding Funding for this study was provided by the Biotechnology and Biological Sciences Research Council (BBSRC) Institute Strategic Programme Grant awarded to the Roslin Institute (BB/J004324/1; BBS/E/D/20241864).

Competing interests None declared.

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