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| PROJECT/STUDY TITLE: | Towards A Greater Understanding Of Contagious Ovine Digital Dermatitis: An Epidemiological Approach |
| PRINCIPAL APPLICANT(S) | Dr. Jennifer Duncan |
| GRANT AWARDED | January 2011 |

Lay summary of project outcomes, achievements and potential impact: Max 300 words

Contagious ovine digital dermatitis (CODD) is a cause of severe lameness in sheep that was first recorded in the UK in 1997. It was considered to be a new foot disease of sheep, with a different clinical presentation to the common and well known foot disease of footrot. Very little was then known about CODD and the aim of this study was to gain a greater understanding of this disease and provide practical information for its control on farms.

Our epidemiology studies were a postal survey of 511 farmers and an on farm detailed study of 6 farms over one year (6,515 sheep were examined). Here we found that CODD was common on farms with 35% of farms in the survey affected. Typically 2% of sheep had the disease although it could be as high as 50% of sheep. During the survey nearly half of farmers thought the disease had arrived due to buying in sheep. The farmers also reported other risk factors for CODD which we went on to study in our on-farm work.

Our on-farm risk factor study found that sheep having footrot greatly increased the risk of having CODD. There was a seasonal trend in disease from late summer/early autumn, and it was found that flock size, lowland pasture, lush pasture and poached pasture all increase the risk of CODD in sheep. These risk factor studies have helped us provide farmers with management advice to reduce the risk of CODD in their flocks.

To measure the impact of CODD on sheep welfare we developed a lameness scoring tool. We found that 1) the tool was reliable for same person scoring sheep; 2) less reliable for early mild lameness; 3) sheep with early stages of disease may not be lame at all; 4) CODD is a very severe form of lameness and the severity of lameness corresponds with the severity of the lesion. The findings of this work have implications for treatment and biosecurity practices on farms.

A detailed clinical description and five-point lesion grading system were developed for CODD in

order to aid diagnosis amongst veterinarians and farmers. Histopathology and immunohistochemistry were also used to describe the lesions in more detail. This work now provides the world with the first formal lesion scoring and pathological description system for this novel foot disease and again emphasizes CODD's severity. Furthermore, radiographs also highlighted the extensive damage to soft tissues and bony structures that may occur in advanced clinical cases.

It was important to also investigate treatment options for CODD. We were aware that it is common practice for vets and farmers to treat whole flocks of sheep with injectable antibiotics in order to eliminate CODD from the flock, although there is no scientific evidence to support this. A sister project had shown that treponeme bacteria are always found in CODD lesions. Following antibiotic sensitivity work in the lab, we found these bacteria were sensitive to many antibiotics including penicillin and macrolide antibiotics. Subsequent to a pilot study, we then undertook a whole flock treatment trial of 24 farms to investigate whether whole flock tilmicosin treatment would eliminate CODD from farms. Whilst tilmicosin was effective at treating clinical cases, we found that there was no statistically significant difference in the *elimination* of CODD, footrot or lameness between control and treatment farms and therefore whole flock antibiotic treatments cannot be recommended for CODD elimination.

Combining knowledge gained from this project and previous CODD research has allowed us to produce clear evidence based advice for the control of CODD for vets and farmers. Many knowledge transfer events have already taken place and more activity is planned during the coming months.

Detailed progress against original objectives: List outcomes against original objectives. Discuss what has been achieved, including any statistical analysis completed as part of the project.

Aims and Hypothesis

The overall aim of the project was to develop evidence based treatment and control strategies for CODD in sheep. Strategies were to be informed by robust epidemiological studies, bacteriological culture and antibiotic sensitivity data and the results from split flock randomised intervention studies.

Objective 1: Estimate the between and within farm prevalence of CODD, and identify farm associated risk factors for CODD, by questionnaire of approximately 3500 sheep farms.

The questionnaire investigated farmers' knowledge and views on contagious ovine digital

dermatitis (CODD). The response rate was 25.6%. The between farm prevalence of CODD was 35.0% and the median farmer estimated prevalence of CODD was 2.0%. The disease now appears endemic and widespread in Wales. Furthermore, there has been a rapid increase in reports of CODD arriving on farms since the year 2000. Risk factors for CODD identified in this study include the presence of bovine digital dermatitis (BDD) in cattle on the farm and larger flocks. Farmers also consider concurrent footrot/interdigital dermatitis, buying in sheep, adult sheep, time of year and housing to be associated with CODD.

This objective was achieved in full and the work is published in the following paper:-

Angell, J.W., et al., *Farmer reported prevalence and factors associated with contagious ovine digital dermatitis in Wales: A questionnaire of 511 sheep farmers*. Preventive Veterinary Medicine, 2014. **113**(1): p. 132-138.

Objective 2: Perform detailed investigation of within farm risk factors for CODD via a longitudinal study of six affected farms, visited over 2 years.

Six farms were studied in North Wales to investigate 1) the prevalence dynamics of CODD, 2) the association between sheep with CODD and potential risk factors and 3) the impact of CODD on lameness in sheep. The farms were visited at approximately two-month intervals between June 2012 and October 2013 and 6,515 sheep were examined.

The mean sheep level prevalence of CODD varied between farms (2.5-11.9%). Within farms, prevalence may increase in the late summer/early autumn and after housing. Environmental risk factors included larger flocks, lowland pasture, lush pasture and poached pasture. Co-infection of a foot with footrot was strongly associated with CODD in that foot (OR: 7.7 95%CI: 3.9-15.5 $P < 0.001$) but negatively associated with co-infection of a foot with interdigital dermatitis (OR: 0.04 95%CI: 0.02-0.1 $P < 0.001$). Reinfection with CODD was observed in 78 individual sheep but there was no re-infection at foot level.

Lameness on all farms reduced during the study and seasonal changes in lameness followed similar patterns to those for CODD. Infection with CODD leads to a greater increase in locomotion score compared to footrot or interdigital dermatitis and CODD lesion grade was strongly associated with being lame. Sheep with CODD in more than one foot were more likely to be lame (OR: 25.0 95%CI: 12.5-49.9 $P < 0.001$) than those with just one foot affected (OR: 10.0 95%CI: 8.6-11.6 $P < 0.001$).

The biggest risk factor for CODD is co-infection with footrot and therefore control of footrot should help reduce the risk of CODD on affected farms. Furthermore, environmental risk factors for

CODD are similar to those for footrot, adding weight for control strategies that target both diseases in tandem. The routine repeated gathering of sheep for the purposes of treating all lame sheep might be an effective control strategy for lameness on some sheep farms. Effective systemic immunity to CODD in sheep appears to be lacking, as 78 sheep were observed to be re-infected with CODD during the survey. However, there is epidemiological evidence that there may be some local immunity within the foot warranting further investigation.

This objective was achieved in full, however the study was completed in 15 months rather than two years as originally planned. This was due to issues with farmer compliance as some of the farms in the study were finding gathering and individually examining the flock a very time consuming task. As sufficient data had been collected it was felt wise to curtail this objective early. It should be noted that this study is one of the largest ever epidemiology studies of individual lame sheep and has generated a vast amount of data which will be analysed in further work.

The remaining financial resources from this work were diverted to allow a far more ambitious treatment trial than one originally envisaged. This change was discussed with the BVA AWF trustees at the mid-point review meeting.

The work described here is published in the following scientific paper:-

Angell, J.W., D.H. Grove-White, and J.S. Duncan, *Sheep and farm level factors associated with contagious ovine digital dermatitis: A longitudinal repeated cross-sectional study of sheep on six farms*. Preventive veterinary medicine, 2015. **122**(1-2): p. 107-20.

Objective 3: Describe the gross and histo-pathological changes associated with CODD lesions.

Diagnosis of CODD by vets and farmers was previously made using broad anecdotal descriptions. The objective here was to firstly, systematically and formally describe the clinical presentation of the disease in terms of 1) a lesion grading system; 2) associated radiographic changes and 3) severity of associated lameness. In the second part of this study the histopathological features of the disease were described along with immune-histochemical localisation of treponeme bacteria.

Part 1: A five-point lesion grading system was developed and applied to 908 sheep affected by CODD from six farms. Sheep with lesions typical of each grade were euthanased and their feet radiographed. Radiographic abnormalities including soft tissue and bony changes were evident in

feet with lesions graded 2-5.

In order to quantify the welfare impact of CODD, all the 908 sheep were locomotion scored. Five hundred and eighty-five (64.5% [95% CI 61.4-67.6]) were lame. The locomotion score for affected sheep increased with worsening pathological changes. Once healing had begun the locomotion score decreased.

In conclusion the 5-point grading system may be used to clinically describe stages of CODD lesions. The radiographic changes revealed examples of deeper pathological changes and there was a strong association between the lesion grading system and locomotion score in affected sheep.

Part 2: The three *Treponema* phylogroups *Treponema medium*/*Treponema vincentii*-like, *Treponema phagedenis*-like and *Treponema pedis* have been associated with clinical CODD. The aims of this study were: (1) to describe the histopathological changes associated with each previously established grade of clinical lesion, and (2) to investigate immunohistochemically the association of the *Treponema*-like organisms with the observed histopathological changes. Early lesions were characterized by lymphoplasmacytic infiltration of the distal digital skin, with suppurative coronitis and intracorneal pustules. In more advanced stages of the disease there was complete separation of the dorsal wall of the hoof with a necrotizing and fibrino-suppurative exudate and dermatitis. The later lesions were mostly resolved, but with milder suppurative changes remaining within the cornified layer and periosteal reaction of the dorsal aspect of the distal phalanx. Large numbers of *Treponema*-like organisms were identified within early grade lesions (as well as later, more advanced grade lesions) and were specifically associated with the observed histopathological changes. The results of this study provide some evidence in support of the hypothesis that the three CODD-associated *Treponema* phylogroups are involved in the aetiopathogenesis of this disease.

This objective was achieved in full, the work is published in the following scientific papers.

Angell, J.W., et al., *Clinical and radiographic features of contagious ovine digital dermatitis and a novel lesion grading system*. Veterinary Record, 2015. **176**(21).

Angell, J.W., et al., *A practical tool for locomotion scoring in sheep: reliability when used by veterinary surgeons and sheep farmers*. Veterinary Record, 2015. **176**(20):521-523.

Angell, J.W., et al., *Histopathological Characterization of the Lesions of Contagious Ovine Digital Dermatitis and Immunolabelling of Treponema-like Organisms*. Journal of Comparative Pathology, 2015. **153**(4): p. 212-226.

Objective 4: Determine the nature and value of the *Treponema* antibody response (for epidemiological and treatment studies) in CODD sheep.

The objective was achieved by employment of assays previously developed for use in digital dermatitis in cattle and sheep. This involved preparation of purified surface antigens from DD-associated treponemes as antigenic targets and usage of these to coat ELISA plates for detection of anti-treponeme antibodies in sheep sera from farms with and without sheep with CODD lesions. In addition, note was made of lameness and lesion scores to attempt to correlate to anti-treponeme antibody titres of individual sheep. The assay worked consistently and useful data was generated.

In the first survey, 153 sheep from North Wales and 41 sheep from a control farm (Leahurst – Ness Heath Farm; CODD-free) were bled and tested for serological reactivity with purified treponeme antigens. The sheep from North Wales were from 8 different farms with different numbers of CODD sheep with varying severity of lesions. The ELISA data clearly indicated that sheep in early to mid-stages of lesion development had the largest antibody response to treponeme antigens. In the later stages of disease, where the lesion was almost “burnt out”, the antibodies had regressed back to almost baseline. However, the bigger picture was that the majority of sheep with CODD were relatively poor immunological responders to treponeme antigens. This may well be indicative of the antibody response not only being weak in this disease but even when present merely being an indicator of a severe lesion with the highest treponeme infection load. Thus, as in cattle, it would appear that the development of DD lesions does not lead to generation of any form of protective immunity. This would explain why DD lesions in cattle and sheep recur. Consequently, whilst serological investigations are of interest in understanding disease pathogenesis and the lack of protective immunity, they are unlikely to be of value as an epidemiological tool for monitoring CODD in sheep on farms. This work is currently being prepared for submission to Veterinary Immunology and Immunopathology.

Objective 5: Assess efficacy of control strategies for CODD. These studies will be informed by the findings of the risk factor studies of Objectives 1 and 2 and results of bacterial culture and antibiotic sensitivity spectra from CODD lesions.

This objective was achieved through two studies. The first was a laboratory study of minimum inhibitory concentrations and minimum bacteriocidal antibiotic concentrations of a range of antibiotics against treponeme bacteria isolated from CODD lesions. The second part was a field based cluster-randomized control trial investigating the efficacy of whole flock tilmicosin treatment in the clinical elimination of CODD, footrot and lameness from sheep flocks.

Part 1: The three treponemal phylogroups *Treponema medium*/*Treponema vincentii*-like, *Treponema phagedenis*-like and *Treponema pedis* spirochaetes have been associated with clinical CODD lesions and are considered to be a necessary cause of disease. There is scant

data on the antimicrobial susceptibility of the treponemes cultured from CODD lesions. The aim of this study was to determine *in vitro* the MIC/MBC of antimicrobials used in the sheep industry for isolates of the three CODD associated treponeme phylogroups *T. medium*/*T. vincentii*-like, *T. phagedenis*-like and *T. pedis*. Twenty treponeme isolates from 19 sheep with clinical CODD lesions were used in the study.

A microdilution method was used to determine *in vitro* the MIC/MBC of ten antimicrobial agents for 20 treponeme isolates (five *T. medium*/*T. vincentii*-like, ten *T. phagedenis*-like and five *T. pedis*). The antimicrobials tested were penicillin G, amoxicillin, oxytetracycline, tilmicosin, lincomycin, spectinomycin, tylosin, tildipirosin, tulathromycin and gamithromycin. The treponeme isolates tested showed low MICs and MBCs to all ten antimicrobials tested. They were most susceptible to gamithromycin and tildipirosin (MIC₉₀: 0.0469 mg/L), and were least susceptible to lincomycin, spectinomycin and oxytetracycline (MIC₉₀: 48 mg/L, 24 mg/L and 3 mg/L respectively).

These data are comparable to *in vitro* antimicrobial susceptibility data for treponemes cultured from bovine digital dermatitis lesions. Dependent on local licensing, penicillin and tilmicosin appear the best candidates for future *in vivo* studies.

Part 2: The aim of this second part of Objective 5 was to evaluate the clinical success of whole-flock systemic tilmicosin in eliminating active CODD from sheep flocks for one year.

The trial was a two-armed, cluster-randomized controlled trial. A sample of 30 farms were recruited in the UK and randomly allocated to receive either treatment as usual or a whole-flock treatment with tilmicosin, together with isolation and extended treatment of clinically affected individuals. All farms were visited once at the beginning of the trial to examine all sheep. Sheep with foot lesions on the control farms were treated as per the farmer's normal routine. On the intervention farms, all sheep were treated with tilmicosin 10mg/kg subcutaneously, and those with clinical lesions were isolated and treated again 14 days later. Any new entrants to the intervention flocks during the study period were isolated and treated as well. One year later all the sheep were re-examined to determine the presence/absence of clinical lesions. The primary outcome was the clinical elimination of CODD from flocks. Secondary outcomes were the reduction in prevalence of CODD at flock level, the clinical elimination of footrot and the reduction in prevalence of footrot.

The final analysis included 11 control farms and 13 intervention farms, with initially 3,460 and 4,686 sheep respectively.

For CODD: at follow-up, in the intervention group 6/13 (46.2%) farms had a prevalence of zero compared to 1/11 (9.1%) in the control group (P=0.12).

For footrot: at follow-up, no farms had a prevalence of zero.

The intervention is not recommended for use for the elimination/reduction in prevalence of CODD or footrot.

The aims of this objective were fully achieved and are published in the following scientific papers:-

Angell, J.W., et al., *In vitro* susceptibility of contagious ovine digital dermatitis associated *Treponema* spp. isolates to antimicrobial agents in the UK. *Veterinary Dermatology*, 2015. **26**(6): p. 484-+.

Angell, J.W et al, "Whole-flock, metaphylactic tilmicosin failed to eliminate contagious ovine digital dermatitis and footrot in sheep: a cluster randomised trial."(Under Review *Veterinary Record*)

Objective 6: Disseminate outputs of project to veterinary surgeons, farmers and the scientific community through knowledge transfer program.

The group have been very proactive in disseminating the outputs of the project to the industry. We have formed close links with the red meat industry HCC and AHDB, the Sheep Veterinary Society and Farming Connect and presented our work at many national and international conferences.

Details of the work undertaken so far are listed below in the KE section.

In summary, from this BVAAWF funded research, these are the key messages on CODD that we are in the process of disseminating to vets and farmers

1. CODD
 1. Common, widespread **but not all farms affected**
2. Welfare
 1. Most severe form of sheep lameness
 2. Damage to deep tissues of foot and (bone)
3. Draw up plan with vet considering
 1. Diseases present
 2. Risk factors and patterns of diseases
 3. Resources available (time and money)
4. Biosecurity
 1. Draw up a biosecurity plan with your vet as part of your health plan
 2. Many farmers believe bought in disease with infected sheep
 3. Quarantine bought in sheep
 4. Not all sheep with CODD are lame therefore individually check feet on arrival
5. Treatment
 1. Individual or group basis
 2. Isolate affected sheep
 3. Treponeme bacteria susceptible to a number of antibiotics including penicillin and macrolide group (tilmicosin and LA amoxicillin) duration important –repeat treatments maybe required

4. Whole flock antibiotic treatment is not advised
5. Hoof Trimming- not advised for footrot- not studied in CODD but... infection could be spread on hoof trimming equipment

6. Footrot

1. Same risk factors as foot rot
2. Footrot itself big risk factor for CODD
3. Control footrot
 1. Five Point Plan
 2. Prompt Individual Treatment
 3. Footvax

7. Hygiene

1. Seasonal trend late summer/early autumn
2. Lowland pasture, lush pasture, poached pasture
3. Hoof knives ... infection could be spread on hoof trimming equipment

Were there any challenges or barriers/modifications to the project? Explain the nature of and reasons for any changes in project focus, scope, delivery, schedule or evaluation.

As discussed above, the only significant change was the early curtailment of the planned 2 year on-farm longitudinal study of 6 farms in Objective 2. This was finished early due to some farmers finding the gathering and examining of their whole flocks very time consuming. We had collected sufficient data at this stage and therefore it was decided to finish this project after 15 months and instead undertake a more ambitious treatment trial phase.

Provide details of knowledge transfer activities to date and any future plans/actions

On all presentations, publications, posters and events the sponsorship of the BVAAWF is clearly referred to by displaying the logo on all work and verbally thanking them for their support.

National and International Scientific Conference Presentations

Angell JW, Grove-White D, Carter SD, Blundell RB, Evans NE, Sullivan LE, Williams H, Clegg SJ, Crosby Durrani "Contagious ovine digital dermatitis, where are we now?" BCVA, Southport 2015

Angell, J.W, Williams H.W, .Carter S.D Grove- White D, Duncan J.S. "Contagious Ovine Digital Dermatitis in the UK, an Emerging Disease". 8th International Sheep Veterinary Society Congress, Rotorua, New Zealand 2013

Duncan, JS, Grove-White, D., Moks, E., Carroll, J., Oultram J.W, Phythian C.J and Williams H.W
“Effect of Footrot Vaccination on Footrot and Contagious Ovine Digital Dermatitis” 8th
International Sheep Veterinary Society Congress, New Zealand 2013

J.S. Duncan, J.W. Angell, L.E. Sullivan, S.D. Carter, N.J. Evans D. Grove-White “Lameness and
Contagious Ovine Digital Dermatitis in the UK.” European College Small Ruminant Health
Management Conference London 2015

J.S. Duncan, J.W. Angell, L.E. Sullivan, S.D. Carter, R.B Blundell N.J. Evans D. Grove-White
“Contagious Ovine Digital Dermatitis, what do we know now?” BCVA Conference Southport 2015

J.W. Angell, L.E. Sullivan, S.D. Carter, R.B Blundell, N.J. Evans, D. Grove-White, J.S. Duncan.
“Dealing with contagious ovine digital dermatitis in sheep – surely it’s just blue spray?” Hybu Cig
Cymru ‘ON-Farm 2016’ technical conference, Gelli Aur College, Carmarthenshire 2016.

J.W. Angell, L.E. Sullivan, S.D. Carter, R.B Blundell, N.J. Evans, D. Grove-White, J.S. Duncan.
“Dealing with contagious ovine digital dermatitis” Sheep Breeders Round Table, Nottingham
2015. 6 posters detailing the studies in more detail were presented for the duration of the
conference.

J.W. Angell, L.E. Sullivan, S.D. Carter, R.B Blundell, N.J. Evans, D. Grove-White, J.S. Duncan.
1) “A clinical and radiographic description of CODD”; 2) “Sheep and farm level factors associated
with contagious ovine digital dermatitis: A longitudinal repeated cross-sectional study of sheep on
six farms.” International Society for veterinary Epidemiology and Economics, Merida, Mexico
2015.

J.W. Angell, L.E. Sullivan, S.D. Carter, R.B Blundell, N.J. Evans, D. Grove-White, J.S. Duncan.
“Clinical and radiographic features of contagious ovine digital dermatitis (CODD) in 908 sheep
from six farms in North Wales and a lesion grading system.” Sheep Veterinary Society Autumn
Meeting, Shrewsbury 2014.

J.W. Angell, S.D. Carter, N.J. Evans, D. Grove-White, J.S. Duncan. “Contagious ovine digital
dermatitis – a questionnaire survey of 511 sheep farmers in Wales.” 17th International
Symposium and 9th International Conference on Lameness in Ruminants, Bristol 2013.

Farmer/Vet Meetings

In October 2015, we held a knowledge exchange day to disseminate the findings of the project. The meetings was for farmers (especially those who took part in the project), vets, industry representatives, researchers and vet students with over 70 people attending.

2016

J.W. Angell, L.E. Sullivan, S.D. Carter, R.B Blundell, N.J. Evans, D. Grove-White, J.S. Duncan. "Contagious ovine digital dermatitis, what do we know now?" BVA Lakeland Group.

J.W. Angell, L.E. Sullivan, S.D. Carter, R.B Blundell, N.J. Evans, D. Grove-White, J.S. Duncan. "Dealing with contagious ovine digital dermatitis – surely it's just blue spray?" National Sheep Association, Wales AGM, Builth Wells.

J.W. Angell. Talk on lameness in sheep to two farmers' meetings in Wales; Farming Connect

2015

J.W. Angell. Seminar on lameness in sheep, Liverpool Farm Animal Veterinary Students (LFAVS); University of Liverpool.

J.W. Angell. Practical seminar on lameness in sheep, Farm Animal Veterinary Students (FAVS) Congress; University of Nottingham.

J.W. Angell. Consultant for Menter a Busnes as part of their TAG project Ease of Data Collection work stream.

2014

J.W. Angell. Talks on lameness in sheep to 5 farmers' meetings in England and Wales facilitated by Farming Connect and AHDB Beef and Lamb.

J.W. Angell. Practical on-farm workshop on lameness in sheep to a vets/farmers' meeting; Park Vets, Cardiff.

2013

J.W. Angell. Expert advisor for the Farmers Weekly 'Stamp Out Lameness Campaign'.

J.W. Angell. Talk on lameness in sheep to veterinary surgeons in practice; Wern Veterinary Surgeons, Ruthin.

J.W. Angell. Talks on lameness in sheep to 3 farmers' meetings in Wales facilitated by Farming Connect.

J.W. Angell. Sheep lameness investigation and plan, and on-farm workshop for Abbey Farm, Llangollen- a farming Connect demonstration farm.

2012

J.W. Angell. Talk on lameness in sheep to a farmers' meeting in Wales facilitated by Farming Connect.

Articles in Farming Press

2016 AHDB Beef and Lamb: Joe Angell and Jennifer Duncan are consultants on the sheep industry standard guidance on management of lameness in sheep through the EBLEX Manual 7 "Reducing Lameness for Better Returns"

2016 National Sheep Association Annual Report – several reports and comments on our work in this magazine - picking up presentations from other reports and conferences.

2015 Gwlad, Wales: Stamping out lameness at Abbey – technical report on lameness in sheep including CODD.

2015 Daily Post, Wales: Sheep foot disease study in North Wales – report picking up information on *in vitro* MIC/MBC study.

2013 Farmers Weekly: Joe Angell was consultant for the Farmers' Weekly Stamp Out lameness Campaign resulting in a series of articles and case studies.

2012 Farmers weekly: J.W. Angell and J.S. Duncan "Take control of CODD in your flock"

Website

A website has been created detailing the outputs of the CODD research

<https://www.liverpool.ac.uk/infection-and-global-health/research/food-safety/codd/>

Future KE Activity

The work of KE is not yet complete with plans to write articles for Livestock, In Practice, Farmers Guardian and Farmers Weekly. We have plans to deliver presentations at the World Buriatrics Conference in 2016 and the International Sheep Veterinary Conference in 2017

Provide details of any original peer-reviewed research papers, book chapters and books/monographs that have resulted directly from your work supported by this grant.

1. Angell, J.W., et al., *Farmer reported prevalence and factors associated with contagious ovine digital dermatitis in Wales: A questionnaire of 511 sheep farmers*. Preventive Veterinary Medicine, 2014. **113**(1): p. 132-138.
2. Angell, J.W., et al., *Clinical and radiographic features of contagious ovine digital dermatitis*

- and a novel lesion grading system. *Veterinary Record*, 2015. **176**(21).
3. Angell, J.W., et al., *In vitro* susceptibility of contagious ovine digital dermatitis associated *Treponema* spp. isolates to antimicrobial agents in the UK. *Veterinary Dermatology*, 2015. **26**(6): p. 484-+.
 4. Angell, J.W., et al., A practical tool for locomotion scoring in sheep: reliability when used by veterinary surgeons and sheep farmers. *Veterinary Record*, 2015.
 5. Angell, J.W., et al., *Histopathological Characterization of the Lesions of Contagious Ovine Digital Dermatitis and Immunolabelling of Treponema-like Organisms*. *Journal of Comparative Pathology*, 2015. **153**(4): p. 212-226.
 6. Angell, J.W., D.H. Grove-White, and J.S. Duncan, *Sheep and farm level factors associated with contagious ovine digital dermatitis: A longitudinal repeated cross-sectional study of sheep on six farms*. *Preventive veterinary medicine*, 2015. **122**(1-2): p. 107-20.
 7. Duncan, J.S., et al., *Contagious ovine digital dermatitis: An emerging disease*. *The Veterinary Journal*, 2014. **201**(3): p. 265-268.
 8. Sullivan, L.E., et al., *Presence of digital dermatitis treponemes on cattle and sheep hoof trimming equipment*. *The Veterinary record*, 2014. **175**(8): p. 201.
 9. Sullivan, L.E., et al., *The Gastrointestinal Tract as a Potential Infection Reservoir of Digital Dermatitis-Associated Treponemes in Beef Cattle and Sheep*. *Applied and Environmental Microbiology*, 2015. **81**(21): p. 7460-7469.
 10. Sullivan, L.E., et al., *High-Level Association of Bovine Digital Dermatitis *Treponema* spp. with Contagious Ovine Digital Dermatitis Lesions and Presence of *Fusobacterium necrophorum* and *Dichelobacter nodosus**. *Journal of Clinical Microbiology*, 2015. **53**(5): p. 1628-1638.
 11. Sullivan, L.E., et al., *A molecular epidemiology of treponemes in beef cattle digital dermatitis lesions and comparative analyses with sheep contagious ovine digital dermatitis and dairy cattle digital dermatitis lesions*. *Veterinary Microbiology*, 2015. **178**(1-2): p. 77-87.
 12. Sullivan, L.E., et al., *Digital dermatitis treponemes associated with a severe foot disease in dairy goats*. *Veterinary Record*, 2014.

In preparation

1. J.W. Angell, D.H. Grove-White, H.J. Williams, J.S. Duncan "Whole-flock, metaphylactic tilmicosin failed to eliminate contagious ovine digital dermatitis and footrot in sheep: a cluster randomised trial."(*Veterinary Record*)
2. Hayley E. Crosby-Durrani, Simon R. Clegg, Ellen Singer, Joseph W. Angell, Nicholas J. Evans, Stuart D Carter, Richard Blundell, Jennifer S. Duncan. "Severe foot lesions in dairy goats associated with digital dermatitis treponemes: clinical presentation, radiography, pathology and the role of treponemes".(*Journal of Comparative Pathology*)

Have any other funding bodies been involved in supporting the development of the work supported by this grant?

The Welsh levy board Hybu Cig Cymru (HCC) funded the development of the locomotion scoring tool (£4175) Studying outbreak dynamics of lameness in sheep, associated with Contagious Ovine Digital Dermatitis (CODD) J.W. Angell J.S. Duncan D Grove-White

HCC and AHDB Beef and Lamb sponsored the laboratory work on the MIC and MBC's of the treponeme bacteria (£9,450) An Investigation of Treponeme bacteria and their antibiotic sensitivities from Contagious Ovine Digital Dermatitis Lesions. N.J. Evans, J.S. Duncan and J.W. Angell

University of Liverpool: (£3750) Characterisation Of The Pathological Changes Of Caprine Digital Dermatitis, A New Foot Disease Of Goats, Dr Jennifer Duncan, Dr Richard Blundell Ms Hayley Crosby

If any clinical trials been supported by the funding of this grant please enter the title of the trial and briefly describe any key developments or outcomes (Max 300 words)

This clinical trial is described above in Objective 5. As discussed above we were aware that vets and farmers were using whole flock metaphylactic tilmicosin for the control of lameness in sheep, including CODD and footrot. However, there was no scientific evidence base for this approach. The antibiotic used, tilmicosin is considered critically important by WHO for human health and its metaphylactic use in this way could be considered an irresponsible use of antibiotics. However, it can be argued that if the metaphylactic approach was able to eliminate disease from a flock, then the overall long term use of antibiotic would be reduced and that this approach could be justified. To determine if whole flock tilmicosin could eliminate footrot and CODD from sheep flocks we undertook the following clinical trial:

(The work has been submitted for publication to the Veterinary Record)

Whole-flock, metaphylactic tilmicosin failed to eliminate contagious ovine digital dermatitis and footrot in sheep: a cluster randomised trial.

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The trial was a two-armed, cluster-randomised controlled trial. A sample of 30 farms were recruited in the UK and randomly allocated to receive either treatment as usual or a whole-flock treatment with tilmicosin, together with isolation and extended treatment of clinically affected individuals. All farms were visited once at the beginning of the trial to examine all sheep. Sheep with foot lesions on the control farms were treated as per the farmer's normal routine. On the intervention farms, all sheep were treated with tilmicosin 10mg/kg subcutaneously, and those with

clinical lesions were isolated and treated again 14 days later. Any new entrants to the intervention flocks during the study period were isolated and treated as well. One year later all the sheep were re-examined to determine the presence/absence of clinical lesions. The primary outcome was the clinical elimination of CODD from flocks. Secondary outcomes were the reduction in prevalence of CODD at flock level, the clinical elimination of footrot and the reduction in prevalence of footrot.

The final analysis included 11 control farms and 13 intervention farms, with initially 3,460 and 4,686 sheep respectively.

For CODD: at follow-up, in the intervention group 6/13 (46.2%) farms had a prevalence of zero compared to 1/11 (9.1%) in the control group (P=0.12).

For footrot: at follow-up, no farms had a prevalence of zero.

The intervention is not recommended for use for the elimination/reduction in prevalence of CODD or footrot.

Use the space below for any other relevant information you wish to report on at this time

The AWF funded research project has resulted in significant benefits for the staff involved directly in the grant and for many others. Some examples are listed below:-

1.Hayley Crosby-Durrani, Farm Animal Pathology Resident

Hayley is the current Veterinary Pathology Resident at Liverpool Veterinary School. Through the AWF funded CODD research she has worked on the pathology and histopathology of CODD in sheep and a novel treponeme associated foot disease in dairy goats. The scientific publications she has produced from this work will go towards her submission for the European College of Veterinary Pathology Examinations this year. As a result of her involvement in the research group Hayley has now also been accepted to undertake a BBSRC/ Dairy Co funded PhD into Ischaemic Teat Necrosis in Dairy Cattle.

2.Leigh Sullivan EBLEX funded PhD

As a result of obtaining the AWF CODD funding, the research group we were successful in obtaining funding from EBLEX to support Leigh Sullivan in a PhD on "Identifying Digital Dermatitis Infection Reservoirs in Beef Cattle and Sheep." Leigh successfully completed her PhD in 2015 and has published many scientific papers (see above) and contributed enormously to the work of the AWF funded CODD research.

3.Veterinary Student Involvement in Research

Due to the large amount of on farm data collection undertaken in the study, the project required the assistance of many veterinary students over the four years and hopefully encouraged in them

an interest in veterinary research. Two third year students undertook their own research projects. One was a clinical trial on the efficacy of non-antibiotic foot bathing in the control of CODD. The second examined the effect of foot trimming on CODD cases. The pilot data from these projects will be used to inform larger scale projects already planned.

4. Links with the Farming and Veterinary Communities

Because of the large amount of on farm research carried out in the project, we required the support and co-operation of many, many farmers and the help of local veterinary practices. Over 500 farmers helped with the questionnaire and approximately 50 farmers took part in on-farm studies. Many of these farmers and their sheep benefitted greatly from the research in terms of substantially improved CODD control on their farms and contact with the research community at the vet school. Research links with several veterinary practices have also been established which continue to be mutually beneficial.