Final Report

Title

Summary sheet (up to two pages)

Short Title	**Unravelling the Aetiology of CODD** **Dr N Evans, Dr J Duncan, Dr D Grove-White, Dr S Carter**		
Start date	**January 2016**	**End date**	Jan 2020
AHDB Project Number			

Project aim and objectives
The central hypothesis for this study is that '***a specific microbial consortium is responsible for CODD'***. *Therefore the research proposal question is* ***'what are the key microorganisms responsible for CODD, how does the host immune system respond and what are their infection reservoirs?'.*** This study proposes to carry out substantial investigations of CODD lesions to identify the key microbes involved and characterise the host immune response to said microbes. Additional surveys of the host environment should allow for relevant farmer / veterinary guidelines to improve disease control. **Aims** ***1) To monitor transmission of CODD under experimental conditions between symptomatic and naive sheep.*** ***2) To evaluate the temporal changes to the ovine foot microbiome throughout the development of CODD to identify the key associated pathogens.*** ***3) To characterise sheep immune responses during the experimental flock CODD outbreak.*** ***4) To investigate the host environment and faeces for presence of disease associated micro-organisms during the flock CODD outbreak.***

Lead partner	University of Liverpool
Scientific partners	BBSRC
Industry partners	AHDB BEEF AND LAMB, HCC Meat Promotion Wales
Government sponsor	N/A

Has your project featured in any of the following?

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Events	• Meeting with AHDB Beef & Lamb and HCC to describe general research at UoL & further outline BBSRC IPA grant (Jan 7th 2016). • Presentation on sheep lameness at AHDB consultants meeting by Dr J. Duncan: 2016. • AHDB Beef and Lamb Webinar: J. Angell 2017: Contagious Ovine Digital Dermatitis (CODD) in sheep - What do we know now? • Presentations at farmers' meetings in England, Ireland, Wales and Scotland on lameness in sheep including contagious ovine digital dermatitis: J. Angell and J. Duncan: 2018-2019. • London Vet Show November 2018: J. Duncan presented: Lameness in Sheep- Effective Diagnosis and Treatment. • A workshop on Current Research on 'CODD on Sheep" to industry: J. Angell and J. Duncan: 2019. • Contagious Ovine Digital Dermatitis Research at Liverpool University J Duncan MSD Training Event February 2019 • CODD Webinar with National Sheep Association June 2020 • KE meeting to AHDB, HCC and other stakeholders to be organised for winter 2020.
Press articles	Angell, J. W., Grove-White, D. H., & Duncan, J. S. (2017). Contagious ovine digital dermatitis (CODD) - where are we now?. In CATTLE PRACTICE Vol. 25 (pp. 219-224) A practical approach to dealing with contagious ovine digital dermatitis (CODD) on farms. Joe Angell, Dai Grove-White, and Jennifer Duncan. Livestock 2017 22:1, 40-44. Duncan, J., Grove-White, D., & Angell, J. (2018). Understanding contagious ovine digital dermatitis. IN PRACTICE, 40(2). Control of infectious lameness in sheep. Jennifer Duncan and Joseph Angell. Livestock 2019 24:5, 246-251. Tackling CODD in sheep J Duncan for Farmer's Guardian planned July 2020
Conference papers, presentations or posters	Presentation at the Gordon's Biology of Spirochetes Conference, California, USA 2018 by S. Carter describing the various disease manifestations involving digital dermatitis treponemes. Contagious Ovine Digital Dermatitis – Where Are We Now?

	J.S. Duncan*, J.W. Angell, S.D. Carter, N.J. Evans, L.E. Sullivan, D. Grove-White. International Sheep Veterinary Congress Harrogate UK May 2017 Lameness in Sheep- Effective Diagnosis and Treatment. London Vet Show November 2018: J. Duncan Digital Dermatitis in Small Ruminants Sheep Goats J Duncan Ontario Small Ruminant Veterinary Congress June 2019
Scientific papers	Crosby-Durrani HE, Clegg SR, Singer E, et al. Severe Foot Lesions in Dairy Goats Associated with Digital Dermatitis Treponemes. J Comp Pathol. 2016;154(4):283-296. Angell, JW., Clegg, SR., Grove-White, DH., Blowey, RW., Carter, SD., Duncan, JS., Evans, NJ.(2017) Survival of contagious ovine digital dermatitis (CODD)-associated treponemes on disposable gloves after handling CODD-affected feet. Veterinary Record 181, 89. Clegg, S., Angell, J., Grove-White, D., Carter, S., Duncan, J., Evans, N., Blowey, R.(2017) Reducing lameness in sheep. Veterinary Record 181, 149. Angell, J. W., Clegg, S., Carter, S., Evans, N. J., Duncan, J. S., & Grove-White, D. (2017). Digital dermatitis-associated treponemes in a wound in a sheep. Veterinary Record, 180(18), 453. Staton et al., Novel leg lesions in yearling lambs: clinical features, microbiology and histopathology. Submitted to veterinary microbiology. Clegg, Angell et al., A reduced potential for lameness bacterial transmission by Lucilia sericata larvae and flies through metamorphosis. For submission to veterinary microbiology. Dissecting the microbiome of contagious ovine digital dermatitis: For submission to the ISME journal. Impact of CODD research on farming and veterinary practice: For submission to Veterinary Record
Levy communications	Work on CODD has been incorporated into the Sheep Industry National Guidelines on Control of Lameness in Sheep (AHDB Better

	Returns Manual Lameness in Sheep) https://ahdb.org.uk/knowledge-library/reducing-lameness-for-better-returns Reducing Lameness in Sheep J Duncan for AHDB Bulletin Article Planned July 2020
Social Media	• AHDB Beef and Lamb Webinar: J. Angell 2017: Contagious Ovine Digital Dermatitis (CODD) in sheep - What do we know now?
Websites	https://www.liverpool.ac.uk/infection-and-global-health/research/codd/

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Q1 Financial reporting

	Yes	No	N/A
Was the project expenditure in line with the agreed budget?	X		
Was the agreed split of the project budget between activities appropriate?	X		
If you answered no to any of the questions above please provide further details: N/A			

Q2 Milestones: Were the agreed milestones completed on time?

Project milestones	**Proposed completion date**	**Actual completion date**
Experimental CODD flock and CODD farm sampling	Months 1-12, 50% PDR.	Completed by Month 7.
qPCR assay development, DNA extraction & qPCR implementation	Months 1-12, 50% PDR.	Completed by Months 18.
Lesion metagenome generation & subsequent analyses	Months 13-18,100% PDR	Completed by Months 28.
Isolations, further qPCR development & implementation	Months 19-24 months, 50% PDR.	Completed by Month 28.
Environmental/faecal metagenome generation & subsequent analyses	Months 19-30, 50% PDR.	Completed by Months 38.
Immune responses, further isolations & qPCR assays	Months 25-36, 50% PDR.	Completed by Months 48.
Analyses completed and Manuscripts prepared	Months 31-36, 50% PDR.	Completed by Months 48.

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If any of the milestones above are incomplete/delayed, please provide further details:

Observing the transmission of the disease amongst the sheep flock took longer than expected. This had a knock-on effect as the length of the study produced many more samples than originally intended. Therefore, sample extraction and subsequent analyses took much longer. The result was rather than the project taking three years we were able to apply for a no cost extension to the BBSRC (and AHDB and HCC) which was granted so the work took four years to complete.

In addition appointed PDRs kept on gaining lectureships! A good outcome for the PDRs although this presented some delays for us. Joe Angell who completed the disease transmission study subsequently gained a tenure track fellowship at the University of Liverpool. Simon Clegg who completed the DNA extractions and initial qPCR development obtained a lectureship at the University of Lincoln. Project was completed by Gareth Staton.

Q3 Results: What did the work find?

1> Transmission of CODD in sheep was observed in a temporal manner and relevant samples collected on a weekly basis. In addition, transmission of interdigital dermatitis (scald) and footrot were also successfully tracked. Longitudinal clinical, microbiological and serological data/samples were collected from all observed animals (diseased and healthy).

2> In the majority of instances during this study disease progression frequently included scald and footrot prior to CODD suggesting better control of scald and footrot should allow for better control of CODD also.

3> Metagenomics of CODD feet exhibited a reduction of the foot microbiota diversity with key pathogens associated with disease. Significant association with the treponemes was seen in biopsy samples although this was weaker for swab samples.

4> qPCR assays identified increases in pathogen abundance during lesion presence especially for the digital dermatitis associated treponemes. Digital dermatitis treponemes were reported in a sheep wound for the first time.

5> Survival of contagious ovine digital dermatitis (CODD)-associated treponemes on disposable gloves after handling CODD affected feet. This is the first report of this key environmental source of digital dermatitis treponemes. The study also reports the successful use of simple cleaning products to remove contamination of gloves. In term of surveying insect contribution to transmission, whilst DD treponemes were present within maggots collected from lesions, lameness associated bacteria were not present after metamorphosis.

6> There was an association between infection and serological cross-reaction with digital dermatitis treponemes. Further work is now needed to determine whether this may be used as a diagnostic tool.

7> Other short projects included 1) better defining digital dermatitis in goats which demonstrated the importance of digital dermatitis treponemes, 2) characterising novel

leg lesions in yearling lambs: which identified both *Fusobacterium necrophorum* and *Streptococcus dysgalactiae* as likely key to aetiology.

Q4 Discussion: What do the results mean for levy payers?

The successful experimental transmission of CODD (inter-digital dermatitis and footrot) has furthered our understanding of the interrelationship between different infectious foot diseases. One clear message is that if you are better able to control scald and footrot then you should be able to reduce the presence of CODD on farm.

The glove disinfection paper indicates mechanisms for preventing transmission of bacteria between animals by using common chemicals found around a farmyard. This is the first time that this fomite (hands/gloves) has been identified as an infection reservoir for CODD. This is valuable knowledge for sheep and other livestock farmers, especially taken together with previous work where we demonstrated foot-trimming knives as an infection reservoir and epidemiological work by others indicating involvement of foot trimming in transmission. Maggots from CODD lesions contained DD treponemes whilst flies deriving from these larvae did not. This rules out the likelihood that the flies themselves are responsible for transmission.
Armed with more knowledge on the infection reservoirs of CODD- associated treponemes it should now be possible to better limit the spread of treponemes on farm.

Immunological data suggests infection is associated with an immune response to digital dermatitis treponemes and further work is needed to determine whether serology might be useful as a diagnostic for this important disease.

A similar disease to CODD exists in dairy goats and this could mean similar control methods could be used in sheep and goats.

Novel leg lesions in yearling lambs which may initiate through environmental trauma appear to have both *Fusobacterium necrophorum* and *Streptococcus dysgalactiae* as key to aetiology which should help inform treatment and control in the future.

Q5 New knowledge: What key bit of new knowledge has come out of this project?

The presence of contagious ovine digital dermatitis treponemes on gloves and their survival on this niche indicate this as an important, novel infection reservoir that would quickly come into contact with further (potentially damaged) feet in quick succession. We identify removal of these pathogens using common farmyard chemicals such as hand soap which should prevent this route of disease transmission.

Based on this current study and previous epidemiology work from the University of Liverpool it would appear that footrot is important in the development of contagious ovine digital dermatitis. Therefore, effective control of footrot should help reduce the presence of contagious ovine digital dermatitis in sheep flocks.

Q6 Gaps in knowledge: What gaps in knowledge has this project identified?

Further work is needed to determine persistence of contagious ovine digital dermatitis treponemes on different bedding types. Work towards a vaccine against the digital dermatitis treponemes should allow for reduction in disease. Further studies into whether serology can be useful for disease diagnostics. Further studies to dissect transmission between different hosts such as sheep and cattle.

Q7 Additional deliverables: What activity is planned with the results from this project?

Activity	What is planned?	When likely to happen?
Events	KE meeting to AHDB, HCC and other stakeholders to be organised.	Winter 2020
Press articles	We hope to disseminate another press article	Spring/Summer 2021
Conference papers, presentations or posters	0	Pandemic has closed most meetings down in the near future.
Scientific papers	Dissecting the microbiome of contagious ovine digital dermatitis: For submission to the ISME journal.	Spring 2021.
Levy communications	-	-
Social Media	-	-
Other	-	-