Institution:
UNIVERSITY OF LIVERPOOL

Unit of Assessment:
UOA6 - Agriculture, Veterinary and Food Science

Title of case study:
Diagnosis and Control of Neosporosis in Cattle

1. Summary of the impact

The parasite *Neospora caninum* is the leading cause of abortion in cattle in the UK, resulting in around 6,000 abortions per year; and a $1.3b pa international problem. There are no effective drugs or vaccines to control neosporosis. University of Liverpool (UoL) research on the development of diagnostic tests, understanding the pathogenesis, epidemiology and transmission of *N. caninum* has made an important contribution to developing best practise herd health schemes, now offered by the Animal Health and Veterinary Laboratories Agency (AHVLA) and by a commercial company 'myhealthyherd', to eradicate *N. caninum* infection from a herd. This has enabled cattle farmers to improve their businesses by reducing abortion rates and other costs associated with neosporosis.

2. Underpinning research

N. caninum is an important protozoan parasite infecting cattle and dogs. It has its most serious effects in cattle where it is considered responsible for 6,000 abortions per year in England and Wales alone. Worldwide farming losses in 2013 were estimated to be $1.3b; two thirds of those losses occurring in dairy cattle and one third in beef. In dairy cattle, global data indicates that 16% of dairy cattle are seropositive, that figure rising to over 40% in aborting cows.

Research on neosporosis at the UoL was initiated by Professor Sandy Trees (retired 2011), who isolated *N. caninum* for the first time in Europe; a description of this isolate was published in 1995 and led to development of a diagnostic ELISA [1]. This serological test was aimed specifically at diagnosing *Neospora*-associated abortions, but was adapted and validated by UoL for surveillance purposes and subsequent epidemiological work stemmed from development and application of this test.

The serological ELISA test was commercialised in collaboration with a local Merseyside biotechnology company (Mast Diagnostics) and adopted by AHVLA in 1999. Between 1996 and 2010, with funding from several sources including industry, all listed in section 3, UoL Professors Sandy Trees and Diana Williams (1994-present) produced the first analysis of the relative importance of vertical transmission compared to post-natal infection of cattle by showing that in normally calving *N. caninum* infected cattle, transplacental transmission occurred in 95% of pregnancies, and that an infected animal was 7 times more likely to abort compared to uninfected cattle [2].

In 1999, the UoL group showed that most infected cattle harbour chronic infections, most likely to have been acquired congenitally and that post-natal infection was a relatively rare event. UoL research followed this up in 2009 by demonstrating that abortion storms associated with *N. caninum* are more likely to be associated with post-natal exposure of pregnant cattle to oocyst infection [6], complementing a prior study in 2007 which showed that oocyst infection could lead to exogenous transplacental transmission (with or without abortion) but significantly did not lead to persistent infections and subsequent endogenous transplacental transmission [5].

The group developed an experimental challenge system to test the efficacy of potential vaccines in protecting against abortion, developing a highly effective but not commercially viable live vaccine [3,4]. Using this experimental challenge system and infecting cattle at different times during gestation, research showed that the parasite was more likely to cause abortion early in gestation and that this is linked to foetal immuno-competence.

3. References to the research

1. **Williams DJL**, **Davison HC, McGarry J**, Helmick B, Guy F, Douglas P, Hogben D, Otter A and **Trees AJ**. (1999) Evaluation of a commercial ELISA for detecting serum antibody to Neospora caninum in cattle. Veterinary Record 145, 571-575. Citations: 26 Impact Factor: 1.803

2. **Davison HC**, Otter A and **Trees AJ**. (1999) Estimation of vertical and horizontal transmission parameters of Neospora caninum infections in dairy cattle. International Journal for Parasitology, 29, 1693-1689. Citations: 168 Impact Factor: 3.637

3. **Williams DJL**, **Guy CS**, **McGarry JW**, **Guy F**, **Tasker L**, **Smith R**, **MacEachern K**, **Cripps PJ, Kelly DF and Trees AJ**. (2000) Neospora-associated abortion in cattle: the time of experimentally-induced parasitaemia during gestation determines foetal survival. Parasitology 121, 347-358. Citations: 125 Impact Factor: 2.355

4. **Williams DJL, Guy CS**, Ellis JE, **Smith RF**, Bjorkman C and **Trees AJ**. (2007). Immunisation of cattle with live tachyzoites of *Neospora caninum* confers protection against foetal death. Infection and Immunity 75, 1343-1348. Citations: 55 Impact Factor: 4.074

5. **McCann CM**, McAllister MM, Gondim LF, **Smith RF**, **Cripps PJ**, **Kipar A**, **Williams DJL** and **Trees AJ.** (2007). *Neospora caninum* in cattle: experimental infection with oocysts can result in exogenous but not endogenous transplacental infection. International Journal for Parasitology 37, 1631-9 Citations: 14 Impact Factor: 3.637

6. **Williams DJL**, **Hartley CS**, Bjorkman C and **Trees AJ**. (2009) Endogenous and Exogenous Transplacental Transmission of Neospora caninum – how the route of transmission impacts on epidemiology and control of disease. Parasitology 136, 1895-1900. Citations: 31 Impact Factor: 2.355

Key grants

1996-1999. **BBSRC**. The immunopathology of bovine neosporosis, £238,744, PI **AJ Trees**. £238,744

1998 – 2001. **Milk Development Council**. *Neospora* associated abortion in dairy cattle, £178,900, PI **AJ Trees**.

1996 – 1999. **Ministry of Agriculture Fisheries and Food**. Towards the improved diagnosis, prognosis and control of neosporosis in cattle, £217,706, PI **AJ Trees**.

2001– 2004. **European Union**. Epidemiology and Diagnosis of Bovine Neosporosis in Europe, £107,323 (UoL element), PI **DJL Williams** (and 6 other European partners).

2001–2006. **Novartis Animal Vaccines Ltd**. Vaccination against *Neospora*-associated abortion in cattle, £399,480, PIs **AJ Trees** and **DJL Williams**.

2002-2005. **Department of the Environment, Food and Rural Affairs**. Bovine neosporosis: the evaluation of zoonotic risk and the development of evidence-based control strategies, £231,880, PI **AJ Trees**

2002–2007. **Wellcome Trust**. Protective type 1 helper T cell responses induced by *Neospora caninum* infection are detrimental to the maintenance of pregnancy in cattle, £323,000, PI **DJL Williams**.

4. Details of the impact

The Liverpool team has used their research findings to create significant economic benefits for the UK's cattle industry by collaborating directly with AHVLA and Myhealthyherd to design herd health schemes to reduce the economic impact of *N. caninum*. The main beneficiaries of the research are UK dairy farmers, who now have access to information, which enables them to control the disease in their herds and mitigate the massive economic and emotional impact of an outbreak of neosporosis.

Research conducted by the Liverpool team has led to a better understanding of the immunopathogenesis, life cycle and transmission of the parasite together with improved, commercially available diagnostics. As a consequence, as key participants in AHVLA working groups, Williams and Trees were involved in designing herd health schemes to improve control of disease. In 2008/9, two schemes were launched, one a commercial scheme, Myhealthyherd, and the other, AHVLA's Herdsure scheme [7], both based on advice on reducing transmission built on research done at University of Liverpool. A series of roadshows, delivered by Professor Trees in 2008-9 was used to publicise these accreditation schemes. To ensure the widest possible reach, these DEFRA funded roadshows targeted hundreds of veterinarians each of whom were asked to hold multiple farmer meetings. These schemes focus on identifying infected animals within a herd and strategically managing breeding programmes and heifer replacement regimes to reduce the number of infected cows entering the milking herd. Within these programmes, regular nationwide surveillance using bulk tank milk antibody tests are used to monitor levels of *N. caninum* infection within herds typically through NMR/NML. Biosecurity measures including quarantine testing, control of dogs on the farm and covering feed stores to reduce risk of contamination are recommended to control the spread of infection. There has been widespread publicity and it has even featured on the popular BBC 4 soap opera, the Archers.

The team's research into abortion storms and quantifying the risk of post-natal exposure to infection have led to an increase in our understanding of frequency of different routes of transmission of *Neospora*. In addition, advisory meetings were held with AHVLA in 2008 to assist in developing its herd health farm assurance scheme prior to its launch in 2009/10. Information about these two schemes are disseminated to dairy farmers through the farming press, advisory information sent out by AHVLA and through a private scheme with a dedicated website. The Herdsure Neospora protocol has also been accepted under the CHeCS scheme (Cattle Health Certification Standards; an organisation owned by the BCVA, National Cattle Association (dairy), the National Beef Association and Holstein UK [8].

Beneficiaries of these health schemes are dairy farmers in UK. Effective measures to reduce levels of infection within the herd, to protect cows from introduction of *N. caninum* into the herd, through biosecurity measures and to reduce the potential of spread within the herd via dogs, the definitive host for the parasite, all contribute to reducing abortion rates and other costs, such as reduced fertility, associated with neosporosis. By obtaining herd health accreditation or joining 'myhealthyherd,' farmers can create their own herd health plans in conjunction with their vets, manage infectious disease, work out profit opportunities and obtain a Health Visa or herdhealth accreditation, to maximise the sale value of stock. To date, over 5,000 farms now use "Myhealthyherd" in England and Wales – to provide context there are c 14,500 dairy farms in the UK. The knowledge gained from UoL research, together with outputs from other groups, has had an impact on control of neosporosis worldwide.

5. Sources to corroborate the impact

Each source listed below provides evidence for the corresponding numbered claim made in section 4 (details of the impact).

7. AHVLA Herdsure website on effectiveness of its neosporosis programme. *http://www.defra.gov.uk/ahvla-scientific/2010/0903herdsure-launches-first-uk-service-neosporosis/*

8. CHeCS scheme. www.checs.co.uk.

9. The following individuals can confirm the impact of the UoL research to cattle health improvement schemes in the UK.

10. Contact: AHVLA. Individual was responsible for developing the herd health scheme of the AHVLA.

11. Contact: Myhealthyherd.