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Genetic and non-genetic congenital defects in the Irish national cattle population

Key external stakeholders:
Vets, farmers and advisors.

Practical implications for stakeholders:
The outcome/technology or information/recommendation is that a National Congenital Defects Register be set up to monitor known congenital defects and to detect the occurrence of new/emerging defects.

- A national coordinated approach to classifying, recording, testing and reporting on congenital defects will allow differentiation of genetic from non-genetic defects and consequent control strategies such as changes to sire usage or infectious pathogen management to be implemented.

Main results:

(1) The establishment of a pilot study portal for farmers and others to report congenital defects in cattle (mainly calves) showed that this approach is feasible as a passive surveillance national register in live and dead dairy and beef calves.
(2) The prevalence of certain defects (e.g. blocked bowel/intestinal atresia) at the herd-level was much higher than previously thought (considered as sporadic and uncommon).
(3) DNA samples from 206 calves with blocked bowel/intestinal atresia were genotyped; 139 with the HD SNP chip and 67 with the IDB chip to identify genes associated with the defect, the first time this analysis has been run on such samples.

Opportunity / Benefit:
Through the scientific and other publications listed here.

Collaborating Institutions:
UCD,
ICBF,
DAFM,
AgResearch, New Zealand.

Teagasc project team: Dr. John Mee (PI)
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1. Project background:

Bovine congenital defects (CD) are grossly under-diagnosed and reported internationally. This is because there is no coordinated reporting infrastructure, in contrast to those set up for human congenital defects

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(WHO, 2005). In the absence of such a register the extent of occurrence of these conditions is grossly underestimated. This was clearly shown by recent Moorepark research which, using a whole-herd active surveillance study design found congenital defects in all Irish dairy herds studied. This lack of a recording system has led to the gross under-diagnosis of congenital defects in both the Irish dairy and beef cattle populations.

2. Questions addressed by the project:

This project set out to answer the following questions: (1) what is the current state-of-the-art in the scientific literature on bovine CD (2) is it possible to set up a national pilot dairy and beef animal CD register (3) what are the risk factors, pathology and non-genetic causes of the common CDs (4) what are the possible genetic causes of the most common CDs recorded in the CD register.

3. The experimental studies:

Literature review – a literature review on the epidemiology, pathology and causes of common bovine CDs was conducted

Register – a national register was set up within ICBF by ICBF, Teagasc and DAFM. It involved both a telephone/text hot-line and survey questionnaire in ICBF and annual returns from the six veterinary laboratories of DAFM and the Moorepark Postmortem Laboratory. In addition, a photo gallery was compiled and set up on the ICBF website to assist farmers in identifying CD cases. Awareness raising amongst stakeholders was conducted through photo-articles in the *Irish Farmers Journal*.

Risk factors, pathology and non-genetic causes of common CDs - The most common CD recorded was intestinal atresia – a common SOP was devised in Moorepark and shared with veterinary pathologists in the RVLs to standardise recording and the PI visited the RVLs multiple times annually to examine formalin-stored case material.

Genetic causes - for the most common CDs recorded in the CD register, (a) pedigree analysis and (b) genomic analyses were conducted.

4. Main results:

Register – Of 279 CD cases reported, 72% were from farmers and the remainder from non-animal owners (e.g. vets). The three most frequently affected systems were abdominal/internal/genital/anus (48%), appendicular skeleton (33%) and head and neck (21%). The most common individual CD reported was intestinal atresia (15%). These results were confirmed from both the six DAFM veterinary laboratories and the Moorepark Postmortem Laboratory; intestinal atresia was recorded in 55% of DAFM cases of CD in dairy and beef carcasses compared to cardiac defects in 33%.

Risk factors, pathology and non-genetic causes of common CDs – the predominant type of atresia occurring in the Irish national herd (atresia jejuni) appears to be different from that reported in the literature (atresia coli). Results indicate that herd, sex and parity are significant risk factors. The putative non-genetic causes internationally (e.g. early pregnancy diagnosis embryonic attrition, phyto-toxins) do not appear to be as relevant in the Irish management systems suggesting a possible genetic basis.

Genetic causes - for the most common CDs recorded in the CD register the possible genetic causes were explored. While certain sire breeds and certain sires were over-represented in cases vs control calves, deep pedigree analyses are required to confirm these relationships. For intestinal atresia cases phenotyped in Moorepark, 139 cases were genotyped with the HD SNP chip, 67 cases were genotyped with the IDB chip and 6 exemplar cases were submitted for whole genome sequencing. Results are awaited from the external laboratory.

5. Opportunity/Benefit:

The results of this study show the potential benefits associated with a national coordinated approach to classifying, recording, testing and reporting on congenital defects as this affords the opportunity to differentiate genetic from non-genetic defects and to implement consequent control strategies such as changes to sire usage or infectious pathogen management.

6. Dissemination:

Main publications:

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Mee, J.F. (2020) Congenital defects in calves. In: *Neonatal and Perinatal Bovine Medicine* (in press)
Mee, J.F., Sen, I., Aytmirza, A., Abdusalam Uulu, N. and Tas, A. (2019) Risk factors for, and causes of, perinatal calf mortality and implications for calf welfare. *Manas Journal of Agriculture, Veterinary and Life Science*, 9: 35-41.
Mee, J.F., Sanchez-Miguel, C., and Doherty, M. (2015) Influence of modifiable risk factors on the incidence of stillbirth/perinatal calf mortality in dairy cattle. *The Veterinary Journal*, 199: 19-23.

Popular publications:

Mee, J.F. (2019) Investigating bovine fetopathy. *Proceedings of the Ontario Association of Bovine Practitioners Seminar on Reproduction in Practice*, Guelph, Canada, p.1-7.
Mee, J.F. (2019) Morbidity and mortality in extensively reared beef calves. *Proceedings of the XXIV Congreso International Anembe de Medicina Bovina,* Sevilla, Spain, p. 120-126
Mee, J.F. and Kenneally, J. (2019) Causes of death in calves – how accurate is our diagnosis? *Moorepark Open Day Book '19*, p. 161-162.
Mee, J.F. (2018) Calving and calf health. *Teagasc Manual on Calf Rearing*, p. 301-303.
Mee, J.F. (2018) Calf health – Progress to date, current priorities and future perspectives. *Proceedings of the 50th Congresso Nazionale della Societa Italiana de Buiatria*, Bologna, Italy, p. 30-32.
Mee, J.F. (2017) Congenital malformations – why do bovine and human prevalences and typologies differ so much. *Proceedings of the European Buiatrics Forum*, Bilbao, Spain, p.159
Mee, J.F. and Kenneally, J. (2017) Why do calves die at calving and what can you do about it? *Moorepark Open Day Book*, p. 150-151.
Mee, J.F., Sanchez-Miguel, C. and Doherty, M. (2017) Causes of stillbirth and perinatal mortality in dairy calves: a prospective whole-herd, necropsy study. *Proc. World Association of Veterinary Laboratory Diagnosticians*, Sorrento, Italy p. 174.
Mee. J.F. (2017) Survive to 5 – can we keep more newborn calves alive? *Progressive Dairyman Canada*, 2: 26-26.
Mee, J.F. (2017) Congenital anomalies – an interspecies comparison using Irish human and bovine datasets. *Proc. International Stillbirth Association*, Cork, p. 94-95.
McClure, J. et al., (2017) Bovine genetic disease and trait frequencies in Ireland: >85 causative alleles in >1M animals. *Proc. European Association for Animal Production*, Tallin, Estonia, p. 138.
McClure, J. et al., (2017) Searching for, finding, and fixing genetic disease: we can't afford not to. *Proc. European Association for Animal Production*, Tallin, Estonia, p. 142.
McClure, M and McClure J. (2017) Understanding genetics and complete genetic disease and trait definition. www.icbf.com
McClure et al., (2017) A mammary missing her mammaries and other interesting genetic defect information in Irish cattle. *Proc. Cattle association of Veterinary Ireland*, Cork, p.130-131.
Murphy, C. (2017) Deformed calves in the spotlight, *Irish Farmers Journal*, Feb 4. p. 16
Murphy, C. (2017) Udderless heifers cost farmer €20,000. *Irish Farmers Journal*, Mar 25, p. 16.
McClure, J. (2017) Still looking for genetic defects! www.icbf.com
Mee, J.F. (2016) Bovine abortion/stillbirth investigation: a practitioner-focused approach. *Proceedings of the 29th World Buiatrics Congress*, Dublin, p. 93-96.
Mee, J.F. (2015) Congenital defects in calves – are we missing them and if so does it matter? *Cattle Practice*, 23: 369.
Mee, J.F. and Kenneally, J. (2015) Update on the latest calf mortality research at Moorepark. *Irish dairying – Moorepark Open Day Book*, 2015, p. 110-111.
Mee, J.F. (2014) Neonatal orphan disease syndromes – enigmatic challenges for the veterinary practitioner. *Proceedings of the 28th World Buiatrics Congress*, Cairns, Australia, p. 199-203.
Mee, J.F. (2014) Intestinal atresia in calves – new insights. *Proceedings of the PPP Symposium*, Bern, Switzerland, p.4
Mee, J.F. (2014) Are congenital defects much more common than we think? *Proceedings of the 28th World Buiatrics Congress*, Cairns, Australia, p. 84.
Mee, J.F. (2014) Intestinal atresia in dairy calves. *European Pathosurveillance Network Autumn Symposium*, Backweston, p.2.
Mee, J.F., McElroy, M., Sheehan, M., Johnson, A., Fagan, J., Gomez-Parada, M. and O.Muireagain, C. (2014) Preliminary results from a national congenital defect surveillance study on intestinal atresia in calves. *Cattle Practice*, 22|: 286.

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