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Ruminant health research – progress to date and future prospects, with an emphasis on Irish research

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Abstract

This review addresses the progress that has been made in ruminant health research over the last 60 yr, with an emphasis on Irish research. The review focuses on the economically important infectious diseases of dairy and beef cattle and of sheep, calf diseases, regulated and non-regulated infectious diseases, lameness, mastitis and parasitoses. The progress to date, current knowledge and future challenges are all addressed. Paradigm shifts have occurred in many of these diseases, the most profound of which is the change from increasing antimicrobial usage (AMU) to the realisation of the challenge of antimicrobial resistance (AMR) and the current reduction in AMU. Another major change in thinking is the move away from focus on the pathogen exclusively towards a more holistic view of the roles of host immunity and adequacy of management. In the last 60 yr, many new diseases have emerged but in parallel many new technologies have rapidly evolved to monitor and control these threats to animal health. Irish research has contributed substantially to improved current ruminant health. The major future challenge is how to manage ruminant health in a OneHealth world where animal, human and environmental health and sustainability are intimately intertwined and interdependent.

Keywords

Beef • dairy • health • review • sheep

Introduction

Given that this is the 60th anniversary of the *IJAFR*, this paper reviews the progress we have made in ruminant health research over the past half-century, the state-of-the-art today and to horizon scan where developments might take us in ruminant health over the next half-century, where have we come from and where are we going? Both cattle enterprises (dairy and suckler-beef) and sheep are covered. The focus is on animal health, to the exclusion of animal welfare, which is included in the companion paper by Boyle *et al.* (2022). However, this publication dichotomy does not imply the authors believe these subjects are separate; on the contrary, the clear linkages between animal health, wellbeing and productivity are accepted and improvements in one domain improve other domains. Given the scale of the undertaking, reviewing 60-yr research and projecting forward, much of the focus is Irish or Euro-centric, though not exclusively. The major, economically important ruminant health issues, as defined by a Delphi study of Irish agricultural stakeholders (More *et al.*, 2010), are addressed in the alphabetical order: calf health (dairy and beef separately), infectious diseases (both regulated and non-regulated [brucellosis, bovine viral diarrhoea (BVD), bovine tuberculosis (bTB), infectious bovine rhinotracheitis (IBR), Johne's disease (JD) and the transmissible spongiform encephalopathies]), lameness and mastitis (with a focus on control; selective dry cow therapy and antimicrobial use), parasitoses (nematodes, liver and rumen flukes and external parasites) and sheep diseases (causes of mortality, lameness, maedi visna, mastitis, ovine pulmonary adenocarcinoma, pestiviruses and Q-fever). Given the importance of antimicrobial resistance (AMR), it is dealt with under the specific major disease of import separately: calf morbidities and mastitis.

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Calf health research

Given that most of the literature on calf health tends to be enterprise-specific, that is, dairy or beef, we have documented this research separately.

Dairy calf health research

In the interests of brevity, only salient issues are addressed here; for broader recently published narratives on dairy calf health, see Mee (2021a) and Lorenz (2021). Each topic is reviewed under current knowledge, future challenges and knowledge gaps.

Perinatal dairy calf health

Perinatal dairy calf mortality rates (death at full term, >260 d, within 48 h of birth) have improved (declined) in Irish dairy herds in recent years (Mee *et al.*, 2008; Ring *et al.*, 2018a). Though difficult to quantify, genetic selection against dystocia, stillbirth and prolonged gestation using functional genetic selection indices (Miglior *et al.*, 2017) has contributed to a reduction in perinatal problems where selection pressure has been intensive enough (Mee, 2021b). In recent years, our knowledge of perinatal health has advanced beyond the peripartum period. For example, our current knowledge indicates that foetal programming and calfhood performance (e.g. Hayes *et al.*, 2021) have significant impacts on lifetime productivity (Berry *et al.*, 2008), reproductive performance (Cushman & Perry, 2019), health (Perry *et al.*, 2019) and longevity (Berry *et al.*, 2008). Sixty years ago, perinatal health research was confined to effects in humans, for example, the Barker hypothesis (Barker *et al.*, 1989).

The day (Borchers *et al.*, 2017; Horvath *et al.*, 2021) and, to a lesser extent, the time (Titler *et al.*, 2015) of calving can now be predicted with commercially available technologies or algorithms (Fenlon *et al.*, 2017). However, these advances are not without problems with some of these technologies (Mee *et al.*, 2019; Voß *et al.*, 2021). While heretofore movement of cows to the calving unit was recommended within 1–2 d pre-calving (Mee, 2008), recent research has identified a sensitive phase during Stage 1 of calving when movement can be detrimental to cow and calf calving outcomes (Proudfoot, 2019). The behavioural needs of the cow pre-calving have now been incorporated into novel calving accommodation strategies which provide optional seclusion in group calving units to facilitate a more "natural" calving (Proudfoot, 2019).

Current knowledge of timed assistance (Schunemann *et al.*, 2011) suggests that early prudent assistance at calving may not be injurious to the calf or adversely affect the dam (Villettaz Robichaud *et al.*, 2017), though replication of such results is needed.

On the perinate side, the impacts of both calving duration and calving difficulty on perinate vitality have been elucidated (Villettaz Robichaud *et al.*, 2017; Mee, 2021c), and various methods of perinatal vitality biophysical profiling have been established (Murray & Leslie, 2013). Calf resuscitation policies have been evaluated (Mee, 2018a) using various techniques (Stilwell *et al.*, 2020), equipment (Ando *et al.*, 2013) and medications (Ravary-Plumioen, 2009) to revive/resuscitate newborn calves; the simple stratagem of sternal recumbence is still paramount (Uystepruyst *et al.*, 2002). The epidemiology (Raboisson *et al.*, 2013), investigation (Mee, 2020a), immunology (Jawor *et al.*, 2017), microbiology (Mee *et al.*, 2021), pathology (Mock *et al.*, 2020) and control (Szenci *et al.*, 2012) of perinatal mortality have all been advanced.

While congenital defects were traditionally documented as case reports (Mee, 1994), increasingly the epidemiology (Whitlock *et al.*, 2008; Romero *et al.*, 2020), pathology (Gehrke *et al.*, 2019) and aetiology (Mee, 1995; Reinartz & Distl, 2017) of such cases are presented so that our current knowledge has advanced from the singular to the population level. Current advances in genetic diagnostics (Sieck *et al.*, 2020) have added greatly to our understanding of the causes of some of these defects and ultimately their prevention. This area is continually evolving as new causes of congenital anomalies are discovered, for example, Schmallenberg virus (Collins *et al.*, 2019).

Our current knowledge of navel antisepsis in newborn dairy calves indicates that when compared to positive controls in recent randomised controlled trials (RCTs), iodine (7%) (the most commonly used product) performed similarly, though not better (Wieland *et al.*, 2017; Bruno *et al.*, 2018), and results were dependent upon environmental hygiene (Fordyce *et al.*, 2018).

Given the importance of colostrum to the health of the newborn calf and beyond the perinatal period, it is not surprising that there has been an explosion in "colostrology" (Lora *et al.*, 2018) regarding, for example, colostrum quality (Quigley *et al.*, 2013) and hygiene (McAloon *et al.*, 2016a, 2016b, 2016c) over the last 60 yrs. In the early days of colostrum evaluation, a colostrometer (measuring specific gravity) was used (Geiger, 2020), but this has now largely been surpassed by the current optical or electronic Brix refractometers (Lopez *et al.*, 2021). Current recommendations on the volume of colostrum to feed dairy calves are based on body weight, but baseline volume is now larger (4 L) than in the past (Geiger, 2020). This probably reflects larger Holstein calves and the need for higher serum Ig concentrations on modern intensive dairy farms. While traditionally suckling the dam was recommended, then nipple feeding, latterly oro-oesophageal feeding has become a recommended method of colostrum feeding (Godden *et al.*, 2009; McAloon *et al.*, 2021). Though laboratory-based tests for evaluation of passive immunity have been available for decades (e.g. sRID test; McGee and Earley, 2019), recently more practical tests have been developed and compared (Dunn *et al.*, 2018), and thresholds for failure of passive transfer (FPT) are constantly being re-evaluated (Lombard *et al.*, 2020). The development of artificial colostrum has been a qualified success with highly variable results (Mee *et al.*, 1996; Geiger, 2020). While the focus of this paper is on health, the companion paper by Boyle *et al.* (2022) has addressed welfare outcomes of FPT.

Currently, snatch calving (immediate removal of the newborn calf from the dam and calving environment) is a recommended management practice on dairy farms to reduce the risk of infection (especially from *Mycobacterium avium* subspecies *paratuberculosis* [MAP]) in the perinate from a contaminated calving environment (Mee, 2020b), though public perception is now causing a re-evaluation of this practice (Beaver *et al.*, 2019; Placzek *et al.*, 2021).

The future challenges in perinatal dairy calf health research stretch from genomics to farm blindness (Mee, 2020b). Given our current knowledge of the adverse effects of foetal programming, we need to be able to modify this programming so that its impacts are beneficial not detrimental. The impacts of environmental and nutritional factors on foetal development and calf survival have been reviewed recently (Mee, 2021a). Advances in genomics will need to target more refined adverse perinatal phenotypes, for example, weak calf syndrome. The enigma of the "unexplained stillbirth" (Mee, 2013) requires further exploration. Specifically, the role of factors not easily diagnosable at routine necropsy examinations need to be examined, for example, genetic, nutritional and management causes. We need reliable, cost-effective automated methods of monitoring both the dam pre- and intra-partum and her at-risk foetus during and immediately after birth. Translating advanced paediatric resuscitation into the calving pen is a real challenge. Routine low-cost screening for a wider range of deleterious inherited mutations should be a norm within both the beef and the dairy industries. Better preventive protocols for navel-ill are required. Cheaper, more consistent quality colostrum supplements/replacers are a requirement where natural colostrum quality can be variable.

Despite 60 yr of research on perinatal dairy calf health, there are still numerous knowledge gaps that we can now identify. The most pressing in the area of perinatal dairy calf health is the development of automated, reliable wearable technologies for calving cows and term/newborn calves and how we can replicate or augment the beneficial properties of natural colostrum.

Young dairy calf health

The major scientific achievements (as detailed hereunder) in young dairy calf health (calves up to approximately 6 mo of age) over the last 60 yr have, though not exclusively, revolved around the two predominant causes of morbidity and mortality: calf diarrhoea and calf respiratory disease, both in housing and while at pasture. With our current knowledge, we now know that infectious calf diarrhoea is a result of compromised host immunity, infectious challenge and management failure. We have advanced from "white scour" caused by colibacillosis (Wood, 1955) to the recognition of parasites (*Cryptsporidium* spp., *Eimeria* spp.) and viruses (e.g. rotavirus, coronavirus) (Caffarena *et al.*, 2021). This knowledge has meant that both preventive and therapeutic protocols are now more broadly based (Lorenz *et al.*, 2011a), with more emphasis on management and less on microbes. This is particularly true of the management of diarrhoea in calves at pasture due to roundworm infestations where targeted selective therapy is now considered best practice (O'Shaughnessy *et al.*, 2015). As in humans, oral electrolyte solutions (ORS) are considered more important than antimicrobial usage (AMU) (Wenge-Dangschat *et al.*, 2020). While maternal vaccination has a role to play, its effectiveness is highly dependent upon colostrum management (Durel *et al.*, 2017). Maintenance of a milk diet during diarrhoea is beneficial for recovery (Lorenz *et al.*, 2011a) and not a cause of diarrhoea, as previously thought. With increasing knowledge of the gut microbiome, the developments of preventive medications (e.g. prebiotics, probiotics, vaccines, coccidiostats) have been major scientific achievements (Cangiano *et al.*, 2020).

As with calf diarrhoea, we have moved on from calf pneumonia being attributed to a "virus" (Maier *et al.*, 2020) to polymerase chain reaction (PCR) tests for specific viruses and bacteria (Hamad *et al.*, 2019). This achievement has allowed targeted respiratory vaccination protocols to be developed for young calves, even in the presence of maternally derived antibodies (Richeson & Falkner, 2020). Calf-side diagnostics traditionally reliant upon clinical inspection, a thermometer and a stethoscope have been supplemented with transthoracic ultrasonography (TUS), (Cuevas-Gómez *et al.*, 2021; Rhodes *et al.*, 2021). The design of purpose-built calf housing, and latterly, calf hutches (first built in the 1970s) and their modification where necessary (e.g. installation of positive pressure ventilation tubes and adjacent preventives, e.g. calf jackets; Roland *et al.*, 2016; Robertson, 2020) have been major advances, especially as herd and calf group sizes have increased (Nordlund & Halbach, 2019).

An apparent increase in abomasal disorders ("abomasal syndrome") in young dairy calves has occurred in the last 60 yr. While traditionally this was attributed to "stress", as in humans, our understanding has now improved and broadened to include multiple management factors, for example, total solid content and osmolarity of liquid diet (van Kruiningen *et al.*, 2009; Burgstaller *et al.*, 2017).

In addition to these well-recognised calf diseases, the last 60 yr have seen the emergence of "new" calf diseases. Examples include bovine neonatal pancytopoenia, congenital defects, cryptosporidiosis (first reported in 1971), haplotype cholesterol deficiency, Hobi-like mucosal disease, SBV-AHS (Mee, 2018b). Rapid advances in modern diagnostics have allowed us to determine the aetiology of these conditions and adopt ameliorative measures. Across all young calf diseases, there have been advances in the development of whole-calf scoring systems to more objectively assess the degree of morbidity (Boyle & Mee, 2021). More recently, wearable sensor technologies have become commercially available allowing, with variable accuracy, monitoring of health, behaviour, growth and disease (Carslake *et al.*, 2021).

At a farm level, the major future challenges in young calf health remain the same in 2021 (Mee, 2018b) as in the 1960s (Leech *et al.*, 1968) with regard to calf diarrhoea and pneumonia. At an industry level, some challenges are global (e.g. AMR, evolving regulatory frameworks, shifting consumer expectations). At a research level, the genetics of calf diseases (Vinet *et al.*, 2018), automated monitoring of health (Kour *et al.*, 2018), "colostrology" (Lora *et al.*, 2018), accelerated growth pre-weaning (Quigley *et al.*, 2018), lifetime sequelae of calfhood diseases (Chuck *et al.*, 2018) and calf welfare (Neave *et al.*, 2018) are all future challenges. With herd size increases continuing in Ireland, calf rearing will become a specialized vertically integrated dairy enterprise for large units while smaller farms will continue with traditional management. This presents challenges for emerging contract calf rearers to maintain calf health at the standards of home-reared calves (Mee *et al.*, 2018).

Rapid development of pen-side diagnostics (e.g. infrared thermography, pulse oximetry, real-time DNA/RNA sequencing) and wearable wellness (implantable) biosensors (e.g. accelerometers, calving sensors, ear fever tags, nano-biosensors; Costa *et al.*, 2021) present a challenge to independent research to provide evidence-based results demonstrating the benefits or otherwise of such technologies. Similarly, 24/7 data collection and storage (the "calf cloud") on feeding, behaviour, welfare and intake via automatic feeders will facilitate pre-clinical diagnosis smart phone alerts of the individual calf and group deviations from expected norms of health and performance (farm-level "big data"; Morrison *et al.*, 2021).

An overarching challenge is to shift the paradigm from disease therapies to better disease prevention.

Currently, we have major knowledge gaps around how to manage infectious calf diseases with diminished AMU. How to develop anti-parasitic immune-modulators or vaccines is a knowledge gap constraining progress in control of cryptosporidiosis and coccidiosis. We need to know more about how to evaluate and alter the microenvironment of calf housing to prevent respiratory disease. Our knowledge of the causal web (pathogenesis) for abomasal disorders is incomplete, a fact emphasised when we try to investigate outbreaks and solve group problems. Our ability to interpret and use the outputs from the multitude of precision livestock farming (PLF) data sources is hampered by the emerging nature of this discipline and our limited knowledge base of its evidenced-based benefits.

Beef calf health research

The most important diseases – diarrhoea and respiratory disease – of beef calves are addressed here. Underlying each of these morbidities is the suckler cow colostrum passive immunity.

Beef-suckler cows colostrum

Colostrum-derived passive immunity is central to the health, performance and welfare of neonatal beef-suckler calves, and economics of beef-farming enterprises. The IgG immunoglobulins are divided into two subclasses, IgG_1 and IgG_2. IgG1 is selectively transported by the udder from the circulation to the lacteal secretions and is the principal IgG for passive immunisation of the calf. IgG_2 is more homogeneous than IgG_1 and is found in high concentrations in bovine serum (McGee & Earley, 2019). The transfer of IgG_1 from blood to mammary secretions is greater for beef × dairy cows compared to most beef breed types (McGee *et al.*, 2005). First-milking colostrum yield is higher for beef × dairy cows than for beef × beef and purebred beef breeds and higher for multiparous than for primiparous cows, but generally colostrum immunoglobulin concentration is relatively similar for each of the respective categories. Consequently, colostrum immunoglobulin mass (volume × concentration) production in beef cows seems to be primarily limited by colostrum volume (McGee *et al.*, 2005, 2006).

The effect of maternal nutrition during late gestation on colostrum yield is not well documented; however, most studies provide evidence that colostrum immunoglobulin concentration is not adversely affected by under-nutrition (McGee & Earley, 2019). Colostrum immunoglobulin mass ingested relative to birth weight post-parturition is the most important variable determining calf passive immunity. From a practical perspective, research has shown that feeding the beef-suckler calf 5% of birth weight in colostrum volume using a tube feeder within 1 h post-calving, with subsequent suckling of the dam (or a second feed) 6–8 h later, ensures adequate passive immunity, equivalent to a well-managed suckling situation where the calf suckles "naturally" within 1 h after birth, with unlimited access to the dam subsequently (McGee *et al.*, 2006). Compared to older cows, calves from younger cows, especially primiparous animals, have lower serum immunoglobulin concentrations.

Young beef calf health

In a recent study on calf health in Ireland, Todd *et al.* (2018) reported that 20.4% of suckler-beef calves were treated with antibiotics for disease by 6 mo of age. The leading cause of morbidity from birth to 6 mo of age was diarrhoea, accounting for 44% of the disease events. The second and third most frequent causes of morbidity in calves during the first 6 mo of life were bovine respiratory disease (BRD) and navel infection, respectively.

Calf diarrhoea

Calf diarrhoea is one of the main causes of calf morbidity and mortality in suckler-beef herds (Waldner & Rosengren, 2009). In Ireland, calf diarrhoea remains the number one cause of mortality in calves <1 mo of age (Department of Agriculture, Food and the Marine [DAFM], 2019) with rotavirus and *Cryptosporidium* being the two most commonly identified pathogens. Dehydration, acidosis, impaired growth rate or death are the major consequences (Gunn & Stott, 1998). Although the majority of incidences of calf diarrhoea occur in the first 2 wk of life (Clement *et al.*, 1995; Bendali *et al.*, 1999a, 1999b), diarrhoea can also occur in older calves due to a variety of different enteropathogens. A number of preventive measures have been adopted to control calf diarrhoea. However, changes in management practices, such as better management of colostrum feeding, can help lower the incidence of calf diarrhoea significantly (Clement *et al.*, 1995; Lorenz *et al.*, 2011a, 2011b).

Bovine respiratory disease

Bovine respiratory disease (BRD), a disease of the lower respiratory tract of cattle, has a multifactorial aetiology of infectious agents, host factors, environmental stress factors and their interactions, resulting in bronchopneumonia. Predisposing factors are those that affect the magnitude of the infectious challenge (e.g. overstocking, poor hygiene, inappetence, inadequate ventilation) and those that affect immuno-competence. These include stress, draughts and fluctuating temperatures, poor nutrition and/or concurrent disease. In most cases, it would appear that the primary infective agent is viral, producing respiratory tract damage that is subsequently extended by secondary bacterial infections. Viruses are unaffected by antibiotics; however, antibiotic treatment is usually administered to treat secondary bacterial infections. Vaccines against BRD are available, but their use is not mandatory and the timing of administration can vary.

Bovine respiratory disease is the most prevalent disease of recently weaned beef calves in Ireland, accounting for 34.3% of deaths in calves between 1 and 5 mo old (Murray *et al.*, 2017; DAFM, 2019). In addition, BRD is also the most prevalent disease of recently weaned feedlot cattle in Ireland (Murray *et al.*, 2017; Cuevas Gomez *et al.*, 2020) and internationally (Delabouglise *et al.*, 2017; Hay *et al.*, 2017; Wilson *et al.*, 2017) and causes substantial economic losses due to decreased animal performance, higher mortality rates and increased costs associated with treatment (Cernicchiaro *et al.*, 2013; Blakebrough-Hall *et al.*, 2020) as well as negatively impacting animal welfare (Lynch *et al.*, 2011; Wolfger *et al.*, 2015a, 2015b; Earley *et al.*, 2017).

Early and accurate BRD diagnosis

Early and accurate diagnosis of BRD is essential to guide more prudent use of antimicrobials, lower relapse rates and reduce animal mortality. Nasal or deep nasopharyngeal swabs, transtracheal or bronchoalveolar lavage samples can be used for virology, bacteriology, cytology and parasitology (Lorenz *et al.*, 2011b). Nonetheless, the diagnosis of BRD remains a challenge due to the lack of an ante-mortem “gold standard” diagnostic method, meaning that delayed and under-detection of BRD is a significant problem. Numerous methods such as auscultation, clinical respiratory score charts (including evaluation of nasal discharge, ear dropping, rectal temperature, cough and so on), and automated behaviour or temperature monitoring systems are used as diagnostic methods for BRD (Wolfger *et al.*, 2015a, 2015b). However, these methods usually fail to detect lung lesions associated with BRD in animals of all ages, often resulting in a variable number of cases going undetected (Leruste *et al.*, 2012).

Respiratory signs can be evaluated using the Wisconsin clinical respiratory score (CRS) (McGuirk & Peek, 2014). The CRS is based on the assessment of five clinical signs including elevated rectal temperature, cough, eye and nasal discharge, and ear position. Each clinical sign is partitioned into four levels of severity (from 0 to 3) where 0 indicates the lowest risk of being sick and 3 with the greatest risk of BRD. It is recommended to treat animals with the respiratory disease if the CRS is ≥5 and to observe calves with scores of 4. Calves with ≤3 are considered clinically healthy. Some of the drawbacks of using scoring systems alone include the subjective nature of ranking the severity of clinical signs as well as the inability to identify animals with sub-clinical BRD (sBRD) (White & Renter, 2009). The detection of sBRD in cattle with lung lesions without showing clinical respiratory signs can only be confirmed using TUS. The combination of CRS with TUS provides a better classification of BRD and sBRD. A recent study performed at Teagasc Grange showed that 18% (28/153) of recently weaned suckler-beef calves (Cuevas-Gómez *et al.*, 2020) had lung lesions that were not detected using the Wisconsin calf respiratory scoring chart in the 28 and 30 d, respectively, post their arrival to the research centre. Beef HealthCheck is an Animal Health Ireland (AHI)-led programme which was developed in collaboration with the Irish Cattle Breeding Federation, the DAFM, Meat Industry Ireland and Veterinary Ireland. Thus, for every batch of cattle slaughtered at a Beef HealthCheck participating factory, farmers will receive a report indicating a disease score relating to any liver and lung conditions present at slaughter.

Novel diagnostics for BRD

New technologies are being used for the identification of viral and bacterial infectious agents causing BRD. Viruses and bacteria associated with BRD are generally diagnosed using culture on Petri dishes, quantitative PCR (qPCR) or mass spectrometry. However, these diagnostic techniques take between several hours and several days to return results and will not identify novel or unknown viruses which may be causing the disease. More recently, two new molecular-based diagnostic techniques for the identification of bacteria and viruses (both known and novel) causing BRD are being used (Johnston *et al.*, 2017; McCabe *et al.*, 2018). The first approach is called 16S rRNA gene amplicon sequencing. Using this technique, *Mycoplasma* and *Pasteurellaceae* have been identified, and in addition, a novel bacterium in the *Leptotrichiaceae* family was detected in lesioned lung tissue from BRD-affected calves (Johnston *et al.*, 2017). The second approach is Oxford Nanopore MinION Sequencing, a molecular nucleic acid sequencing-based technique that is optimised for the diagnosis of viruses causing BRD. McCabe *et al.* (2018) tested the potential of untargeted nanopore sequencing on the MinION Mk1B for rapid simultaneous identification of a mixture of DNA and RNA viruses that are associated with BRD. McCabe *et al.* (2018) reported correct simultaneous identification of the combined DNA and RNA viral species involved in BRD by PCR-free rapid (10 min) tagmentation-based library preparation and nanopore sequencing on the portable Oxford Nanopore Technologies MinION Mk1B sequencer. The MinION has the capability of becoming a rapid point-of-care diagnostic test for the identification of viral and bacterial species causing BRD, directly on farm. These new diagnostic approaches will enable prudent antibiotic usage for the treatment of animals affected by BRD.

AMR and calf health

Antimicrobial resistance is currently recognised as one of the most challenging problems for human and animal health. The use and misuse of antimicrobials can contribute to the development of antimicrobial resistance (FAO, 2016; O'Neill, 2016). In a recent stakeholder survey in Ireland, AMR was ranked first by farmers and professional service providers with respect to the dairy and beef fattener/finisher sectors (Meunier *et al.*, 2020). A recent study quantified AMU and identified specific life stages, and diseases within calves, including dairy and beef animals (Earley *et al.*, 2019). A total of 123 (79 beef and 44 dairy) farms, comprising 3,204 suckler-beef calves and 5,358 dairy calves, representing 540,953 and 579,997 calf-days at risk, respectively, were included in the study. All calves were raised on farm of origin and most of the studied herds were closed herds. In this study, only animals showing signs of disease were treated with antimicrobials and no mass administration of antibiotics was practised. The highest risk period for disease in the study was between birth and 1 mo of age, with approximately two-thirds of all disease events occurring during this time period (Figure 1).

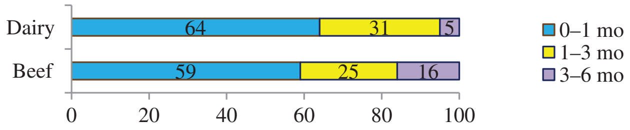

Figure 1. Proportion of antimicrobial treatments (%) for suckler-beef and artificially reared dairy calves from birth to 6 mo of age.

Non-regulated infectious diseases

The landscape of cattle disease control programmes has altered over the past decades. Previously control programmes focussed solely on regulated diseases, for example, bTB (More & Good, 2006), bovine brucellosis (Hayes *et al.*, 2009) and transmissible spongiform encephalopathies (TSEs; Sheridan *et al.*, 2005). The absence of a coordinated approach to non-regulated disease control was highlighted by More (2007, 2008), and a move from government-led disease eradication programmes to a public–private partnership approach was proposed. The European Animal Health policy provided the stimulus for this change; "prevention is better than cure" (European Commission, 2007). The formation of AHI was central to this change. AHI is an industry-led, not-for-profit partnership between all key stakeholders of animal health, including livestock producers, processors, representative farming organisations, service providers and DAFM (More *et al.*, 2011). A Delphi study was conducted to establish the priority order, and three biosecure diseases were highlighted for priority: bovine virus diarrhoea (BVD), IBR and JD (More *et al.*, 2010).

Bovine virus diarrhoea (BVD)

Bovine virus diarrhoea virus (BVDV) is an economically important pathogen and is endemic in many countries worldwide (Ridpath, 2010; Richter *et al.*, 2019) and across Europe (EFSA, 2017). The ability of the non-cytopathic biotypes to establish a lifelong persistent infection of the foetus prior to 120 d of gestation is a key feature in the epidemiology of the disease, with both persistently infected (PI) and transiently infected (TI) animals playing a role in disease propagation (Houe, 1999). In Ireland, BVDV was first reported in ruminants during the 1970s (Hamilton & Timoney, 1973). The work conducted during the

1990s indicated that a high proportion of diagnostic samples from feedlot cattle was positive for BVDV (Healy *et al.*, 1993). National figures generated between 2005 and 2008 by the Central Veterinary Laboratory on diagnostic submissions reported seropositivity between 64% and 69%. Whereas herd-level seroprevalence of 98%–99% was reported in non-vaccinated herds in Ireland (Cowley *et al.*, 2012) and Northern Ireland (Cowley *et al.*, 2014).

Much of Europe has been subject to varying national or regional eradication programmes over the past two decades (Lindberg & Alenis, 1999, 2006; Synge *et al.*, 1999; Houe *et al.*, 2006; Ståhl & Alenis, 2012; Booth *et al.*, 2016; Wernike *et al.*, 2017; Richter *et al.*, 2019), with a number of Scandinavian countries achieving effective eradication (Bitsch *et al.*, 2000; Hult & Lindberg, 2005; Valle *et al.*, 2005; Norström *et al.*, 2014). Earlier programmes were based on an initial herd serological screen followed by investigations to identify PI animals (Lindberg & Alenis, 1999, 2006; Synge *et al.*, 1999; Ståhl & Alenis, 2012). The advent of identification tags that facilitated the collection of a tissue tag sample has paved the way for more recent eradication programmes in Germany (Wernike *et al.*, 2017), Switzerland (Presi *et al.*, 2011), Ireland (Barrett *et al.*, 2011; Graham *et al.*, 2014, 2015) and Northern Ireland (Charoenlarp *et al.*, 2018). Prior to embarking on an eradication programme, it was estimated that BVD was costing €102M annually in Ireland (Stott *et al.*, 2012), with the estimated annualised benefits of eradication far exceeding the cost by multiple factors for all herd types.

The Irish BVD eradication programme

From January 2013, all calves born in Ireland were required to undergo tissue tag testing for the presence of BVD viral antigen (Graham *et al.*, 2014). The science and policy of BVD is guided by AHI's BVD technical working group (BVD TWG), while the BVD implementation group (IG), representing the financial, advisory and farming organisations stakeholders, has steered the programme. Perhaps somewhat ironic, the first step in managing a non-regulated disease is to regulate it, and the BVD Order 2012 (DAFM, 2012) set out the legal requirement to partake in the compulsory programme. The regulations have been revised over the period to reflect the evolving control programme (DAFM, 2014, 2017, 2020b). Herd owners are encouraged to remove positive calves, and supports are available for herds complying with the programme requirements (DAFM, 2021a, 2021b). As with similar BVD control programmes (Wernike *et al.*, 2017), progressive control measures have been implemented overtime to improve compliance with the programme. Herds that fail to partake in testing and herds that disclose positive animals are subject to herd movement restrictions (AHI, 2021a). Since 2016, herds disclosing a BVD virus-positive animal have been required to undergo a mandatory investigation to determine the likely infection source (Graham *et al.*, 2021). In addition, in 2021, this investigation also extends to a whole herd test for all animals and vaccination of eligible females for a 2-yr period, to reduce the risk this herd poses to itself and others (AHI, 2021a). The prevalence of BVD in the national herd has reduced considerably in Ireland since 2013. Herd prevalence reduced from 11.27% of breeding herds in 2013 to 0.53% in 2020 (AHI, 2021b).

Factors influencing the prevalence of BVD

Herd level and animal factors have been demonstrated to influence the prevalence of BVD within the cattle population. Research conducted early in the eradication phase in Ireland highlighted the importance of prompt removal of positive calves (Graham *et al.*, 2015). Herds that retained positive calves the longest (>170 d) were 4.42 (confidence interval [CI], 3.06–6.35) times greater risk of being classified a positive herd the following year compared with herds that did not disclose a BVD positive the previous year. Dairy herds display a higher odds of BVD infection compared with beef herds (Presi *et al.*, 2011; Barrett *et al.*, 2020; van Roon *et al.*, 2020). Herd size was reported as a significant factor in both Ireland (Graham *et al*, 2015) and Northern Ireland (Charoenlarp *et al.*, 2018). Data collated in the Irish programme indicated the odds increase by 1.95 for each 2.7-fold increase in herd size (Graham *et al.*, 2015). The movement of animals is an important influence on BVD risk, and in Ireland, there is a large number of farm-to-farm movements annually (McGrath *et al.*, 2018). The risk of BVD infection disclosure was higher in herds that introduced animals (OR, 1.41; CI, 1.18–1.69) or participated in shows or marts (OR, 1.45; CI, 1.10–1.91) compared with those that did not (van Roon *et al.*, 2020). The infection pressure within the neighbourhood has been evaluated and is considered an important risk factor in both Ireland (Graham *et al.*, 2016) and Northern Ireland (Charoenlarp *et al.*, 2018), and the odds ratio associated with any BVD-positive neighbour early in the Irish compulsory programme was 1.92 (CI, 1.37–2.7) compared with herds with no positive neighbouring herd.

Future prospects – the pathway to BVD freedom

In order to progress to a disease-free status enhanced control measures, with immediate movement restrictions, whole herd testing and compulsory vaccination have been introduced in 2021 to ensure Ireland can meet the definition of BVD freedom under the new European Animal Health Law (AHL; AHI, 2021a). The new AHL came into force from April 2021 and makes provision for national eradication programmes to be officially approved and for BVD-free countries to be formally recognised (European Commission, 2016, 2020a). Planning is underway to pursue official programme approval and, in due course, to apply for recognition of freedom under these regulations by 2023. To achieve BVD freedom under the

AHL, Ireland must achieve 18 mo without a confirmed case of BVD, with 99.8% of bovine holdings, covering 99.9% of the bovine population, categorised as negative herd status, and vaccination against BVD has been prohibited for bovine animals (European Commission, 2019). Once BVD-free status is obtained, the use of vaccination may be authorised in the event of a disease outbreak.

Infectious bovine rhinotracheitis (IBR)

Infection with bovine herpes virus 1 (BoHV-1) is economically important (Sayers, 2017), occurs worldwide (reviewed by Ackermann & Engels, 2006) and is endemic in Ireland (Cowley *et al.*, 2012; Martinez-Ibeas *et al.*, 2015; Sayers *et al.*, 2015; Sayers, 2017). Following primary infection, a lifelong latent infection is established if the animal survives (Ackermann *et al.*, 1982), and reactivation may occur under stress and lead to episodic excretion of virus (reviewed by Muylkens *et al.*, 2007). While the reproductive syndromes were described in the 19th century in Europe (reviewed by Ludwig & Gregersen, 1986), the respiratory form (IBR) was first described in the United States (Schroeder & Moys, 1954) and subsequently in Europe (Gründer *et al.*, 1960). Infection with BoHV1 was first described in Ireland in 1971, with 12 further outbreaks recorded by the Central Veterinary Laboratory until 1992 (Moore *et al.*, 2000). Estimates of prevalence were historically low with a 9% seroprevalence reported in feedlot cattle during the 1980s (Gunn & Wilson, 1991). More recent studies have suggested that prevalence has increased (O'Grady *et al.*, 2008; Cowley *et al.*, 2011), with Sayers *et al.* (2015) reporting 80% of bulk milk samples test positive for BoHV1. Reproductive syndromes have been detailed by Graham (2013), and reduced milk yields reported by Stratham *et al.* (2015) and Sayers (2017). Economic modelling indicated that profitability was reduced by €60 per cow annually where the dairy herd was classified as seropositive. At 29 cents per litre, this equated to a 22% reduction in profit (Sayers, 2017).

Since its establishment, AHI has viewed IBR as a priority disease (Graham *et al.*, 2013). An IBR eradication programme will be important to support the health status of live exports within Europe and worldwide. A recent study conducted by Hanrahan *et al.* (2020) suggests that potential costs of the absence of an IBR eradication or control programme could be in excess of €100 million per annum. The Terrestrial Manual of the OIE (OIE, 2021) outlines the requirements for a country to qualify for disease-free status, while the Commission delegated Regulation (EU) 2020/689 (European Commission, 2020a) prohibits vaccination and sets out the requirement to achieve 99.8% of bovine establishments, representing at least 99.9% of all cattle are free from BoHV-1. Eradication programmes have been successful elsewhere in Europe (reviewed by Ackermann and Engels, 2006). Nonetheless, the challenge to move to eradicate IBR in Ireland is clear, especially given the high seropositivity in Irish cattle herds. Currently, a national IBR programme is under consideration by the IBR IG, led by AHI, and the IBR TWG is developing and refining a proposed programme. Modelling studies, funded by DAFM, are being conducted to investigate the epidemiology of BoHV-1 infection in Irish herds (Brock *et al.*, 2020). Further research, including abattoir and bulk milk tank surveillance, is being undertaken presently by AHI and DAFM. Ultimately, it will be the stakeholders of the IBR IG who decide as to whether a national eradication programme is undertaken or not.

Johne's disease (JD)

Johne's disease is a chronic infectious disease, caused by infection with "MAP"; it is characterised clinically by chronic continuous or intermittent watery diarrhoea. Clinical disease is the tip of the iceberg (Whitlock & Buergelt, 1996); pre-clinical animals are infectious, and the aim of a control programme is to identify and remove pre-clinical infection from herds and prevent exposure of young calves in particular from infection. Economic losses are associated with its occurrence (Richardson & More, 2009), and McAloon *et al.* (2016a, 2016b, 2016c) outlined the reduction in milk yield associated with JD positivity. Only limited reports of JD were notified to DAFM up to the year 1992 (92 cases), suggestive that JD was not prevalent before the introduction of the European Single Market when controls on imported bovines were relaxed (Good *et al.*, 2009). A further 232 cases were notified to DAFM between 1995 and 2002 (Good *et al.*, 2009). O'Doherty *et al.* (2002) highlighted the risk of disclosing JD in imported cattle, as 36% of 36 herds had disclosed at least one enzyme-linked immunoassay (ELISA)-positive imported animal. Based on a serological survey in 2005, the estimated animal-level prevalence was 3% while the herd-level prevalence was 20% (Good *et al.*, 2009). More recently, McAloon *et al.* (2016a, 2016b, 2016c) reported that the probability of a herd containing at least one truly JD-positive animal in Irish dairy herds was 28% (CI, 23–34%). A comprehensive review conducted in Europe suggested variation in animal-level prevalence, with the true prevalence estimated at 20%, with some countries considerably lower between 3% and 5% (Nielsen & Toft, 2009). Management practices relating to dry cow and calving pen management have been highlighted as important risk factors for JD infection (McAloon *et al.*, 2017), while a survey of management practices on Irish dairy farms highlighted that the presence of risk factors associated with JD transmission is frequently observed on Irish farms (Kennedy *et al.*, 2014).

The Irish Johne's Control Programme (IJCP)

JD control programmes have been initiated worldwide (Sockett, 1996; Geraghty *et al.*, 2014; Whittington *et al.*, 2019), often in response to economic pressures and potential public health implications. The science of the JD control programme in Ireland has been guided by the JD TWG of AHI and by disease control modelling (Sergeant *et al.*, 2018). The IJCP is a voluntary national programme and is managed by AHI under the guidance of the JD IG (Animal Health Ireland, 2021c). The objectives of the programme are addressed through a combination of risk assessment, voluntary assurance and national surveillance (Jordan *et al.*, 2020). The IJCP enables participating herd owners to have increasing confidence in the absence of infection in their herds and to achieve significant control or elimination, and it underpins the quality of Irish dairy and beef produce in the international marketplace. The programme provides a long-term approach to the control of JD in Ireland (Gavey *et al.*, 2021).

Regulated infectious diseases

The Department of Agriculture, Food and the Marine (DAFM) is the competent authority responsible for the implementation of national and European Union (EU) legislation relating to regulated disease programmes in Ireland. The so-called “regulated” diseases include exotic diseases which are not present in Ireland and for which there is a legislative basis for their exclusion and elimination in the event of an outbreak, such as foot-and-mouth disease. There are also those diseases which, for public health and trade reasons, are also regulated and for which there are national eradication programmes. Bovine Tuberculosis (bTB), brucellosis and bovine spongiform encephalopathy (BSE) have considerable public health and trade implications, and DAFM has made substantial commitments to their eradication over the years. The delivery of these eradication programmes has been underpinned by evidence-based research carried out in Ireland.

Bovine tuberculosis

Bovine TB is a chronic infectious disease caused by *M. bovis* which affects cattle, several domestic and wildlife mammal species as well as humans (O’Reilly & Daborn, 1995). The main concerns regarding bTB relate to its economic losses to the cattle industry and government due to losses in productivity, trade restrictions and control costs (Zinsstag *et al.*, 2016). A voluntary bTB eradication programme commenced in Ireland in 1954, which became compulsory in 1962 (Good, 2006). Considerable progress was made in the early years of the programme, but this progress stalled from the mid-1960s. In late 1980s, DAFM identified a lack of scientific evidence in the development of the policy which underpinned the bTB eradication and so the TB investigation unit was established at University College Dublin in 1988. This later evolved into the Centre for Veterinary Epidemiology and Risk Analysis (CVERA).

Extensive research has been conducted on herd-level risk factors for bTB in Ireland. Over a broad range of studies, three factors have consistently placed herds at the greatest risk of being diagnosed with bTB, namely herd size, location (including bTB prevalence in the area) and bTB history (More & Good, 2015). Irish research has provided conclusive evidence in support of badgers playing an important epidemiological role in the epidemiology of cattle bTB in Ireland (Martin *et al.*, 1997; Griffin *et al.*, 2005). The transmission of bTB between badgers and cattle is believed to occur through both direct and indirect transmission routes (More & Good, 2006; Ward *et al.*, 2010; Corner *et al.*, 2011). Badgers are considered to be a maintenance host with spillback to cattle – essentially, an upstream driver of infection (More, 2009).

In light of this evidence, Ireland has implemented a national programme of badger culling, specifically to reduce badger density in areas with chronic problems of bTB in cattle herds (Byrne *et al.*, 2013). Culling is initially in the environs of the affected farm, but this may be extended up to 2 km beyond the farm boundary (Byrne *et al.*, 2013). In contrast to UK findings (Pope *et al.*, 2007; Prentice *et al.*, 2019), this culling has not led to badger perturbation and increased TB risk (Olea-Popelka *et al.*, 2009).

There has also been a comprehensive research programme on the development of bTB vaccines for badgers over the years. Initial studies were mainly pen-based experiments to determine if the BCG vaccine had a protective effect against bTB in badgers (Corner *et al.*, 2009). A recent field study concluded that vaccination matched targeted badger culling in four counties in the control of bTB in Ireland (Martin *et al.*, 2020). Such findings have directed the programme away from badger culling to badger vaccination to reduce the risk of bTB from badgers to cattle.

The gamma interferon test, as an ancillary test, has been used in high incidence herds to uncover any residual infection and has laterally been used as a quality control tool to monitor the effectiveness of tuberculin testing at the herd level (Clegg *et al.*, 2016).

The DAFM has outlined the ambition to eradicate bTB by 2030. However, a recent review has concluded that this is not considered likely without additional measures in the areas of addressing the bTB risks from wildlife, implementing additional risk-based cattle controls and enhancing industry engagement (More, 2019).

Bovine brucellosis

Brucellosis in cattle is caused by *Brucella abortus*. Brucellosis is widespread globally and affects the reproductive tract, resulting in abortion in females and infertility in males. It is a zoonosis, and infection occurs in humans through contact with infected animals or their body fluids or via consumption of unpasteurised dairy products. Disease in humans can range from asymptomatic infection to chronic problems including fever, arthritis, endocarditis and bone lesions.

A national brucellosis eradication scheme commenced in 1966. A programme using a combination of vaccination, serological testing and anamnestic testing using Br. abortus strain 45/20 vaccine (Cunningham & O'Connor, 1971), and the slaughter of reactors made considerable progress towards eradication. By the mid-1980s, the number of herds being restricted for brucellosis had been reduced to between 300 and 500 annually. However, prior to final eradication being achieved, the programme was relaxed, with the discontinuation of vaccination in 1984, the removal of the annual herd test (1986) and pre-movement test (1988). A dispute with veterinary practitioners and the expansion of the national suckler herd in the early 1990s were thought to have led to the increased spread of brucellosis (Sheahan *et al.*, 2006).

In 1998, a renewed effort to eradicate brucellosis was commenced. These measures included the introduction of a 30-d compulsory pre-movement test, a full round of annual herd serological testing, rapid depopulation of infected herds, lime treatment of cattle slurry in infected herds to kill any brucella bacteria present, improved diagnostic tests for both milk and serum samples, extended rest periods particularly where contiguous herds were infected and serological testing of cull cows at slaughter (Sheahan *et al.*, 2006). Considerable progress was made in reducing the prevalence of brucellosis over the following 8 yr, until the last recorded case of brucellosis was diagnosed in Ireland in 2006 (Anon., 2021).

In the years subsequent to 2006, the intensity of the programme was reduced with the gradual removal of the intensified herd serological screening programme and pre-movement tests. In recent years, passive surveillance provided by the Regional Veterinary Laboratory (RVL) network and the cull cow monitoring programme have evolved as the main elements of the surveillance programme for brucellosis in Ireland. Following the declaration of Brucellosis freedom in 2009, the post eradication surveillance was reviewed and incrementally reduced. However, until 2016 up to 250,000 cows were sampled, which prompted an analysis to devise a more targeted approach having demonstrated the suitability of the Irish cull cow serological sample archive as a basis for establishing countrywide freedom from infection, and, more generally, provided a roadmap for how such surveillance resources could be used in Ireland more efficiently to provide assurance of freedom and to calculate prevalences for a range of endemic diseases (Tratalos *et al.*, 2018).

Bovine spongiform encephalopathy

Bovine spongiform encephalopathy (BSE), a progressive neurodegenerative disorder of adult cattle, was first recognised in the United Kingdom in 1985 (Wells *et al.*, 1987) and the first case was diagnosed in Ireland in 1989 (Bassett & Sheridan, 1989) (Figure 2). The disease is caused by the feed-borne transmission of an infectious prion protein agent (Wilesmith *et al.*, 1988).

In 1989, BSE became a compulsory notifiable disease by S.I. No. 61 of 1989 (Diseases of Animals Act (Bovine Spongiform Encephalopathy) Order 1989). Ireland adopted a robust approach to the eradication of BSE from 1990 where a policy of herd depopulation was applied, which was over and above the approach adopted in other European countries, where only the birth cohorts and progeny of confirmed positive cases were culled. The occurrence of BSE was one of the main driving forces behind the European legislation which required the development of national bovine registration and movement databases to facilitate the tracing of progeny and birth cohorts of BSE cases. In 1990, there was an initial ban on the feeding of animal protein to ruminants. In 1996, the occurrence of a new variant CJD in the United Kingdom was linked to BSE (Will *et al.*, 1996) and created considerable anxiety among European consumers. As a result, an enhanced feed ban came into effect in 1996.

In 2001, the EU feed ban came into place, which banned the inclusion of processed animal protein in farmed animal feed. In 2001, all casualty, emergency slaughter and fallen animals over 24 mo of age and all healthy animals slaughtered for human consumption over 30 mo of age were tested for BSE, which was the basis of the active surveillance system for BSE. In 2009, these age limits increased to 48 mo for all categories. The age threshold for testing healthy animals slaughtered for human consumption over 30 mo increased to 72 mo in 2011 and was removed altogether in 2013.

Since 1989, there have been 1,662 confirmed cases of BSE in Ireland (Figure 2), with the greatest number of cases confirmed in 2002 (n = 333), which coincided with the introduction of the active surveillance programme. A spatio-temporal analysis of BSE in Irish herds was carried out from 1996 to 2000. The risk of a herd having a case of BSE increased with increasing herd size and was higher for mixed and dairy herds than for beef-suckler herds. Using the spatial scan statistic, clusters of BSE cases were identified in counties Monaghan, Wexford and Cork, with evidence of spatial association between cases and some large feed suppliers (Sheridan *et al.*, 2005). Although there was a marked decline in the incidence of BSE following the various enhanced controls on animal feed, BSE cases continued to occur in animals born after the various enhancements to the feed ban, the so-called born after the reinforced feed ban or BARB cases. An analysis of such cases concluded that the clustered spatial pattern of Irish BARB cases, and the finding that dairy herd type is a significant risk factor (as was the case for the earlier two phases of the epidemic), is evidence against the hypothesis that BARB cases arise spontaneously and is supportive of the hypothesis of locally distributed feed-borne exposure (Ryan *et al.*, 2012).

A wider study carried out by European Food Safety Authority (EFSA) concluded that the BARB cases were related to

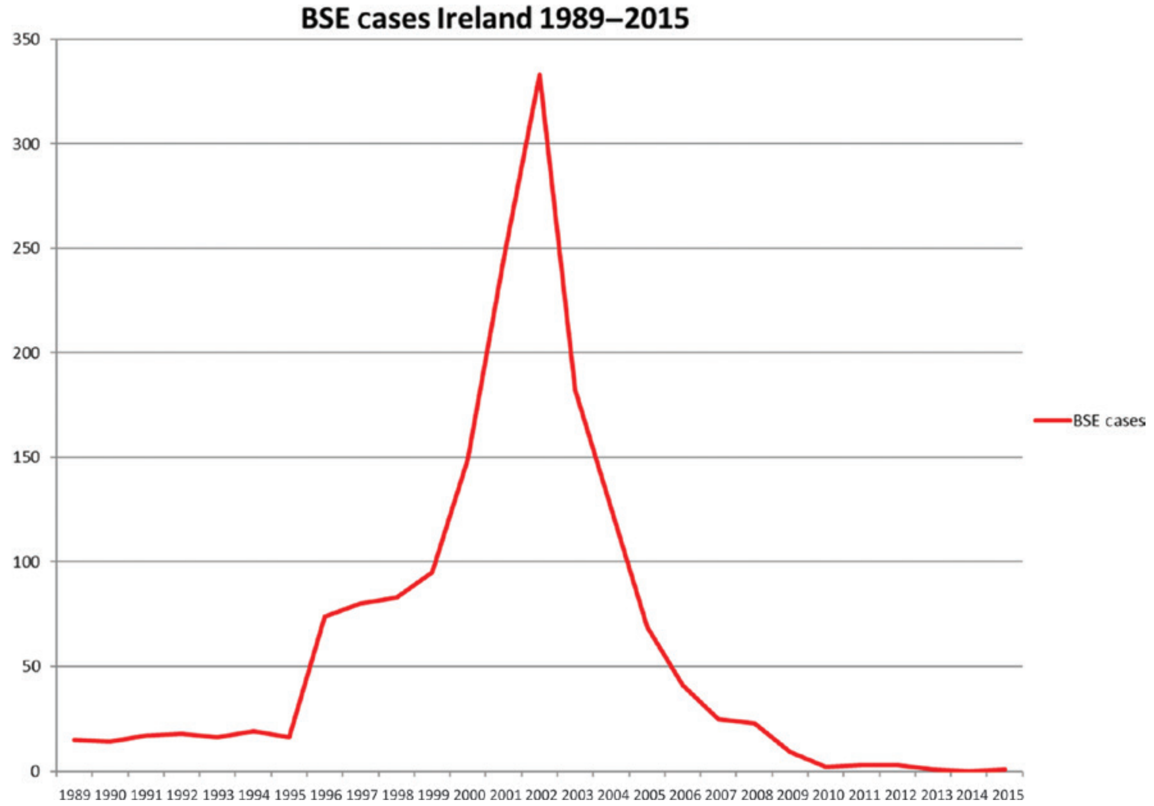

Figure 2. BSE cases in the Republic of Ireland (1989–2015).

historic exposure to contaminated feed, and the data are consistent with exponential decline from epidemic peak to zero (Ricci *et al.*, 2017). In recent years, Ireland has had one case of classical BSE in 2015 in a 2010 born cow and two cases of atypical BSE in 2017 and 2020 in 18-yr-old and 14-yr-old cows, respectively. Atypical BSE is considered a spontaneous pathological change in all cattle populations at a very low rate and has only been identified in older cattle. It occurs spontaneously in cattle, which is in contrast to classical BSE which is associated with the ingestion of prion material. Ireland achieved the OIE BSE negligible risk status in 2021, which was 11 yr after the birth of the last classical case in 2010. Bovine spongiform encephalopathy negligible risk status represents the lowest level of BSE risk status and is of importance in accessing international markets for Irish beef.

Lameness research

Bovine lameness is a major global problem that severely impacts cow welfare (Shearer *et al.*, 2013), longevity (Booth *et al.*, 2004), fertility (Garbarino *et al.*, 2004) and milk production (Bicalho *et al.*, 2008), causing huge economic loss ($11B in the US; Kang *et al.*, 2021) and threatening the sustainability of the entire dairy sector. Limited studies on lameness in beef herds report prevalences of below 3%, but this is likely an underestimation (Fjeldaas *et al.*, 2007). This review focuses on lameness in dairy herds only. The worldwide prevalence of dairy cow lameness is approximately 26% (Cook, 2016), but rates as high as 63% have been reported in indoor systems (von Keyserlingk *et al.*, 2012). Lower rates are reported for pasture-based systems; Irish research has documented lameness rates of between 6% and 15% (Somers *et al.*, 2015; O'Connor *et al.*, 2020; Crossley *et al.*, 2021). Herd-level risk factors for lameness in indoor systems include environmental factors related to housing design, cubicle size and comfort, and standing times (Espejo & Endres, 2007; Sarjokari *et al.*, 2013; Solano *et al.*, 2015). Risk factors in outdoor systems differ, with a greater focus on roadway infrastructure and cow handling on roadways (Chesterton *et al.*, 1989, Ranjbar *et al.*, 2016). Individual cow level risk factors are similar for both systems and include parity, genetics and body condition score (Solano *et al.*, 2015).

Until recently, compared with other major health concerns of dairy cows such as fertility and mastitis, lameness has been under-researched (Huxley, 2012), possibly because its prevalence may have been underestimated, and the associated costs are often not well understood (Dolecheck & Bewley, 2018). In recent years, however, a greater appreciation for the multiple and severe impacts of lameness has resulted in greater research focus in this area.

A major advancement in our understanding of lameness concerns its pathogenesis. Previously, the development of claw horn lesions was explained by the "laminitis" theory; high levels of concentrate feeding result in ruminal acidosis and consequent inflammation throughout the body, including in the laminae of the corium which attach the pedal bone to the hoof wall (Maclean, 1965; Vermunt & Greenough, 1994). While it is clear that lameness and ruminal acidosis are linked, research to date does not support a causal relationship (Danscher *et al.*, 2010). It is now understood that the causes of lameness involve a number of factors acting synergistically. Enzymes released at the time of parturition degrade connective tissue in the reproductive tract to allow parturition to occur but also affect the connective tissues that hold the pedal bone within the hoof capsule. Consequently, the connective tissues weaken (Tarlton *et al.*, 2002), allowing the pedal bone to sink within the hoof capsule and damage the layer of horn-producing germinal cells beneath, resulting in the formation of defective horn sole. Additionally, environmental factors that increase the standing time of the cow or the forces acting on the hoof increase pressure in this area (Cook & Nordlund, 2009). Finally, changes to the structure of the hoof, including thinning of the digital cushion in cows with low BCS (Bicalho *et al.*, 2009) and new bone formation on the distal phalanx, as a result of lameness episode (Newsome *et al.*, 2016) result in a hoof that is vulnerable to external pressures. The structural changes that occur in the hoof following a lameness episode explain why the risk of a cow becoming lame is far greater for a cow that has had a previous lameness episode (Randall *et al.*, 2018) and in older cows (Browne *et al.*, 2021) which highlights the critical importance of preventing lameness occurring in the first instance.

A significant body of Irish research has examined the effects of various management strategies on hoof health and cow mobility. Increased comfort in cubicles improved claw health in heifers (Leonard *et al.*, 1994) and overcrowding had a negative impact (Leonard *et al.*, 1996). Cows kept on out-wintering pads during the dry period did not experience worse hoof health or lameness (O'Driscoll *et al.*, 2008), and yearling heifers kept on an out-wintering had reduced limb lesions (Boyle *et al.*, 2008). Hoof health and mobility were improved in cows that were milked once a day (O'Driscoll *et al.*, 2010) because cows had more opportunity to rest. Nutritional management of grazing cows also impacts mobility; certain aspects of mobility were worse in cows that did not receive an adequate daily herbage allowance, possibly because sub-optimal nutrition resulted in a thin digital cushion (O'Driscoll *et al.*, 2015).

Recent research has demonstrated the huge importance that early detection and treatment of lame cows has in ensuring their recovery. Cows that are detected earlier in the course of the disease are far more likely to make a full recovery (Thomas *et al.*, 2016). This is of particular relevance to Ireland, as a recent study (N. Browne, personal communication) revealed that the vast majority of Irish farmers do not engage proactively in mobility scoring of cows, thus severely limiting their ability to minimise the impacts of lameness on the productivity and welfare of their herds.

Research has shown the benefits that non-steroidal anti-inflammatory drugs (NSAID) have in the treatment of lameness, reducing pain (Wagner *et al.*, 2017; Warner *et al.*, 2021) and improving recovery rates (Thomas *et al.*, 2015). However, the use of NSAID in the treatment of lame dairy cows in Ireland is low, with only 3% and 8% of farmers reporting their use in the treatment of mildly and severely lame cows, respectively (N. Browne, personal communication). Using a block on the unaffected claw of lame cows also improves recovery (Thomas *et al.*, 2015), though it is not currently clear how widely blocks are used in the treatment of lame cows in Ireland.

The role of genetics has recently come to the fore also. Previous research has demonstrated that genetics play a significant role in the likelihood of a cow becoming lame (Zwald *et al.*, 2004) and recent Irish research supports this (Ring *et al.*, 2018b; O'Connor *et al.*, 2020; Browne *et al.*, 2021). Therefore, it is likely that an increased emphasis on lameness traits in breeding programmes could significantly reduce herd lameness.

As agriculture becomes increasingly sensor based, so too has the area of lameness detection. A number of methods exist for automated detection of lameness in cows, including accelerometers, pressure-sensing mats and cameras (Kang *et al.*, 2021). Problems remain with these systems, however, including cost and lack of sensitivity and specificity, which thus far have limited their use on farms.

Reducing lameness prevalence is critical to improving cow welfare, the importance of which is highlighted in Ireland's recently published first Animal Welfare Strategy (DAFM, 2021c). Although Ireland's 10% herd-level lameness prevalence (Crossley *et al.*, 2021) is markedly lower than many other countries, it nevertheless indicates that a significant proportion of cows are suffering unnecessarily and failing to realise their full production potential because of pain and reduced mobility. The dairy sector is under increasing scrutiny from a cow welfare perspective (Wolf *et al.*, 2016) and demonstrating that the Irish dairy production system is sustainable and welfare friendly is vitally important to maintain consumer confidence. It is also key to maximise market returns for increased production in competitive markets worldwide (DAFM, 2015).

The European Green Deal aims to overcome the threat of climate change and environmental degradation by making the economy of the EU sustainable. As part of this, the 2030 Climate Target Plan targets a 55% reduction in greenhouse gas emissions by 2030 (European Commission, 2020b). Given that lameness can significantly increase the environmental impacts of milk production (Chen *et al.*, 2016; Mostert *et al.*, 2018), it is vital that reducing lameness is prioritized as a means by which this target can be reached. The Farm to Fork Strategy targets a 50% reduction in the sales of antimicrobials for farm animals by 2030 (European Commission, 2020c). Lameness is one of the top reasons for antimicrobial use in dairy cows (Obritzhauser *et al.*, 2016; Redding *et al.*, 2019). Currently, antibiotics are the most commonly used medication in the treatment of lame cows on farms in Ireland (N. Browne, personal communication); further research investigating the reasons underlying this is required. Reducing lameness within herds is key to reducing antimicrobial use, but it is also critically important that those involved in the care of lame dairy cows receive correct training and guidance on appropriate treatments such as hoof paring.

Scientific progress over recent years has greatly improved our understanding of how and why lameness develops. Consequently, we are now well equipped to prevent, effectively detect and treat it. While many areas of lameness undoubtedly require further study, we nonetheless have much of the knowledge required to reduce its prevalence in Irish herds; therefore, it is the implementation of lameness prevention and management strategies on farms that is urgently required.

Knowledge gaps remain. The role of NSAIDs in the treatment of lameness in pasture-based herds has not been researched to date, and an understanding of their current low level of use is lacking. Investigation of appropriate management systems to prevent the first time occurrence of lameness, particularly in heifers, is needed. Further research is required to optimise automated lameness detection methods. A barrier to further research is the current lack of consistently recorded high-quality claw lesion and lameness data, such as that that exists for the recording of somatic cell count (SCC). Huge scope exists for improvement in this area.

Mastitis research

The purpose of this section is to review the research on mastitis control, selective dry cow therapy, AMU and AMR. Mastitis is one of the most common diseases of dairy cows and one of the most economically important (Dohoo *et al.*, 2011; Oliveira & Ruegg, 2014).

Mastitis can be caused by bacteria from different sources. Environmental mastitis is caused by bacteria present in the cows' environment (e.g. manure, bedding material) such as *Streptococcus uberis*, *Escherichia coli*, *Strep. dysgalactiae*, among others (Cobirka *et al.*, 2020). Contagious mastitis occurs when a healthy teat comes in contact with an infected gland or milk, mainly during milking through the milking cluster or the milker's hands (Neave *et al.*, 1969; Cobirka *et al.*, 2020). The most common contagious pathogens are *Staphylococcus aureus* and *Strep. agalactiae.*

Mastitis control

Dodd *et al.* (1969) and Neave *et al.* (1966, 1969) developed fundamental work on our understanding of mastitis control. Their work revealed that the average proportion of cows infected in a herd could be reduced by 75% when reducing the new infections and the average duration of infections by 50% (Dodd *et al.*, 1969). Therefore, these are the two pillars of mastitis control.

The research by Dodd *et al.* (1969) led to the development of a systematic mastitis control plan referred to as the "five-point" plan (Ruegg, 2017). It consists of effective post-milking teat disinfection, appropriate treatment of clinical cases, antibiotic dry cow therapy, culling chronically infected cows and milking machine maintenance, which will be reviewed in the following paragraphs.

The practice of applying effective disinfectant to the teat and especially the teat end immediately after milking has been shown to be a very effective practice to reduce new infections: close to 50% according to Neave *et al.* (1969) and Pankey *et al.* (1984). The aim of this practice is to remove pathogens on the teats to eliminate most of the bacterial contamination that occurs during milking therefore preventing pathogens from colonizing lesions and teat ducts (Neave *et al.*, 1966; Bramley & Dodd, 1984). However, this practice is not equally effective against coliforms and many streptococcal mastitis (Pankey *et al.*, 1984).

The second practice of the mastitis control plan, appropriate treatment of clinical cases, can help reduce the duration of each infection (Neave *et al.*, 1966). The limitations of this practice for mastitis control are that only a fraction of infections are clinical (Neave *et al.*, 1966) and that treating clinical cases not knowing the aetiology of the disease results in unnecessary antimicrobial treatments due to reduced efficiency of treatments in cases where there is no growth or growth of certain Gram-negative pathogens (Ruegg, 2021). The wide range in bacteriological cure (27%–95%) can vary the success of the strategy depending on the herd management, the cows and the type of bacteria present

(Ruegg, 2021), and therefore treatment effectiveness should be evaluated on each herd.

Work showing that antibiotic therapy for treating staphylococcal infections at the end of the lactation was more effective than in lactation treatment (Dodd *et al.*, 1969) led to the recommendation of application of antibiotic dry cow therapy of all cows. Dry cow therapy also helps prevent many new infections over the dry period, which is a high-risk period for acquiring new infections (Bradley & Green, 2004; Ruegg, 2017). Using antibiotic dry cow therapy can reduce on average 78% of existing infections depending on the pathogen present on the herds (over 90% of streptococcal and 50% of staphylococcal infections) (Neave *et al.*, 1966; Halasa *et al.*, 2009). However, variable cure rates of dry cow therapy (Halasa *et al.*, 2009) can result in PI cows, particularly older cows, which can provide a reservoir of pathogenic bacteria. Therefore, sometimes, culling chronically infected cows from the herd at drying off could have a greater influence than dry cow therapy in reducing the prevalence of infection (the number of infected cows) in many herds (Browning *et al.*, 1994).

The final measure in the mastitis control plan is related to the maintenance of the milking equipment. The milking machine needs to provide adequate vacuum level and vacuum stability and allow a short milking to reduce the risk of mastitis (Thompson *et al.*, 2006). Additionally, the milking machine plays a role in the maintenance of teat condition, which can impact infections (Thompson *et al.*, 2006). Advances in milking machines have greatly improved vacuum stability, duration and teat condition (Mein, 2012; Ruegg, 2017) making milking machine factors less predominant as the main cause of mastitis problems (Mein, 2012).

Additional milking management practices that have been shown to reduce bacterial contamination of teat ends can be important mastitis control measures. Wearing gloves for milking cows is absolutely necessary to avoid the spread of contagious pathogens (Neave *et al.*, 1966). Pre-milking disinfection of teats (not udders) if followed by effective drying can reduce the development of infections caused by *Strep. uberis* (Galton *et al.*, 1988). Separate milking of cows infected with *Staph. aureus* has been shown to reduce the prevalence of infection significantly (Wilson *et al.*, 1995). Additionally, regular SCC recording is a key tool in monitoring intramammary infection and allows for improvements in mastitis control (LeBlanc *et al.*, 2006). In Ireland, regular milk recording of approximately 40% of herds is conducted and only on average 4.5 times in the lactation (More *et al.*, 2017).

The implementation of the five-point plan has led to a reduction of infections and a change in the aetiology of mastitis in many countries (Bradley & Green, 2004; Zadoks & Fitzpatrick, 2009). In Ireland, most mastitis problems remain associated with contagious mastitis pathogens and especially *Staph. aureus*. Several studies have shown that *Staph. aureus* was the most common pathogen found in cows infected at dry off (range 60–90% of infections) (Egan & O'Dowd, 1982; McParland *et al.*, 2019; C. Clabby, personal communication), in sub-clinical mastitis samples (21%; Barret *et al.*, 2005) and in clinical mastitis samples (38%; Keane *et al.*, 2013), followed by *Strep. uberis*.

CellCheck, the national mastitis control programme, coordinated and facilitated by AHI has contributed to reducing SCC in dairy herds on a national basis. However, currently, many farms still have sub-optimal levels of milk quality. Data collected by DAFM showed that in 2018, 38% of herds had an annual bulk tank SCC of >200,000 cells/mL (AHI, 2019). Having information of individual cow SCC combined with the measures in the five-point plan can have a great impact in further improving udder health in national herds.

AMU and selective dry cow therapy

Legislation on AMU on animals (Regulation 2019/6) will come into effect in the EU from 28 January 2022 (European Parliament and the Council of the European Union, 2019) which includes regulation on the preventive use of antimicrobials in groups of animals (e.g. dry cow therapy).

In Canadian dairy farms, Saini *et al.* (2012) reported AMR to penicillin by *Staph. aureus* strains in 28% of the herds examined (Saini *et al.*, 2012). Similar results were reported by McDougall *et al.* (2014) in New Zealand dairy herds. Holko *et al.* (2019) observed that 62% of isolated mastitis-causing pathogens were resistant to at least one antimicrobial. *Strep. agalactiae* was resistant to at least one antimicrobial in 100% of isolates, while resistance was found in 86% of *Strep. uberis* and 79% of *E. coli* isolates (Holko *et al.*, 2019). Resistance to penicillins by *Staph. aureus* has been shown to vary greatly between different geographical regions (likely due to treatment decisions and poor stewardship) and temporal trends can be recognised (Aarestrup & Jensen, 1998), which highlights the importance of evaluating resistance profiles for each country. In Ireland, there are limited current data on AMR or mastitis-causing pathogens (Aarestrup & Jensen, 1998). Keane (2016) found that of 53 *E. coli* isolates from clinical mastitis, 16% were resistant to at least one antimicrobial (most commonly tetracycline), while three isolates were multidrug resistant. Aarestrup & Jensen (1998) reported that 90% of 100 *Staph. aureus* isolates were resistant to penicillin; however, there was no reference to the resistance profiling methodology applied in that study. There is a need for current data on resistance profiles for the most common pathogens causing clinical and sub-clinical mastitis in Irish dairy herds.

Mastitis accounts for the majority of antimicrobials administered to dairy cows (Pol & Ruegg, 2007; Saini *et al.*, 2012). Stevens *et al.* (2016) reported that approximately 60–70% of all antimicrobials administered on dairy farms are for preventing and treating mastitis. More *et al.* (2017) showed a yearly decrease in intramammary tubes sold for the treatment of mastitis in lactation since 2003 in Ireland; however, a higher percentage of critically important antimicrobials (i.e. an antimicrobial that is the sole or one of few therapies available for serious human diseases and that is used to treat diseases transmitted to humans from non-human sources or may acquire resistance genes from non-human sources) were being prescribed.

Blanket dry cow therapy (treatment of all quarters of all cows at the end of lactation) was an important measure targeted at curing existing infections and avoiding new infections over the dry period (Dodd *et al.*, 1969). This practice has been widely adopted in Ireland with an estimated adoption of 100% of herds in 2015 (More *et al.*, 2017) which is an increase of the estimated 92.7% coverage in 2010 reported by More *et al.* (2012). Given the impending legislation to prevent the prophylactic use of antimicrobials, selective dry cow therapy (treatment only of cows that have a proven infection, while the rest receive a teat seal) will become a common practice. International studies have mostly shown that there is no negative impact on SCC by replacing the use of antimicrobials with a teat seal at dry off in uninfected cows (Bradley *et al.*, 2010; Vasquez *et al.*, 2018; Rowe *et al.*, 2020). A study conducted in research herds in Ireland evaluated the effect of treating cows that had no clinical mastitis nor a high SCC recording (>200,000 cells/mL) with teat seal only compared with antibiotic plus teat seal (McParland *et al.*, 2019). Results showed that cows treated with teat seal only had a significantly higher average SCC in the following lactation compared to cows receiving antibiotic plus teat seal (roughly a 2% higher somatic cell score or 8,200 cells/mL difference when back transformed) (McParland *et al.*, 2019). Reports from a study conducted in five commercial Irish dairy herds found similar results with a large variation between herds, with one herd not showing differences in SCC between the teat seal-only and teat seal plus antibiotic groups (C. Clabby, personal communication). This highlights the importance of mastitis control during the lactation to reduce the risk of implementing a selective dry cow therapy approach because, particularly with *Staph. aureus*, more new infections are likely to occur in herds with high levels of infected cows (Berry & Hillerton, 2002).

Future research on mastitis control adapted to Irish dairy farms and safe implementation of selective dry cow therapy are warranted with the increased pressure to reduce antimicrobials on dairy farms, which will limit the implementation of blanket dry cow therapy while maintaining the industry goals of udder health and milk quality.

Parasitoses research

Ireland's grass-based production system, coupled with our mild and humid climate, ensures that the challenge of grazing livestock with a variety of endo- and ectoparasites is a perennial problem. The major endoparasites of concern in ruminant production include protozoa (e.g. *Eimeria* spp., *Neospora caninum*, *Toxoplasma gondii*, *Babesia divergens*), nematodes (e.g. the lungworm *Dictyocaulus viviparus* and a variety of gastrointestinal nematode [GIN] species) and trematodes (e.g. the liver fluke *Fasciola hepatica*) (Murphy *et al.*, 2006). Major ectoparasites of concern include mite infestations, leading to mange or sheep scab, and lice infestations (chewing and sucking lice). Parasitic infections result in significant economic losses, primarily due to reduced production efficiency and treatment costs. The total cost of infections of cattle and sheep in Ireland due to the helminth parasites *D. viviparus*, *F. hepatica* and GIN has recently been estimated at almost €240 million per annum (Charlier *et al.*, 2020).

Parasite control

For the past 60 yr, the control of parasites has been heavily dependent on the availability of effective anti-parasitic veterinary medicines. Initial compounds, such as phenothiazine, were subsequently replaced by a series of highly effective, safe anti-parasitics that were developed throughout the 1960s–1980s (Gordon, 1961; Turton, 1969; Lucas, 1971; Wolff *et al.*, 1983). The golden era for anti-parasitic development arguably culminated with the launch on the market of ivermectin in 1981 (Campbell *et al.*, 1983). This broad-spectrum anthelmintic, which has activity against human as well as veterinary parasites, was developed at Merck Research Laboratories in the United States by a team led by Irishman William Campbell, an achievement for which he was jointly awarded the Nobel Prize in Physiology or Medicine in 2015 for "discoveries concerning a novel therapy against infections caused by roundworm parasites". However, there has been a dearth of new anti-parasitics launched onto the global market in recent years with only two new anthelmintic classes developed: the amino-acetonitrile derivatives and spiroindoles (Kaminsky *et al.*, 2008; Little *et al.*, 2011) with both of these classes licenced for the control of nematodes in sheep only.

Anti-parasitic resistance (APR)

The lack of new effective anti-parasitics coming on-stream is a cause for concern, as the emergence of drug-resistant parasites is now a threat to our pasture-based production system. Anthelmintic resistance is now widespread among GIN of sheep and cattle in Ireland (Keegan *et al.*, 2017; Kelleher *et al.*, 2020). Worryingly, GIN that are simultaneously resistant to all three commonly available anthelmintic classes (benzimidazole, levamisole and macrocyclic lactones) have also been identified (Keegan *et al.*, 2015). Among trematodes, *F. hepatica* resistant to triclabendazole have been confirmed in Ireland (Mooney *et al.*, 2009) and resistance is likely to be widespread (Rose Vineer *et al.*, 2020). As this anthelmintic class is the only flukicide with efficacy against all stages of *F. hepatica*, resistance raises the spectre of uncontrollable liver fluke disease due to early immature stages. Tolerance to the insecticide deltamethrin has also been demonstrated in *Bovicola bovis* (chewing lice) (Mckiernan *et al.*, 2021). While APR has not been documented in Ireland for a number of commercially important parasites such as *Nematodirus* spp. or *D. viviparus*, the lack of regular monitoring or national surveillance programmes for resistance may be responsible for this lack of detection. Ultimately, continued widespread use and misuse of anti-parasitic products will apply an ongoing selection pressure for resistance development and will inevitably culminate in the emergence of further resistance.

A variety of approaches will be required to manage the threat posed by APR. The distribution of parasites in the host is often over-dispersed (Barger, 1985). Hence, the development of novel, cheap, pen-side diagnostics/sensors or infection indicators will facilitate targeted treatment of at-risk individuals or groups of animals at the appropriate time. Irish research has made significant advances in understanding *F. hepatica* antigenic determinants and the associated immune response (Dalton & Heffernan, 1989; Mulcahy *et al.*, 1998; Mulcahy *et al.*, 1999), which facilitates the design of immunological solutions, such as novel vaccines (Molina-Hernández *et al.*, 2015). By stimulating natural immunity against disease, vaccines are highly effective, easy to administer and have broad consumer acceptance. Increased uptake of existing vaccines (such as lungworm vaccination) should also be encouraged, and research to optimise the use of such vaccines in the context of our pasture-based, spring calving system is required (Downey, 1984). Research on management strategies that slow the further development of APR and approaches to manage parasites in the face of existing and emerging APR are now urgently required. Refugia, the proportion of the parasite population not exposed to resistance selection pressure, is a key determinant for the development and spread of APR (van Wyk, 2001). The concept of refugia management will need to become commonplace on Irish farms and research to optimise refugia within Irish farming systems is required. Breeding animals for resistance to parasitic disease will also improve sustainability and reduce reliance on anti-parasitics. While the heritability of many disease traits is low, heritability of resistance to GIN is moderate in cattle and sheep ($h^2 = 0.2–0.3$) (Gasbarre *et al.*, 1990; Keane *et al.*, 2018). Breeding values for resistance to liver fluke infection have recently become available in Ireland for AI bulls, and these will be incorporated into breeding indices in time.

Changes in the prevalence of parasite pathogens have also been reported over the last 60 yr, such as the decline in the incidence of bovine babesiosis (Gray & Harte, 1985; Gray *et al.*, 1996; Zintl *et al.*, 2014b). The emergence of new parasitic diseases is also an area of concern. In recent years, there has been an apparent increase in the prevalence of rumen fluke in Ireland (Murphy *et al.*, 2008; Zintl *et al.*, 2014a). While adult rumen fluke appear to be relatively well tolerated, a large number of larvae in the intestine has been associated with clinical disease (Millar *et al.*, 2012). One hypothesis for the increase in the prevalence of paramphistomosis is the importation (in ruminants) and spread of a new paramphistomum species. Early work identified rumen fluke in the United Kingdom and Ireland as *Paramphistomum cervi* (Willmott, 1950); however, more recently it has been demonstrated that the major species present is *Calicophoron daubneyi* (Zintl *et al.*, 2014a; Martinez-Ibeas *et al.*, 2016). Future research may determine whether the recent increase in rumen fluke prevalence is the result of the importation of a new species or a change in local conditions, which favours the transmission of an existing species. The impact of *C. daubneyi* on ruminant health and production efficiency also remains to be elucidated. While an aquatic snail is the intermediate host for *P. cervi*, *C. daubneyi* and *F. hepatica* share an intermediate host, *Galba truncatula*, and co-infection of livestock with both species occurs on many farms (Jones *et al.*, 2017). The impact of the increasing prevalence of *C. daubneyi* on *F. hepatica* prevalence and the possibility of competition between the two species within the intermediate host warrants further investigation. In addition, only a single product, oxyclozanide, has efficacy against rumen fluke and so there is a need to guard against the development of resistance to this product.

The local environment has a significant effect on the lifecycle and transmission of many parasites (Ollerenshaw, 1966; O'Connor *et al.*, 2006; Morgan & van Dijk, 2012). Climate or land use change may therefore have a major impact on the epidemiology of livestock parasitic diseases by changing the risk period for infection, the window of transmission for specific species or providing habitat for disease vectors (van Dijk *et al.*, 2010). Changed climatic conditions may support the lifecycle and transmission of parasite species, such as *Haemonchus contortus*, not currently commonly found in Ireland. An increase in mean temperatures may also enable the spread of arthropod vectors in Ireland, with a concomitant increase in vector-borne parasitic diseases.

Future research in this field needs to address predicting the influence of climate change on host–parasite dynamics and mitigating the negative consequences of any change in parasite transmission dynamics.

Sheep disease research

This section will give a broad overview of the research into the health status and the most prevalent endemic diseases of sheep in Ireland and internationally over the past 60 yr.

In the sheep census, the population of sheep in Ireland was just over 3.7 million with 35,186 flocks. This gives an average of 106 sheep per flock, but the flock size is skewed with many flocks below 100 and few above 300 (Gov.ie Sheep Goat census; http://www.askaboutireland.ie/enfo/sustainable-living/farming-in-ireland-overvi/sheep-farming/#:~:text=In%20total%2C%20as%20of%20December,%2C%20Mayo%2C%20Kerry%20and%20Wicklow).

Causes of ovine mortality

A mortality study of Irish flocks (*n* = 33) was carried out by DAFM laboratories in 2016 (Murray *et al.*, 2019). The median overall submission rate of dead sheep of all ages from sentinel lowland flocks of 13.8% is in line with other international studies. Data for mortality rates in sheep of all ages internationally have not been published for comparison.

Ovine diseases

The health status of a flock has major implications for the welfare, productivity and profitability of sheep farming. (Hosie & Clark, 2007) The health status of the flock also affects the potential for antimicrobial and anthelmintic resistance. Health issues which have a big effect on productivity include lameness, mastitis and teeth problems. The iceberg diseases that are present in Ireland include ovine pulmonary adenocarcinoma (OPA), maedi visna (MV), caseous lymphadenitis (CLA), JD. Iceberg diseases are slow-onset diseases which cause chronic wasting and are referred to as iceberg diseases, as the thin, wasting ewes are the tip of the iceberg, with the vast majority of their negative health issues and productivity losses hidden below the surface (Ogden *et al.*, 2019).

Internal and external parasites are also major issues for sheep health and productivity; they are dealt with in a separate section.

Ovine abortion

The two most important causes of infectious abortion in Ireland are *Chlamydophila abortus* (EAE) and *Toxoplasma gondii* infection. In the 2016 All-Island Surveillance Report (DAFM, 2016), approximately 23.5% of ovine abortions submitted to DAFM Regional Veterinary Laboratories were diagnosed as due to *Toxoplasma gondii* and about 16% due to EAE (*N* = 713). Mearns (2007) found that together these make up over 70% of diagnoses of abortion material at veterinary disease surveillance centres throughout England, Scotland and Wales.

Ovine lameness

Lameness is a major issue for sheep farmers as it impacts welfare, productivity and labour demands. In the work by Bohan *et al.* (2019), the costs/ewe/day associated with lameness in Ireland were €0.25. Thus, lameness has a huge impact worldwide on the economics of sheep production. The main causes of lameness in Irish sheep are footrot, “scald” and contagious ovine digital dermatitis (CODD). Footrot is a highly infectious bacterial disease caused by two bacteria – *Fusobacterium necrophorum* and *Dichelobacter nodosus*. Vaccines have been developed over the last 40 yr to try to combat footrot (O’Meara *et al.*, 1993).

Interdigital dermatitis (scald) results in the skin between the claws becoming red and swollen and covered by a thin layer of white discharge. There is no under-running of the hoof wall or sole. It is more common in lambs, especially when underfoot conditions are wet. Contagious ovine digital dermatitis is caused by treponeme bacteria and often occurs in conjunction with footrot. There has been no Irish and only limited international research on lameness in sheep.

Ovine mastitis

Mastitis in sheep is often underappreciated as a productivity and welfare constraint. In the work by Bohan *et al.* (2019), the costs/ewe/day associated with mastitis were €0.24. In Ireland, McLaren *et al.* (2020) estimated that 19.2% of sheep are culled due to mastitis/udder problems. In the 2016 Irish sheep mortality study, 4.6% of deaths in adult sheep were attributed to mastitis (Murray *et al.*, 2019).

Ovine dental problems

As sheep are ruminants, and in Ireland, the majority of their feed intake is from forage, good dentition is a prerequisite to productivity and longevity in the flock (Nolan & Black, 1970). Incisors are commonly examined by flock owners and sheep are culled on findings; however, overgrown, worn and absent molar teeth and jaw abscesses cause problems with mastication of fibrous feeds and subsequent weight loss. It is estimated in Ireland that 20.9% of sheep are culled for problems with teeth (aged) compared to 38.9% in the United Kingdom (McLaren *et al.*, 2020).

Ovine pulmonary adenocarcinoma

Ovine pulmonary adenocarcinoma (OPA) is caused by the jaagsiekte retrovirus (JSRV). It is characterised by the development of invariably fatal lung tumours primarily in adult sheep. Affected sheep show breathlessness, exercise intolerance and repeated moist coughing. In Irish surveillance work carried out by Lee *et al.* (2017), lungs from 1,911 adult sheep were examined macroscopically in the abattoir and 369 were removed for further testing due to the presence of gross lesions of any kind. All 369 were subject to histopathology and real-time (RT) PCR and 46 to immunohistochemistry (IHC). Thirty-one lungs (31/1,911, 1.6%) showed gross lesions and were positive for JSRV by RT-PCR and/or IHC, but only 10 cases of OPA were confirmed (10/1911, 0.5%). Jaagsiekte retrovirus-positive sheep tended to cluster within the same flocks.

Maedi visna

Maedi visna (MV) in sheep is caused by a lentivirus (MVV). The lungs and mammary glands are the main organs affected, with occasionally affected sheep developing nervous signs. In 2020, the first cases of MV in Ireland were diagnosed by Regional Veterinary Laboratory (Kilkenny, Ireland) in two flocks. Surveillance studies carried out by DAFM laboratories on serum collected in 2018 and 2019 suggest, as yet, a very low prevalence (0.25%) in Irish sheep (unpublished). A study by Ritchie *et al.* (2012), using a random sample of UK flocks, found that the prevalence of infected flocks appeared to have doubled between 1995/1996 and 2010 (1.4%–2.8%, $P = 0.015$).

Pestiviruses

The DAFM has carried out a number of seroprevalence studies in the past number of years (unpublished). In 2019, a seroprevalence study on pestiviruses (border disease and BVD) and Q-fever was carried out in four flocks. The main finding of the study was that there was very low lamb seroprevalence (0.19%) of pestiviruses. Flock seroprevalence was 2% (4/196 flocks positive). There seems to be no significant epidemiological link between the sheep flocks where pestivirus was demonstrated to be circulating and the presence of BVD in cattle on those establishments.

Q-fever

The major finding of the DAFM study (unpublished) on Q-fever is the lower seroprevalence of *Coxiella burnetii* antibodies in sheep flocks. The animal-level seroprevalence of 0.45% is down from the 0.7% found by Ryan in a 2011 prevalence study (Ryan, unpublished) and flock seroprevalence is down to 6.4% from 8.4%. This compares to a serological survey using an indirect ELISA, carried out on 15,186 sheep and goats in The Netherlands in 2008. In total, 2.4% (95% CI, 2.2–2.7) of the sheep and 7.8% (95% CI, 6.9–8.8) of the goats were seropositive for antibodies against *Coxiella burnetii* (van den Brom *et al.*, 2013).

Future ovine health research

Lameness, mastitis and ovine dental problems are the areas that need more research, as they have a major impact on sheep health and productivity, but there is very little available research. Areas for further research on mastitis are the infectious agents involved and genetic and management factors. Key areas for further research on ovine dental problems are the effects of diet and the extent of problems with molar teeth and jaw abscesses. Further research is also needed into the seroprevalence of JD and CLA in sheep in Ireland. Research into mastitis in milking goats in Ireland is also needed.

Conclusions

The last 60 yr have seen an exponential increase in ruminant health research in Ireland and worldwide associated with technological developments. Some of this has been proactive, but most has been reactive to changing agri-industry (or societal, e.g. AMR) priorities. The advances have been most marked in the economically important infectious diseases, particularly those of regulatory concern. This has sometimes (e.g. BVD, brucellosis), but not always (e.g. bTB), been associated with disease reduction or eradication. Our basic understanding of the causes and effective control measures for ruminant diseases has evolved with each scientific paper, resulting sometimes in re-evaluation of old dogma as the consensual evidence-base strengthened. Improvements in the scientific method (e.g. the use of meta-analyses) have contributed to these incremental gains. The ruminant health research agenda of the future will need to address not just ruminant health but also public perception of the priorities in ruminant health, as has already occurred with animal welfare research.

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