Cardiac disease in cats has a prevalence of 15%: myocardial and endocardial inflammation has been documented. Cardiac biomarkers, high sensitivity Troponin I (hsTnI) and NT-proBNP have been used as markers of myocyte damage and cardiac chamber remodelling in cats. Little information exists on the use of acute phase proteins (APPs) as markers of cardiac inflammation in cats. Research funded by a University of Glasgow Veterinary Fund grant facilitated collaboration of Dr Anne French and team with ReactivLab Ltd and IDEXX Laboratories to measure cardiac biomarkers (hsTnI and NT-proBNP) and APPs (haptoglobin, serum amyloid A, C-reactive protein and alpha-glycoprotein) in a cohort of cats with well characterised cardiac/non-cardiac disease.

Dairy herd health monitoring

Dairy herd health monitoring is an increasingly important component of commercial veterinary and consultancy services on dairy production units. Effectively monitoring herd performance in areas including nutrition, mastitis, fertility, lameness, infectious disease and replacement rearing allows the farmer to make improvements where necessary and maximise animal welfare and efficiency of production.

Mr Lorenzo Viora and team developed a project that combines provision of routine veterinary services and herd health consultancy with active research in herd health monitoring with 2 large commercial dairy farms in central Scotland. The project benefits the farmers by providing service delivery and access to up to date knowledge on developments in herd health, and benefits the School of Veterinary Medicine by gaining access to commercial production units for teaching (undergraduate and postgraduate) and development of applied research projects.

Research projects completed to date include work on fertility manipulation (Viora et al., in press) and monitoring of pathogens associated with mastitis (Viora et al., 2014). Currently ongoing projects include optimising neonatal calf health and developing non-invasive methods of monitoring udder health during the last stages of pregnancy in replacement heifers.

The project still has 3 years to run (with option to extend at that time); both parties are very satisfied with the outputs to date.
Developing technologies for the control of viral diseases in cats

In Europe, over 30 million domestic cats are vaccinated each year against three core virus infections. Research performed by the University of Glasgow has made a significant contribution to controlling the major feline viral diseases, supported by industrial collaborations.

Feline leukaemia virus (FeLV) was discovered by University of Glasgow researchers in 1962, associated with lymphoma and leukaemia in cats; in 1993, University of Glasgow and Merital collaborated to develop a new FeLV vaccine; University of Glasgow provided FeLV constructs based on the Glasgow-1 virus strain and tested vaccine efficacy. This highly efficacious vaccine is used widely to protect cats against FeLV infection.

The feline lentivirus feline immunodeficiency virus (FIV), is widespread worldwide and induces clinical signs resembling human acquired immunodeficiency syndrome (AIDS). University of Glasgow researchers Margaret Hose and Brian Willett, supported by funding from research councils, charities and industrial partners, have contributed significantly to the understanding of immunity to FIV and in vaccine development.

Since 2010, University of Glasgow has hosted the European reference laboratory for feline calicivirus (FCV), funded by Merital SAS. Data from this project will potentially improve understanding of immunity against FCV infection; this has comparative significance for the development of vaccines against the closely related human norovirus, a leading cause of acute gastroenteritis.

Biomarkers to assist decision making in veterinary neurology

Dr Mark McLaughlin and Prof. Jim Anderson’s group is comprised of clinicians and scientists who aim to identify biomarkers of canine neurological disorders affecting the spinal cord from a range of biological fluids including CSF, urine and blood. One potential biomarker of canine degenerative myelopathy (DM) called apolipoprotein J (or clusterin) has been identified in CSF. DM is associated with a mutation in the gene encoding superoxide dismutase (Sod1), implying that DM is a naturally occurring animal model of the human condition familial amyotrophic lateral sclerosis (ALS). Validation of this and other potential biomarker(s) to demonstrate specificity and reliability (e.g. discrimination between DM and vertebral disc disease) is required.

A achieving translational medicine outcome requires the development of a rapid and convenient analytical method for emerging biomarkers. It is likely that CSF derived biomarkers can inform on the disease mechanisms and therefore assist in identifying targets for drug design. It is envisaged that progress in the understanding and treatment of DM will also provide relevant information on human ALS. The group is looking to work with organisations developing analytical systems for a clinical setting to generate a readout while the animal is in clinic to assist in treatment planning.

EPIC centre of expertise in animal disease outbreaks

Prof. Dominic Mellor is part of this consortium among collaborating Universities and MRPAs in Scotland brings together a substantial body of epidemiological expertise to address the risks of, and response to, animal disease outbreaks.

The basis of this, and a previous programme, is the provision of epidemiological advice to support Scottish Government policy decisions about all aspects of animal disease management and control. A close working relationship with the farming, food and other rural industries has been a vital component of the programme, with representatives of these comprising part of the project’s steering group, and regular KE through industry stakeholder groups forming an essential communication pathway for industry focused research questions and their answers. Much of the work is dedicated to epidemiological modelling of infectious disease transmission, and of potential alternative control options, including their economic impact. Scenario planning exercises have engaged broad-based stakeholder groups to consider alternative long term futures for Scottish cattle and sheep industries under different conditions of, among other things, technological development and adoption. Such exercises offer valuable insights into potential future drivers for disease spread that can be accounted for and mitigated against. In addition to their direct outputs, these inclusive discussions have taught all participants a great deal about working at the science/industry/policy interface.

Use of acute phase protein CRP in canine lymphoma

Acute phase proteins are useful for disease monitoring and prognosis in human lymphoma, and Dr Joanna Morris and colleagues sought to investigate whether this was also the case with dogs.

As part of treatment investigations and at each chemotherapy visit, routine bloods were collected from canine patients and ReactivLab was approached to run an assay for C-reactive protein (CRP) on these. Pilot data indicated that CRP is high in untreated lymphoma and reduces as dogs go into clinical remission.

A larger sample size investigated as an MSc project confirmed these findings and showed CRP at time of diagnosis is related to serum albumin, disease stage and subtype. The research benefitted the Glasgow oncology service by illustrating the work on canine lymphoma, whilst benefitting ReactivLab by highlighting an important use for their CRP assay. Dr Morris hopes to collaborate on future projects with Avacta Animal Health (bought ReactivLab) who currently market the canine lymphoma blood test (cLBT) which utilises the serological levels of CRP and Haptoglobin, in combination with other clinical information to aid diagnosis of lymphoma.

Minimising risk in horse racing

This body of work has evolved over the last 10 years through multiple contacts made with racing jurisdictions around the world. Dr Tim Parkin’s underlying science is based on epidemiological and statistical analysis of data to identify risk factors for which we use multi-level logistic regression techniques and other predictive modelling procedures such as machine learning to develop predictive models. This research has progressed from the identification of risk factors to the identification of ‘at risk’ horses, with the main driver being to ensure that the work has a practical impact on the welfare of racehorses.

There are three ongoing projects in North America and GB which either aim to better identify the ‘at risk’ horse or modify racing conditions and owner/trainer understanding of injury risk such that the likelihood of fatal or non-fatal injury is as low as possible. These different approaches are attractive to racing jurisdictions around the world and it is anticipated that others will request the group conduct similar projects in the years to come.
Clinical development of Trilostane for canine Cushing’s disease

In the 1970s canine Cushing’s disease was treated with mitotane. However this drug was expensive and cytotoxic, demanding specific dog handling requirements and discouraging this treatment regimen. Trilostane, a steroid synthesis inhibitor, was first used in dogs in 1997 and the benefits were immediately obvious. This prompted Dechra Pharmaceuticals (at that time called Arnold’s) to use Prof. Ramsey’s expertise in a canine clinical trial, which involved recruiting cases and managing them with trilostane.

The combination of Arnold’s experience at getting drugs authorised for veterinary use and clinical skills found in University of Glasgow led to a provisional authorisation being obtained for trilostane to be sold as Vetoryl within 3 years. Further trials comparing dosing regimens and delivery followed. Today, in 2014, Vetoryl (trilostane) sales are worth just over ten millions of pounds in Europe per year, with just over thirty thousand dogs (and even some cats) being treated. These figures do not include USA sales. Working with Dechra, numerous continuing professional development sessions were provided around the world. As a result of this work, the University of Glasgow is now established as a centre for clinical research into canine Cushing’s disease, with trials on new condition monitoring methods currently underway.

Evaluation of a culture-based pathogen identification kit for bacterial causes of bovine mastitis

Accurate identification of mastitis-causing bacteria supports effective management, allowing selective treatment and providing the opportunity to reduce unnecessary antimicrobial use, an important issue in food producing animals. On-farm culture-based pathogen detection kits (allowing crude identification of pathogens within 18-24h) have been used successfully for this purpose in US dairy herds, but no reports are available on UK dairy herd samples. The culture-based mastitis pathogen detection test kit ('VetoRapid', Vétoquinol) results were compared with standard laboratory culture by Mr Lorenzo Viora and team to evaluate whether they could be used to inform a selective treatment programme. In conclusion, the kit provided rapid preliminary identification of five common causes of bovine mastitis under UK field conditions, likely to be suitable for informing selective antimicrobial treatment of clinical mastitis caused by Gram-positive organisms.

A recent training day for the UK-Ireland Vétoquinol team discussed the practicality of the test kit, the main outcomes of this project, and a possible future collaboration.

Birds, dogs and horses: Investigating influenza and viral emergence

Influenza or ‘the flu’ is a common infectious disease caused by a virus that affects many of us each year, causing symptoms such as fever, headache, runny nose and coughing. Unfortunately, in some people it causes much more serious disease and results in thousands of deaths each year worldwide. The flu virus is constantly adapting and changing and has the ability to move between host species including birds, pigs, horses, dogs and people. The emergence of new influenza viruses can result in global pandemics, the most famous of which was the 1918 Spanish flu. Influenza viruses have emerged -4 times in people in the last 100 years.

At the Centre for Virus Research (CVR) and Weipers Centre Equine Hospital (WCEH) we are trying to better understand the ways in which flu viruses are able to emerge and adapt to new species. Veterinary species provide us with two excellent models that allow us to study viral emergence. The first is the jump of avian influenza from birds to the horse and the second is the jump of equine influenza from the horse to the dog. By studying these viruses, we aim to better understand flu and the general processes that underpin viral emergence in all species. With this knowledge, we can develop effective strategies to prevent influenza infection in animals and humans.

Wounds in people and horses: Can we increase the rate of healing?

Skin wounds, particularly those involving the lower limb, have significant welfare implications in humans and horses and have been neglected in research. Across the globe, the emotional and economic effects of these injuries are of major significance. To date it has not been possible to ‘speed-up’ the wound healing process and healing can be prolonged and complex. Across the globe, veterinary surgeons and horse owners employ a myriad of wound treatments, many of these are of dubious efficacy, some are perhaps detrimental.

During wound healing in humans and horses, communication between cells occurs via proteins called gap junctions. Recent work suggests that the gap junction protein Cx43 plays a central role with problem and complex wounds, undergoing delayed wound healing, showing increased concentrations of this protein.

Providing veterinary care to an underserved population of working horses, donkeys and mules

There are currently approximately 100 million working equids across the world, many of which have no access to veterinary care, indeed it is said that 99% of the world’s vets treat only 10% of the world’s equids. The link between human and animal health is well established and with equids (horses, donkeys and mules) thought to be responsible for around 75% of traction power in the underserved world, a healthy working equid can increase family income and therefore socioeconomic status considerably. Work by the Donkey Sanctuary suggests that a healthy donkey can increase family income by up to 500%.

The School of Veterinary Medicine, in conjunction with the American Fondouk, an NGO based in Fes, Morocco, is the first veterinary school to offer a working equid rotation, with approximately 35 students per year attending a 4-week placement. Providing veterinary care to these animals can be challenging and there are many aspects to consider including: cultural and language issues, dealing with unfamiliar diseases, working in a low resource environment, and coping with different standards of animal welfare. There are often fundamentally different views regarding treatment and euthanasia. In addition some workers have questioned the effectiveness and sustainability of providing veterinary care in underserved areas. Evidence suggests that the educational benefits for students are diverse and result in life long benefits professionally and personally. In addition the school offers a yearlong rotating internship for Moroccan employees of the American Fondouk at the Weipers Centre Equine Hospital. Weekly scheduled ward rounds, and several post graduate research studies are also underway. The two-way exchange of teaching, clinical work and research work between the University of Glasgow and the American Fondouk provides a template for similar initiatives across the globe that have the potential to significantly improve human and equine welfare.
In acute surgical wounds, undergoing normal healing, Cx43 synthesis is reduced in cells at the wound edge within the first 24–48 hours. At the same time it can be shown that Cx43 synthesis increases in blood vessels and activated neutrophils (white blood cells). Applying a Cx43 specific antisense gel (C43asODN) to an acute wound reduces the amount of Cx43 in wound edge cells faster and prevents the production of Cx43 in blood vessels. The overall result is that the wounds heal twice as fast with reduced swelling and evidence of inflammation. In humans, clinical trials suggest that the use of Cx43asODN as a single application on venous leg ulcers speeds their healing when compared with control wounds treated with gel alone. There is little doubt that normal wound healing can be speeded up by down regulating the synthesis of Cx43. Whilst this finding in itself is important the development of the method is better applied to situations where wound healing is abnormally slow or difficult to achieve, such as in working animals presented on a single occasion in the underserved world.

Our project is exploring the dynamics of connexin expression in the wounds of horses with naturally occurring wounds healing normally and in those with complex non-healing wounds seen to determine the effect of the use of Cx43asODN treatment in problem equine wounds in addition to the use of “best practice” wound healing techniques.

This project brings together an international group interested in tissue regeneration and wound healing, and clinicians with access to naturally occurring problem equine wounds in the UK and the developing world. The long-term goal is to develop effective wounds treatments, reduce healing time and improve human and animal welfare.

**Passive smoking in pets:** understanding the risk and helping motivate owners to give up

Exposure to environmental tobacco smoke (ETS) through second hand smoke (SHS) can be significant in both adults and children and is a known cause of smoking related disease. In dogs, ETS exposure appears to increase the relative risk of cancer of the lung, nasal cavity and paranasal sinuses and was associated with increased populations of macrophages and lymphocytes and macrophage anthracosis in the bronchoalveolar lavage fluid in Yorkshire Terriers. In cats exposure to ETS is associated with increased expression of oncogenic p53 in oral squamous cell carcinoma and an increased relative risk of lymphoma. In cats self grooming is likely to increase the amount of nicotine and tobacco carcinogens ingested, which may explain the association with cutaneous and lymphoma (particularly if it were to increase the risk of intestinal lymphoma). Tobacco smoke has been shown to play a significant role in the development of IBD in humans increasing the risk of developing Crohn’s disease by a factor of 1.8–4.8.

At the School of Veterinary Medicine we have shown that both dogs and cats absorb just as much smoke as children in the home by assessment of hair nicotine concentration. We are finalising a study looking at the impact of ETS exposure on biological ageing parameters in pet dogs and still collecting data for a study to assess if cats with gastrointestinal diseases or lymphoma have greater hair nicotine concentrations. Further studies are looking at pet owners' attitudes to the issue of passive smoking to establish how veterinary surgeons can improve their advice to owners better. By performing these studies we are raising awareness of the dangers of passive smoking to all members of the household and identifying mechanisms by which passive smoking may be having a deleterious effect on both pets and their owners.

**Canine degenerative myelopathy: a unique, natural, companion animal model of fALS**

Canine degenerative myelopathy (DM) is a progressive neurological disorder associated with a mutation(s) of the Sod1 gene. This, together with the clinical and pathological features, has lead to the conclusion that DM is a comparable animal model of familial Amyotrophic Lateral Sclerosis (fALS) where mutations in the SOD1 gene have also been identified. The mechanisms responsible for the SOD1 mediated neurological disorder remains unclear. In both DM and fALS there is variability in disease penetrance and therefore a need for biomarkers to assist in diagnosis. There are currently no effective treatments available for either DM or fALS. Our group of clinical veterinary neurologists, pathologists and neuroscientists are actively investigating the mechanisms associated with DM and searching for biomarkers. A panel of fluorescently tagged wild type and mutant Sod1 constructs have been generated and will provide the basis of an in vitro programme investigating the toxic pathways associated with SOD1 mutant protein. A pathological study is also ongoing to identify in vivo characteristics to explain clinical neurological features of the disorder. This combined strategy may provide a more complete understanding of the disease process and aid in identifying therapeutic targets that would benefit not only DM but potentially fALS suffers.

Currently there are many hypotheses about possible sources of infection as this bacteria is able to infect and generate contaminating spores in a variety of warm-blooded animals. These include potential for healthy human carriers, as well as domestic animal carriers and infection through food and water. To investigate this further, clinicians at the School of Veterinary Medicine and researchers in the Institute of Infection Immunity and Inflammation are testing faecal samples from companion animals and livestock as well as environmental samples from soil and water. We will type any isolates of C. difficile at the Scottish National Clostridium difficile reference laboratory and compare these with types of C. difficile found in human cases. This research will identify potential sources of C. difficile infection for humans, and may offer opportunities to reduce the burden of disease.

**If you go down to the woods today:** Investigating ecological drivers of Lyme borreliosis in Scotland

Lyme borreliosis is a disease caused by bacteria which people can contract after an infected tick bite. The sheep or deer tick which transmits these bacteria is widely distributed in woodland, grassland and moorland in the UK, and while normally feeding on wild animals or livestock, this tick will also bite humans. Symptoms of Lyme borreliosis can include headache, muscle and flu type symptoms and in more serious cases the heart, brain and joints can be affected. Around 4% of ticks in the UK are infected, though this can vary substantially. Cases of Lyme borreliosis in Scotland and the UK have increased sharply over the last decade, and knowledge of environmental factors affecting the distribution of ticks and whether ticks are infected or not are of great interest.

At the School of Veterinary Medicine and Institute of Biodiversity Animal Health and Comparative Medicine we are using a number of approaches to study the ecology of Lyme borreliosis, including surveys of forested sites across Scotland and at Loch Lomond. Other work investigates the role of deer, songbirds and invasive grey squirrels on the number of infected ticks (hazard of Lyme borreliosis) in the environment. The results of this project will help us understand environmental factors which affect the hazard of Lyme borreliosis and improve recommendations to reduce the risk to humans.

**Investigating the environment and animals as sources of Clostridium difficile for community acquired infections in humans**

Clostridium difficile infection (CDI) is the most common cause of antibiotic-associated diarrhoea in the developed world with significant morbidity and mortality in the elderly. Whilst most commonly associated with health care settings, infection of the elderly, adults and children living within the community is a globally emerging problem. By definition, community associated disease represents patients suffering disease who have no recent history of visits to healthcare facilities. At present, the source and risk factors for this type of infection remain unclear.

[Image of a graph illustrating the different aspects of Lyme borreliosis research at the University of Glasgow. Clockwise from top left: Blanket dragging surveys of woodlands to collect ticks, other studies investigate the role of invasive grey squirrels, the role of songbirds, and the effect of deer density on ticks and Lyme borreliosis.]
The internationally accredited school provides expert referral services for animal owners, referring practitioners and researchers throughout the UK and beyond via:

- Small Animal Hospital
- Weipers Centre Equine Hospital
- Scottish Centre for Production Animal Health & Welfare (Cochno Farm and Research Centre)
- Veterinary Diagnostic Services

www.glasgow.ac.uk/schools/vet