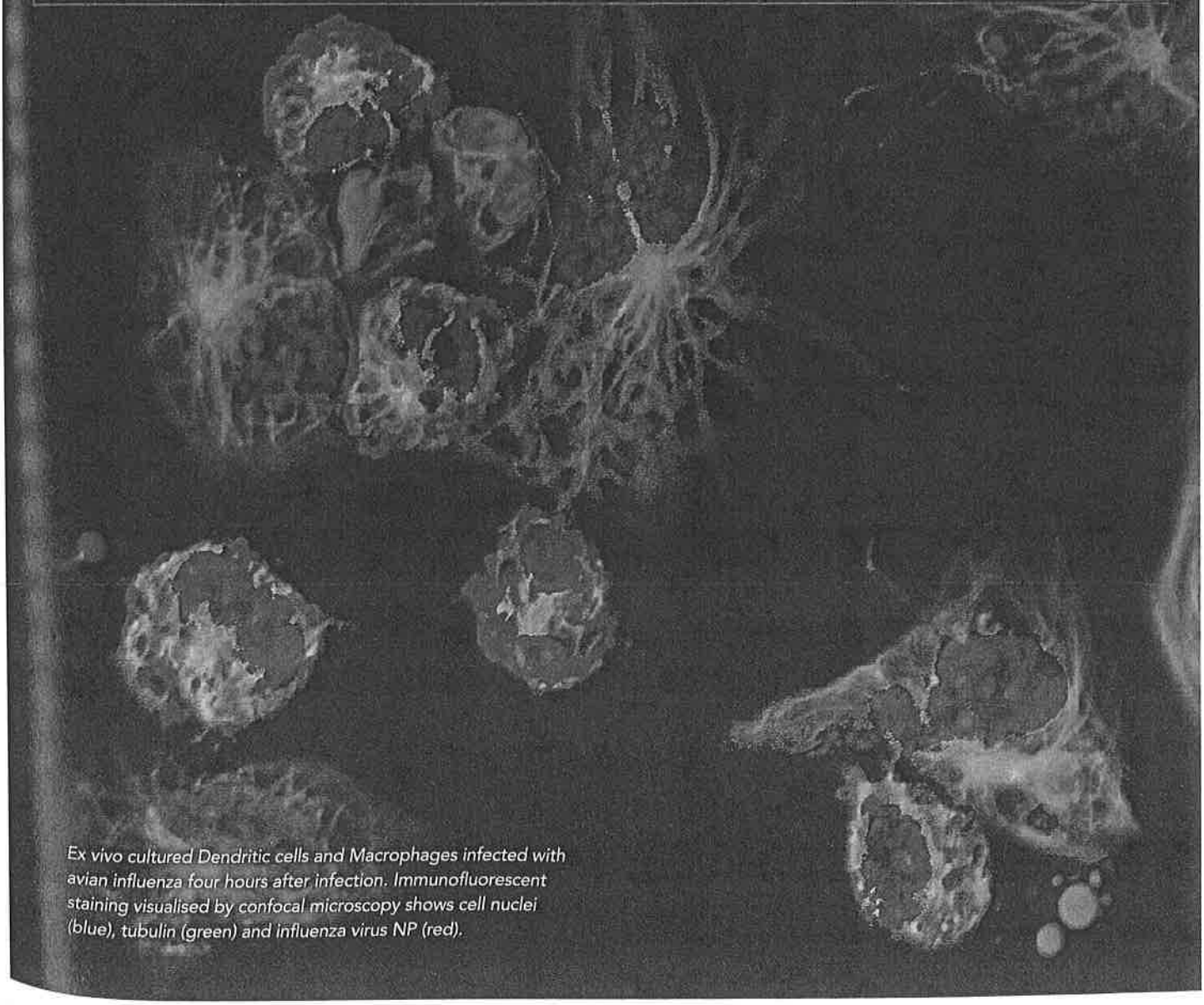
Case study

Towards a 'universal vaccine' to protect chickens against different subtypes of avian influenza virus

The Institute is also investigating other vaccine approaches to the control of avian influenza virus (AIV) in poultry. Dr Colin Butter's group, in collaboration with colleagues from the University of Oxford, has developed the concept of a "universal vaccine" for influenza in chickens. Whereas traditional AIV vaccines are only effective against one subtype of flu virus, Dr Butter's team is developing a strategy whereby new-generation vaccines will protect against different subtypes of AIV.

The approach involves human adenovirus and modified vaccinia virus Ankara as recombinant vaccine viruses that carry the nucleoprotein and matrix protein genes from an H3 subtype human influenza virus strain. These highly conserved internal proteins then become the targets of cell-mediated immunity that protects across different influenza virus subtypes, including AIVs.

By experiment, Dr Butter's group found that this strategy produced appropriate immune responses to the H3 subtype derived vaccine that protected chickens against challenge with unrelated H7 subtype AIV. The use of such recombinants is likely to be much more sustainable than vaccines that produce only antibody-mediated immunity, as the latter drive the target virus to escape through antigenic variation. This work continues through the framework of the Jenner Institute, which brings together medical and veterinary vaccinologists.



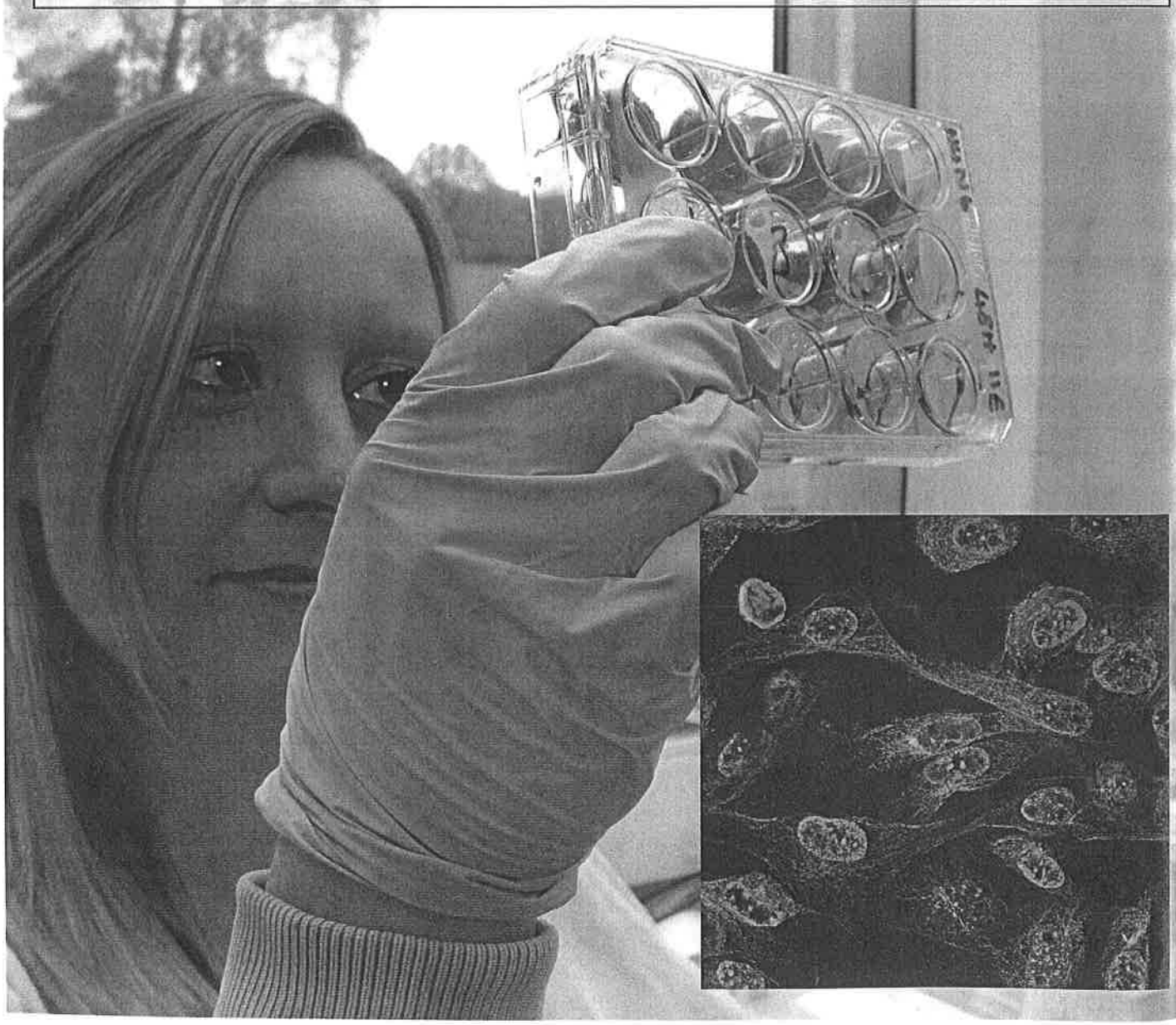
Ex vivo cultured Dendritic cells and Macrophages infected with avian influenza four hours after infection. Immunofluorescent staining visualised by confocal microscopy shows cell nuclei (blue), tubulin (green) and influenza virus NP (red).

Case study
Investigating the threat of avian influenza virus to humans

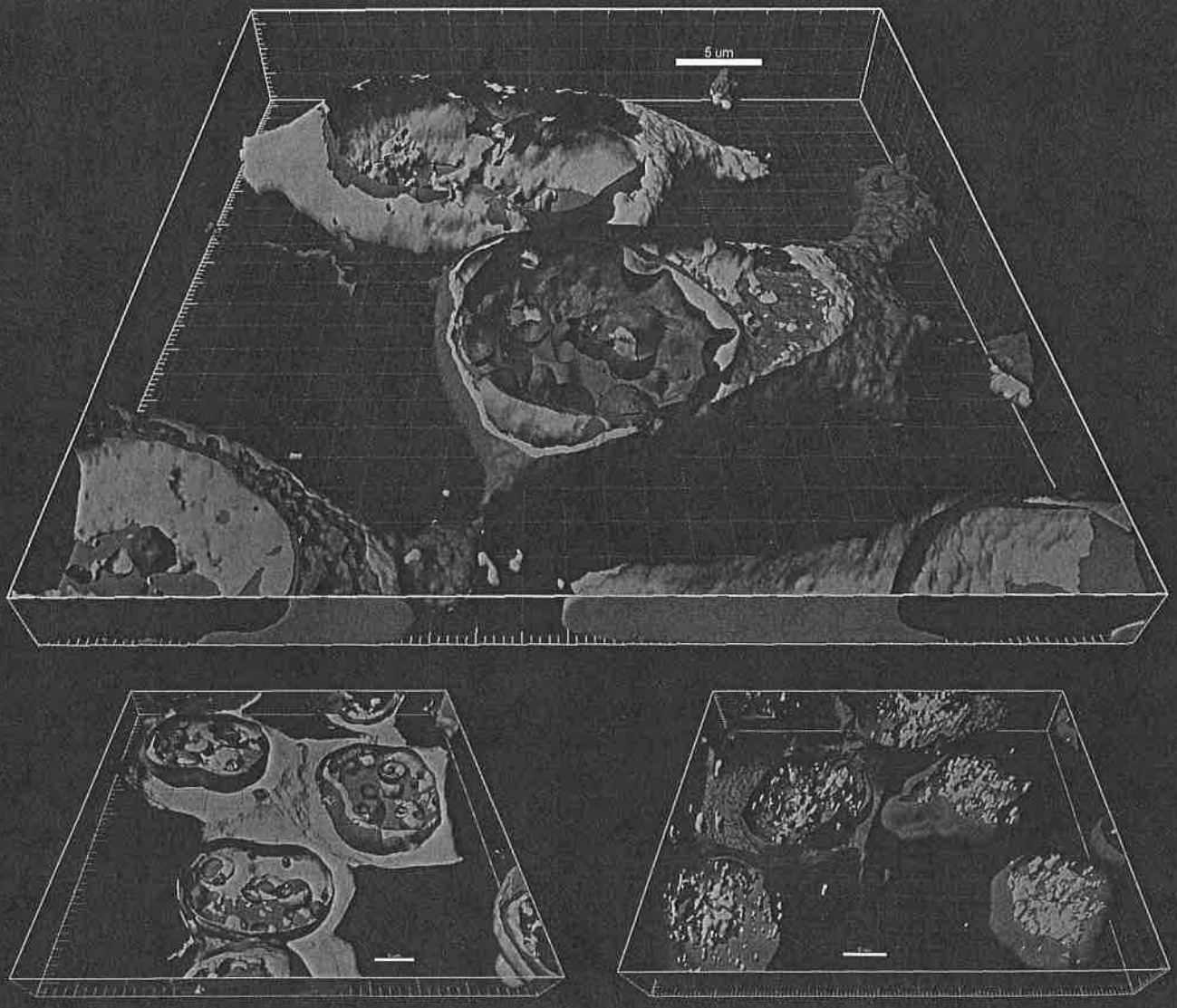
Domestic animals such as poultry and pigs can act as a gateway for influenza to pass from the wild bird reservoir to humans, due to their close proximity. Dr Holly Shelton's group is investigating the potential of avian influenza viruses (AIVs) to infect humans, and whether some AIV subtypes can resist human anti-viral drugs.

One objective is to establish which AIV subtypes can attach, replicate and transmit in domestic poultry populations, as only a handful of the 17 subtypes have ever infected humans, and widespread infection of chickens has also been limited to only a few subtypes. Dr Shelton is using differentiated culture systems, such as chicken tracheal organ cultures (illustrated: ciliated cells, red; green indicates cells infected with H4N6 subtype AIV from a Mallard duck), which mimic the sites of replication in poultry (respiratory and enteric tract), to develop an understanding of why some avian subtypes replicate well and others do not in the poultry host. This will allow development of improved diagnostic tests and inform surveillance programmes.

Another approach, through fitness studies, is to determine whether strains of influenza that grow well in domestic poultry are capable of maintaining mutations that render them resistant to anti-viral drugs.



Viral nucleic acids have to be translated into proteins by the host machinery and so scientists at The Pirbright Institute are studying the key component - ribosomes. Using state of the art microscopic techniques ribosomal subunits can be visualised in 3D within cells, as seen below.



All known viruses are dependent on cellular translation machinery known as ribosomes to meet their intense protein synthesis needs. Scientists at The Pirbright Institute hope to develop strategies to control and prevent viral diseases by studying the mechanisms by which viruses hijack the ribosomes for their own benefits. The ribosome is a very complex macromolecular structure that is extremely difficult to harness but thanks to a novel system recently developed by Prof Vincent Mauro from the Scripps Research Institute, La Jolla, California, it is possible to address some of the functional and regulatory properties of ribosomes; particularly those exploited by viruses.

Using state of the art microscopic techniques with 3D image reconstruction software (research led by Dr Abdessamad Tahiri-Alaoui in collaboration with Prof Vincent Mauro) it has been possible to visualise ribosomal subunits inside cells that are programed to produce recombinant ribosomes:
***Top image**: 40S subunit (seen in red) and native 60S subunit (seen in green) with the nucleus (shown in blue).*
***Lower right image**: The novel ribosomal system can be established without disturbing the homeostasis of ribosome biogenesis as it uses existing nucleoli (seen in green).*
***Lower left image**: The research has allowed the identification of specific spots within the 40S ribosomal subunits that if mutated, can prevent ribosome biogenesis.*

Livestock Viral Diseases programme

Head of programme: **Dr Bryan Charleston**

The ever growing populations of livestock worldwide, and the continual increase in intra- and intercontinental trade of livestock, meats and products derived from them, are increasing the risk posed by livestock virus diseases. For example, the UK foot-and-mouth disease (FMD) epidemic of 2001 was not only devastating to British livestock and their owners, it also brought other rural businesses to a stop, and cost billions of pounds for control actions and compensation.

Mitigating these threats requires research to underpin control measures within our borders and to contribute to better disease control in those countries where the diseases are endemic; reducing the disease abroad means minimising the risk to the UK.

In addition to FMD virus, we are also studying the causative viruses of classical swine fever, peste des petits ruminants of sheep and goats, and calf pneumonia (bovine respiratory syncytial virus), and are in a position to investigate additional emerging viruses, such as swine influenzas, which can be a threat to people as well as livestock.

Foot-and-mouth disease

FMD is perhaps the most feared disease amongst owners of cloven-footed animals. The major susceptible species under threat in the UK are cattle, sheep and pigs. The virus (a picornavirus) is present on three continents – Africa, Asia, and South America.

Classical swine fever

Classical swine fever is caused by a pestivirus which occurs in much of Asia, Central and South America, parts of Africa – and in parts of Europe. It is a highly contagious disease. In Europe outbreaks are controlled by slaughter.

Peste des petits ruminants

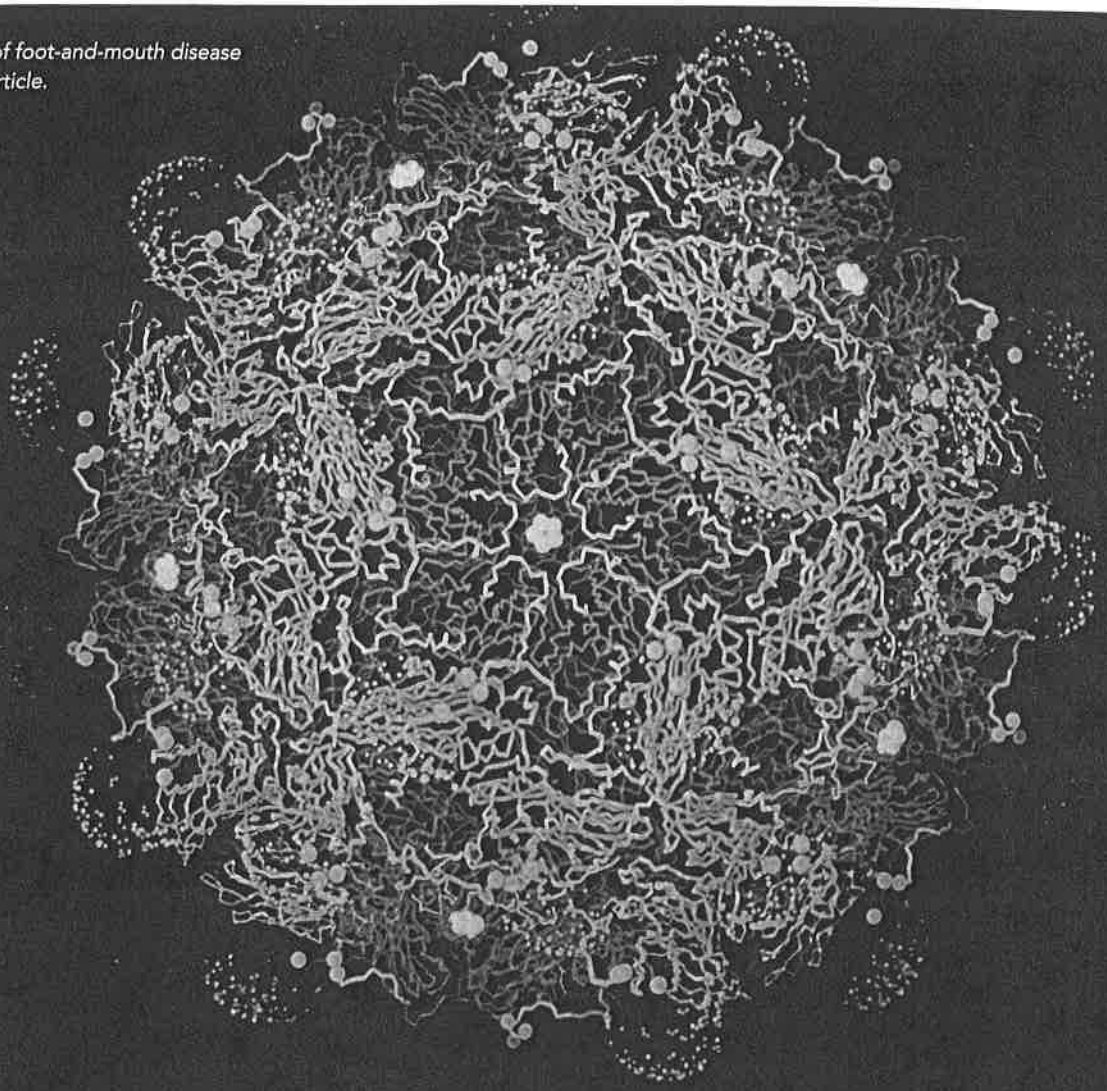
Peste des petits ruminants virus (PPRV, a morbillivirus), which causes disease in sheep and goats in Africa and Asia, is a close relative of rinderpest which has recently been eradicated globally. Research at the Institute is aimed at producing better vaccines and diagnostics for the control of PPR, with the possibility of eradicating it.

Bovine respiratory syncytial virus

Bovine respiratory syncytial virus (a pneumovirus) is endemic in the UK, causing pneumonia and serious losses in calves. We also study it because it serves as a model for the closely related human respiratory syncytial virus which causes particularly severe pneumonia in young children.

Unique resources

- Vesicular Virus Reference Laboratory and associated collections of viruses and surveillance data.
- An interdisciplinary team of experts comprising diagnosticians, epidemiologists, immunologists, molecular biologists, pathologists, vaccinologists, and virologists who can provide an emergency response capacity. New laboratories and large-animal experimentation facilities at very high bio-containment levels (SAPO 3 and 4) for research on viruses from overseas.
- Cattle and inbred pigs of known genetic background (defined MHC Class I haplotypes).
- Cattle MHC genes that determine protective immune responses.



Model of foot-and-mouth disease virus particle.

Scientific priorities are to understand:

- Why viruses emerge and persist, and what determines their capacity to spread and evolve.
- The features of the viruses and their replication processes that enable them to grow well, and how they induce and avoid protective immune responses in the host.
- How livestock immune systems combat viral infections, and how this is affected by genetic differences amongst individuals and breeds of livestock.

Research has additional impact arising from:

- The design of improved disease control strategies.
- Its underpinning of the diagnosis service provided by our Vesicular Virus Reference Laboratory.
- Modelling of the diseases, for prediction of emergence and spread.
- The Pirbright Institute being a hub for collaboration.
- Development of diagnostic tools for internal and worldwide use.
- Development of vaccines.
- Training of livestock industry professionals, diagnosticians and students.

Recent and current supporters include:

BBSRC, Defra, The Department for International Development (DfID), Wellcome Trust, vaccine developers (Merial Animal Health, MSD, Okairos), and diagnostics manufacturers (Prionics), Food and Agriculture Organisation (FAO), World Organisation for Animal Health (OIE), the European Union, US Department of Homeland Security.

More information: www.pirbright.ac.uk/ISPG/LVD.aspx

Livestock Viral Diseases programme
Recent achievements

Control of foot-and-mouth disease:

- **Enhanced understanding of virus-host interactions for FMDV, resulting in the development of improved FMD vaccine formulations.**

> Identification of follicular dendritic cells within lymph node germinal centres as a site of long term persistence of FMDV in cattle, sheep and African buffalo.

> Demonstration of the role of CD4+ T cell responses in the development of neutralising antibodies to FMDV in cattle.

> Defining the functional consequences of the interaction between FMDV and myeloid and plasmacytoid dendritic cells in cattle.

> Developed and patented an in vitro system to make FMD empty capsids, stabilised by targeted mutagenesis to survive heat and pH changes, which have the potential for the safer production of vaccines with better shelf life, and greater potency.

> Determined the infectious period of FMDV in cattle is shorter (mean 1.7 days) than currently realised and that animals are not infectious until, on average, 0.5 days after clinical signs appear.

> Identification of the palatine tonsil as a major site of viral persistence in African buffalo.

> Established a role for sar1 (a key endoplasmic reticulum exit site protein) in FMDV replication.

> Shown that FMDV triggers autophagic signalling during cell-entry and that autophagy is favourable for FMDV replication.

> Used viral vectors (recombinant human adenovirus 5 and recombinant modified vaccinia virus Ankara) to induce effects on bovine migrating dendritic cells with a view to improving immune response to vaccination.

> Developed a method to identify broadly cross-reactive neutralising antibody epitopes for FMDV, which will support the development of better vaccines.

- **Better preparedness for another FMDV outbreak.**

> A better global early warning system through coordination of an international network of FMD Reference Laboratories to predict threats and vaccine suitability.

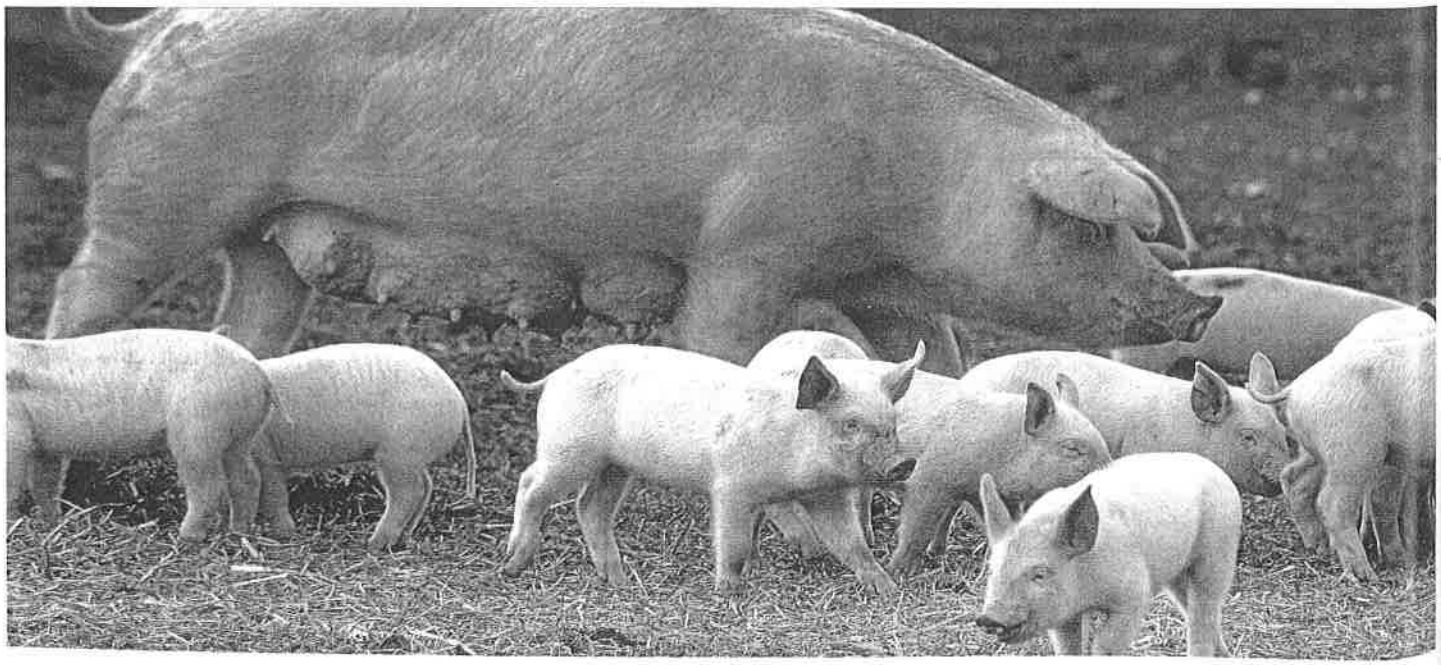
> The launch of a fully validated FMD lateral flow device for penside detection.

> Better models to select the most suitable outbreak control measures (e.g. culling versus vaccination) as a result of our experimental transmission studies.

> Accurate tracking of farm-to-farm spread by whole genome sequencing.

> Better prospects for using vaccinate-to-live in support of eradication due to enhanced understanding of how to substantiate post-vaccination freedom from infection.

> Improved understanding of how thermal imaging could be used to assist in recognition of affected cattle.



- **Improved prospects for global FMD control through advice to international agencies on concepts for regionalised efforts and trade incentives.**

- **Controlling FMD overseas.**

> High resolution molecular epidemiology approaches to assist (in real-time) in the control of FMD incursion into Bulgaria and to understand the spread of the virus in East Asia (China, Japan, Korea and the Russian Federation).

> Sequencing and tailored diagnostic tools to address the upsurge of FMD cases due to the SAT 2 serotype in North Africa.

> Launch of the FAO and OIE global FMD control strategy that puts Pirbright at the centre of the first five-year phase of work.

> Demonstration that combined LAMP-lateral flow device can give highly sensitive field detection of FMD from epithelia or air samples with minimal sample processing.

> Use of mathematical modelling to predict protective levels of antibody for vaccines and to aid vaccine selection.

- **Pioneered the use of next-generation sequencing to monitor intra and inter-host evolutionary dynamics during FMD infection.**

- **Developed a process for rapid adaptation of FMDV field strains to cell culture and identified a novel point mutation that expands tropism for cultured cells regardless of virus serotype.**

Other achievements

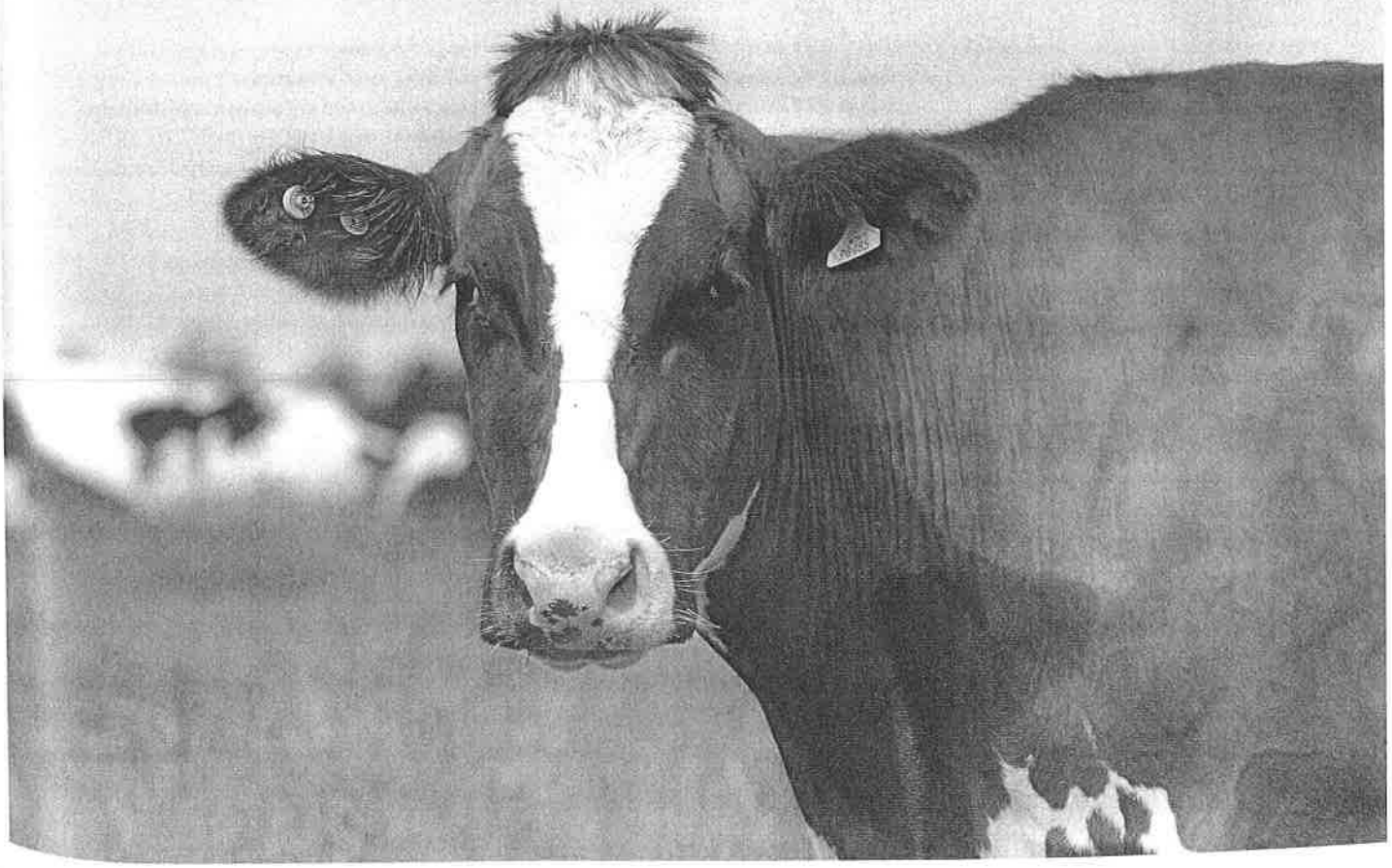
> Demonstration that morbilliviruses with different host tropisms use a variety of different mechanisms to block type-1 interferon induction and modify cell function.

> From structure-function studies, identified a mechanism to define immunodominant CD8+ T cell epitopes in cattle to help define protective immune responses.

> Demonstrated effectiveness of a new viral-vector method of vaccinating against bovine respiratory syncytial virus.(RSV) that also has potential for control of human RSV.

> Demonstrated effectiveness of a new viral-vector method of vaccinating against peste des petits ruminants (PPR).

> Established reverse genetics for PPR virus.



Livestock Viral Diseases programme
People and key scientific questions

The LVD programme comprises many avenues of investigation.

Research leaders within or contributing to the LVD programme	
Dr Bryan Charleston	Immunology of Exotic Virus Infections group, and Head of LVD
Dr Michael Baron	Paramyxovirus and Bunyavirus group
Dr Simon Gubbins	Mathematical Biology group
Dr Jef Hammond	Vesicular Diseases Reference Laboratory
Dr John Hammond	Immunogenetics group
Dr Pippa Hawes	Bioimaging
Professor Terry Jackson	Picornavirus Structure group
Dr Don King	Molecular Characterisation and Diagnostics group
Professor Satya Parida	FMD Vaccine Differentiation group
Professor David Paton	Transmission Biology group
Dr Geraldine Taylor	Vaccinology group
Dr Toby Tuthill	Picornavirus Molecular Biology group

Key scientific questions

Why do viruses emerge and persist and what determines their transmissibility and evolution?

Objectives include:

- Understanding and modelling of factors affecting spread and persistence of viruses at the population level and mechanisms and drivers for virus evolution.
- Defining viral strain distributions and interpreting the significance of viral mutations for tracing outbreaks and risk mapping.
- Understanding in vivo virus replication, shedding and transmission routes as a means of predicting and modelling viral dissemination and of protection afforded by vaccines.

What are the viral determinants of productive infection and drivers of protective immunity?

Objectives include:

- Identifying mechanisms of viral infection including cell entry, virus/host-cell membrane interactions, and virus disassembly and assembly.
- Identifying mechanisms by which viruses evade host innate and adaptive immune responses and how this contributes to host restriction.
- Identifying determinants of pathogenesis and persistence within hosts.
- Identifying viral antigens critical for and predictive of immune protection.

How do livestock immune systems combat viral infections and how is this influenced by polymorphisms in immune response genes?

Objectives include:

- Defining fundamental mechanisms of resistance to pathogens of livestock and the functional importance in cattle of gene families with a key role in the immune response.
- Developing immunological tools, reagents and assays to analyse immune responses in cattle.
- Dissecting anti-viral immune responses.

Case study
Understanding dendritic cells to improve vaccination

Dendritic cells (DC; image) are important immune cells that trigger immune responses via T-cells following infection or vaccination. Dr Bryan Charleston's group has been successful in collecting these cells from living cattle and using them to study the detailed interaction of these cells with different vaccines.

Collection of migrating DC by cannulation of afferent lymphatic vessels is technically challenging but rewarding; they can be used to examine the interaction of DC with potential vaccine antigens ex vivo without extensive in vitro manipulations. Viral vectors expressing an antigen of a pathogen e.g. FMDV, are a much safer means of vaccination than using the pathogen itself, even when inactivated.

Dr Bryan Charleston's group examined the interaction of afferent DCs with three viral vectors: recombinant replication-defective human adenovirus 5 (rhuAdV5); recombinant modified vaccinia virus Ankara (rMVA); and recombinant fowlpox virus (rFPV), all expressing green fluorescent protein (GFP). The adenovirus vector rhuAdV5 successfully produced GFP in the DC, whereas the rMVA and rFPV caused apoptosis. Delivery of FMDV antigens to DC was also most effective by the adenovirus vector, resulting in significantly greater CD4+ T cell proliferation. Delivery of the adenovirus vector in oil adjuvant in vivo was effective in enhancing DC-vector contact. This study showed that the interaction between viral vectors and afferent lymph DC ex vivo can predict the outcome of in vivo immunization and provide a means of rapidly assessing the effects of vector modification, important for expediting vaccine development.

Cubillos-Zapata C, Guzman E, Turner A, Gilbert SC, Prentice H, Hope JC, Charleston B (2011). **Differential effects of viral vectors on migratory afferent lymph dendritic cells in vitro predict enhanced immunogenicity *in vivo***. Journal of Virology 85, 9385-94.

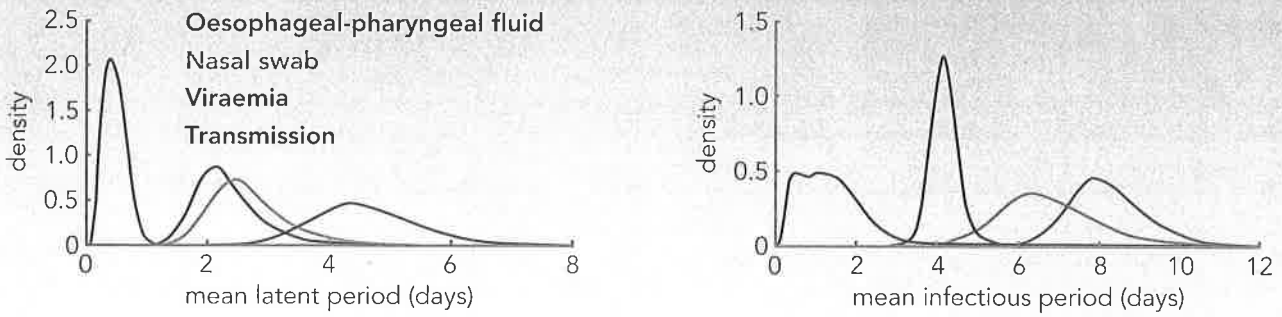
Guzman, E, Cubillos-Zapata C, Cottingham MG, Gilbert SC, Prentice H, Charleston B, Hope JC (2012). **Modified vaccinia virus Ankara-based vaccine vectors induce apoptosis in dendritic cells draining from the skin via both the extrinsic and intrinsic caspase pathways, preventing efficient antigen presentation.** Journal of Virology 86, 5452-5466.

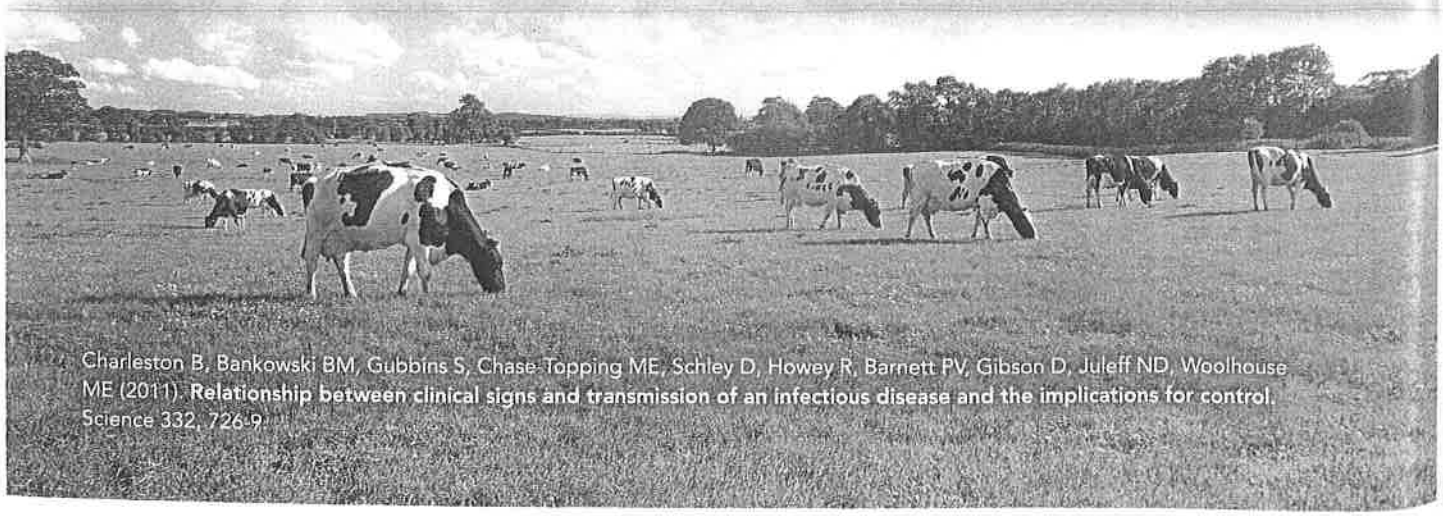
Case study
Early detection of foot-and-mouth disease: potential for alternative control measures

One-to-one transmission studies along with molecular, mathematical and pathological analysis of the first few days of experimental infection of cattle with FMDV have revealed a window of opportunity for alternative approaches to controlling outbreaks. The fraction of the transmission, to in-contact cattle, of newly-formed infectious FMDV that occurred before clinical signs appeared was less than half the value expected from detecting virus in body fluids, the standard proxy measure of infectiousness. This was because the duration of the infectious period, in terms of transmission to in-contact cattle, was shorter than previously realised (mean 1.7 days; Figure, part B, black line), plus the animals were not infectious until, on average, 0.5 days after clinical signs appeared.

Quantitative reverse transcription polymerase chain reaction (qRT-PCR) detected viral replication before infectious virus was released and before clinical signs appeared. Consequently, there is the potential for diagnosing FMD in individual cattle on-farm before clinical signs are detectable and before transmission has occurred – not possible currently. Application of viral genome detection methods on farms with at-risk cattle would have a number of advantages. Firstly, FMDV-positive animals could be detected, and then killed, before they had released any virus, thus reducing the spread of the disease and limiting an outbreak. Secondly, cattle in the immediate area of an infected farm and which remained negative would not necessarily have to be pre-emptively killed. The Institute, with Defra support, is working to develop technology further to enable sensitive tests to be performed on-farm. One promising technique, combining sensitivity and ease of use, involves isothermal genome amplification followed by visualisation of product on a lateral flow strip test.

FMDV transmission biology





Charleston B, Bankowski BM, Gubbins S, Chase-Topping ME, Schley D, Howey R, Barnett PV, Gibson D, Juleff ND, Woolhouse ME (2011). **Relationship between clinical signs and transmission of an infectious disease and the implications for control.** Science 332, 726-9.

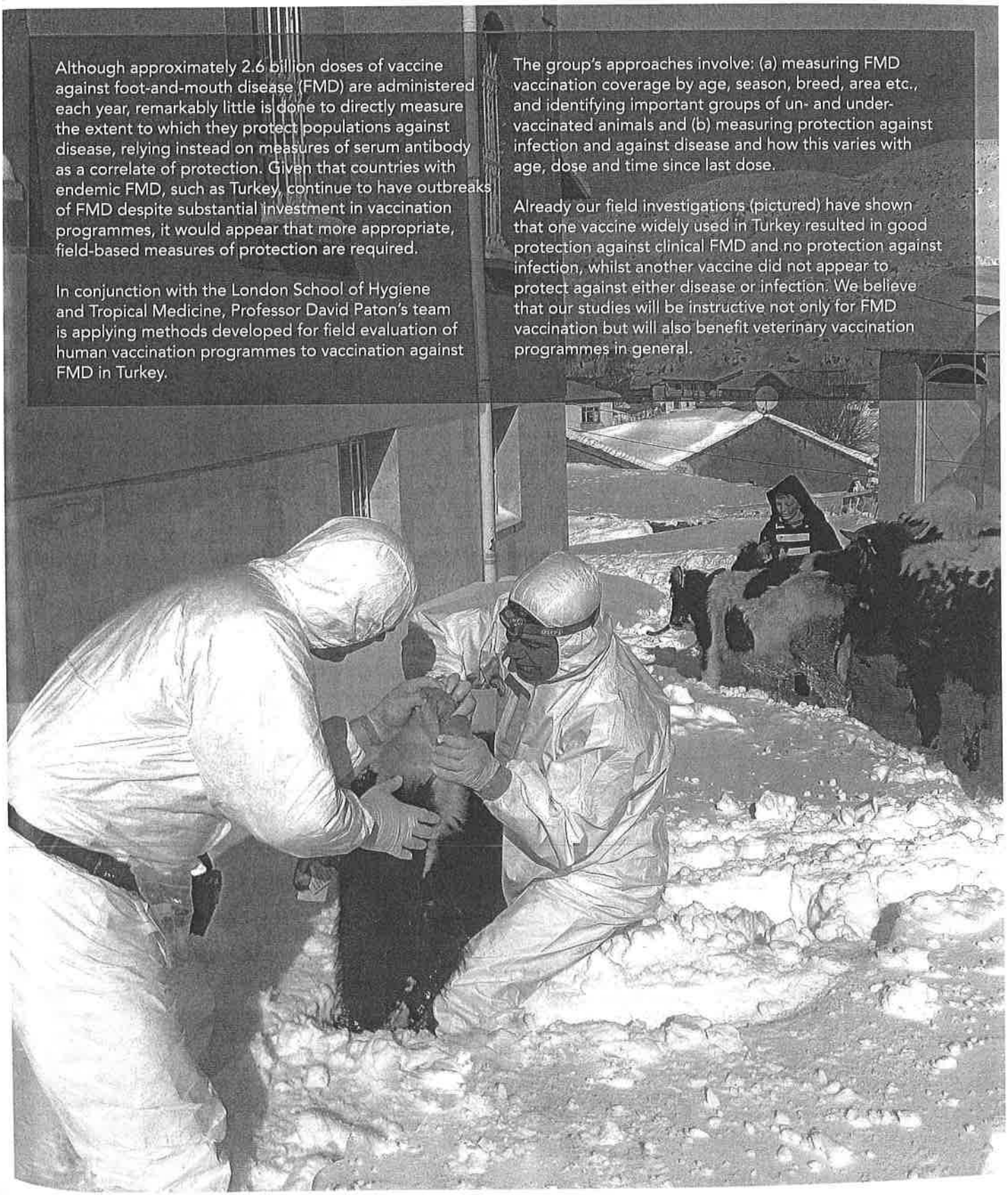
Case study
Evaluating the effectiveness of foot-and-mouth disease vaccination in the field

Although approximately 2.6 billion doses of vaccine against foot-and-mouth disease (FMD) are administered each year, remarkably little is done to directly measure the extent to which they protect populations against disease, relying instead on measures of serum antibody as a correlate of protection. Given that countries with endemic FMD, such as Turkey, continue to have outbreaks of FMD despite substantial investment in vaccination programmes, it would appear that more appropriate, field-based measures of protection are required.

In conjunction with the London School of Hygiene and Tropical Medicine, Professor David Paton's team is applying methods developed for field evaluation of human vaccination programmes to vaccination against FMD in Turkey.

The group's approaches involve: (a) measuring FMD vaccination coverage by age, season, breed, area etc., and identifying important groups of un- and under-vaccinated animals and (b) measuring protection against infection and against disease and how this varies with age, dose and time since last dose.

Already our field investigations (pictured) have shown that one vaccine widely used in Turkey resulted in good protection against clinical FMD and no protection against infection, whilst another vaccine did not appear to protect against either disease or infection. We believe that our studies will be instructive not only for FMD vaccination but will also benefit veterinary vaccination programmes in general.

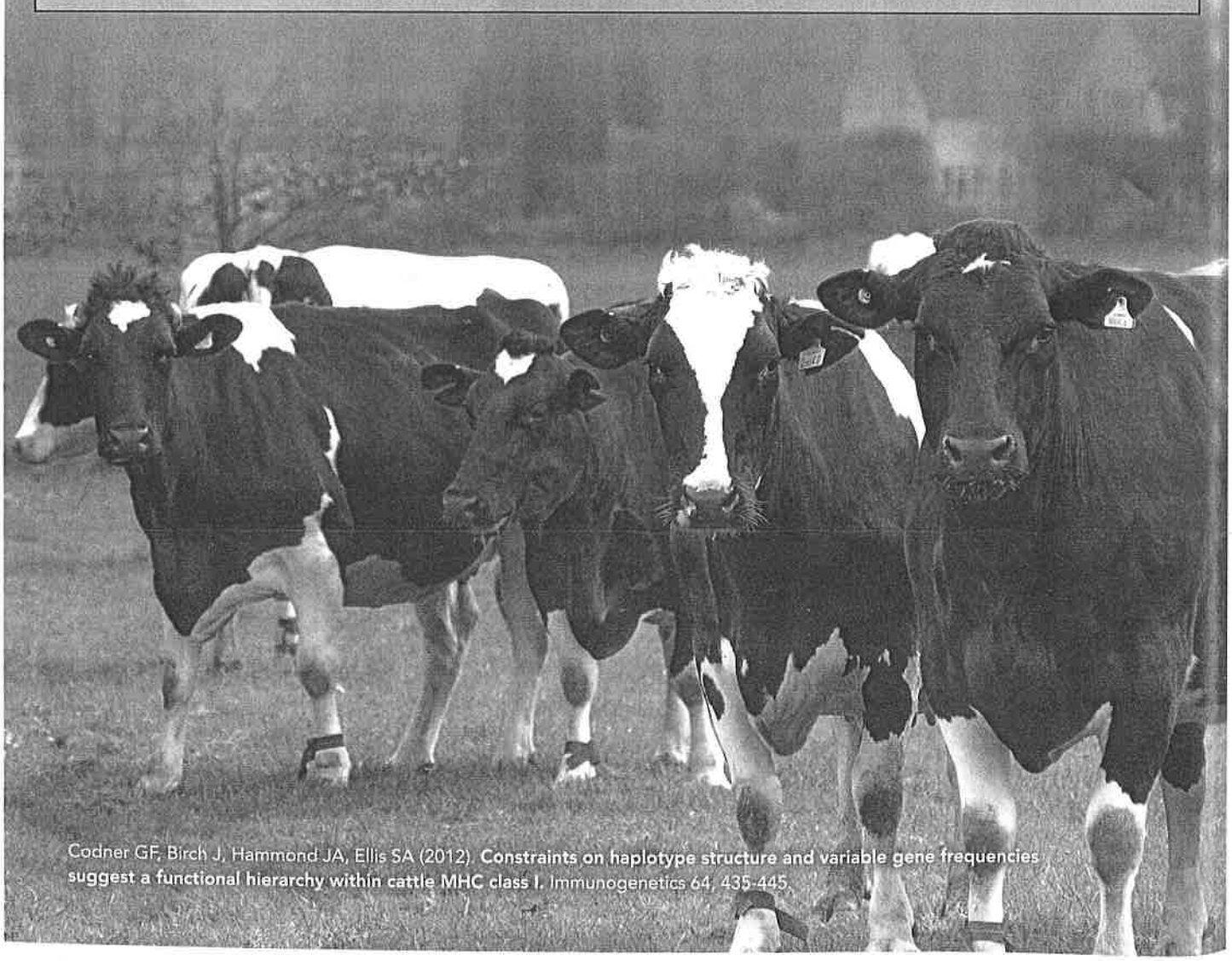


Case study
Researching variation in immune genes to underpin breeding strategies

Natural killer (NK) cells are crucial cytotoxic lymphocytes for both the immediate (innate) and subsequent (adaptive) immune responses to virus infection. Receptors on the NK cells (NKR) recognise ligands e.g. fragments of viral proteins, presented at the surface of infected cells by major histocompatibility complex (MHC) proteins. The NK cells then release cytokines to signal to other immune cells or directly kill the infected cells. The nature of the NK response subsequently influences how the rest of the immune system responds. Understanding the mechanisms and genetic basis of these responses will therefore help design better vaccines and breed for more disease resistant cattle.

Five mammalian lineages have independently expanded NKRs that likely all recognise diverse MHC class I ligands. Cattle are the only species to have expanded and diversified the KIR3DX genes, and the only species to have diversified LRC and NKC genes.

Dr John Hammond's group is characterising these cattle NKR gene families from the Institute's MHC-defined Holstein-Friesian herd, a globally important dairy breed. Using genome enrichment methods with contemporary high-throughput DNA sequencing techniques, the first maps of these highly naturally diverse regions have been constructed. These receptors interact with MHC on infected cells to control NK cell immune functions. By using the MHC-defined herd at the IAH Dr Hammond will be able to test how animals with dissimilar NK cell receptors and ligands respond differently to infection. The aim is to identify receptor and ligands pairs that significantly influence disease progression.



Codner GF, Birch J, Hammond JA, Ellis SA (2012). **Constraints on haplotype structure and variable gene frequencies suggest a functional hierarchy within cattle MHC class I.** Immunogenetics 64, 435-445.

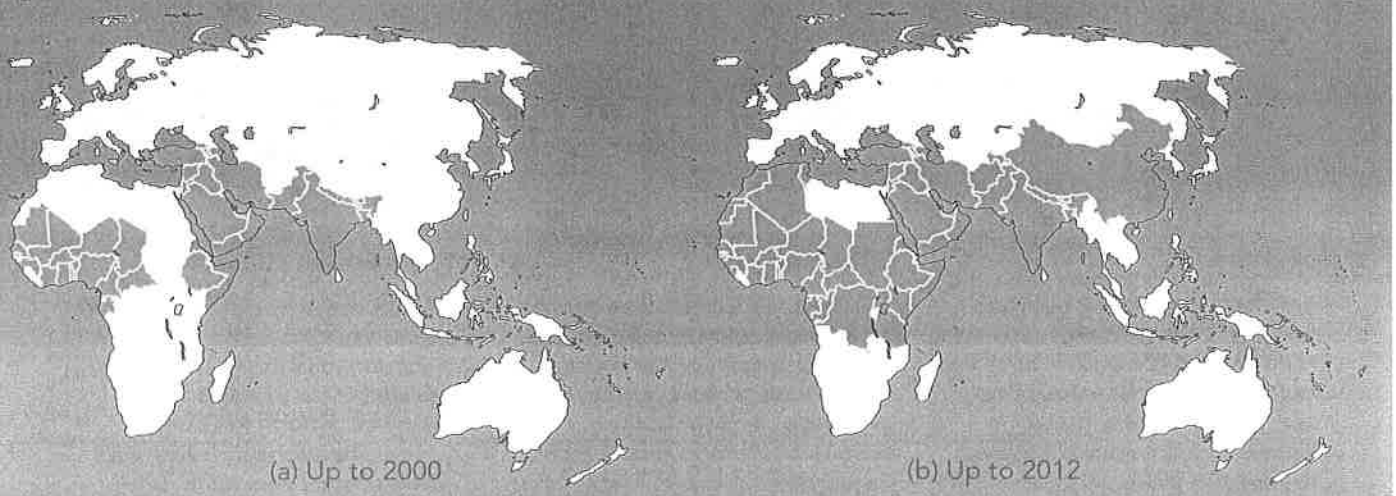
Case study
Towards the eradication of a second virus of ruminants

Peste des petits ruminants virus (PPRV) causes disease in sheep and goats, which are of great socio-economic importance amongst poorer livestock keepers in many developing countries. The eradication of rinderpest virus has provided a road-map to the elimination of the closely related PPRV, which has been spreading in recent years (Figure, showing countries reporting PPR outbreaks from 1990 up to (a) 2000 and (b) 2012)).

Vaccination and surveillance are at the heart of a PPR eradication programme. Unfortunately, when animals have been vaccinated with conventional live PPR vaccine they produce the same spectrum of antibodies as the animals that have been infected by virulent virus; distinguishing infected and vaccinated animals (DIVA) is not possible.

The immune response to a single PPRV protein, the H protein, is sufficient for protection. Consequently, the Institute is investigating the use of recombinant fowl pox virus and adenovirus expressing the H protein as DIVA vaccines to control PPR; a vaccinated animal would have antibodies only to the H protein, whereas an infected animal would also have antibodies to other PPRV proteins. This permits differentiation.

We are also working with a diagnostics company on another important tool for PPRV control: a robust test for the virus itself that can be used in the field. The test is a Lateral Flow Device (similar to a pregnancy test kit) based on that originally developed by the Institute to help eradicate rinderpest.



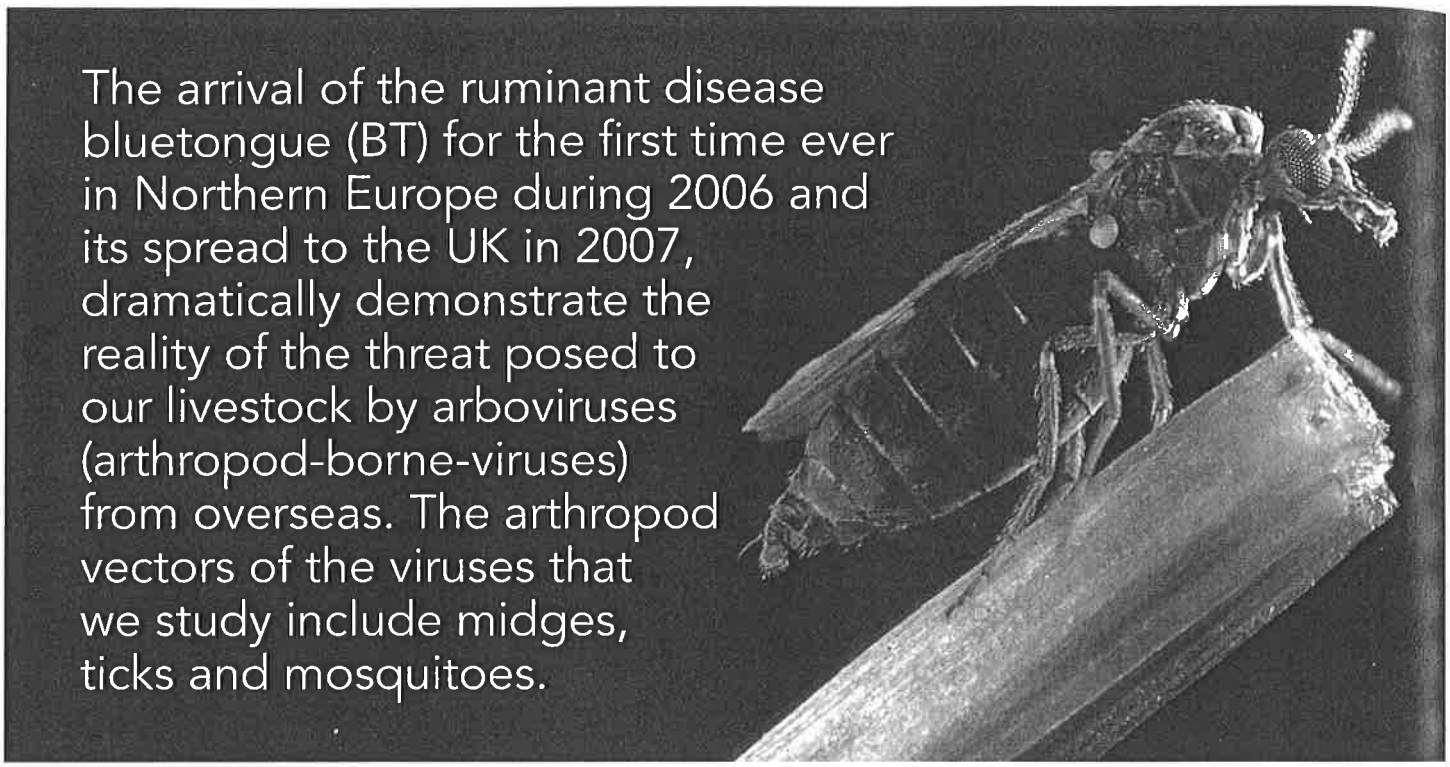
(a) Up to 2000

(b) Up to 2012

Baron MD, Parida S and Oura CA (2011) **Peste des petits ruminants: a suitable candidate for eradication?** Veterinary Record 169, 16-21.

Vector-borne Viral Diseases programme

Head of programme: **Professor Peter Mertens**



The arrival of the ruminant disease bluetongue (BT) for the first time ever in Northern Europe during 2006 and its spread to the UK in 2007, dramatically demonstrate the reality of the threat posed to our livestock by arboviruses (arthropod-borne-viruses) from overseas. The arthropod vectors of the viruses that we study include midges, ticks and mosquitoes.

Bluetongue

Biting midges transmit bluetongue virus and related viruses of ruminants and horses that are endemic in Africa as well as many other areas of the world, and are already present in countries on the edges of Europe. The Institute's efforts, in partnership with many others, including farmers, veterinarians, vaccine producers, Defra, scientific colleagues in other countries and oversees authorities, resulted in the 2007 BT outbreak in the UK being 'nipped in the bud'. In contrast, the disease outbreak which had started one year earlier in continental Northern Europe, when no vaccine was available, eventually spread across most of the EU, infecting a high proportion of the ruminant populations of several countries, bringing livestock movements and trade to a halt, and killing many thousands of animals, mainly sheep.

Other orbiviruses

The Institute's expertise extends to orbiviruses related to the BT virus, including epizootic haemorrhagic disease virus, which also affects ruminants, and two viruses of horses and other equines, equine encephalosis virus and African horse sickness virus. The latter would probably kill more than 90% of horses if a widespread outbreak occurred in the UK.

African swine fever

African swine fever virus (an asfavirus) kills virtually 100% of affected pigs. The tick-borne virus was transported inter-continentally in 2007 from sub-Saharan Africa to Georgia, from where it spread devastatingly, including close to the border with the European Union.

Nairobi sheep disease

Nairobi sheep disease virus (NSDV, a bunyavirus) occurs in Africa and is transmitted by ticks. It is closely related to (and provides an important model for) Crimean Congo haemorrhagic fever virus, which affects humans.

Vectors

Mosquito-borne viruses are posing an increasing threat beyond their traditional territories. The Institute is studying the interactions of arthropod vectors with both viruses and mammalian hosts, and the involvement of climate. The growth of some viruses in arthropod vectors, such as midges, mosquitoes and ticks, which then transmit the virus to mammals whilst taking a blood meal, hugely adds to the risk of these viruses spreading great distances in a very short time and, consequently, complicates our capacity to defend against them.

Multidisciplinary research

Defending against arboviruses requires expertise in molecular biology, diagnosis, entomology, epidemiology, genetics, immunology, vaccinology, mathematical modelling, and virology; all of which are present within the Vector-borne Virus Diseases (VVD) programme. The Institute also receives essential meteorological input from a collaboration with the UK Met Office.

Zoonotic diseases

In recent years a significant number of zoonotic arboviruses (able to infect people) have been detected or have caused outbreaks in Southern Europe. Although these events have not been as widespread or as dramatic as the outbreaks caused by BTV, they indicate an additional and increased threat to both animal and human populations. These viruses include West Nile virus, Chikungunya virus, Toscana virus, Crimean Congo haemorrhagic fever virus and Dengue virus as well as other agents such a Rift Valley fever virus. The Seadornaviruses, such as Kadipiro virus and Liao Ning virus, represent further areas of study.

Unique resources

- A cadre of experts concerning the biology, transmission and control of arboviral diseases.
- New laboratories and large-animal experimentation facilities at very high bio-containment levels (SAPO 3 and 4) for research on viruses from overseas.
- Insectaries in which researchers rear colonies of midges, ticks, and mosquitoes.
- Cattle and inbred pigs of known genetic background (defined MHC Class I haplotypes).
- Collections of different virus strains from all around the world suitable for vaccine and diagnostic test development and evaluation, as well as further research work.

Scientific priorities are to understand

- Why certain arthropod-borne viruses emerge in Europe, and what factors determine changes in their distribution, persistence in the environment, and evolution.
- The features of the viruses that enable their interaction with both their arthropod and livestock hosts, affecting the range of arthropods and mammals that are affected, the virulence of the virus, and the nature of the disease.
- The role of arthropod vectors in the distribution and intensity of arbovirus outbreaks.
- How the immune systems of livestock and vectors combat arboviral infections.

All with a view to exploiting this knowledge for the health of livestock and sustainable production.

Research has additional impact arising from:

- Its underpinning of the diagnostic service provided by the Institute's Non-Vesicular Virus Reference Laboratories.
- Emergency response capacity for the UK.
- Modelling of the diseases, for prediction of emergence and spread within Northern Europe.
- The Pirbright Institute is a hub for collaboration with research and surveillance partners in the UK and worldwide.
- Development of diagnostic tools for internal and worldwide use.
- Development of vaccines.
- Training of livestock industry professionals, diagnosticians and students.

Recent and current supporters include:

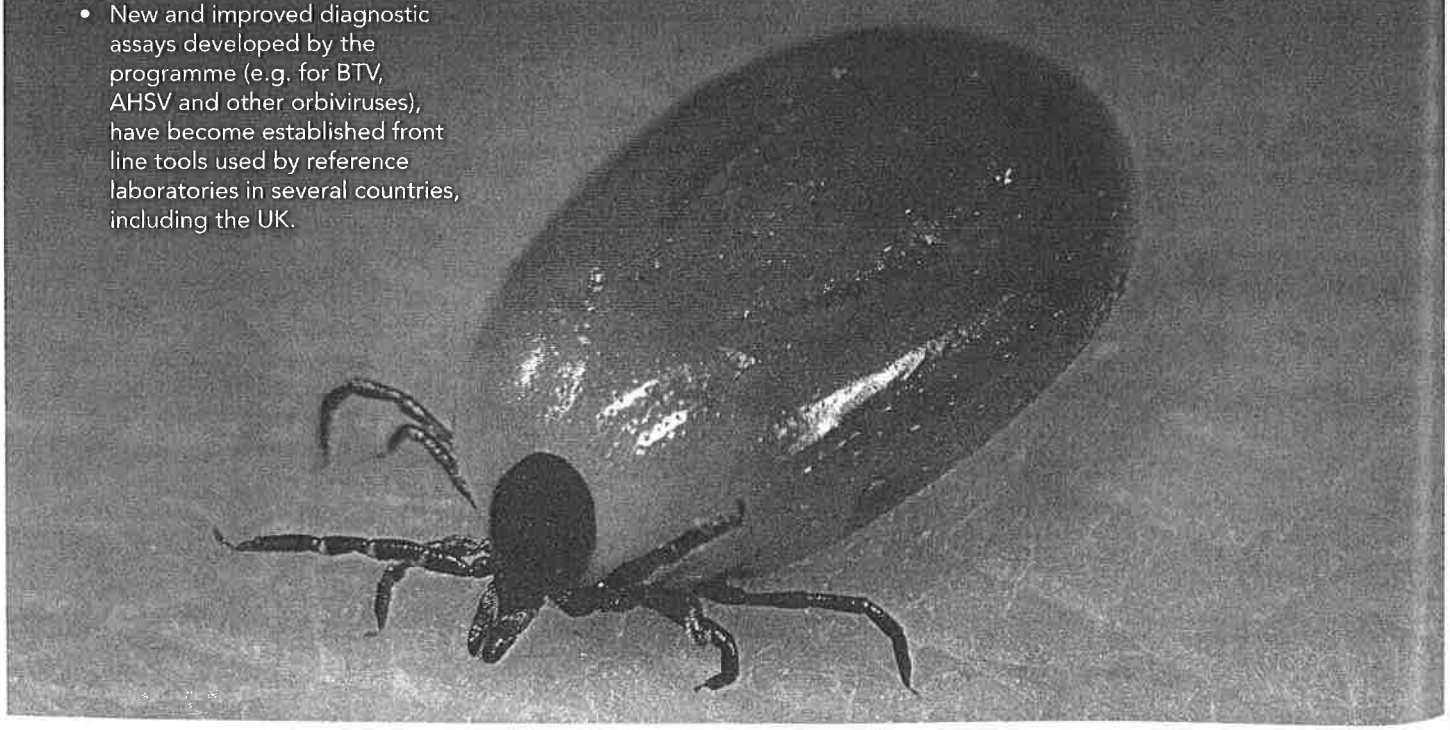
BBSRC, Defra, The Department for International Development (DfID), Wellcome Trust, European Union (EU), vaccine developers and diagnostics manufacturers (Qiagen, Laboratoire Service International, Biological Diagnostic Supplies Limited, Pfizer), Food and Agriculture Organisation (FAO), World Organisation for Animal Health (OIE), and the Commonwealth Comission.

More information: www.iah.ac.uk/ISPG/VVD.aspx

Vector-borne Viral Diseases programme
Recent achievements

- Advice given to Defra and UK farming and veterinary communities on bluetongue virus (BTV) control measures, including advising purchase and use of BTV-8 vaccine, made a major contribution to the success of the Joint campaign Against Bluetongue (JAB) campaign, preventing re-emergence of the disease in the UK – the only country in Europe to control BTV-8 during 2008. It has been estimated that the Institute's contribution to BTV control saved the UK economy £485 million per annum.
- At Pirbright, there are reference collections, complete genome sequence datasets and databases for BTV, African horse sickness virus (AHSV), other orbiviruses, and African swine fever virus (ASFV), that represent important global resources for studies of strain distribution, variation and evolution, gene function and virus/host interactions, supporting development of diagnostic assays, diagnosis, vaccine development and disease control.
- New and improved diagnostic assays developed by the programme (e.g. for BTV, AHSV and other orbiviruses), have become established front line tools used by reference laboratories in several countries, including the UK.
- The Non-Vesicular Reference Laboratory (NVRL) provides a vital interface between research and diagnosis in the UK, Europe and further afield. It supports disease surveillance and characterisation of BTV, AHSV and ASFV strains, informing the design and implementation of control strategies with demonstrable global impact.
- BTV assay systems and databases developed at Pirbright have provided a basis for identification of the first novel BTV types for over 30 years, (type 25 in Switzerland and type 26 in Kuwait).
- Sequencing and phylogenetic studies have identified seven novel orbivirus species.
- A 'pan-orbivirus' diagnostic RT-PCR and sequencing technology have been developed for the detection and characterisation of any orbivirus.
- Novel vaccine candidates have been developed for several arboviruses, including BTV and AHSV, which have associated DIVA assays (Differentiating Infected from Vaccinated Animals).
- The establishment of arbovirus reverse genetics technologies at Pirbright provides enhanced capability to study viral gene function and virus host interactions.
- The *Culicoides* Reference Laboratory is a world leader in identification and monitoring of *Culicoides* midge populations, helping us to understand risks and combat the diseases they transmit.
- The identification of immune correlates of protection against ASFV and the demonstration that immunisation of pigs with one ASFV genotype can protect against several heterologous genotypes enhances prospects for the development of an effective ASFV vaccine.

The Institute maintains the world collection of tick cell lines, which are indispensable for research on many tick-borne pathogens.



Vector-borne Viral Diseases programme
People and key scientific questions

The Vector-borne Viral Diseases programme comprises five areas of research:

1: Immunology and vaccinology
2: Reference laboratories and surveillance
3: Vector biology and arthropod genomics
4: Arbovirology molecular research
5: Mathematical biology and distribution modelling

The research is undertaken by a multidisciplinary team dealing with arboviral diseases from the molecular level through to populations.

Research leaders within or contributing to the VVD programme	
Professor Peter Mertens	Arbovirus Molecular Research group and Head of the VVD programme
Dr Michael Baron	Paramyxovirus and Bunyavirus group
Dr Mark Boyce	Institute Fellow in Arbovirus Molecular Research
Dr Simon Carpenter	Entomology
Dr Linda Dixon	African Swine Fever group
Professor John Fazakerley	Arbovirus Pathogenesis group
Dr Mark Fife	Genetics and Genomics group
Dr Rennos Fragkoudis	Institute Fellow in Rift Valley fever virus
Dr Simon Gubbins	Mathematical Biology group
Dr Terry Jackson	Picornavirus Structure group
Dr Geraldine Taylor	Vaccinology group
Dr Anthony Wilson	Institute Fellow in Mathematical Biology of Vector-borne Diseases
Dr Carrie Batten	Non-Vesicular Reference Laboratory
Dr Lesley Bell-Sakyi	Tick-borne Viruses group
Dr Geraldine Taylor	Vaccinology group
Dr Anthony Wilson	Institute Fellow in Mathematical Biology of Vector-borne Diseases
Dr Carrie Batten	Non-Vesicular Reference Laboratory
Dr Lesley Bell-Sakyi	Tick-borne Viruses group

Vector-borne Viral Diseases programme
People and key scientific questions continued

Key scientific questions

Why do certain arboviruses emerge and what factors determine changes in their distribution, persistence and evolution?

Objectives include:

- Understanding vector, host and environmental factors that influence the spread and transmission of arbovirus diseases, developing models to help predict associated risks and designing appropriate control measures.
- Identifying different arbovirus strains, determining their distribution, tracing outbreaks, interpreting the significance of viral mutations, and understanding the mechanisms/drivers of arbovirus evolution.
- Developing novel diagnostic systems to identify the causes of disease outbreaks, trace strain movements and origins.

Ornithodoros ticks transmit African swine fever

How does arbovirus structure and function control interactions with hosts and vectors?

Objectives include:

- Understanding how arbovirus structure-function determines replication and transmission mechanisms.
- Determining high resolution structures and molecular organisation of arbovirus particles and proteins, using x-ray crystallography and cryo-electron microscopy.
- Determining the significance of insect saliva proteins in the interactions between host, vector and virus.

What is the role of arthropod vectors in the distribution and intensity of arbovirus outbreaks?

Objectives include:

- Exploring the genetic basis for arbovirus transmission competence by Culicoides vectors.
- Defining the distribution and variation of arthropod vector species and predicting disease movements/risks using sequence-based technologies/assays and studies of vector ecology.
- Determining the vector capacity of indigenous and exotic arbovirus vectors, including alternative transmission mechanisms and their susceptibility to infection by different arbovirus strains.

How does the livestock immune system combat arboviral infection and how can this be used to develop better vaccines?

Objectives include:

- Understanding host immune responses to BTV, AHSV, and ASFV; identifying correlates of protection, and defining fundamental mechanisms of resistance.
- Improving vaccination strategies: identifying type-specific and cross-reactive viral antigens and mechanisms used to evade innate and adaptive host immune responses.
- Developing novel subunit vaccine-candidates and associated DIVA assays.

Case study
Meteorological influences on *Culicoides* biting midges

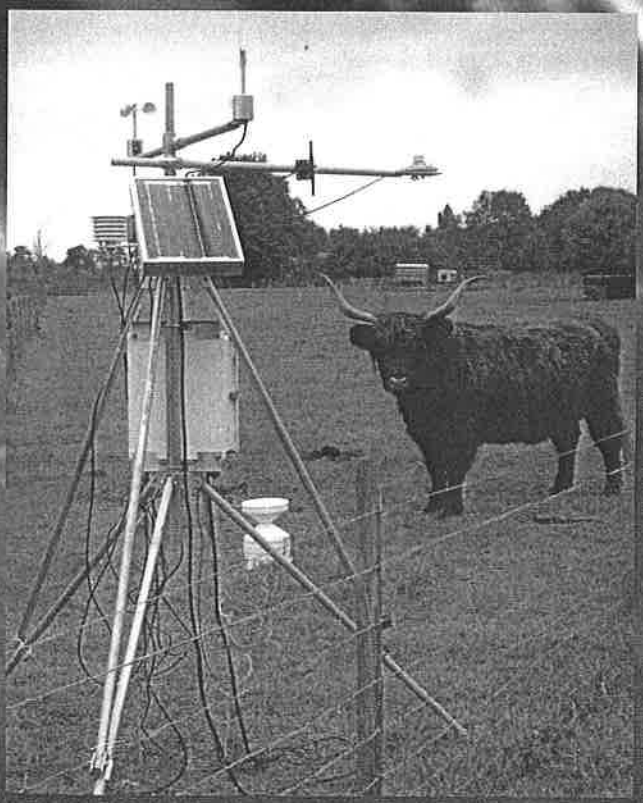
Understanding the ecology and behaviour of vector *Culicoides* species is a key element in predicting the incursion and spread of the pathogens they transmit.

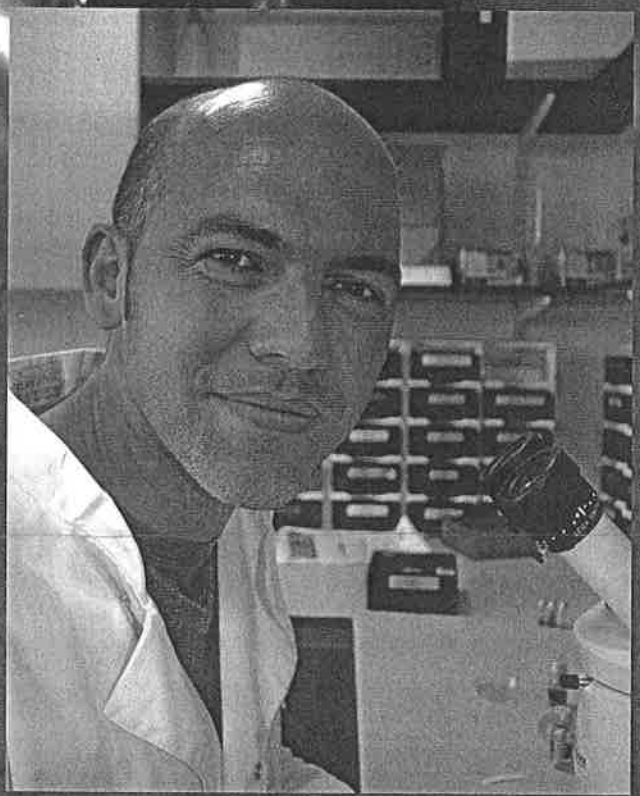
Meteorological conditions strongly influence the activity and abundance of *Culicoides*. The Institute, in collaboration with Rothamsted Research, the Met Office and the Natural Resources Institute, examined the effect of season and meteorological parameters on the daily presence and abundance of *Culicoides* captured in a network of 12m high Rothamsted suction traps at 12 sites across England.

Most sites demonstrated greater *Culicoides* abundance during spring (April/May) and autumn (September/October), although C. chiopterus peaked later in the year. Correlation with the peak of infection during autumn in the 2006-2008 outbreak of bluetongue virus (BTV) in northern Europe may be coincidental but it could reflect the increased abundance of a more efficient vector of bluetongue at that time of year.

Livestock-associated species were recorded at all sites, with increased *Culicoides* abundance correlated with greater densities of livestock. However, the presence of livestock-associated species in traps in drier arable areas where livestock were rare implies a greater dispersal potential of *Culicoides* over land than previously thought.

The Bayesian model developed in this study for daily *Culicoides* abundance has been incorporated into the latest Pirbright Institute-Met Office advisory service for the prediction of risk of infectious, wind-borne *Culicoides* reaching the UK from continental Europe.





Sanders CJ, Shortall CR, Gubbins S, Burgin L, Gloster J, Harrington R, Reynolds DR, Mellor PS and Carpenter S (2011) **Influence of season and meteorological parameters on flight activity of Culicoides biting midges.** Journal of Applied Ecology 48, 1355-1364

Case study
Transmission of arboviruses and vaccine development

With environmental change, insect and tick-borne viruses – arboviruses (**ar**thropod **bo**rne **viruses**) – are likely to become more problematic in many parts of the world. Professor John Fazakerley's research group studies transmission of these viruses and does research with a view to vaccine development.

Several arboviruses are capable of causing disease in livestock; Schmallenberg virus is a recent example but viruses such as Rift Valley fever virus and Nairobi sheep disease, currently in Africa, may have the potential to spread to other regions of the world. Some of these arboviruses which have reservoirs in animal species are important threats to human health, examples include Rift Valley fever virus, West Nile virus and chikungunya virus.

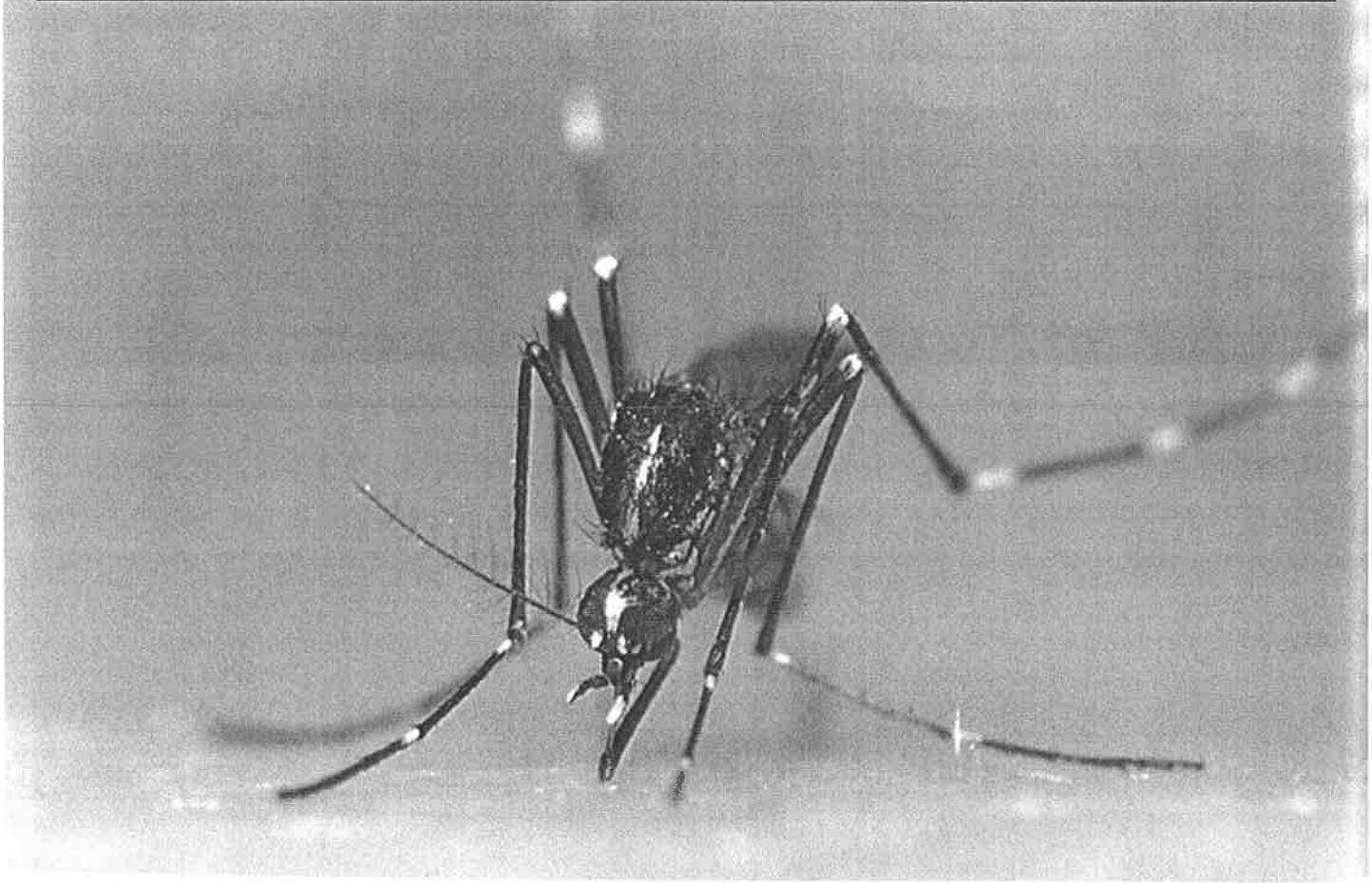
Chikungunya virus is endemic in Central Africa and SE Asia and in 2005 spread from Central Africa across the Indian Ocean into India affecting millions of people and causing debilitating joint and muscle disease.

Using the specialist insectary, high containment laboratories, international collections of arthropod cells and arboviruses at Pirbright, studies are underway to understand the transmission of viruses such as Rift Valley fever virus, chikungunya virus and tick-borne encephalitis virus between arthropods, animals and humans and to develop novel vaccines.

Dr Lesley Bell-Sakyi's group manages the world's global collection of tick cell lines, a unique collection of difficult to establish and difficult to maintain cells which are used by research groups worldwide. The group is investigating how viruses such as tick-borne encephalitis virus, Crimean-Congo haemorrhagic fever virus and African swine fever are able to persist for long periods of time in ticks.

Professor John Fazakerley coordinates a large international programme designed to understand the transmission and pathogenesis of chikungunya virus and develop a vaccine.

Dr Rennos Fragkoudis leads a group looking at improving vaccines for Rift Valley fever virus.



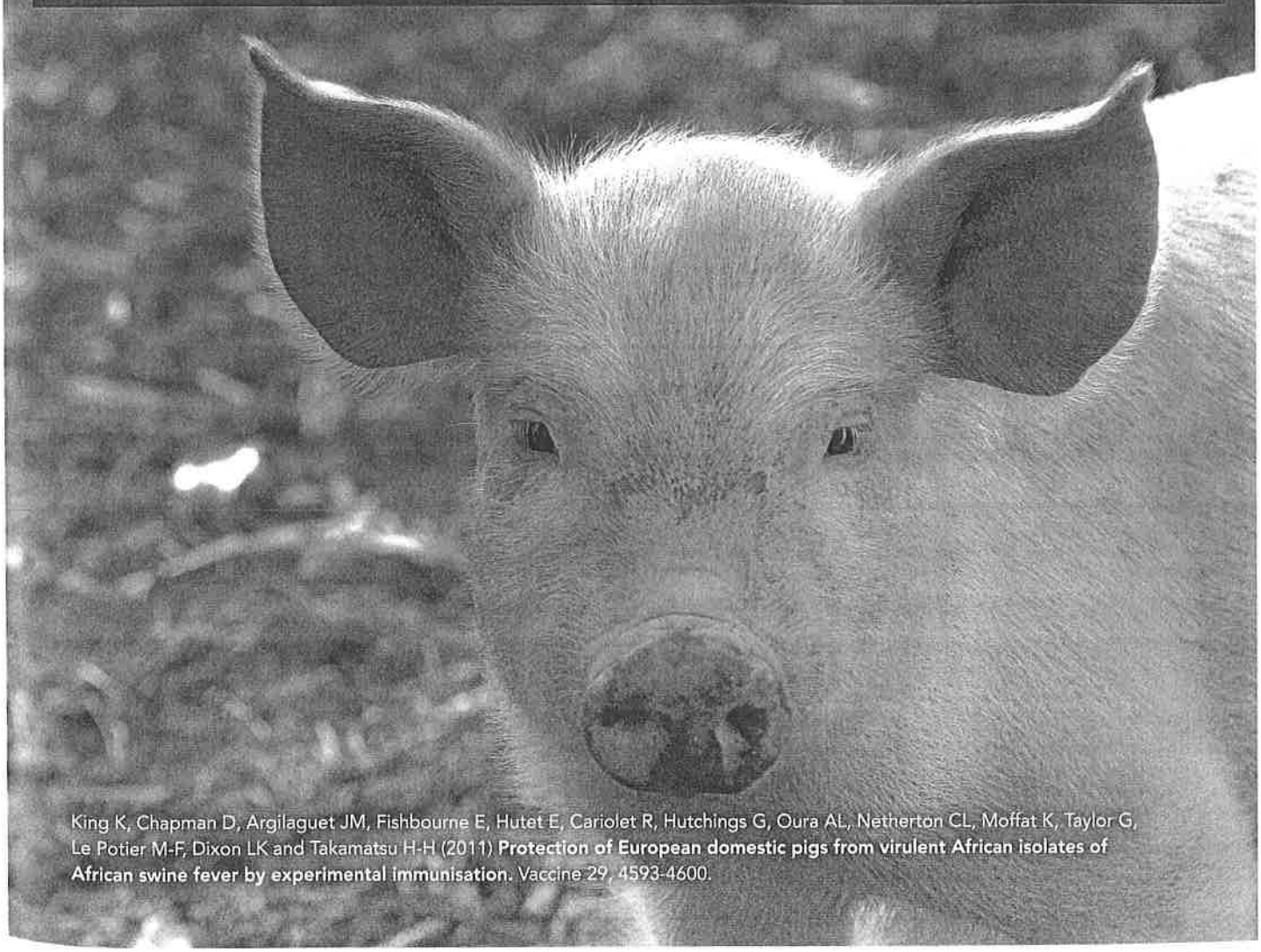
Case study
Towards a safe and effective vaccine against African swine fever

African swine fever virus (ASFV) causes a highly contagious, haemorrhagic disease of domestic pigs, with virulent strains causing high mortality. Attempts to produce killed vaccine strains have proven to be unsuccessful. Attenuated strains can induce protective immunity but there are concerns about their use in the field due to possible post-vaccination reactions and/or their capacity to persist in hosts.

The Pirbright Institute's ASF programme, led by Dr Linda Dixon, is directed towards a greater understanding of the immune responses to ASFV and the identification of the virus genes involved in virulence and immune evasion, with a view to genetically modifying the virus to produce an effective and safe vaccine.

Another concern is that a given ASF vaccine might protect against only the corresponding (homologous) genotype; there are 22 genotypes of the virus. Recent research at the Institute has shown that vaccination with a non-virulent strain, followed by a booster with a virulent strain, both of the same genotype, induces protection against a heterologous as well as homologous genotype i.e. the animal is protected against more than one strain of the virus. This is promising for the eventual control of ASF by vaccination; a single vaccine might be effective in a region where there are several genotypes.

Researchers at the Institute have also shown that the ability of different ASFV isolates to stimulate type II interferon production from immune pig lymphocytes correlated with the ability to induce cross-protection against different isolates. Consequently the assay is useful to predict cross-protection and vaccine efficacy.



King K, Chapman D, Argilaguet JM, Fishbourne E, Hutet E, Cariolet R, Hutchings G, Oura AL, Netherton CL, Moffat K, Taylor G, Le Potier M-F, Dixon LK and Takamatsu H-H (2011) **Protection of European domestic pigs from virulent African isolates of African swine fever by experimental immunisation.** Vaccine 29, 4593-4600.

Case study
Genetic mapping of *Culicoides* biting midges

Culicoides biting midges inflict substantial economic damage on global livestock production and trade by acting as vectors of arboviral pathogens such as bluetongue virus (BTV). Genetic variation within a species of *Culicoides* may influence the vector competence (the ability to transmit a virus) for transmission of BTV strains, with consequences for the epidemiology of this virus worldwide.

The Pirbright Institute's Genetics and Genomics group, led by Dr Mark Fife, has established a world-leading consortium to systematically investigate the vector competence of the Institute's colonies of *C.sonorensis* for BTV and African horse sickness virus. The consortium includes the Institute's own Head of Entomology, Dr Simon Carpenter; the BBSRC Genome Analysis Centre; and Dr. Paul Kersey at the European Bioinformatics Institute.

In addition to providing insights into *Culicoides*-BTV interactions, the collaboration will also generate the first annotated *Culicoides* genome, providing new opportunities for research on this genus, not least through comparative genomics with other diptera (e.g. mosquitoes) for which genome sequences are already available.

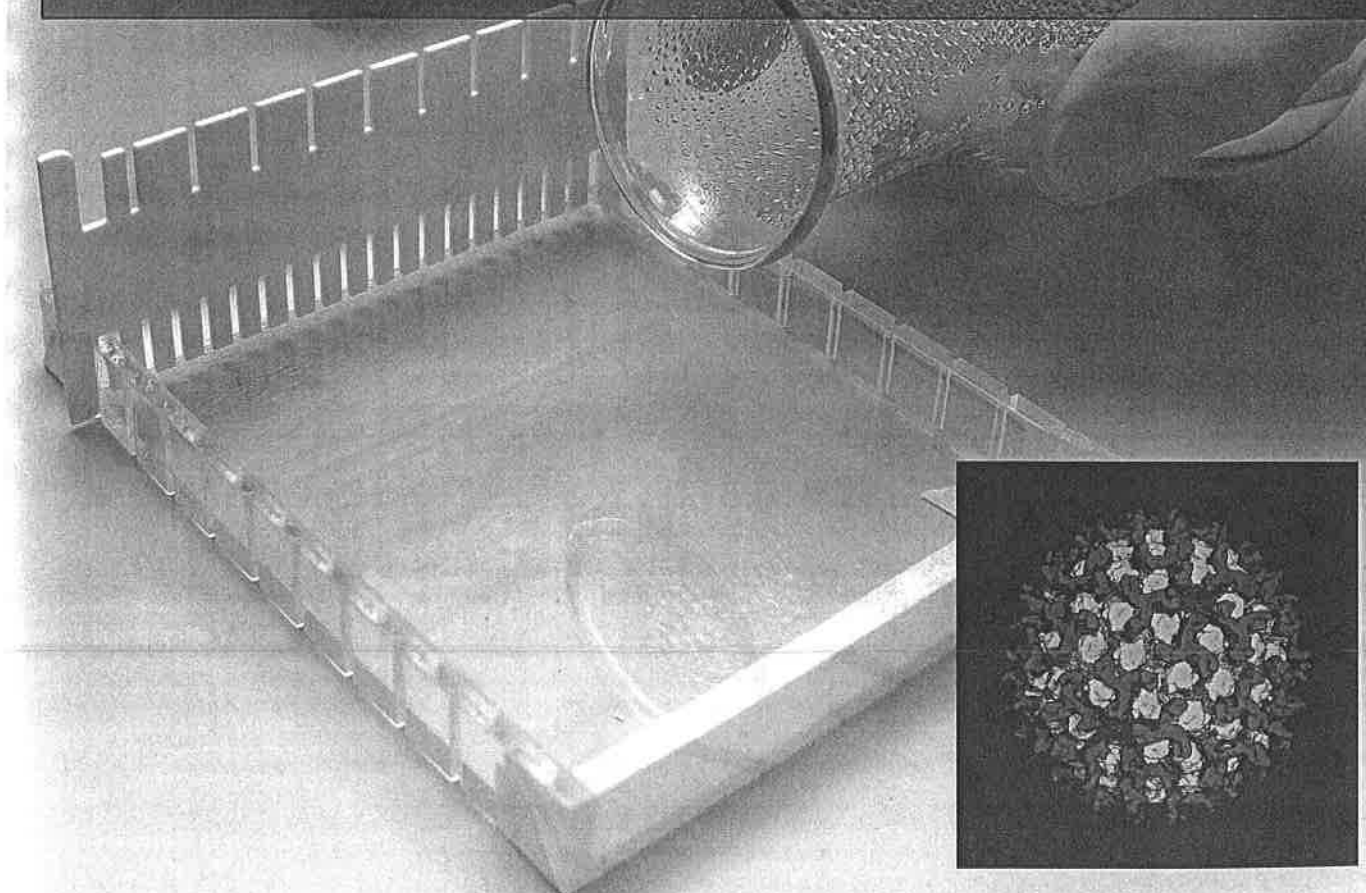
Case study
Fundamental molecular biological studies of orbiviruses

In addition to the strategic and applied research of the vector-borne viral diseases programme the Institute undertakes fundamental studies on the molecular biology of bluetongue virus (BTV) and other members of the Orbivirus genus within the Reoviridae family.

Recently, a team at the Institute, led by Dr Terry Jackson, has shown that BTV-1, like BTV-10, can infect cultured cells via an entry mechanism that is clathrin and cholesterol-independent, but requires dynamin, and shares certain characteristics in common with macropinocytosis.

BTV infects a wide variety of cell types in its mammalian hosts and also replicates in insect cells. It is likely that this broad tropism results in part from an ability to use multiple entry routes to initiate infection. Moreover, BTV can exist in at least three different forms that are all considered to be infectious. These include intact virus particles, infectious sub-viral particles, and virus-cores. These different particle types have different surface components, and may therefore also use different entry mechanisms for infection.

Orbiviruses have ten-segmented double stranded RNA genomes. Our studies of epizootic haemorrhagic disease virus and BTV have shown that in addition to the monomeric form of a given segment there can also be concatamers and partial gene duplications. Concatamers could provide an important source of diversity in the molecular evolution of all members of the Reoviridae.



Gold S, Monaghan P, Mertens P and Jackson T (2011) **A clathrin independent macropinocytosis-like entry mechanism used by bluetongue virus-1 during infection of BHK cells.** PLoS One 5, e11360.

Anthony SJ, Darpel KE, Belaganahalli MN, Maan N, Nomikou K, Sutton G, Attoui H, Maan S and Mertens PPC (2011) **RNA segement 9 exists as a duplex concatamer in an Australian strain of epizootic haemorrhagic disease virus (EHDV): genetic analysis and evidence for the presence of concatamers as a normal feature of orbivirus replication.** Virology 420, 164-171.

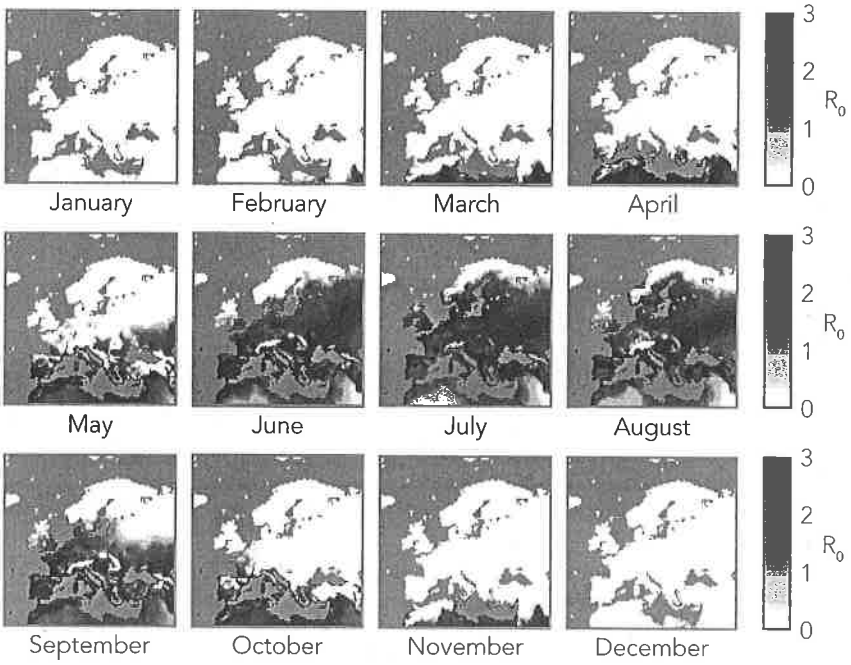
Centre for Integrative Biology

Epidemiology, mathematical modelling, bioinformatics and statistics at The Pirbright Institute are embedded in a virtual centre consisting of world-class experts in these fields. The Centre cuts across all three core research programmes (Avian Viral Diseases; Livestock Viral Diseases; Vector-borne Viral Diseases) and fosters an interdisciplinary approach to investigating the dynamics of livestock diseases at all scales.

Systems approaches are increasingly being used to help understand the often large and complex data-sets produced in biological research. They also allow integration of data across scales from genomes and individual cells, through.whole animals to entire countries

The centre has a dual role, undertaking mathematical, computational, and bioinformatics research in collaboration with field and laboratory scientists at the Institute; and providing support for colleagues who are involved in quantitative biology, strengthening the design and analysis of *in vitro*, *in vivo*, and *in silico* studies.

The Centre's research on foot-and-mouth disease in particular is seeking to bridge the gap between small-scale animal experiments and real life epidemics. Using state-of-the-art mathematical and statistical approaches researchers in the Centre helped discover that the window of infection in foot-and-mouth disease is considerably narrower than first thought – knowledge that will be important for policy makers who are tasked with developing and implementing control measures in the event of an outbreak in the UK.



Bluetongue Seasonal

An important area of work in recent years has been predicting how bluetongue could spread in the UK and the likely impact of different control strategies. To do this the Institute developed models to describe how bluetongue is transmitted between animals on a farm and between farms using data from previous outbreaks, in particular that in northern Europe in 2006. An important component of the model is the dependence of vector activity and lifespan on temperature. Combining meteorological data, laboratory data and entomology fieldwork, the model predicts the effect of different vaccination programmes, and contributed to the development of a successful control strategy, which is estimated to have saved the UK economy £485 million and protected 10,000 jobs. We have recently applied similar approaches to other viral diseases, such as Schmallenberg virus, which first appeared in Western Europe in 2011.

Bioimaging

The Pirbright Institute is unique in the UK as a facility where some of the most serious viruses can be studied both in the lab and in the host animal. Bioimaging is a core facility with collaborations across all three of the Institute's research programmes.

At the Institute, microscopy is mostly used to investigate basic research questions. For example, Institute researchers have used confocal microscopy to identify the mechanism of entry of bluetongue virus into host cells in culture. Investigators have also recently developed a confocal microscope protocol which makes it possible to locate fluorescently-labelléd viral proteins within tissue sections taken from host animals.

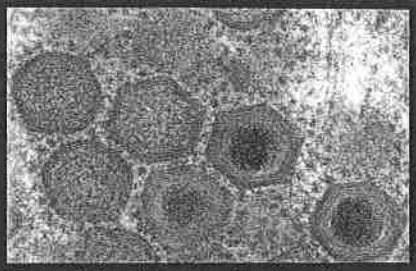
Current molecular biology techniques allow proteins to be fluorescently tagged so they are visible in a **live cell imaging** microscope system. Virus behaviour plays out before the eyes of researchers who have, for example, successfully followed rinderpest virus replication in real time.

Modern **transmission electron microscope** cryo-preparation techniques developed at the Institute have answered a long-standing question about African swine fever virus structure. The virion has only one membrane layer which is important information because it gives clues to how the virus assembles in host cells.

According to Head of Bioimaging, Dr Pippa Hawes, the two most significant advances in microscopy in recent years have been the development of super-resolution light microscopy techniques and **electron tomography** (ET) and it is in the latter that the Institute really excels.

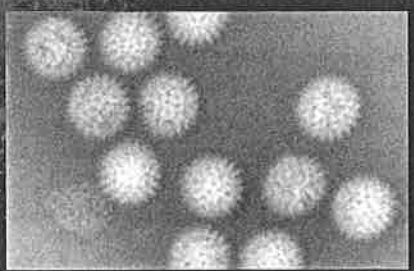
In an ongoing project at the Institute, African swine fever virus precursor structures are being investigated by electron tomography in host cells. The advantage of ET is that it can produce 3D models that show connections between membranes and viruses in a cell that would normally be impossible to see. With this information researchers can deduce how viruses replicate, and potentially develop a strategy to block this process.

High biocontainment facilities raise some unique challenges, and sample preparation needs particularly careful consideration. Often it is the positioning of microscopes that determines available techniques. For example, both live cell imaging and cryo-electron microscopy use samples that include live virus. Because of this, the microscopes are housed within the highest biocontainment areas of the Institute.



Transmission electron microscope image of intracellular African swine fever virus in the replication factory, showing mature particles with dense DNA core and immature particles without the DNA core.

Uninfected dividing cell in culture labelled with antibody against tubulin (red) and stained with fluorophore-conjugated Phalloidin to indicate location of actin (green), and DAPI to indicate location of DNA (blue).



Transmission electron microscope image of negatively stained bluetongue virus core particles.

Uninfected cell in culture labelled with antibody against vimentin (red), and DNA stained with DAPI (blue). Imaged using a confocal laser scanning microscope.

3Rs: Reduction, Refinement and **Replacement** in experiments involving animals

The Institute has been successful in applying the 3Rs – **Reduction, Refinement, Replacement** – to the use of animals in research.

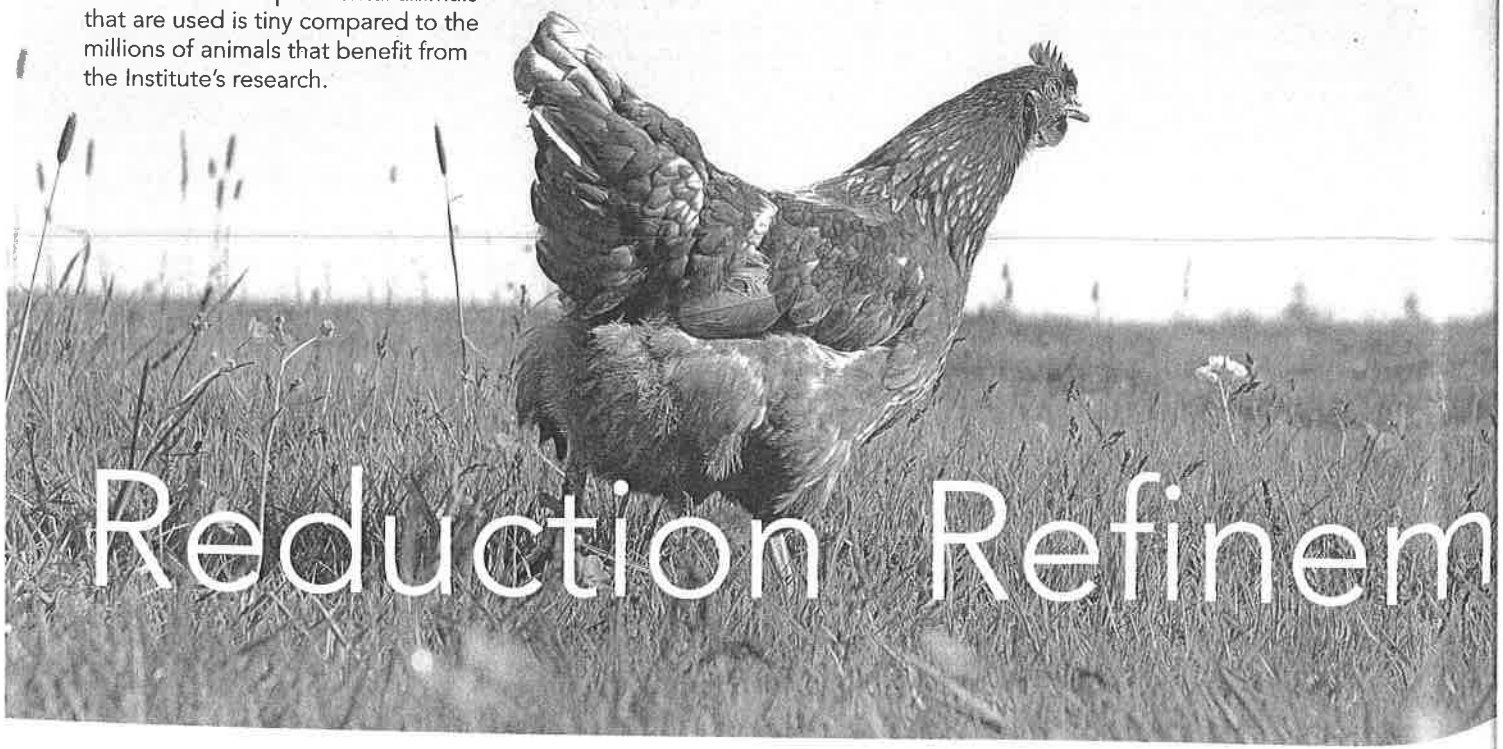
Improvements in veterinary medicines and diagnosis are the result of years of research and development. Much of the time is spent doing research in laboratories. However, the sheer complexity of diseases and the hosts' immune responses to them mean that experiments with animals are essential. At The Pirbright Institute this usually entails working with the species for whose improved health the research is directed (cattle, poultry, sheep and pigs), and we also use small numbers of mice and rabbits. All experimental protocols are subject to scrutiny by the ethical review process, before submission to the Home Office for licensing approval. A fundamental consideration when writing and reviewing such protocols is the application of the 3Rs, and impact on animal welfare.

The number of experimental animals that are used is tiny compared to the millions of animals that benefit from the Institute's research.

Notwithstanding, the Institute strives to apply the principles of the 3Rs for the benefit of animals involved in research and for the quality of the data that they yield. Below are some examples of the progress that has been made:

African swine fever virus kills virtually 100% of the pigs that it infects. All attempts to date to make a killed vaccine against it have failed. It is still necessary to use primary cells derived directly from pigs to grow the virus. The Institute has reduced the number of pigs that are used to obtain primary cells following the discovery that porcine bone marrow cells produce more virus than the previously used porcine alveolar (lung) macrophage. Institute researchers are investigating host factors that determine the susceptibility of cells to ASFV infection in order to develop laboratory-grown cell lines that support replication, obviating the need for primary cells.

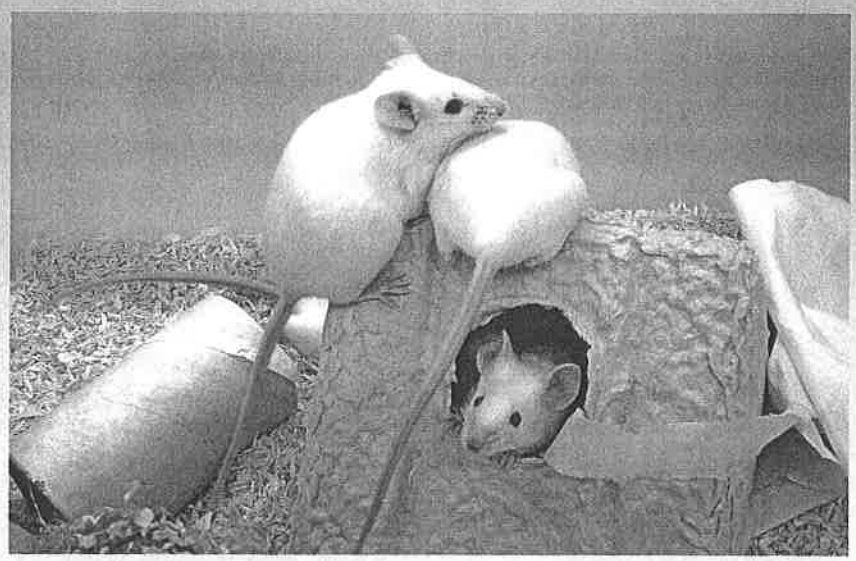
Foot-and-mouth disease virus (FMDV) is an extremely variable virus. Successful control involves identifying the right vaccine to use and demonstrating the efficacy of batches of the selected vaccine. This used to involve vaccination of cattle (a group of cattle for each vaccine to be assessed) which would then be challenged (inoculated) with virus. The Institute now uses serologically-based methods that have greatly reduced both the number of cattle that are used and those that are challenged. Together with mathematical modellers at Glasgow University Institute researchers are



working towards a robust and challenge-free computational-based model for the assessment of FMD vaccine efficacy.

Many FMD diagnostic tests require virus capture using FMDV-specific antibodies. This necessitates the frequent production of serum in rabbits or other small rodents. We have shown, through our fundamental research, that the FMDV cell receptor, integrin avb6, can bind FMDV, regardless of virus serotype, via a highly conserved RGD motif in the GH loop of VP1. Thus avb6 has the potential to be used as a "universal capture ligand", to replace capture antibodies in diagnostic tests. A key aim currently is to develop processes which can reliably produce the integrin avb6 or mimic it to a scale adequate to support these diagnostic tools.

Colonies of biting midges and mosquitoes were traditionally fed using mice. The Institute has shown that the insects can be fed successfully using artificial membrane-based feeding units, and now uses only the latter for insect colonies.

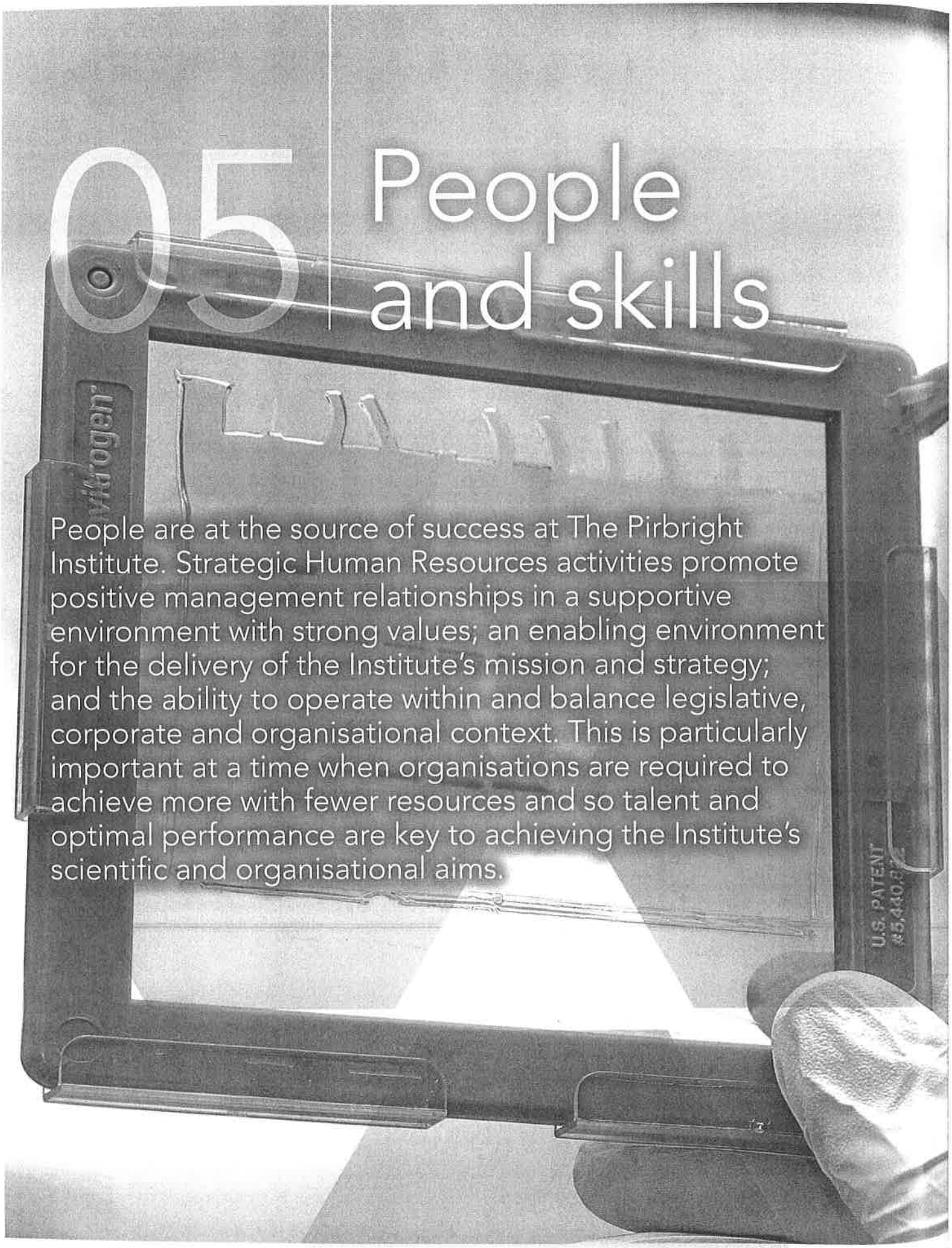


Former colleague Prof. Mark Stevens, in conjunction with collaborators at the University of Cambridge and University College London, did research to identify targets within gastroenteritis-causing Salmonella and Escherichia coli bacteria for the development of treatments against them. He developed a system whereby he was able to screen 475 mutant bacteria using a single animal, a huge reduction in animal numbers. For his achievements in the 3Rs he was awarded the Intervet Dieter Lütticken Award in 2007.

Refinement includes environmental enrichment for animals used in experiments in animal accommodation. The Institute's pigs have easy to clean and hard wearing items like brush heads, dog toys and pieces of hose with which they can play. Background music is also played in the corridor. The introduction of these methods has not only prevented the onset of abnormal behaviour but has also improved the welfare of the animals.

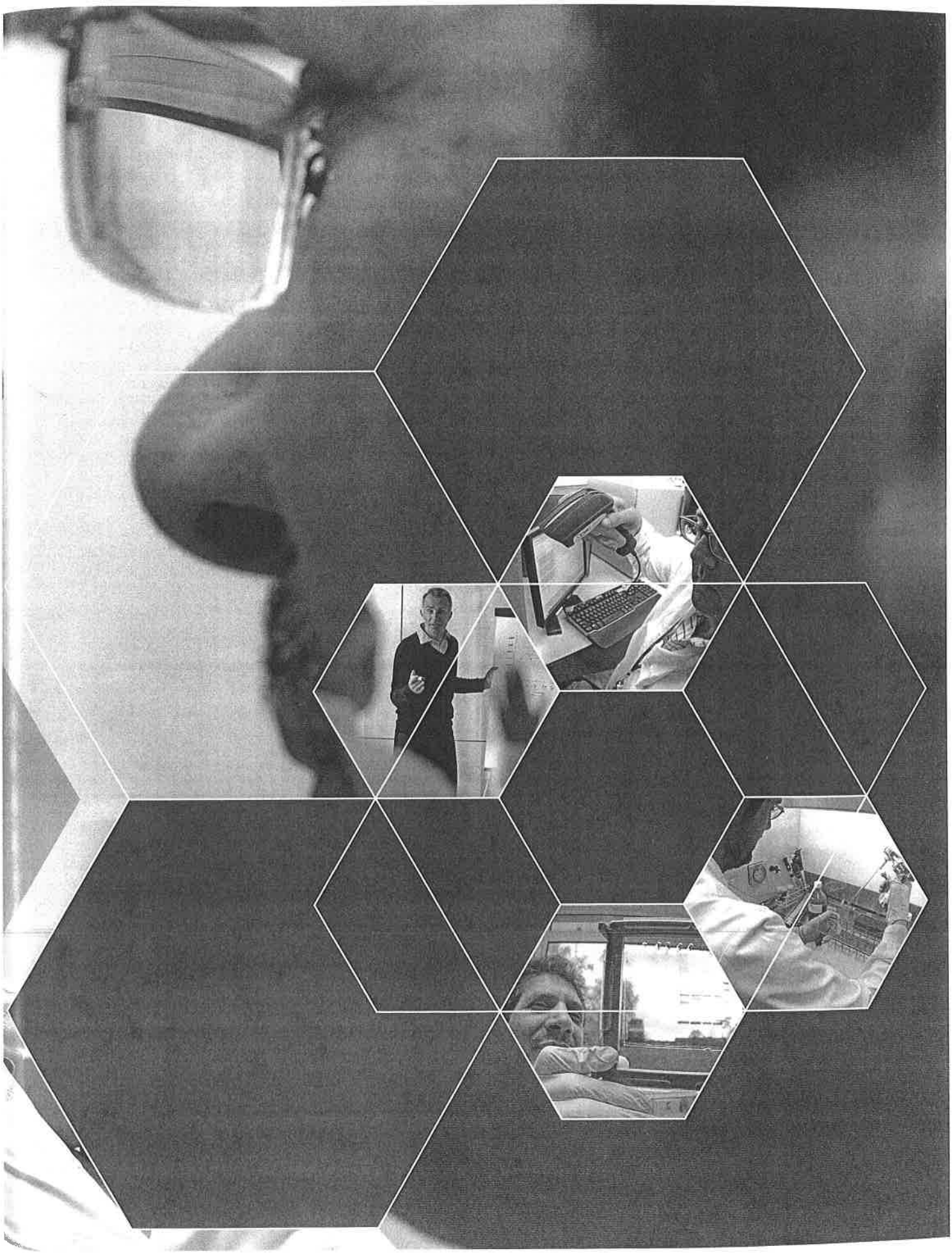
The Institute has also enriched the environment of many of its breeding chickens by replacing mesh cages and flooring with floor pens. Researchers at the Institute demonstrated that these resulted in significant improvements in the health and appearance of the birds as well as higher fertility in the majority of the chicken lines.

ent Replacement



05 People and skills

People are at the source of success at The Pirbright Institute. Strategic Human Resources activities promote positive management relationships in a supportive environment with strong values; an enabling environment for the delivery of the Institute's mission and strategy; and the ability to operate within and balance legislative, corporate and organisational context. This is particularly important at a time when organisations are required to achieve more with fewer resources and so talent and optimal performance are key to achieving the Institute's scientific and organisational aims.



People and Skills

The community of scientific and operational staff at The Pirbright Institute is diverse in every respect; it is the variety of perspectives, experiences and skills that drives creativity and innovation and ultimately success. Professional excellence and confidence are valued highly along with cooperation, collaboration, leadership and respect.

Staff at The Pirbright Institute are experts in a range of scientific, technical and administrative specialities and are actively encouraged and enabled to maintain and develop their skills and knowledge. The next generation is supported through MSc, PhD, and professional and technical apprenticeships and succession planning in niche areas of expertise is taken seriously and approached strategically. Mentoring is available to staff at all levels and schemes exist to promote a positive culture for career progression and advancement.

When well-managed performance and inherent talent, creativity and innovation combine with a highly rigorous academic and professional approach, genuine team work and partnership, and equality of opportunity and experience, there is no stopping an organisation. The Pirbright Institute is committed to supporting and developing its staff to this end.

Institute Fellowships

As part of The Pirbright Institute's long term strategy, the organisation wishes to attract and encourage the best scientists to join the Institute. In order to help achieve this aim, a Fellowships Scheme has been introduced to enable outstanding early-career scientists to develop their own research programme within the remit of the Institute.

Postgraduate Skills Training

An important aspect of the Institute's strategy is to develop the next generation of scientists to take forward research on infectious disease biology.

As part of the commitment to fulfil this responsibility, each year the Institute enrols 10 to 12 graduate students from the UK and elsewhere into its Postgraduate Training programme to study for a PhD or MSc. The ambition is that these students will form the research leaders of the future at the Institute, elsewhere in the UK and worldwide.

The Institute has a unique learning environment providing its students with the opportunity to work on multidisciplinary projects with real disease agents in the target species. They also benefit from access to world experts in their chosen subject, availability of facilities, such as specialised animal accommodation and equipment, and to a network of other research laboratories internationally. In addition, students have access to the expertise and facilities of the universities at which they are registered. All students receive training in transferable skills providing them with the necessary grounding for work in many fields.

Studentships at the Institute are funded by a variety of sources including the BBSRC, industry, the Association of Commonwealth Universities and foreign governments as well as the Institute itself. This creates an exciting international community of young researchers and typifies the ethos of the Institute as an organisation of international learning, training, and knowledge exchange.

It is a priority to encourage industry to take part in our programme to provide students with experience and to further our collaborations.

Students trained at The Pirbright Institute are highly regarded in the research community for the level of training they have received and have little difficulty finding employment. The majority of students go on to post-doctoral positions either in the Institute or in laboratories elsewhere in the UK and around the world.

In addition to research, the skills acquired by Institute-trained scientists are also in demand for other related activities in industry, Government and research councils and university scientific administration.

Overseas students often return home, taking with them expertise and knowledge and also thereby helping to fulfil part of the UK's international development responsibilities.

Continuous Professional Development

The Pirbright Institute is committed to being a top choice for employment and training, leadership capability, and performance management, underpinned by dedication to equality of opportunity and experience. For the Institute to fulfil its goals and grow in all ways as an organisation, the professional and personal development of people at all levels is vital.

To maintain and develop expertise and to ensure competence in scientific, technical and administrative disciplines and skills in leadership and management, there is an embedded culture of continuous professional development and a strategic approach to staff development. There are also many ways of working that are unique to the Institute, making induction training a vital part of maintaining an effective workforce. Training in standard operating procedures for biosecurity, health and safety, and technical operations enables the Institute to maintain the highest standards of working that protect people and the environment and to meet the requirements of regulators and inspectors.

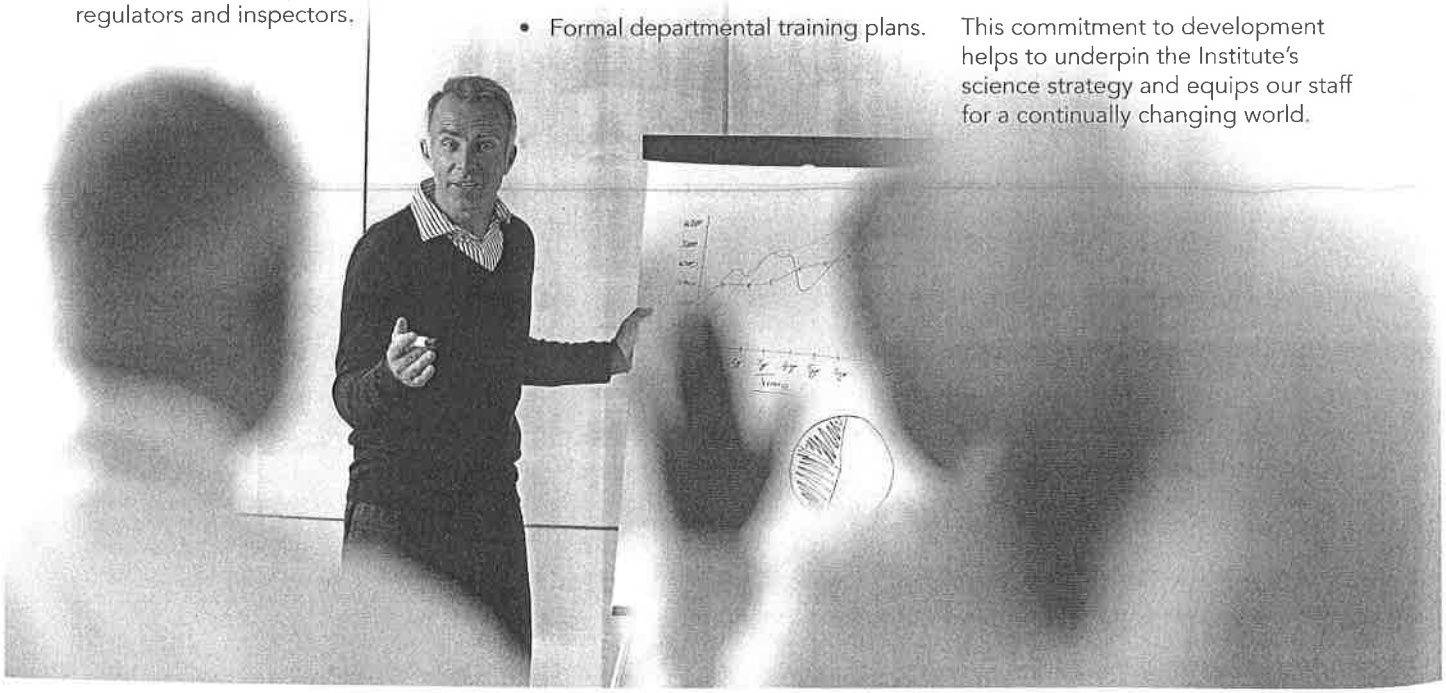
The Institute's Learning & Development Manager supports this by providing:

- Induction training.
- Annual staff development reviews through a PPDR (Personal and Professional Development Review) process.
- An Institute training events calendar.
- A transferable skills programme for research students and post-docs.
- Apprenticeships.
- Mentoring scheme.
- An Individual Learning & Development requests scheme.
- Formal departmental training plans.

The Institute funds a diverse range of training to support all our staff. Examples of these are:

- Financial qualifications.
- Further education sponsorship in MSc and Part-time PhDs.
- Chartered qualifications and qualifications from professional bodies.
- Home Office licences.
- Veterinary qualifications.
- Engineering qualifications.
- Compliance qualifications.
- Farm practices.

This commitment to development helps to underpin the Institute's science strategy and equips our staff for a continually changing world.



Strategic HR activities

The success of publicly-funded science comes from the talent and performance of scientists and support staff employed in the organisation. The Pirbright Institute has a unique staff with a national and international reputation for delivering high quality, high impact science.

Leadership and management

Career progression can involve transitions into management roles and for scientists these transitions can be particularly sharp. The importance of supporting the progression of staff with targeted training and development and continuing to support those who have been in a management role for some time is recognised at The Pirbright Institute.

The Institute expects all leaders to espouse values of, and develop skill in, inspirational and visionary leadership; leading by example and being a role model; staff development at all levels; acting as a change agent; and effective communication skills.

To this end, there is a formal competency approach for leaders; all recruitment managers are trained in recruitment and selection and pre-interview screening; and schemes are in place for coaching and mentoring, identifying and nurturing talent and potential, and continuous professional development.

Succession planning

Since 2012 a formal succession planning scheme has been in place. This is particularly important for The Pirbright Institute where certain roles include niche skills and knowledge that are unique to the Institute and can only be developed through experience of the unusual environment therein. The scheme ensures that values are reinforced and sustainability is ensured through an approach that provides the right people at the right time with the right skills and capabilities in all areas of the organisation to deliver the Institute's aims.

Equality of opportunity

Recruiting and retaining women and other minorities in senior positions is a recognised challenge across the science, technology, engineering and mathematics sector. There are many ways to address this challenge and at the time of writing The Pirbright Institute is in the early stages of collaboration with the Athena SWAN scheme, which recognises good practice in the employment of women in science. The Institute aims for membership of the scheme in order to increase the visibility of senior women in science and to use its guiding principles as a catalyst for change. In this way, good practice will be encouraged that will, it is hoped, in turn attract women into senior positions at the Institute.

Fellowships scheme

The Pirbright Institute has an established internal fellowships scheme that enables outstanding early-career scientists to develop their own research programme. There are fellows working across the Institute's science portfolio and opportunities in particular areas are advertised from time to time. Applications for these posts are welcomed from high-calibre, ambitious scientists who are able to demonstrate their potential for becoming an established group leader.

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Director of Science
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Head of Avian Viral Diseases programme
Professor Venugopal Nair
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Head of Livestock Viral Diseases programme
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Head of Vector-borne Viral Diseases programme
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Head of Microbiological Services
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Head of Information Services
Toby Fenton
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Head of Compliance, Regulatory Affairs & Risk
Steve Copping
Email: steve.copping@pirbright.ac.uk

BBSRC bioscience for the future

The Institute receives strategic funding from BBSRC

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Director

Professor John Fazakerley BSc, MBA, PhD, FSB, FRCPath

Institute Executive Board

Professor John Fazakerley, *Director*
Mr Richard Shaw, *Director of Operations*
Professor David Paton, *Director of Science*
Dr Bryan Charleston, *Head of the Livestock Viral Diseases programme*
Mr Steve Copping, *Head of Compliance, Regulatory Affairs and Risk*
Mr Alan Garmonsway, *Change Director*
Dr Mike Johnson, *Head of Engineering and Estates*
Professor Peter Mertens, *Head of the Vector-borne Viral Diseases programme*
Professor Venugopal Nair, *Head of the Avian Viral Diseases programme*
Mr Keith Simpson, *Head of Finance*
Ms Carol Smith, *Head of Human Resources*

Trustee Board

Professor Joe Brownlie (*Chair*)
Ms Alison Craig
Mr Paul Gemmill
Dr Theo Kanellos
Mr Tim Key
Professor Quintin McKellar
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Science Advisory Board

Professor Keith Gull (*Chair*)
Professor Maggie Dallman
Professor Richard Elliott
Dr Lesley Heppell
Professor Duncan Maskell
Professor Thomas Mettenleiter
Professor John Pickett
Professor Alan Rickinson
Professor Mark Rweyemamu

About The Pirbright Institute

The Pirbright Institute is a world leading centre of excellence in research and surveillance of virus diseases of farm animals and viruses that spread from animals to humans. Based in the UK and receiving strategic funding from the Biotechnology and Biological Sciences Research Council (BBSRC), the Institute works to enhance capability to contain, control and eliminate these economically and medically important diseases through highly innovative fundamental and applied bioscience. With an annual income of around £30 million from grants and commercial activity, and a total of £76.9 million strategic investment from BBSRC during 2011-12, the Institute contributes to global food security and health, improving quality of life for animals and people.

For more information see **www.pirbright.ac.uk**

THE Pirbright INSTITUTE

PAGE 1

PIPESTONE®

PAGE 2 PIPESTONE

Overview

- **Pipestone Holdings** is an internationally recognized leader in large scale livestock production management, veterinary advisory and marketing services.
- **Four Business Operating Units:**
  - Pipestone Veterinary Services
  - Pipestone System (PVC Management II)
  - BigStone Marketing
  - Pipestone International
- **Pipestone's** complementary skill set, collective wisdom and demonstrated expertise provide immediate access and opportunities for clients seeking progressive swine production.

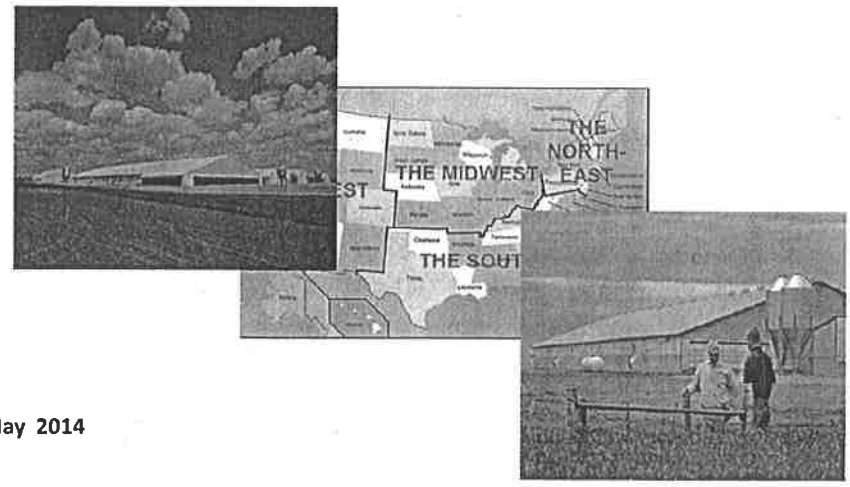
Vision & Values

Helping farmers today create the farms of tomorrow

Integrity
Caring
Commitment
Growth
Teamwork

PIPESTONE®
Advancing Animal Care Every Day™

PIPESTONE®



May 2014

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US Operations

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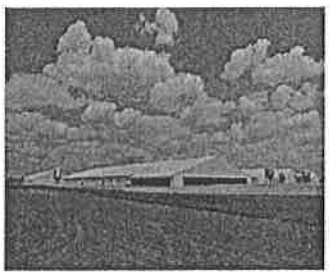
  - Livestock marketing
  - Project and facility design, construction and operation
- Headquartered in Pipestone, Minnesota.



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- Established 1942
- 3 Locations
  - Pipestone, MN
  - Independence, IA
  - Ottumwa, IA
- 30 Veterinarians:
  - 15 100% swine practice
  - 3 recognized as Swine Practitioner of the Year by American Association of Swine Veterinarians
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- $40+ million in product sales in 2013
- Recognized innovative industry leader in research related to genetics and animal health products (Pipestone Applied Research Initiative)
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- Have consulted or lectured in every major swine production area in the world

PIPESTONE®

VETERINARY SERVICES

- Established 1990
- 700+ employees
- Manage ~170,000 sows
  - 50+ separate sow farms in Minnesota, Iowa, South Dakota and Nebraska
  - 27 PSY (sow yield)
  - 14.5 Total Born per Sow
- 6th largest Hog producer in US based upon number of sows
- Manage ~500,000 finishing pigs annually
- Information and record keeping systems that allow management to track progress as well as to respond to challenges real time

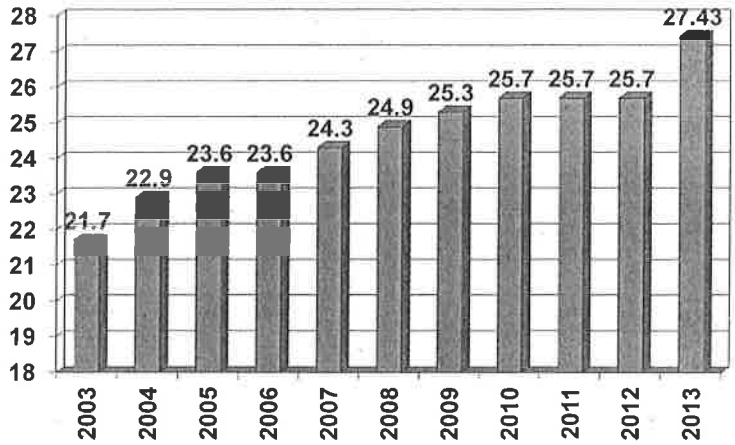
PIPESTONE®

SYSTEM

Top 25 U.S. Pork Powerhouses[1] 2013
A Successful Farming Exclusive Report

2013 Ranking	Company/Headquarters	# of Sows in 2013	# of Sows in 2012
1	[illegible]	961,000	952,000
2	[illegible]	781,500	710,500
3	[illegible]	532,000	512,000
4	[illegible]	505,000	536,000
5	[illegible]	173,000	155,000
6	[illegible]	163,500	150,000
7	Pipestone System/Pipestone, MN	153,000	115,000
8	[illegible]	151,000	115,000
9	[illegible]	101,500	103,000
10	HMC Management Services/Audubon, IA	101,000	52,300
11	[illegible]	95,000	49,300
12	[illegible]	95,000	52,300
13	[illegible]	94,000	58,300
14	[illegible]	94,000	35,300
15	[illegible]	52,500	50,000
16	[illegible]	51,500	49,300
17	[illegible]	48,000	48,300
18	[illegible]	48,000	42,300

PIPESTONE SYSTEM Pigs Weaned Per Mated Female



Big Stone Marketing

Big Stone Marketing

- Established 2009
- 1.8M Market Hogs annually
- Strategic contractual arrangements with:
  - Cargill Meat Solutions
  - Hormel Foods
  - Tyson Fresh Meats
  - JBS
  - John Morrell
- Market optimization tools and services for customers

Farm Design & Construction

PIPESTONE SYSTEM

- Pipestone has real-world experience in the design and construction of swine facilities.
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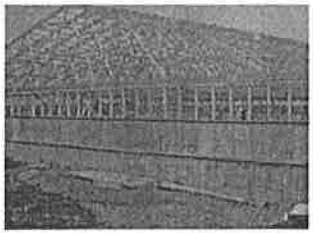
- Pipestone's extensive network of US based equipment suppliers is leveraged for the benefit of Pipestone clients.



Herd Health

PIPESTONE SYSTEM

- Pipestone has extensive and valuable experience designing overall production systems for long-term health & performance.
- Unique disease challenges present a significant economic risk
- Swine operations that consistently seek to reduce and ultimately operate free of;
  - PRRS
  - PEDV
  - PCV
  - M. hyopneumoniae
- Will enjoy a competitive production and economic advantage

Genetics Strategy

PIPESTONE INTERNATIONAL

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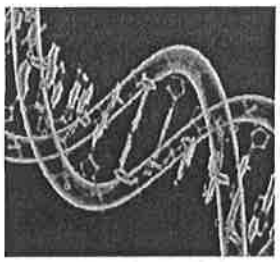

Health and bio-security

PIPESTONE SYSTEM

Bio-security

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The **focus and improvement in the areas of bio-security** have led to a reduction in disease incidence in Pipestone managed farms

Pipestone's animal health focus can and will be transferred to swine clients.

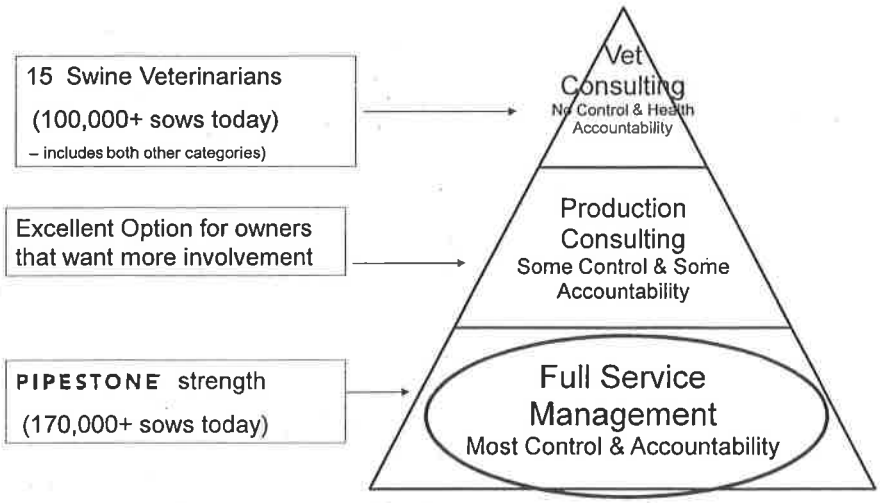
PIPESTONE

Pipestone is a USA Swine Industry Innovator:

- Weaned pig production model
- Large scale sow farm management
- Internal gilt multiplication
- Semen/Boar stud management
- Field Application of filter technology
- Field based research barns
- Attracting and retaining world class Swine Veterinary Team

PIPESTONE

PIPESTONE Management Service Levels



Executive Team

- **Dr. Gordon Spronk (Chairman of BOD, Pipestone)** is a native of the Pipestone, MN area. After completing his education at the University of Minnesota College of Veterinary Medicine in 1981, he returned to Pipestone to practice at the Pipestone Veterinary Clinic. Dr. Spronk is the co-founder of the "Pipestone System" and numerous affiliated companies under Pipestone Holdings. Dr. Spronk is the recipient of the 2000 AASV Swine Practitioner of the Year Award and the 2011 Leman Science in Practice Award. Dr. Spronk and his wife, Deb, live near Pipestone and have three children, Courtney, J.J., and Morgan. In his free time, Dr. Spronk enjoys traveling and spending time with his family.

- **Dr. Luke Minion (CEO, Pipestone)** grew up in southwestern Minnesota and began his career with the Pipestone Veterinary Clinic in 2000 after graduating from the University of Minnesota College of Veterinary Medicine. Dr. Minion serves as the CEO of Pipestone Holdings, LLC and oversees the operations of the clinics management and livestock marketing companies. Dr. Minion and his wife, Betsy, enjoy golfing and keeping up with their son, Landon and twin daughters Claire and Lauren. Dr. Minion was honored in 2013 with the 40 under 40 award in Agriculture by Vance Publishing.

- **Dr. Barry Kerkaert (Vice President, Pipestone)** grew up in southwest Minnesota and began his career with the Pipestone Veterinary Clinic in 1994 after graduation from the University of Minnesota College of Veterinary Medicine. Dr. Kerkaert serves as Vice President of Pipestone management and veterinary operations and leads the System Grow Finish team. Dr. Kerkaert and his wife Karen live near Pipestone, Minnesota with their three children and enjoy 4-H activities including showing sheep and swine in local and national competitions. Dr. Kerkaert was honored in 2013 with the Swine Practitioner of the Year award from the American Association of Swine Veterinarians. Barry enjoys spending his free time hunting and fishing with his friends and family.

- **Brian Stevens (CEO, Big STONE)** grew up on a diversified livestock farm in Eastern Nebraska, attended the University of Nebraska where he received his Bachelor's degree in Animal Science. After graduation he began what would become a 19 year career with Hormel Foods. His last 7 years there he was Director of Hog Procurement and oversaw all activities related to hog buying and carcass evaluation. Brian is President of Big Stone Marketing which was established to help independent producers with negotiating packer contracts, open market sales, benchmarking among other producers, risk management through forward contracting, process verification programs and overall marketing performance and opportunities.

MORE INFORMATION:

www:pipestonesystem.com
www:pipevet.com

PIPESTONE SYSTEM
PIPESTONE VETERINARY SERVICES

Vision & Values

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Integrity
Caring
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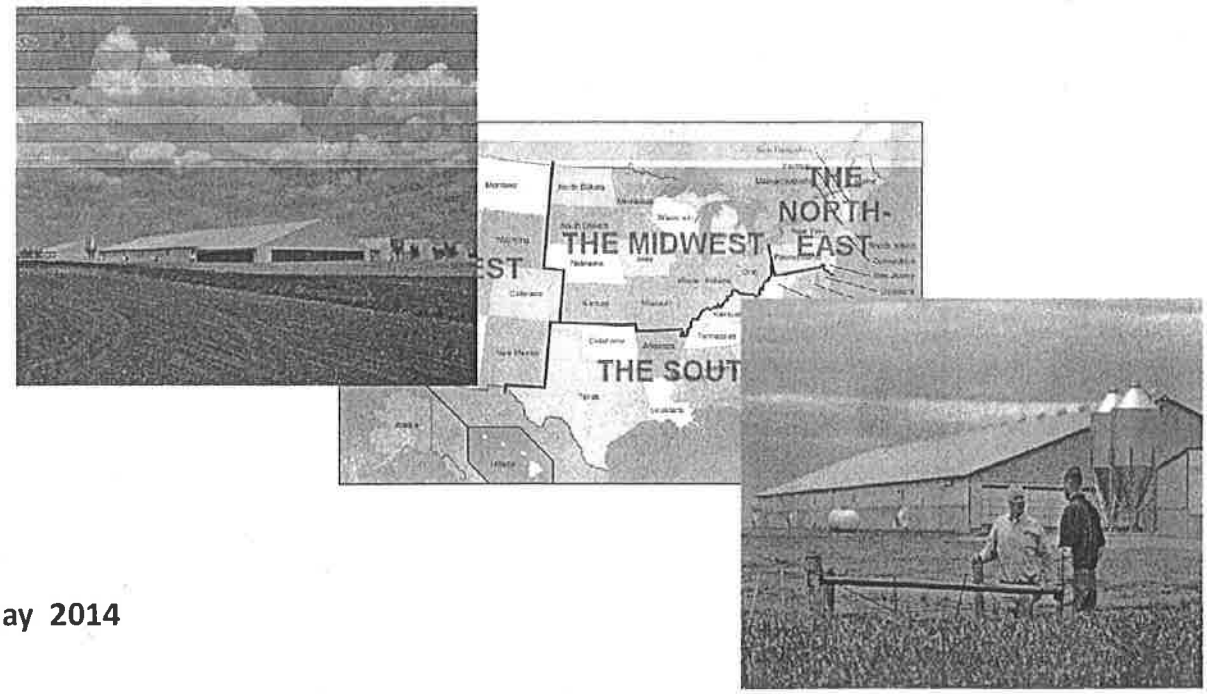

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2013 Ranking	Company/Headquarters	# of Sows In 2013	# of Sows In 2012
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2	Triumph Foods/St. Joseph, MO (Includes Christensen Farms: 158,300 sows, Hanor: 82,800, Allied Producers' Cooperative: 60,500, New Fashion Pork: 52,000, and Eichelberger Farms: 30,000 sows.)	381,500	328,500
3	Seaboard Foods/Shawnee Mission, KS	217,000	217,000
4	The Maschhoffs/Carlyle, IL	208,000	196,000
5	Prestage Farms/Clinton, NC	170,000	185,000
6	[illegible]	160,000	160,000
6	Pipestone System/Pipestone, MN	160,000	145,000
8	Cargill/Minneapolis, MN	153,000	136,000
9	Carthage System/Carthage, IL	104,500	103,500
10	AVINC Management Services/Audubon, IA	100,000	82,000
11	Maxwell Foods/Goldsboro, NC (Now includes Indiana operation.)	90,000	69,000
12	Tyson Foods/Springdale, AR	80,000	52,000
13	Hormel Foods/Austin, MN	54,000	54,000
13	TriOak Foods/Oakville, IA (Bought sows from AgFeed.)	54,000	35,000
15	Pillen Family Farms/Columbus, NE	52,500	50,000
16	Hatfield Quality Meats/Hatfield, PA	51,500	49,900
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18	Wakefield Pork/Gaylord, MN	45,300	42,900

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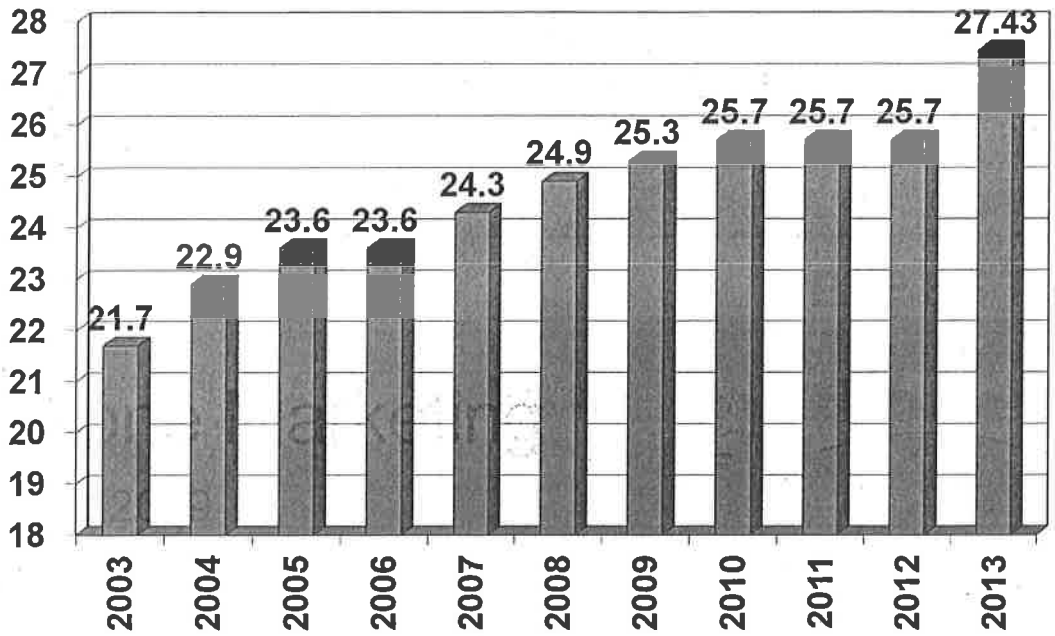

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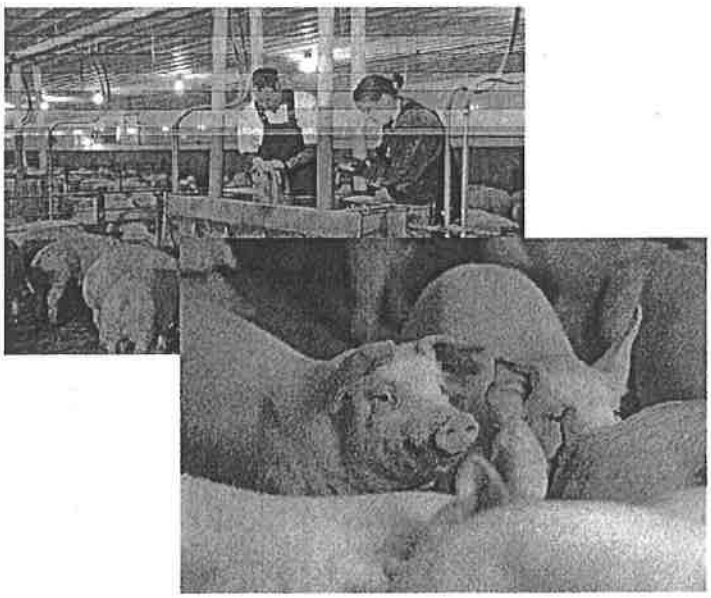

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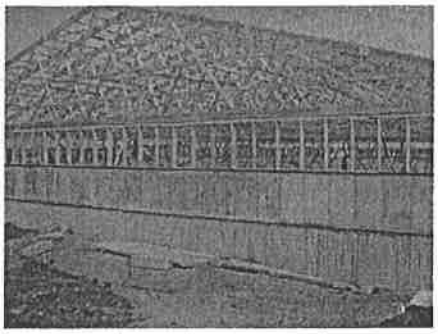

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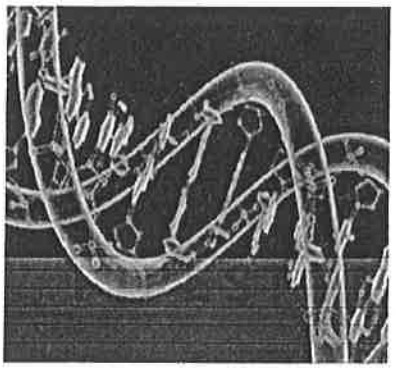

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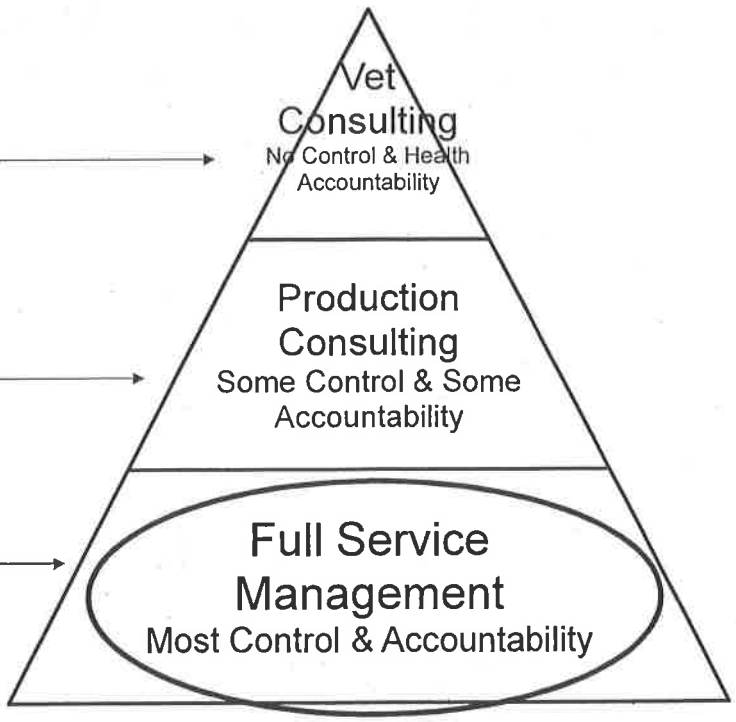
PIPESTONE®

PIPESTONE® Management Service Levels

15 Swine Veterinarians
(100,000+ sows today)
– includes both other categories)

Excellent Option for owners that want more involvement

PIPESTONE® strength
(170,000+ sows today)



Executive Team

- **Dr. Gordon Spronk (Chairman of BOD, Pipestone)** is a native of the Pipestone, MN area. After completing his education at the University of Minnesota College of Veterinary Medicine in 1981, he returned to Pipestone to practice at the Pipestone Veterinary Clinic. Dr. Spronk is the co-founder of the "Pipestone System" and numerous affiliated companies under Pipestone Holdings. Dr. Spronk is the recipient of the 2000 AASV Swine Practitioner of the Year Award and the 2011 Leman Science in Practice Award. Dr. Spronk and his wife, Deb, live near Pipestone and have three children, Courtney, J.J., and Morgan. In his free time, Dr. Spronk enjoys traveling and spending time with his family.

- **Dr. Luke Minion (CEO, Pipestone)** grew up in southwestern Minnesota and began his career with the Pipestone Veterinary Clinic in 2000 after graduating from the University of Minnesota College of Veterinary Medicine. Dr. Minion serves as the CEO of Pipestone Holdings, LLC and oversees the operations of the clinics management and livestock marketing companies. Dr. Minion and his wife, Betsy, enjoy golfing and keeping up with their son, Landon and twin daughters Claire and Lauren. Dr. Minion was honored in 2013 with the 40 under 40 award in Agriculture by Vance Publishing.

- **Dr. Barry Kerkaert (Vice President, Pipestone)** grew up in southwest Minnesota and began his career with the Pipestone Veterinary Clinic in 1994 after graduation from the University of Minnesota College of Veterinary Medicine. Dr. Kerkaert serves as Vice President of Pipestone management and veterinary operations and leads the System Grow Finish team. Dr. Kerkaert and his wife Karen live near Pipestone, Minnesota with their three children and enjoy 4-H activities including showing sheep and swine in local and national competitions. Dr. Kerkaert was honored in 2013 with the Swine Practitioner of the Year award from the American Association of Swine Veterinarians. Barry enjoys spending his free time hunting and fishing with his friends and family.

- **Brian Stevens (CEO, Big STONE)** grew up on a diversified livestock farm in Eastern Nebraska, attended the University of Nebraska where he received his Bachelor's degree in Animal Science. After graduation he began what would become a 19 year career with Hormel Foods. His last 7 years there he was Director of Hog Procurement and oversaw all activities related to hog buying and carcass evaluation. Brian is President of Big Stone Marketing which was established to help independent producers with negotiating packer contracts, open market sales, benchmarking among other producers, risk management through forward contracting, process verification programs and overall marketing performance and opportunities.

MORE INFORMATION:

www:pipestonesystem.com

www:pipevet.com

PIPESTONE SYSTEM PIPESTONE

PEDV SUMMARY

7.11.14

Dr. Barry Kerkaert

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VETERINARY SERVICES

Data and information source acknowledgement

- Dr. Bob Morrison
- University of Minnesota
- Pipestone Applied Research Team (PAR)
  - Dr. Scott Dee, Director
- Pipestone Swine Veterinary Staff
  - Dr. Luke Minion
  - Dr. Barry Kerkaert
  - Dr. Adam Schelkopf
  - Dr. Steve Menke
  - Dr. Todd Williams
  - Dr. Scott Dee
  - Dr. Cameron Schmitt
  - Dr. Bryan Myers
  - Dr. Gordon Spronk
  - Dr. Spencer Wayne
  - Dr. Joel Nerem
  - Dr. Emily McDowell
  - Dr. GF Kennedy

Pipestone Weekly Health Status

May 12, 2014 report

- Summary
  - 9 sites PEDV
  - 1 site PEDV and SDEV
  - 1 site TGEV
- 2 sites PEDV elimination completed
- 11 sites in various stages of Elimination protocols

Level	Farm ID	Herd Size	Herd Vet	Status Date	Days in Level
Level-2	Windy Plains	3329	Barry Kerkaert	1-Mar-07	2515
Level-2	Farmers Pork	3053	Carissa Odland	14-Apr-11	1110
Level-2	Grassland Pork	2750	Emily McDowell	19-Jan-12	830
Level-2	Eagle Ridge	3256	Adam Schellkopf	19-Jan-12	830
Level-2	Silver Top	2846	Emily McDowell	18-Apr-12	740
Level-2	Alliance Family Farms	5591	Adam Schellkopf	17-Dec-12	497
Level-2	Fox Run	5158	Luke Minion	19-Dec-12	495
Level-2	Jackrabbit Family Pork	5236	Barry Kerkaert	17-May-13	345
Level-2	R&F MO, LLC	2915	Steve Menke	20-Jun-13	312
Level-2	Stormy Hollow, LLC	2900	Steve Menke	20-Jun-13	312
Level-2	Coyote Ridge	3387	Joel Nerem	4-Sep-13	236
Level-2	Skyline	5275	Bryan Myers	15-Sep-13	225
Level-2	Horseshoe Hill	1296	Carissa Odland	10-Oct-13	200
Level-2	Prairie Gold	2792	Adam Schellkopf	11-Oct-13	199
Level-2	Duckdel	2514	Bryan Myers	17-Dec-13	132
Level-3	Twin Rock	5024	Dr. Scott Dee	9-Oct-12	566
Level-3	Buffalo Run	3127	Spencer Wayne	6-Nov-12	538
Level-3	Whitetail Run	3178	Gerald Kennedy	22-Apr-13	371
Level-3	Pheasant Run	3105	Spencer Wayne	8-Jul-13	294
Level-3	Ten Brook 1	2500	Scott Dee	22-Aug-13	249
Level-3	Hawkeye-9	3400	Bryan Myers	3-Oct-13	207
Level-3	Blue Stem	3478	Carissa Odland	11-Oct-13	199
Level-3	Classic Farms	2965	Luke Minion	17-Oct-13	193
Level-3	Buttercup	3253	Gordon Spronk	31-Oct-13	179
Level-3	Hawkeye-7	3550	Bryan Myers	2-Jan-14	116
Level-3	Hawkeye-1	3230	Joel Nerem	23-Jan-14	96
Level-4	HIAWATHA	2201	Barry Kerkaert	22-May-12	706
Level-4	Remitle Run	1327	Carissa Odland	22-May-12	706
Level-4	Cougar Run 1	5529	Bryan Myers	2-Aug-12	634
Level-4	Calumet	1457	Adam Schellkopf	1-Nov-12	543
Level-4	HIAWATHA- West	0	Barry Kerkaert	29-Nov-12	515
Level-4	Nokomis-Winnemissa	3040	Gerald Kennedy	25-Mar-13	399
Level-4	Ten Brook 3	3041	Scott Dee	15-May-13	348
Level-4	Hawkeye-2	3200	Joel Nerem	5-Jun-13	327
Level-4	Cougar Run 2	2811	Bryan Myers	27-Nov-13	152
Level-4	Hawkeye-4	3300	Gordon Spronk	27-Feb-14	60
Level-4	Rosewood	3458	Gordon Spronk	15-Apr-14	13
Level-4	Prairieview Pork	2721	Spencer Wayne	15-Apr-14	13
Level-4	Ten Brook 2	2500	Scott Dee	21-Apr-14	7
Level-5	Hillcrest Pork	1584	Todd Williams	26-Sep-13	214
Level-5	WAPCI	1272	Adam Schellkopf	24-Dec-13	125
Level-5	Sleepy Hollow	2906	Jeff Blythe	16-Jan-14	102
PEDV	Legend	5215	Joel Nerem	9-Jan-14	109
PEDV	New Prairie	1370	Barry Kerkaert	9-Jan-14	109
PEDV	Dakota Superior	3261	Gerald Kennedy	11-Jan-14	107
PEDV	Shellit	3058	Gerald Kennedy	13-Jan-14	105
PEDV	North View	1332	Carissa Odland	15-Jan-14	103
PEDV	Deer Run Pork	2977	Emily McDowell	22-Jan-14	96
PEDV	Fox Ridge Pork	1374	Todd Williams	25-Jan-14	93
PEDV	Schmitz Grain Farm	2504	Barry Kerkaert	29-Jan-14	89
PEDV	Lyon-One	1500	Spencer Wayne	30-Jan-14	88
PEDV	Hawkeye-6	3750	Gordon Spronk	22-Feb-14	65
TGEV	Hawkeye-3	3000	Gordon Spronk	5-Feb-14	82

PEDV

- Porcine Epidemic Diarrhea Virus (PEDv)
- Identified in USA in April/May, 2013
  - Corona virus family
  - Similar to TGE virus
- Only infectious in swine
- First observed in England in 1971
- Asian epidemics of the virus in the 80's, continued into 90's and 2000's
  - China – big increase in 2008 to 2013
- USA virus sequence is 96.5 to 99.9% similar
  (Marthaler et al, 2013)

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PEDV Clinical Signs

- PEDV replicates in the epithelial cells of the small intestine
- Incubation period: 1-2 days
- Shedding in feces: 7-11 days (up to 35 days)
- Profuse, watery diarrhea
  - Dehydration, anorexia, vomiting, poor nutritional absorption
- High morbidity, low mortality in growing swine
- Devastating impact on sow farm
  - High morbidity and high mortality in piglets less than one week of age

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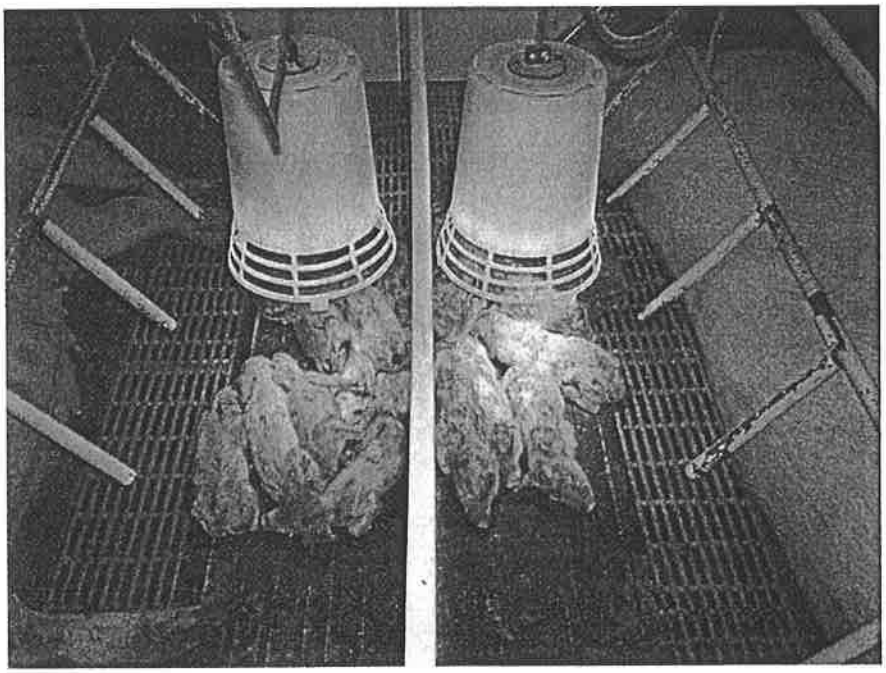
Litters less than 1 week old (photo



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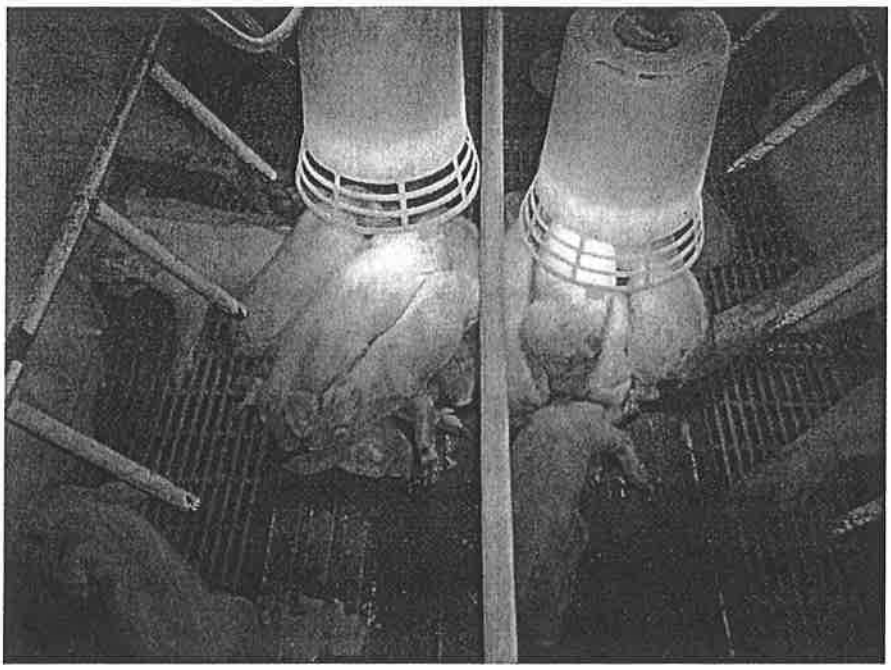
Litters 1-2 weeks old



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Litters 2-3 weeks old

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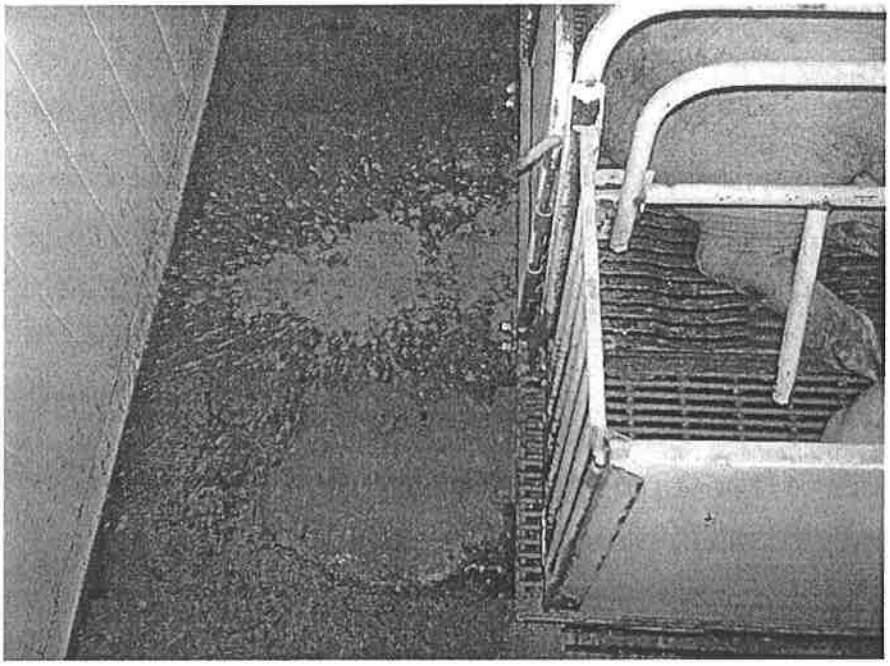
Sow Clinical Signs



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PEDV

- PEDV replicates in the epithelial cells of the small intestine
- Incubation period: 1-2 days
- Shedding in feces: 7-11 days (up to 35 days)
- Immune response: mucosal and serological: serum antibodies at 7-14 dpi

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PEDV in USA

- Identified in USA in April, 2013
  - Corona virus family
  - Group 1 – Like TGE
  - Enveloped
- Only infectious in Swine
- First observed in England in 1971
  - Primarily in feeder pigs and market pigs
  - Expressed itself in winter months similar to TGE

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PEDV in USA

- Milestone dates:
  - April, 2013 – first detection in USA
  - January 2014 – "new" PEDV detected in USA
  - February 14, 2014- first detected in Canada
  - February, 2014 –SDCV; deltacorona virus detected in Ohio

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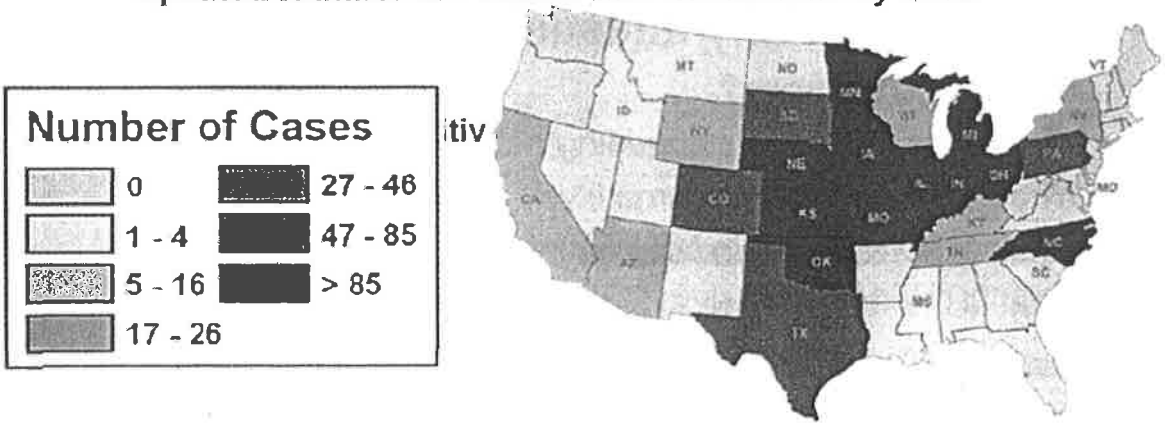
PEDV Diagnostic Tests

- U of Minnesota, ISU, SDSU
- Virus isolation:
  - Difficult to grow in vitro
- Electron Microscopy:
  - low sensitivity
- <u>Histopathology:</u>
  - atrophic enteritis
  - same as TGEV and Rota
- <u>Real time PCR:</u>
  - sensitive and specific
  - available in US laboratories
  - Fecal or OF
  - Very quick turnaround time:
    - Samples to lab by noon: same day results

Porcine Epidemic Diarrhea Virus Reporting

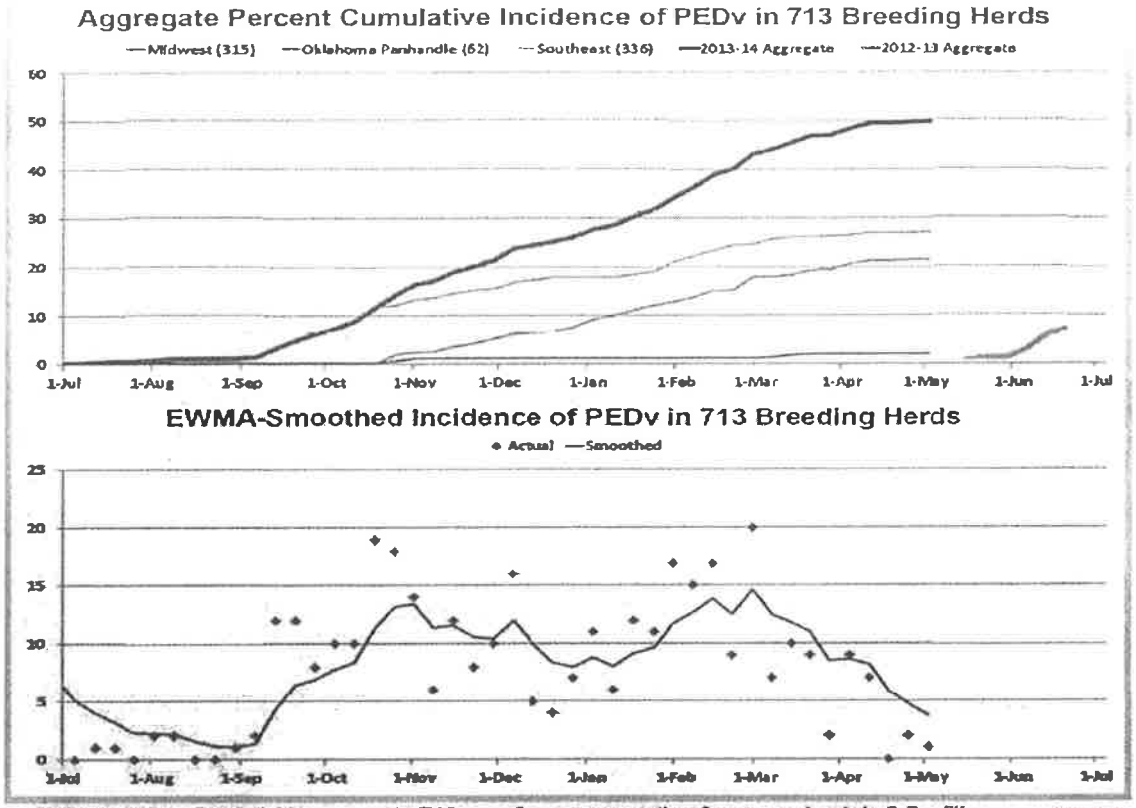
Collated by APHIS, VS, NVSL, National Animal Health Laboratory Network & Univ of MN VDL. Reporting Laboratories include: ISU, KSU, OH Department of Agriculture ADDL, SDSU, Univ of MN, Univ. of GA, NE VDC, Purdue, MSU. Data through 6/3/2014

Updated Number of Positive Lab Accessions by State



STATE	IA	OK	MN	IN	CO	KS	OH	NY	WI	MD	CA	SC	MT	ND	VT
CASES	1930	370	1057	349	78	253	297	5	14	1	11	2	1	1	1

	PA	MI	KY	IL	MO	SD	NC	TX	TN	NE	WY	ID	AZ	MS	
	82	147	15	640	152	71	629	72	13	109	8	3	5	1	



Editor's note - Our total is now up to 713 sow farms accounting for approximately 2.5 million sows. The vets from the 16 participating systems report only new infections out of a known number of sow herds at risk and therefore, we can report % incidence.

NATIONAL PORK PRODUCER COUNCIL

Reporting 16 of 16 Systems

PEDV Control/Elimination from a herd

- Depends on many questions:
  - How is PEDV spread?
  - What is the duration of shedding?
  - What is the duration of immunity?
  - What is the variation in strains?
  - What is the environmental stability of the virus?
- Pipestone sow herds:
  - 100% breed to wean
  - With on site GDU
  - 2000 to 5000 sows

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PEDV Spread

- Fecal-oral transmission
  - High quantities shed in feces, highly infectious
  - Pencil eraser-size manure diluted in 26,000 gallons water
- Easily spread on fomites
  - Vehicles
  - Shoes/clothing
- Spread through birds/rodents unknown
  - Likely based on research with TGE
- Evidence of aerosol component to spread
  - PCR positive air samples up to 10 miles (University of Minnesota, 2013)
- Feed and feed products

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Duration of Shedding

- Shedding in individual pigs >28 days (Hesse 2013)
- Quantity shed over time unknown
- Shedding in populations unknown
  - Dynamics within populations not completely understood

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Duration of Immunity

- Individual antibodies may persist >1 year (Song et al 2012)
- Antibodies to PEDV spread through milk to piglets
- Protection for piglets depends on titer of sow
- Specifics of PEDV immunology unknown

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Variation in Strains

- Currently, 2 major strain isolates in USA with genetic sequence completed
  - "mild" and "wild"
  - Share ~94% homology
- RNA virus – high propensity to mutate
- Cross protection between strains unknown
- Implications for vaccine creation

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Environmental Stability

- Very stable in cold temperatures
- Livability in fecal slurry (Hesse, 2013)
  - >28 days at -20C
  - >14, <28 days at room temperature
- Livability in feed
  - >28 days in wet feed mixture at room temperature
  - <14 days in dry feed at room temperature
- In dry fecal mater – unknown
- Aerosolized - unknown

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New Strain Detected

- **ISU - Jan 24 to 29, 2014**
  - Sequencing performed on 15 cases
    - 10 cases were similar
      - 99.1 – 100%
      - Also similar to April 2013 cases
    - 5 cases were not
      - 93.9 – 94.6%

Courtesy of R Main, Iowa State University

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PEDV Risk Factors

- Virus survivability in the environment
  - Shed in feces in high amounts
  - Cold and wet favor the virus
  - Survives better than PRRS outside the pig
- Likely means of transmission:
  1. Dirty trailers and other mechanical vectors
  2. Feed
  3. Air

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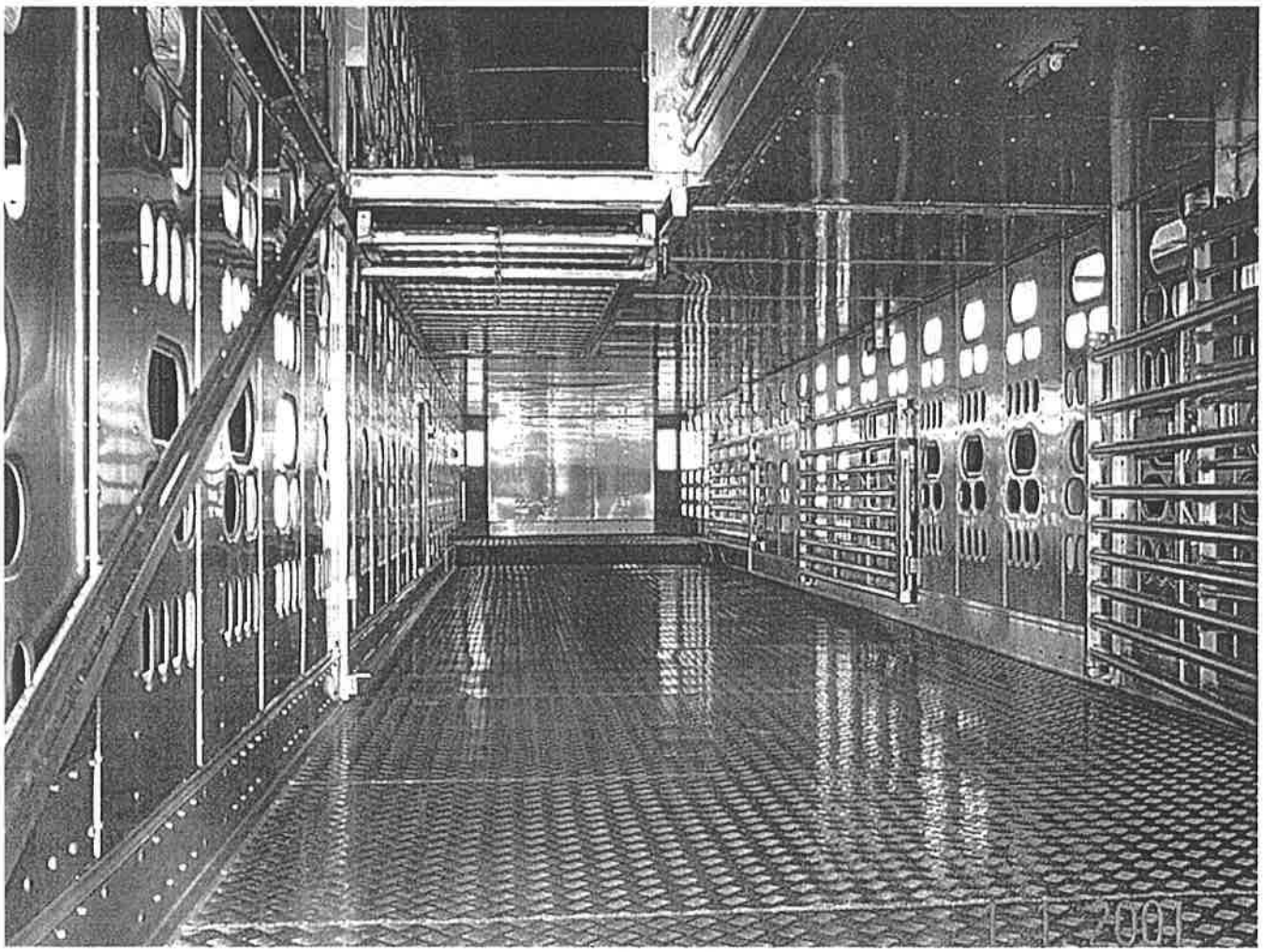

Feed Mill Assessment Project

- Objectives:
  - Share latest PEDV information with Pipestone associated mills
  - Gather information from mills on current operational and biosecurity practices
  - Collect samples for PEDV PCR testing
- Sample Categories
  - Environmental
  - Feed ingredients of animal origin

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Feed Mill Assessment Aggregate Results

Mills sampled	22
Mills with positive samples	9
% positive mills	40.91%

Total Samples	126
Positive Samples	12
% positive samples	9.52%
ct value range	30.4-37.4

Positive Samples by type:	
Office	5
Feed ingredients (animal)	7

FEED MILL ASSESSMENT RESULTS

Feed Ingredients	Positive	Total	CT Range	% Positive
Bone/Meat & Bone Meal	4	6	34.45 - 37.04	66.7%
Fat Products	1	3	30.42	33.3%
Blood/Plasma/PepNS	2	9	35.17 - 36.07	22.2%
Other Feed Ingredients	0	9		0.0%
Finished Feed	0	5		0.0%

Environmental	Positive	Total	CT Range	% Positive
Office/Control Rm	5	23	32.55 - 37.1	21.7%
Feed Mill System	0	21		0.0%
Feed Truck	0	21		0.0%
Ingredient Receiving	0	28		0.0%

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PEDV Prevention on your Farm

- Direct Fecal-Oral transmission
- All trucks considered contaminated
  - Feed trucks, livestock trucks, truck washes
  - Trucks need to be thoroughly cleaned and disinfected
  - Load crew never steps into chute from truck
  - Boots coveralls worn
  - Pigs prevented from exiting trailer
  - Barn lime in chutes to stop virus
- Rendering high risk
- Feed ingredients of animal origin – Review feed sources/ingredients
- Aerosol risk
- Birds?

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USDA

March 28th, 2014

Swine Health Monitoring Project

pork checkoff

PED virus infection associated with bird feces

courtesy of Bob Blomme, Audobon-Manning Veterinary Clinic

Two sow farms provide pigs to a series of nurseries in Kansas. One sow farm is in upper Midwest, the second is in South-central US. To date, both sow farms are PEDv negative.

The week of 3/2/14, three of the nursery sites were confirmed PEDv infected via PCR on oral fluids. Two nurseries (A and B) are within 1.0 mile of each other and are sourced from the upper Midwest sow farm. Nursery C is sourced out of the South-central US sow farm. A third nursery site (site C) has three buildings; the middle building has had clinical signs of PED and has been confirmed positive. The two buildings on site C that flank the middle building have remained clinically normal and are still PCR-negative in oral fluids as of March 26th despite a compost pile between one of them and the middle site into which PEDv-contaminated dead animals were placed. These barns each have individual caretakers which may speak to the importance of diligent biosecurity in the face of close proximity to infective material. Site C is a few miles away from Sites A and B. The region is considered low-density for pig production.

Trucking has been ruled out as the pigs in the affected nurseries were on split loads and the other nurseries that shared the truck have remained unaffected. All nurseries received the same feeds from the same feed mill. No cross traffic of personnel has occurred between nursery sites A, B, and C.

SEABOARD FOODS

HOLDEN

Iowa Select Farms

PILLEN

Elimination and Eradication

- Elimination is possible from individual farms
  - Pipestone successful in 2/2 PEDV eliminations
  - All other farms elimination protocols implemented
- Eradication from USA very unlikely
  - Too many factors unknown
  - No effective vaccine currently
- Many areas to research and learn

PIPESTONE VETERINARY SERVICES

Current & proposed projects

- Time to stability project
- Improved diagnostics
- Sow challenge study ("mild" → virulent)
- Coordinated outbreak investigation
- Risk assessment for feed
- Case / control for alleged feed cases

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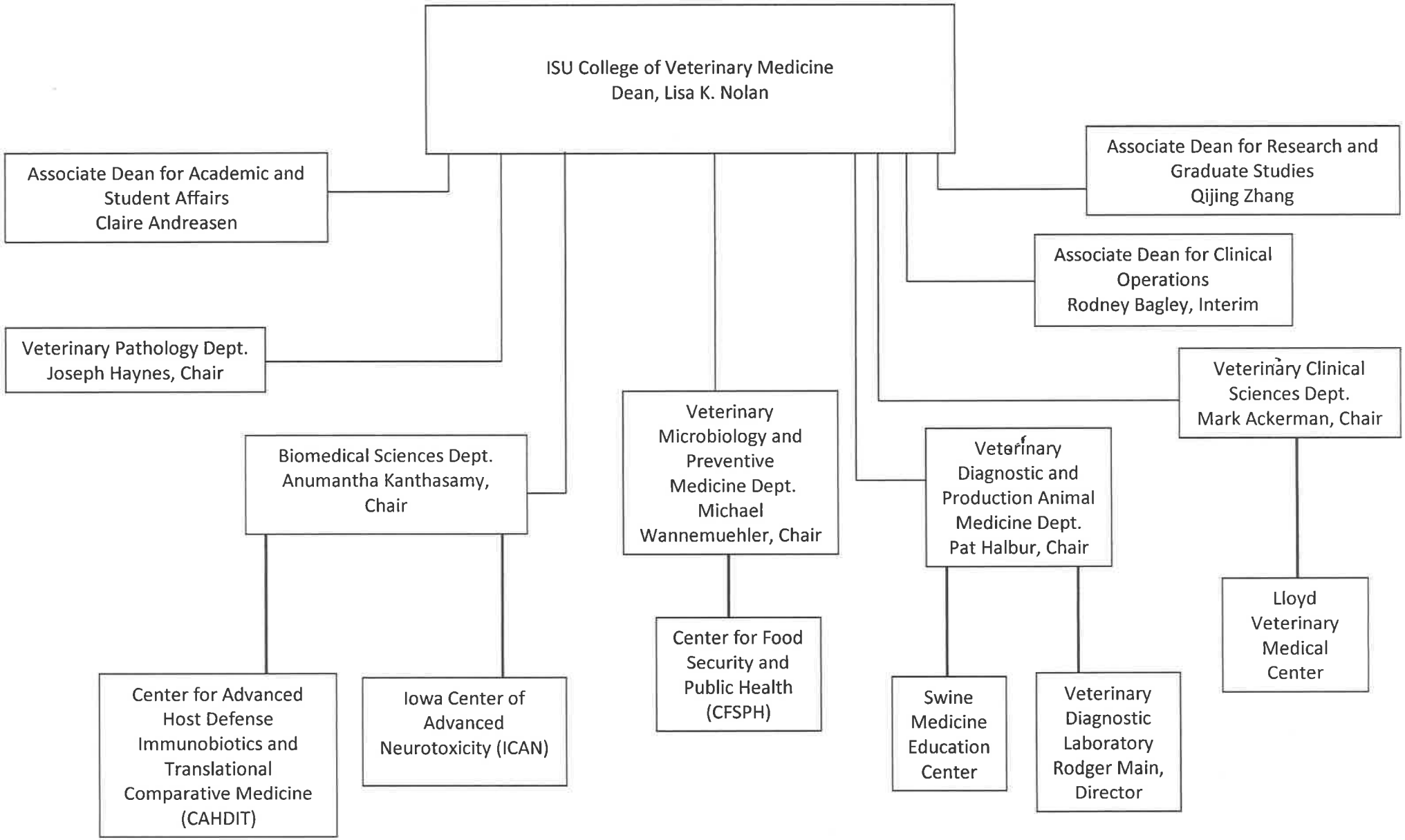
Iowa State University

College of **Veterinary Medicine**

dedicated to enhancing
the **health** and **quality** of life
of **animals** and **humans**

IOWA STATE UNIVERSITY
College of Veterinary Medicine


ISU College of Veterinary Medicine
Dean, Lisa K. Nolan
Associate Dean for Academic and Student Affairs
Claire Andreasen
Associate Dean for Research and Graduate Studies
Qijing Zhang
Associate Dean for Clinical Operations
Rodney Bagley, Interim
Veterinary Pathology Dept.
Joseph Haynes, Chair
Veterinary Clinical Sciences Dept.
Mark Ackerman, Chair
Biomedical Sciences Dept.
Anumantha Kanthasamy, Chair
Veterinary Microbiology and Preventive Medicine Dept.
Michael Wannemuehler, Chair
Veterinary Diagnostic and Production Animal Medicine Dept.
Pat Halbur, Chair
Lloyd Veterinary Medical Center
Center for Advanced Host Defense Immunobiotics and Translational Comparative Medicine (CAHDIT)
Iowa Center of Advanced Neurotoxicity (ICAN)
Center for Food Security and Public Health (CFSPH)
Swine Medicine Education Center
Veterinary Diagnostic Laboratory
Rodger Main, Director

Veterinary Diagnostic and Production Animal Medicine Professional Curriculum Courses

65 Required and Elective Courses (Updated 09-21-13)

Course No.	Course title	Date Introduced or Revised	VM Year	Credits	Semester S	Semester SS	Semester F	Location	Beef	Swine	Dairy	Small Ruminant	Poultry	Other/Aquatics	Epidemiology	Business	Diagnostic Medicine
VDPAM Courses Required For Veterinary Students																	
VDPAM 312	Veterinarian in Society II	2009	1	1	X			ISU	X	X	X	X	X	X			
VDPAM 426	Veterinary Toxicology	1998	3	3	X			ISU	X	X	X	X	X				
VDPAM 445	Clinical Medicine	1998	3	3	X			ISU	X	X	X	X	X				
VDPAM 450	Disturbances of Reproduction	1998	3	4			X	ISU	X	X	X	X	X				
VDPAM 477	Food Animal Medicine and Surgery	1998	4	1-4	X	X	X	ISU	X		X	X					X
Requirements in addition to the above for Food Animal or Mixed Animal Track																	
VDPAM 455	Diagnostic Laboratory Practicum	2001	4	1	X		X	ISU	X	X	X	X	X	X		X	X
VDPAM 488	Laboratory in Clinical Microbiology	2001	4	1	X		X	ISU	X	X	X	X	X	X			X

VDPAM Elective Courses

Course No.	Course title	Date Introduced or Revised	VM Year	Credits	Semester S	Semester SS	Semester F	Location	Beef	Swine	Dairy	Small Ruminant	Poultry	Other/ Aquatics	Epidemiology	Business	Diagnostic Medicine
VDPAM 308	Spanish for Veterinarians	2010	1,2,3,4	2	X			ISU	X	X	X	X	X				
VDPAM 309	Intro to Production Animal Informatics	2007	1,2,3	1	X			ISU	X	X	X	X			X	X	
VDPAM 310	Intro to Production Medicine	2007	3	2	X			ISU	X	X	X				X		
VDPAM 340	Clinical Foundations I	2005	1,2,3	1	X		X	ISU/Neb	X	X	X	X			X	X	
VDPAM 351	Bovine Embryo Transfer & Related Technology	2010	2,3	2	X			ISU	X		X						
VDPAM 365	Animal Welfare Judging	2011	1,2,3,4	1		X	X	ISU	X	X	X	X					
VDPAM 402	Advanced Dairy Production Informatics	2008	1,2,3	2	X		X	ISU			X						
VDPAM 407	Evidence Based Clinical Decision Making	2007	1,2,3,4	1	X			ISU							X		
VDPAM 408	Poultry Medicine and Disease Prevention	1998	1,2,3,4	2	X			ISU					X				
VDPAM 409	Veterinary Practice Mgmt & Organization	2003	1,2,3,4	3			X	ISU								X	
VDPAM 414	Veterinary Practice Entrepreneurship	2003	2,3,4	3	X			ISU								X	
VDPAM 415	Bovine Reproduction Evaluation Lab	1998	3	1	X		X	ISU	X		X						
VDPAM 419	Advanced Swine Production Informatics	2007	2,3,4	1			X	ISU		X						X	
VDPAM 420	Appl. Mixed Animal Preceptorship	1998	4	1-6	X	X	X	Various	X	X	X	X	X	X			
VDPAM 421A	GPVEC: Fall/Spring Calving	2007	4	1	X		X	Nebraska	X								
VDPAM 421B	GPVEC: Bull Breeding Soundness	207	4	1	X			Nebraska	X						X		
VDPAM 421C	GPVEC: Clinical Calving	2007	4	1	X			Nebraska	X						X		
VDPAM 421D	GPVEC: Feedlot Mgmt	2007	4	1	X		X	Nebraska	X						X		
VDPAM 421E	GPVEC: Weaning Mgmt	2007	4	1			X	Nebraska	X						X		
VDPAM 421F	GPVEC: Preg Exam	2007	4	1			X	Nebraska	X						X		
VDPAM 421G	GPVEC: Bovine Repro	2007	4	1			X	Nebraska	X						X		
VDPAM 421J	GPVEC: Lambing	2009	4	1	X			Nebraska				X			X		
VDPAM 421K	GPVEC: Equine Dentistry	2011	4	1	X			Nebraska						X			
VDPAM 421M	GPVEC: Preconditioning	2011	4	1		X	X	Nebraska	X								
VDPAM 421P	GPVEC: Gomer Bull Surgery	2011	4	1			X	Nebraska	X								
VDPAM 422A	Southern Plains: Cattle Marketing	2011	4	2	X	X	X	Missouri	X						X		
VDPAM 422B	Southern Plains: Beef Cattle Processing	2009	4	2	X	X	X	Oklahoma	X						X		
VDPAM 422C	Southern Plains: Feedlot Mgmt	2009	4	2	X	X	X	Oklahoma	X						X		
VDPAM 422D	Southern Plains: Beef Enterprise consulting	2009	4	2	X	X	X	Oklahoma	X						X		
VDPAM 422E	Southern Plains: Beef Cattle Calving	2009	4	2	X	X	X	Missouri	X						X		
VDPAM 422F	Southern Plains: Stocker Exp	2011	4	2	X	X	X	Missouri	X						X		
VDPAM 424X	Veterinary Pathology Preceptorship	2012	4	1-6	X	X	X	ISU	X	X	X	X	X	X			X
VDPAM 436	Beef Records Analysis	2001	1,2,3	1	X		X	ISU	X								
VDPAM 437	Dairy Herd Problem Identification	1998	4	2	X	X	X	Wisconsin			X				X		
VDPAM 438	Mastitis Problem Investigations	1998	4	2	X	X	X	Wisconsin			X				X		
VDPAM 439	Fresh Cow & Calf Problems	1998	4	2	X	X	X	Wisconsin			X				X		
VDPAM 451	Clinical Embryo Transfer	2007	4	2	X	X	X	ISU	X		X	X					
VDPAM 456	Vet. Diag. Lab Methods & Applications	2007	2,3,4	1			X	ISU	X	X	X	X	X		X		X
VDPAM 463	Feedlot Production Medicine	2012	4	1	X		X	ISU	X								
VDPAM 464	Advanced Feedlot/Stocker	2009	4	2	X		X	ISU	X						X	X	X
VDPAM 465	Clinical Animal Welfare	2011	4	2			X	ISU	X	X	X	X	X				
VDPAM 466X	Animal Welfare Preceptorship	2012	4	2	X	X	X	ISU	X	X	X	X	X				
VDPAM 476	Food Animal Field Service	2007	4	2	X		X	ISU	X	X	X	X					
VDPAM 479	Appl Swine Prod Med Preceptorship	1998	4	1-6	X	X	X	ISU		X					X		
VDPAM 480	Swine Production Medicine	1998	4	2	X	X	X	ISU		X					X		
VDPAM 481	Advanced Cow/Calf	2010	4	2	X			ISU	X						X	X	X
VDPAM 482	Appl Beef Prod Med Preceptorship	1998	4	1-6	X	X	X	ISU	X						X		
VDPAM 483	Beef Production Medicine	1998	4	2	X	X	X	ISU	X						X		
VDPAM 484	Dairy Production Medicine	1998	4	2		X	X	ISU			X				X		
VDPAM 485	Appl Dairy Prod Med Preceptorship	1998	4	1-6	X	X	X	ISU			X						
VDPAM 486	Introduction to Small Ruminant Prod Med	1998	3	1	X			ISU				X					
VDPAM 487	Livestock Disease Prevention	1998	UG,1-4	3			X	ISU	X	X	X	X	X		X		
VDPAM 489	Issues in Food Safety	2005	1,2,3,4	1	X			ISU	X	X	X	X	X		X		
VDPAM 490	Independent Study	1998	1-4	1-5	X	X	X	ISU	X	X	X	X	X	X	X	X	X
VDPAM 490BL	State Fair Animal Health	2007	4	2	X	X	X	ISU	X	X	X	X	X			X	
VDPAM 491	Advanced Ruminant Nutrition	2009	2,3	3	X			ISU	X		X						
VDPAM 494	Advanced Dairy Production Medicine	2009	4	2	X			ISU			X						
VDPAM 492/496	International Preceptorship	2005	2	1-12	X	X	X	Various	X	X		X				X	
VDPAM 495	Advanced Small Ruminant Prod Med	2009	4	2	X		X	ISU				X			X	X	X

Mixed Food Animal Focus	Dairy Focus	Poultry Focus	Welfare Focus
Beef Focus	Swine Focus	Equine Focus	Small Ruminant Focus

http://vetmed.iastate.edu/vdpam/students

http://vetmed.iastate.edu/academics/curriculum

2013-14 Catalog

(For the Class of 2015 - present)

The list below is the core curriculum for students at the College of Veterinary Medicine. Every effort has been made to make the list accurate as of the date of publication. However, all policies, procedures, fees, and charges are subject to change at any time by appropriate action of the faculty, the university administration, or the Board of Regents, State of Iowa. See policy updates for the most current information.

The Iowa State University Catalog

VM - 1 Curriculum

Fall Semester Course	Title	Credits
BMS 330	Principles of Morphology I *(anatomy)*	5
BMS 333	Biomedical Sciences I *(microscopic anatomy/physiology-cells)*	6
BMS 335	Molecular & Cellular Biology	1
BMS 336	Nutritional Biochemistry	2
BMS 339	Clinical Foundations I	1
BMS 345	Case Study I	1
VCS 311	Veterinarian in Society I *(careers)*	R
VCS 391	Radiology Imaging	1
		17

Spring Semester Course	Title	Credits
BMS 331	Principles of Morphology II *(anatomy)*	4
BMS 334	Biomedical Sciences II *(microscopic anatomy/physiology-systems)*	6
BMS 337	Neuroanatomy	3
BMS 346	Case Study II *(clinical correlations)*	1
VMPM 380	Veterinary Immunology	2
VPth 342	Anatomic Pathology I	3
VCS 312	Veterinarian in Society II *(animal behavior and welfare)*	1

		20

VM - 2 Curriculum

Fall Semester Course	Title	Credits
VMPM 386	Veterinary Microbiology I	5
VPth 372	Anatomic Pathology II	4
VPth 376	Veterinary Parasitology	4
VPth 377	Case Study III *(clinical correlations)*	2
VCS 313	Veterinarian in Society III *(ethics)*	1
VCS 393	Principles of Surgery	3
		19

Spring Semester Course	Title	Credits
BMS 354	General Pharmacology	3
VMPM 378	Case Study IV	2
VMPM 387	Veterinary Virology	3
VMPM 388	Public Health	3
VCS 394	Principles of Surgery Lab	1
VCS 395	Small Animal Surgery	2
VCS 398	Anesthesiology	1
VPth 425	Clinical Pathology	4
		19

VM - 3 Curriculum

Fall Semester Course	Title	Credits
BMS 443	Pharmacology and Therapeutics	3
VCS 314	Veterinarian in Society IV (*Communication/leadership*)	1
VCS 436	Small Animal Internal Medicine	3
VCS 444	Small Animal Medicine	4

VCS 445	Equine Medicine	2
VCS 449	Surgery Laboratory	3
VDPAM 450	Disturbances of Reproduction	4
VCS 385	Seminar	R
		20

Spring Semester Course	**Title**	**Credits**
VMPM 437	Infectious Diseases and Preventive Medicine	3
VPth 409	Intro to Vet Cytology and Lab Techniques	1
VDPAM 426	Veterinary Toxicology	3
VDPAM 445	Large Animal Clinical Medicine	3
VCS 399	Ophthalmology	1
VCS/VDPAM 440	Introduction to Clinics	R
VCS 448	Diagnostic Imaging and Radiobiology	3
VCS 315	Veterinarian in Society V (*veterinary law*)	1
VCS 385	Seminar	R
		15

VM - 4 Curriculum

The fourth year is designed to be flexible and to provide for species emphasis. Students must complete 44 credits during their fourth year. They must take a required block and one option block. The required block rotations are multi-species oriented and exist in all types of clinical practice. Preceptorship credit can be earned at approved government agencies, research laboratories, veterinary practices, and other approved university hospitals.

In several cases, students are given the option of choosing between two courses to meet a requirement. For instance, the required block equine requirement can be met by taking either VCS 457 (Equine Medicine) or VCS 464 (Equine Field Services). In such cases, students are given the opportunity to provide their preference in the schedule optimizer. However, there are not always sufficient slots to meet all preferences, so some students will not receive their first choice, but will be assigned to the alternative course.

ISUCVM Fourth Year Curriculum; Approval Dates: ISUCVM Faculty, April 29, 2008; Faculty Senate

Curriculum Committee, Sept 11, 2008, Revised by ISUCVM Curriculum Committee for implementation – 04-03-2009

Required Block: (Total 20 Credits required of all students)

Course	Title	
VCS 463	Primary Care	2
VCS 453	Small Animal Medicine I or II	2
VCS 473	Small Animal Surgery (1 week Ortho and 1 week Soft Tissue)	2
VCS 460	Radiology	2
VCS 466	Anesthesiology	2
VCS 468	Intensive Care/ Emergency Med	4
VCS 457 or VCS 464	Equine Medicine (457) or Equine Field Service (464) (as assigned by the schedule optimizer)	2
VDPAM 477	Food Animal Medicine and Surgery	2
VPTH 456 and VPTH 457	Necropsy and Clinical Pathology (Taken together as one 2-week block)	2
VCS 495	Seminar (non-credit)	R
Total required		20

Electives:

May include external experiences for credit (i.e., preceptorships) that fulfill the requirements for VCS 419 (Preceptorships in small animal or equine) or VDPAM preceptorships (VDPAM 420, 424X, 466X, 479, 482, or 485) or Zoo and Exotic preceptorship (VMPM 494) or any rotations offered in the 4th year.

Electives required per option:

Small animal = 6, Mixed animal = 10, Equine = 6, Food Animal = 10.

Preceptorships must follow guidelines to qualify for credit.

Additional Time Off (Total = 4 blocks [8 weeks]):

This time will fall randomly throughout the schedule to allow time for interviews, unapproved preceptorships, additional rotations and/or personal time.

Small Animal Option:

Required courses for all tracks listed above (20 credits) plus,

Required courses for Small Animal Track ONLY = 12 credits plus,

Selectives: 6 credits required, plus,

Electives: 6 credits required

Required courses for Small Animal Track ONLY:

Course	Title	
VCS 453/454	Small Animal Medicine	2
VCS 455 or VCS 459	Soft Tissue Surgery (455) or Small Animal (Over) Population Medicine and Surgery (459)	2
VCS 456	Orthopedic Surgery	2
VCS 446	Neurology	2
VCS 452	Dermatology *(repeatable by permission)*	2
VCS 469	Ophthalmology	2

Selectives (Total = 6 credits required): *Selectives can usually be taken more than once.*

Course	Title	
VCS 459	Small Animal (Over) Population Medicine and Surgery	2
VCS 471S	Small Animal Reproduction	2
VCS 476	Anesthesiology	2
VCS 409X	Oncology	2
VCS 455	Soft Tissue Surgery	2
VCS 441	Canine Rehabilitation	2
VDPAM 488 and VDPAM 455	Clinical Microbiology and D Lab (Taken together as one 2-week block)	2
VCS 470	Radiology (instructor permission required)	2
VCS 453/454	Small Animal Medicine	2
VCS 463	Primary Care	2
VCS 475X	Cardiology *(not offered at ISU 2012-13 yr)*	1-2
VCS 456	Orthopedic Surgery	2
VMPM 486	Public Health	2
VCS 467	Pain Mgmt	1
VDPAM 465	Animal Welfare	2

VCS 422	Blank Park Zoo* *(not repeatable)*	4

Equine Option:

Required courses for ALL Tracks (Total = 20 credits) Plus,

Required Courses for Equine Track ONLY (Total = 6 credits) plus,

Selectives: 12 credits, plus

Electives: 6 credits

****Equine option students, VCS 457 and 464 each must be taken at least once. One of the courses satisfies the overall required block requirement, the other satisfies the equine option requirement.**

Required courses for Equine Track ONLY:

Course	Title	
VCS 471E	Equine Reproduction	2
VCS 458	Equine Surgery	2
VCS 457 or VCS 464	Equine Medicine (457) or Equine Field Services (464)**	2

Selectives (Total = 12 credits required): Selectives can usually be taken more than once

Course	Title	
VCS 471E	Equine Reproduction	2
VCS 471C	Comparative Reproduction	2
VCS 458	Equine Surgery	2
VCS 465	Farrier	2
VCS 457	Equine Medicine **	2
VCS 464	Equine Field Services	2
VCS 469	Ophthalmology	2
VCS 446	Neurology	2
VCS 452	Dermatology *(repeatable by permission)*	2
VCS 476E	Equine Anesthesia	2
VCS 467	Pain Mgmt	1-2
VCS 481X	Equine Dentistry	2

Mixed Animal Option:

Required courses for ALL Tracks (Total 20 credits) Plus,

Required courses for Mixed Animal Track ONLY (Total = 6 credits)

Selectives: Group A = 6 required, Group B = 2 required, plus

Electives: 10 credits required

Required courses for Mixed Animal Track ONLY:

Course	Title	
VDPAM 488 and VDPAM 455	Clinical Microbiology (488) and D Lab (455) (Taken together as one 2-week block)	1
	Dermatology	1
VCS 452	Ophthalmology	2
VCS 469		2

Selectives: Group A (Total = 6 credits required) ***Selectives can usually be taken more than once***

Course	Title	
VDPAM 477	Food Animal Medicine and Surgery	2
VCS 457	Equine Medicine	2
VCS 458	Equine Surgery	2
VDPAM 476	Large Animal Ambulatory ***(prereq. VDPAM 310)***	2

Courses listed as required selectives for the Food Animal Track or Equine Track

Selectives: Group B (Total = 2 credits required)

Course	Title	
VCS 446	Neurology	2
VCS 471E,S or F	Equine, Small Animal, or Food Animal Reproduction	2
VCS 452	Dermatology *(repeatable by permission)*	2
VCS 453	Small Animal Medicine	2
VCS 455	Soft Tissue Surgery	2
VCS 456	Orthopedic Surgery	2
VCS 463	Primary Care	2
VCS 469	Ophthalmology	2
VCS 475X	Cardiology *(not offered at ISU 2012-13 yr)*	1-2
VCS 409X	Oncology	2

VCS 470	Radiology (instructor permission required)	2
VCS 476	Anesthesiology	2
VMPM 486	Public Health	2
VCS 459A, B or C	Small Animal (Over) Population Medicine and Surgery	2
or Courses listed as required selectives for the Small Animal Track		
	ELECTIVES:	10

Food Animal Option:

Required courses for ALL Tracks (Total = 20 credits) Plus,

Required courses for Food Animal Track ONLY = 2 credits Plus,

Selectives: 12 credits required plus,

Electives: 10 credits required

Required courses for Food Animal Track ONLY:

Course	Title	
VDPAM 488 and VDPAM 455	Clinical Microbiology and D Lab (Taken together as one 2-week block)	1 1

Selectives (Total = 12 credits required): ***Selectives can usually be taken more than once.***

Course	Title	
VDPAM 424X	Diagnostic Pathology preceptorship	2
VDPAM 483	Beef Production Medicine ***(prereq. VDPAM 310)***	2
VDPAM 484	Dairy Production Medicine ***(prereq. VDPAM 310)***	2
VDPAM 480	Advanced Swine ***(prereq. VDPAM 310)***	2
VDPAM 420	Preceptorship in Veterinary Medical Practice	1-6
VDPAM 421A-K	Great Plains Vet Education Center (*see dept. complete listing)*	1
VDPAM 422A-F	Cattle Marketing, processing, mgmt ,consulting *(see dept for complete listing)*	1-2
VDPAM 479	Applied Swine Production Medicine ***(prereq. VDPAM 310)***	1-6
VDPAM 482	Applied Beef Production Medicine ***(prereq. VDPAM 310)***	1-6
VDPAM 485	Applied Dairy Production Medicine ***(prereq. VDPAM***	1-6

	484)	
VDPAM 451	Embryo Transfer	2
VDPAM 477	Food Animal Medicine and Surgery	2
VDPAM 476	Large Animal Ambulatory ***(prereq. VDPAM 310)***	2
VPTH 456 and VPTH 457	Necropsy (456) and Clinical Pathology (457) (Taken together as one 2-week block)	1 1
VDPAM 488 and VDPAM 455	Clinical Microbiology (488) and D Lab (455) (Taken together and one 2-week block)	1 1
VDPAM 495	Advanced Small Ruminant Production Medicine ***(prereq. VDPAM 486)***	2
VDPAM 437	Basic Clinical Skills for Production Medicine (Wisconsin)	2
VDPAM 438	Mastitis Problem Investigations (Wisconsin)	2
VDPAM 439	Clinical Investigations of Fresh Cow and Calf Problems (WI)	2
VDPAM 463	Iowa Feedlot (requires 421D)	1
VDPAM 464	Advanced Feedlot ***(prereq. VDPAM 310)***	2
VDPAM 481	Advanced Cow/Calf ***(prereq. 2 sem. of VDPAM 436)***	2
VDPAM 465	Animal Welfare	2
VDPAM 494	Advanced Dairy Production Medicine ***(prereq. VDPAM 310)***	2
VCS 471F	Food Animal Reproduction	2
Electives:		10

Credits required during senior year: 44

Graduation Requirements: 158

To be awarded the degree Doctor of Veterinary Medicine, candidates must have passed all required courses in the curriculum of veterinary. Candidates must have earned at least 4 elective credits during the VM1-3 year on a graded basis of A, B, C, D while enrolled in the College of Veterinary Medicine and a minimum 2.0 grade point average in the veterinary medicine curriculum. Candidates must also have given a grand rounds presentation (VCS 495-Seminar).

Revised 10/10/12

Serving Food Animal Agriculture

Comprehensive Diagnostic Service, Teaching, and Discovery

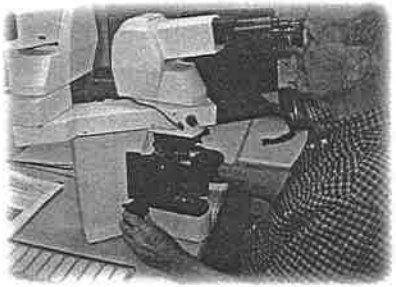
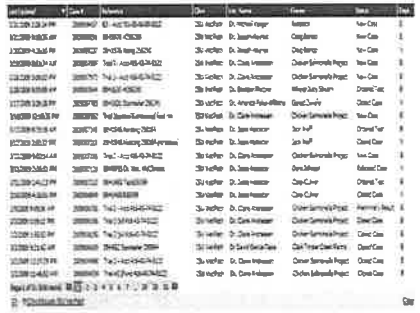
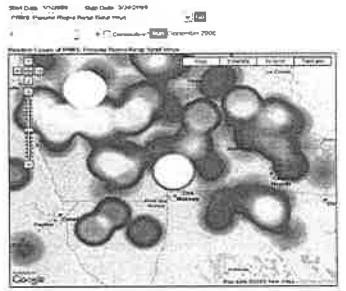
(Iowa's only Full-Service & Fully Accredited Veterinary Diagnostic Laboratory)










Processing 50,000 cases/year from livestock producers

Applying world-class technology to solve real-world problems

Veterinary Diagnostic Laboratory
Iowa State University

ISU VDL Diagnostician receives the case from the local veterinarian

50,000/year

Select diagnostic tests based on history and gross lesions

- Serology
- Molecular Diagnostics
- Histopathology
- Bacteriology
- Toxicology & Nutrition
- Virology
- Clinical Pharmacology

Results coordinated to arrive at a diagnosis

Informs teaching and research programs

Transmit diagnosis to and assist local veterinarian with intervention strategies and establishment of best practices

VDPAM Course Descriptions: Fall 2013-Summer 2014

Courses primarily for professional curriculum students:

VDPAM 308. Spanish for Veterinarians.
Cr. 2. S. *Prereq: Basic knowledge of Spanish*
This course is designed to meet the needs of veterinary students who will practice in an environment in which the use of Spanish for accurate client communication is essential which includes much of our food animal industry in the state of Iowa. This is not a traditional Spanish language course. To be successful, students taking the course should have a basic knowledge of Spanish pronunciation, grammar and syntax.

VDPAM 309. Introduction to Production Animal Informatics.
Cr. 1. S.
The fundamentals of how clinical, diagnostic, production and financial information is obtained and used by production animal operations. Students will acquire skills to create and use spreadsheets for manipulating and summarizing data. They will also acquire knowledge of where to find inexpensive and readily available resources with information on how to use spreadsheets and other software. Students will also have the opportunity to work with different record keeping programs used by swine, beef and dairy operations.

VDPAM 310. Introduction to Production Medicine.
Cr. 2. S. *Prereq: Classification as second or third year veterinary student or permission of instructor*
The role of the veterinarian in the management of animal health and production in dairy and beef cattle herds, beef feedlots and swine herds will be described. Provides veterinary students with a starting point to understand the principles and techniques that are the basis of food-animal health management programs.

VDPAM 312. Veterinarian in Society II.
Cr. 1. S. *Prereq: Classification as a first year veterinary student*
A continuation of the Veterinarian in Society series. An introduction to the topics of animal behavior, animal welfare, and the human animal bond.

VDPAM 340. Clinical Foundations.
Cr. 1. F.S. *Prereq: Classification in veterinary medicine*
One week course at Iowa State University and Great Plains Veterinary Educational Center in Clay Center, Nebraska. An introduction to Food Supply Veterinary Medicine covering overviews of major animal agriculture species (beef, dairy, pork, sheep), production systems, behavior, welfare, handling and restraint, examination techniques, biosecurity, epidemiology and food safety. Visits to production units are utilized to introduce the application of clinical skills. Biosecurity policies require documentation of your presence in the USA 5 days immediately prior to the start of class if international travel has occurred.

VDPAM 351. Bovine Embryo Transfer and Related Technology.
Cr. 2. S. *Prereq: Classification as a second or third year veterinary student*