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Comparative medicine - with some thoughts about the integration of medical and veterinary education

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ABSTRACT

The common pool of knowledge between veterinary and medical medicine has been frequently exploited to provide insights into basic biomedical science and its application in such areas as vaccine development, therapeutics and diagnostics.

In this paper the essential interplay between the disciplines of medicine and veterinary medicine is discussed and illustrated in detail in such areas as prion diseases, zoonotic infectious diseases and genetic diseases of dogs.

Considerations are also made about the integration of medical and veterinary education, with indications of the critical needs for maximizing the opportunities for "One Medicine" both in medical and veterinary education and for research.

The essential and fascinating interplay between medicine, veterinary medicine and basic biomedical sciences can do more to advance knowledge in both medicine and veterinary medicine than either can achieve on their own.

Key words: Comparative medicine, One Health, Medical and veterinary education

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"Between animal and human medicine there is no dividing line-nor should there be. The object is different but the experience obtained constitutes the basis of all medicine" – Rudolf Virchow (1821-1902).

Virchow's view on animal and human medicine is as pertinent today as it was over 100 years ago. He recognized the interdependence of animal and human health and their reliance on a common pool of medical and scientific knowledge.

The term 'One Medicine' or 'Comparative Medicine' emphasizes the importance of the interaction between veterinary and human medicine which has long been recognised in veterinary medicine (1, 2, 3). The common pool of knowledge between the two sectors has been frequently exploited to provide insights into basic biomedical science and its application in such areas as vaccine development, therapeutics and diagnostics.

Today, the regular emergence and re-emergence of infectious diseases are significant challenges for both human and animal health. They provide clear evidence of the need to understand the interplay between animal and human medicine. In addition to the study of emerging infections, the One Medicine concept also applies to many areas of current biomedical research in cancer, infectious diseases, autoimmunity and genetics.

The ever growing list of global biomedical

and human health issues which are pertinent to the One Medicine agenda are:

- Animal and human disease surveillance
- Food safety, food production and security of the food chain
- Fundamental biomedical research
- Opportunities for translation of basic research to clinical problems
- Impact of animal genomics and genomic technologies in human medicine
- Genetics of diseases resistance and susceptibility in man and animals
- Use of animals in biomedical research
- Spread of antibiotic resistance between animals and man
- Environmental health.

I am a veterinarian and an immunologist and my exposure to One Medicine has always been a feature of my entire career. I did my PhD with a very distinguished immunologist and veterinarian Professor Robin Coombs. Robin Coombs was one of the founding fathers of immunology and inventor of the Coombs test for haemolytic diseases of the newborn and much else. His Immunology Division in the Department of Pathology in Cambridge was a wonderful environment of medics, vets and scientists without boundaries caused by our professional training. In Robin Coomb's laboratory it did not matter what species you worked on what mattered was the questions you asked. He would often say "ask the right question and you have got half the answer" (4, 5).

In a professional context medicine and veterinary medicine are separate since the veterinary and medical schools have distinct educational goals essential to their respective missions. Veterinary medicine is concerned with such issues as farm and companion animal medicine and surgery, animal welfare and veterinary public health. Medicine has of course its focus on human health. However there are many areas where there is no boundary between the two but considerable overlap especially in the fields of infectious diseases, genetic diseases, cancer and public health. In this paper I shall discuss the essential interplay between our disciplines of medicine and veterinary medicine and illustrate how they apply in such areas prion diseases, zoonotic infectious diseases and genetic diseases of dogs.

PRION DISEASES OF MAN AND ANIMALS

Prion Diseases of man and animals rank as a classical example of One Medicine. Before the advent of Bovine Spongiform Encephalopathy (BSE), prion diseases were well recognised in other species including man but not well understood. In animals the prion diseases are scrapie of sheep, transmissible mink encephalopathy (TME) and chronic wasting disease (CWD) in elk and deer in the USA. TME has occurred from time to time in mink farms in the USA where mink have been fed condemned carcases of sheep or cattle which contain prions - an early example of a food borne prion disease. In humans there are a range of well known prion diseases such as Kuru and Creutzfeld Jakob Diseases (CJD) which includes both sporadic, familial and iatrogenic forms as well as the human form of BSE known as variant CJD (vCJD) (6).

The prion diseases of scrapie, kuru, CJD and BSE are all caused by novel infectious agents known as a prions (7). These have been the cause of not one but two TSE epidemics, one in cattle (BSE) and the other, tragically in man, of vCJD. In spreading through the animal and human food chain BSE had extensive consequences for animal health and the many industries involved in food ranging from animal feed industries to supermarkets. The crisis also impacted severely on farming, public health, and public trust in Government. Rarely in the history of veterinary medicine could an obscure and rare brain disease of ruminants come to have had such a huge impact on global aspects of agriculture, food, human health and public trust in Government and science.

I have always regarded BSE as a kind of animal health Chernobyl. It drew into its fall-out veterinarians, medics, scientists as well as a wide range of Government departments of Agriculture, Environment, Health, Treasury, Education and Science. A wide range of industries such as farming, food and health care as well as the animal feed industry, the pharmaceutical industry and even the cosmetics industry were all affected. The cost to the UK taxpayer was in the region of £12 billion. The BSE crisis also spread out to involve the EU proving at that time to be a bigger issue than the European single currency. The effects of the BSE crisis have been global involving many other countries such as Canada, the USA and Japan (8).

Scrapie of sheep

Sheep scrapie is the prototype prion disease which has been recognised since 1750 in European sheep breeds originating in the Merino breed in Spain. It is so called because the sheep

scratch and nibble and tear at their fleece. They also show gait abnormalities, twitching, shivering and a range of limb paralysis.

It is a classical TSE with characteristic brain pathology and is 100% fatal within 16 months to two years after the onset of symptoms. Scrapie is endemic in many countries with the exception of Australia and New Zealand which are scrapie free. In sheep scrapie, infection is sustained between ewe and lamb by perinatal infection and contamination of pastures. Scrapie has never been shown to cause any human CJD- like disease.

In the context of naturally occurring TSE diseases of animals it is instructive to look at what happens in endemic and naturally occurring scrapie. Although scrapie presents as a neurological disease infection begins very early on in the gut. Infectious prions can cross the gut epithelium through the specialised M cells and the first sign of prion replication can be detected in the Peyer's patches of the gut associated lymphoid tissue. This is then followed by neuroinvasion via the parasympathetic and sympathetic nerves and ganglia to the brain and spinal cord. This replication in the gut associated lymphoid tissue and peripheral nervous system can be bypassed by direct inoculation of prions into the CNS as is frequently done experimentally. In considering the aetiology of natural scrapie it is the early events in the gut associated lymphoid tissue that trigger the process of prion development in the enteric nervous system which eventually results in the characteristic spongiform encephalopathy in the CNS.

Kuru in man

Kuru, which means shivering, was a mysterious illness mainly affecting women and children and was first recognized in the Fore tribes in the Eastern Highlands of Papua New Guinea. Clinically all cases had difficulty in standing, lacked co-ordination and developed paralysis. Kuru was shown to be associated with the practice of ritualistic cannibalism and later shown to be experimentally transmissible to animals (9). Amongst the Fore tribes it was the commonest cause of death in women and young children at the height of the epidemic. The kuru epidemic was brought to an end when the Australian Health Authorities persuaded the Fore people to end ritualistic cannibalism. The epidemic went into decline with no new cases after 1960 and died out in the younger age groups as the source of infection had been stopped. Those infected before 1960 continued to die and as the incubation period is very long, up to 50 years some cases, affected individuals are still being seen to this day.

The relevance of kuru to BSE is twofold:

- It was the first example of a "food borne" TSE disease – albeit a highly unusual source of food – your dead relatives
- When ritualistic cannibalism which was fuelling the epidemic stopped , the epidemic went in to decline

Kuru is a fascinating story of truly pioneering medical science by Dr. Carleton Gajdusek and his colleagues Dr. Joe Gibbs and Dr. Michael Alpers (10). Their research led to the understanding of this disease and its link to the practice of ritualistic cannibalism.

The early studies that began to unravel the nature of kuru as a disease also owe much to a veterinarian, Dr. Bill Hadlow (11) who had done much research on scrapie. He was struck by the similarities between the pathology of kuru and scrapie that he published a very important and prescient paper on scrapie in the Lancet wherein he concluded that:

"Thus it might be profitable, in view of veterinary experience with scrapie, to examine the possibility of the experimental induction of kuru in a laboratory primate, for one might surmise that the pathogenetic mechanisms involved in scrapie - however unusual they may be - are unlikely to be unique in the province of animal pathology".

This observation, by Hadlow captures the essence of One Medicine and influenced the subsequent attempts by Gajdusek and his colleagues to investigate kuru by attempting to transmit the disease to experimental primates.

Creutzfeld Jakob Disease (CJD)

CJD occurs sporadically affecting men and women in late middle age (65-75 years) and has a worldwide incidence of 1.3 cases per million. It is rapidly progressive, always fatal and was shown to be transmissible to experimental animals. The first cases of CJD were recorded by two German physicians Creutzfeld and Jakob in the 1920s.

There are two other forms of CJD. Familial CJD accounts for about 15% of all CJD cases and is a genetic disease arising through point mutations in the PrP gene leading to progressive dementias. Although a genetic disease, one of the forms of familial CJD was shown to be is experimentally

transmissible to primates. Iatrogenic CJD is passed on by the accidental transmission through medical or surgical procedures. This emphasises the transmissibility and health risks of human to human transmission of CJD and is a major issue for current handling of variant CJD. Iatrogenic CJD was a 'near miss' of an epidemic in man caused by the injection of human growth hormone to cure dwarfism in children. The human growth hormone used was contaminated by prions since it had been derived from a pool of pituitary tissue that contained CJD material. It was sheer luck that this was not a major medical catastrophe-genetically engineered growth hormone is now used instead to avoid this kind of medical mistake.

Kuru, scrapie and CJD can all be regarded as a classic example of One Medicine in that they are all caused by the same mechanism. Prion proteins can be isolated from brain extracts from any of the prion diseases be it kuru, scrapie or CJD and if inoculated into laboratory animals result in disease onset after a long incubation period of several months or years. The brain of the lab animal shows typical spongiform change but more importantly the infectivity can be recovered and repeatedly passed to more animals of either the same or different species.

This is what defines such encephalopathies as "transmissible" and fulfils Koch's postulates for an apparently "infectious" disease. Transmission within a species is easier than transmission between species and this can be done. The relative resistance to transmission of prions between species is due to the effect of the species barrier and determined significantly by the polymorphisms in the PrP gene. Experimental transmission of TSEs opened up important new avenues for the study of prion diseases and was the key evidence that linked all three diseases together.

Until these groundbreaking experiments in animals were done these three diseases of kuru , scrapie and CJD were regarded as quite separate.

- Scrapie was regarded as an obscure infectious disease of sheep of interest only to veterinarians and farmers
- Kuru was a strange tropical disorder afflicting the Fore tribes in New Guinea whose rituals were bizarre
- The human forms of CJD were puzzling but very rare disorders occurring worldwide at a level of 1 in a million people
- Iatrogenic CJD was a medical risk

Historically, this failure to see the common threads between the TSE diseases and to compartmentalize them as different problems illustrates the barriers to understanding which can arise when there is no or little cross-talk between medical and veterinary disciplines when confronted with new and threatening disease problems.

Although BSE has been a story of tragedy it has also brought some considerable gains for scientific understanding of the TSEs and a greater understanding of how to handle epidemics in animal health that affect public health.

In summary the advantages have been:

- Huge strides in understanding of prion diseases
- New scientific understanding of neurodegenerative and protein misfolding diseases (cfr. Alzheimer's Disease)
- Better understanding and control of zoonotic diseases
- Improved TSE diagnostics for man and animals
- Recognition of the linkage between animal health, food safety and public health. The importance and need for openness and transparency with the public in emerging infectious diseases to gain trust and confidence in matters of animal and public health.

ZOONOTIC INFECTIOUS DISEASES

At the start of the 21st Century the global concern was about "millennium bugs" (i.e. computer viruses). However millennium bugs turned out to be the real thing -viruses and bacteria. These range from the spread of flu, SARS and West Nile Fever virus and many other that can all be regarded as emerging infections. We urgently need to better understand these infectious diseases and to be better prepared for them (12). Infectious diseases do not respect geographical boundaries and our modern world makes the reach of such infections extensive and ever threatening. Recent epidemics of animal diseases including those that transmit to man are wake up calls. We live on a global farm where an outbreak of swine flu in a farm in Mexico rapidly becomes a global infection of man and animals (13).

The global reach of infectious agents is considerable. In recent years examples of the major viral threats have been:

Avian and swine influenza (H5N1, H1N1), Sever Acute Respiratory Syndrome (SARS), West Nile Fever (WNF), Monkey Pox, Nipah and Hendra virus, Ebola, Rift Valley fever.

Nipah and Hendra virus (the Henapaviruses) are of particular significance since wildlife, in this case bats, are carriers of these viruses and spill-

overs from the bat reservoir of Henapaviruses to pigs, horses and man is well recorded. Hendra virus - a measles-like virus of the Morbillivirus group - has caused fatal infections in horses and man.

Once infectious agents have emerged or jumped species there are plenty of risk factors that promote their spread. There is international trade in food products and long distance transport of livestock which resulted in the extensive spread of foot and mouth disease (FMD) outbreak in the UK in 2001. New reservoirs of WNF are now widespread in the mosquito populations of the USA. There are also political risk factors – e.g. the planned expansion of the EU to include such countries as Turkey brings with it the concern of further incursion of say FMD or Blue Tongue virus (BTV) in sheep.

We should not imagine for one minute that we shall ever escape the biological interaction between pathogens, animals and humans. To put it in the context of the "war on bugs" - there will always be new threats - containment and not conquest is the way forward.

Many health authorities are now fully aware of the significance that global travel may play in the rapid spread of zoonotic diseases. The statisitics of air travel are interesting in this regard in that no city on earth is more than 24 hours away from any other and the volume of air passenger traffic can accelerate such spread as we have seen with SARS and WNF. The SARS epidemic dramatically illustrated the role of travel in rapid disease spread. The number of cases across the globe grew at an alarming rate until the application of strict public health strategies and isolation contained further spread. It remains a puzzle as to how WNF got in to the US-explanations are inadvertent passenger aircraft transport of mosquitoes from the middle east to the USA.

Avian influenza, especially that caused by H5 N1 is highly infectious for birds and has to be regarded with utmost seriousness. Although H5N1 has not as yet become a major human flu pandemic - and one hopes never will - avian flu is an accomplished species jumper. Although human cases of H5N1 flu have been in the low hundreds (in contrast to millions of bird cases) so far there have only been about 200 deaths mainly through direct contact with infected birds. Nonetheless the mortality rate of those becoming infected is around 50% which is extremely high for a zoonotic flu virus.

Some of the causes of exotic diseases emergence include:

- Genetic changes in pathogens
- Genetic changes in farmed animals
- Ecological changes
- Changes in land use
- Urbanisation
- Intensive agriculture
- Animal movements.

The increased demand for meat and meat products, the enormous international trade in food and food products together with increased movement of livestock and open animal markets are all factors in the global spread of infectious agents. To this can be added the rapid growth in human and animal air travel and the enlargement of international trading blocks to include countries with endemic and poorly controlled infectious diseases.

Avian flu and its spread emphasizes the key issues for animal and human health authorities in the control of zoonotic diseases. Speed of clinical detection, rapid diagnosis and rapid action must be applied to outbreaks. Rapid diagnosis of infectious agents in the field using state of the art molecular diagnostic technologies are essential.

Preparedness can of course be at many levels. Preparedness based on huge stockpiles of vaccines and antiviral drugs is crucial but so also is awareness and biosecurity. In developing countries and in rural areas simple attention to limiting spread of infections through early reporting is essential. There are many lessons that have been learned and many more yet to be learned.

My conclusions on the key needs for control of infectious diseases of man and animals can be summarized as:

- Surveillance, vigilance and containment
- Integration of medical and veterinary surveillance needs
- Effective regional, national and global co-ordination in surveillance
- Better understanding of animal and human demographies
- Oversight of the international trade in pets, livestock and wildlife
- International funding in support of disease control in developing countries
- Recognition by Governments that animal diseases are highly significant not only to the economy but more importantly to public health.

CANINE GENETIC DISEASES

I now want to turn to another large area in One Medicine where the study of naturally occurring genetic diseases in their target species is opening up

new avenues of understanding for human medicine. Genetic diseases of companion animals is a goldmine for comparative medicine (14, 15).

The wolf is the wild ancestor of the domestic dog. The domestication of the dog from its ancestor is one of the biggest genetic enterprises of a domestic animal breeding going back for thousands of years. As a result of some 15 000 years of selective breeding for desired traits ranging from hunting, rat catching and lapdog companionship there are now some 400 distinct breeds and a global dog population of about 400 million animals.

There are a large number of diseases traits "fixed" in inbred dogs. The "breed barrier rule" operated by many breed societies has led to a relatively closed genetic pools in inbred dogs. Different dog breeds represent distinct genetic lineages analogous to the development of inbred lines of mice. As a result there are now some 430 genetic diseases recognized and 70% of the diseases are inherited as autosomal recessive traits.

The healthy dog can be the carrier of a defective gene (e.g. in canine muscular dystrophy) and because the same dog may be used for multiple matings there is a high degree of consanguinity in the pedigree dog population derived from one sire over many years. The spread of the disease carrying allele can arise without it being known and subsequent matings between heterozygote carriers in the derived offspring can result in the disease trait being expressed. Many of the disease conditions are representative of human diseases and there are close identities with such diseases as increased cancer susceptibilities, autoimmune diseases, epilepsy, deafness and possibly behaviour. Because there is extensive clinical surveillance of most pedigree dogs there is now a large amount of clinical data on the many genetic conditions.

What makes these diseases interesting in the context of One Medicine is that the selectively bred dogs share the environment with man and are exposed to a similarly wide range of microbiological and environmental challenges to health from very young to old age. This is in stark contrast to the inbred laboratory animal in genetic diseases research as these are kept in relatively sterile and non-challenging environments with short life spans. Thus the genetic diseases of companion animals represent a unique and rich source of the "experiments of nature" which in human medicine have often revealed fundamental insights into biology and medicine.

What has given this field enormous significance has been the work on understanding the canine genome (16-18). Genes which predispose to certain diseases are more common in some breeds and in others the disease is rare. One of the reasons for this is that there is a strong founder effect through the use of popular sires that may be a carrier for the disease allele. Many of the traits are due to the action of several genes but there are three conditions where the precise gene mutation is known and mapped and its mechanism of causing disease established: these are hereditary renal cancer; narcolepsy and the genes involved in progressive retinal atrophies some of which are equivalent to early onset night blindness or retinitis pigmentosa in man.

Probably the best example at present which illustrates the One Medicine concept in the context of genetic diseases of man and dogs is in the understanding of narcolepsy. Narcolepsy in man is a well known genetic disease with an incidence in the population of about 1/2 000. This used to be a poorly understood disease recognised clinically as a sleep-wake disorder. Patients show excessive day time sleepiness, sleep paralysis and the disease has a close association with MHC Class II genes. It is a disorder with a marked similarity to canine narcolepsy.

Canine narcolepsy is seen in such dogs as Dachsunds, Poodles, Labradors, and Doberman Pinchers. The studies by Lin et al (19) "woke up the field of medical research on human narcolepsy" when they showed that canine narcolepsy was a simplified genetic system where the defect was due to a deletion in the cell membrane of the orexin receptor (Hcrtr2 gene) in CNS for the sleep modulating neuropeptide -orexin/hypocretin.

This work was the first data to link the hypocretin gene family to sleep disorders and led directly to the identification of the defect in some forms of human narcolopsy where there is a more complicated genetic system than in the dog. The defect in man is now known to be a mutation in the neurotransmitter which leads to its defective synthesis. It is not an identical mechanism to that in the dog but part of the function of the sleep modulating neurotransmitters in the CNS.

The canine narcolepsy story then is one of the classic examples of One Medicine. It also shows the remarkable speed of medical progress made possible by the genome revolution in man and animals resulting in the space of a few years of a new understanding of a puzzling human condition arising from the study of a rare canine disease.

Canine genetic diseases are a fast growing area of animal genetics and clinical veterinary medicine (20). Some 10% of the genetic abnormalities now

reported have the same genetic abnormality as seen in human diseases and genetic tests for these mutations are becoming available (17). Examples where the gene defects in canine disease in different breeds are well established seen with:

- X-linked muscular dystrophy (dystrophin deletion) - Belgian Shepherd
- X-linked SCID (IL2 receptor deletion) - Basset Hound
- Narcolepsy (orexin receptor mutation) - Doberman , Rottweiler, Chihiuahua
- Epilepsy (tandem repeat expansion of EPm2 gene) - Dachsund
- Progressive retinal atrophy (rod-cone dystrophies) - Corgi, Collies, Briard
- Mammary carcinoma (association with BRCA1 and 2) - English Springer Spaniel
- Diabetes Mellitus (SNPs in IL4 and IL10) - Cairn terriers, Labradors
- Copper toxicosis (deletion in Cu metabolism gene) - Bedlington terrier
- QTL loci identified associated with growth (IGF 1 and IGF2), longevity.

Canine genetic diseases are also helping us to understand the complex aetiologies and pathogenesis of more complex polygenic disorders. A particularly good example comes from the studies of canine Diabetes Mellitus (21). Several studies have now shown that there is an increased risk of late onset diabetes in middle aged to old dogs in breeds such as the Samoyed, the Tibetan Terrier and the Yorkshire Terrier. This is in contrast to other inbred dogs where Diabetes is either rarely seen (e.g. the Boxer) or at very low frequencies (German Shepherds). In mixed breed dogs the incidence of diabetes is about 0.36% but the Samoyed has about 15 times this risk. There is a marked association with a particular MHC Class 11 haplotype and evidence to suggest that there is an imbalance in T cell subsets in affected dogs some of which have elevated antibodies to tissue antigens (21, 22).

Breed dispositions for cancer susceptibility are also well recognized (23). Histiocytic sarcoma which can present as a lymphoid cell tumour in dogs is seen at greatly increased incidence in certain breeds but most notably in Flat Coated Retreivers and Bernese Mountain dogs. This is an autosomal recessive condition and the familial distribution throughout many offspring generated from one dog emphasizes the popular sire effect where the spread of an autosomal recessive gene through many offspring occurs in the course of repeated breeding and inbreeding of offspring.

VETERINARY AND MEDICAL EDUCATION

Comparative medicine has a proud and enviable record but will it be sustained by the veterinarians of the future? Academic developments in veterinary medicine need to be underpinned by a vibrant culture of research and inquiry. Veterinary undergraduates need to be educated in the substance of science and not in its shadow. All too often this is not achieved because the statutory requirement in veterinary medicine for accreditation on graduation squeezes out intellectual and curiosity driven inquiry. This impacts negatively on the opportunities for research by veterinarians.

Although the requirements for the professional education of medical and veterinary undergraduates precludes integration of much of their clinical education initiatives need to be taken which will encourage integration in pre-clinical medical and veterinary education. The Flexnerian view of the importance of a scientific education during the preclinical education of medical or veterinary students cannot be overstated. Initiatives that should foster the Flexnerian ethos include joint pre-clinical education of medical, veterinary and natural science undergraduates, joint intercalated Honours Degrees, Summer Schools, Research based electives and postgraduate research training.

For the veterinary profession to survive with credibility in today's science led culture it is essential that we nurture a significant number of research educated veterinarians. Without this, the opportunities for veterinarians to play a full part in the "One Medicine" agenda will be progressively lost. This will be to the detriment of advances in basic biomedical science and its application in such diverse and important areas as public health, comparative medicine, animal genetics, zoonotic and wildlife diseases, food security, climate change and use of animals in research. These are all areas critical to the "One Health" agenda which is dependent on collaborative and interdisciplinary research in translating scientific advances from one traditional discipline to another.

The ethos of "One medicine/One health" needs to be embedded in veterinary education and the curriculum. Nor should it be ignored in the undergraduate medical curriculum. Important advances in biomedical science have come from the One Medicine approach and now with the genomics revolution there will be undoubtedly many more significant new developments in basic and clinical medicine.

In my view some of the critical needs for maximising the opportunities for One Medicine in medical and veterinary education are as follows.

- Co-location of veterinary schools and medical schools on the same campus
- Combined preclinical teaching of veterinarians, medics and natural scientists
- Integration of basic science into the clinical curricula
- Admitting more natural scientists to clinical years of veterinary education
- Development of Intercalated Honours Degrees, and Summer Schools
- Development of combined Veterinary/PhD programmes and their funding.
- Culture change in attitudes of veterinary undergraduates to research and non-practice based careers.
- Educational loan debt redemption schemes
- Move to a postgraduate pre-registration year for clinical veterinarians.

At a research level there is a need to maximise the opportunities for research that One Medicine offers. Some of the key issues here are:

- Recognition by research funders of the need for interdisciplinary research
- Recognition by research funders of value of naturally occurring diseases in outbred animal populations.
- Opportunities for long tem strategic research awards in One Medicine
- Provision of tenure track career development Fellowships for veterinary and medical graduates
- Establishing academic centres of excellence in One Medicine in the best Universities.

The Academies of Medicine could play a leading role in fostering such developments. It was almost a century ago that the importance of One medicine was articulated by Sir Clifford Allbutt, Regius Professor of Physic in the University of Cambridge, England. To quote:

> *"To establish in Cambridge a central institute of comparative pathology, which must include professorial units for the diseases of plants and animals and the means of blending these departments with the neighbouring departments of the diseases of man, will no doubt cost much money, but a sum which when compared only with the waste and destruction of stock and crops would prove to be small indeed.*
> *Such is the utilitarian promise, but far beyond this we cannot tell how bright will be the cross-lights which, in a system of comparative medicine, will be thrown reciprocally upon the fields of the several pathologies of all kinds of life"*
> (Sir Clifford Allbutt, Regius Professor of Physic, University of Cambridge).

In this paper I hope I have illustrated that across the wide spectrum of diseases of animals and man whether they be degenerative diseases, genetic diseases or zoonotic infections all illustrate the continuum of medicine, veterinary medicine and basic biomedical science. The essential and fascinating interplay between them can do more to advance knowledge in both medicine and veterinary medicine than either can achieve on their own.

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