One Health Initiative
An in-depth interview with Dr Laura Kahn

RETHINKING VACCINATION
• Feature and interview with The Jenner Foundation
Could you offer an insight into the background of the One Health Initiative and its overall aims and objectives?

The concept that human and animal health is linked is not new. What is new is that in recent years, a number of like-minded individuals across professional spectrums began recognising it as an essential element for advancing research progress for human and animal health. The emergence of West Nile virus in New York City in 1999 was a seminal event. A veterinarian played a key role in recognising that the disease in humans and animals was linked by a newly emerged virus, emphasising the critical role for One Health principles in public health. At that time, I was researching the public health and animal health infrastructures in several U.S. states. One of the veterinarians in the study sent me some veterinary medical literature on bioterrorism, and it struck me how many of the bioterrorist agents and emerging infectious diseases are zoonotic (transmissible from animals to humans). Yet in my research, I found that physicians and veterinarians rarely, if ever, communicated or collaborated with each other.

I published a paper in Emerging Infectious Diseases on the need for medical and veterinary medical professionals to work together in April 2006. Dr Bruce Kaplan, a retired veterinarian and a former epidemiologist with the U.S. CDC and staff officer with USDA Food Safety and Inspection Service in Washington, DC, contacted me, and we formed a most productive One Health partnership which has now been established for over four years. A year after our inception, I approached Dr Tom Monath, an eminent medical virologist and physician, to join us, after I heard him give a terrific speech at an American Society for Microbiology conference. He has worked with a number of veterinarian scientists over the years, and led a multidisciplinary team at CDC working on zoonotic infections, so he knows first-hand the benefits of a One Health approach in addressing disease(s). Dr Jack Woodall, a world-renowned PhD scientist and a co-founder of ProMED-mail, which is inherently One Health in its approach to disease reporting, joined our One Health team in February 2009.

Our foursome works together to promote One Health via newspaper and professional journal publications and through our One Health Initiative website at www.onehealthinitiative.com.

The aim of the One Health Initiative is to increase communication and collaboration between human, animal, and ecosystem health professionals.

Why have there been so few coordinated human and animal medical projects to date? Has there long been a desire for such a collaborative approach and how can this help in disease prevention and the development of new medications?

That’s a very good question. First of all, it is important to recognise that there have been a number of successful collaborative projects in the past, and they do serve as models for future efforts. Examples include the Rockefeller Foundation Virus programme (1951-71), CDC’s National Center for Zoonotic, Vector-borne, and Enteric Diseases, the Eden Project and efforts to control bovine spongiform encephalopathy and avian influenza.

An outstanding example is a livestock drug, Ivermectin, developed in 1981 to treat parasites in livestock,
which became important in the treatment of canine (dog) dirofilariasis (heartworms) and was subsequently approved for human use in 1987. It is now responsible for the elimination of river blindness from huge areas of Africa, and the treatment of lymphatic filariasis and pinworm.

With regard to One Health necessity, virtual elimination of rinderpest by livestock vaccination, supervised by veterinary medical epidemiologists, has improved nutrition for millions of people across sub-Saharan Africa, the Middle East and India. Drug treatment for bovine African trypanosomiasis has opened up huge areas of grazing land in Africa to pastoralists.

However, there are several factors that might explain the rarity of such projects. First, as humans we tend to be more focused on our own health needs than on other species. It is only natural, and so we forget that our health is intimately tied to animal and ecosystem health. Second, as medical knowledge has exploded in the past century, we have become increasingly reductionistic in our approach to health and disease. We are good at building areas of specialisation which certainly has its benefits, but narrows our scope so much that we stop seeing the forest for the trees. We’re now looking at the veins of the leaves and don’t even see the trees! We need to step back, look at the whole picture, which includes our individual health and public health, the health of other animals, and the health of the planet, if we want to survive. Disease prevention is far better than disease treatment, which is much more expensive.

A more integrated approach would identify the factors that promote infectious disease emergence as well as non-infectious diseases like cancer, cardiovascular disease, obesity, orthopaedic conditions like osteoarthritis; more specifically, human joint prostheses developed primarily by veterinarians in animals continue to serve as significant models for human surgical replacements of knees, hips and other joints. Also, the first flexible coil balloon expandable intracoronary stent was developed for humans by a research team including an interventional physician cardiologist (a former veterinarian) and a pathologist veterinarian in the early 1990s. Nearly 100 per cent of patients undergoing balloon angioplasty for ‘heart attacks’ from heart vessel blockages receive stents.

Are there any particular diseases or global regions that could benefit from your research? Is there a greater prevalence of disease transmission between humans and animals in less developed nations?

I do policy research, so I look at the big picture and develop recommendations on how we can improve our approach to disease control, treatment, and prevention. In the U.S., we’ve largely divorced ourselves from livestock and food animal production since the vast majority of the U.S. population lives in urban areas. I recently took my family to spend a few days on a dairy farm in rural Pennsylvania. My kids and I watched cows get milked, and it was a revelation for them to see where our milk comes from.

In much of the rest of the world, in contrast to the U.S., people live with their livestock. And they implicitly recognise the importance of animal health because if the animals die, then they starve. Of course, if humans live closer to the animals, there is a greater opportunity for disease transmission. The avian influenza (H5N1) illustrates this case. Most of the people who got sick with H5N1 were exposed to sick poultry. On the other hand, there is debate that the increasing incidence of allergic disorders and autoimmune diseases is due to living in too clean an environment. Allergies and autoimmune diseases are rare in African and Asian populations. So perhaps it would be healthier for us if we were more exposed to animals and their parasites beyond just dogs and cats. Clearly, we need more research in this area.

Will the One Health Initiative play an active role in drug and vaccine development and implementation or is your role more of an advisory capacity?

I am not directly involved in drug and vaccine development, but clearly we need to develop therapeutic and preventive strategies in tandem between humans and animals. Our One Health team colleague Dr Tom Monath, a partner in the Pandemic and Biodefense Fund, Kleiner Perkins Caufield & Byers, and also Adjunct Professor, Harvard School of Public Health (USA), is involved in this area. He has emphasised the benefits that would result from a closer collaboration between animal and human health sectors of the pharmaceutical industry. Dr Monath directed research and development on vaccines against dengue, Japanese encephalitis, West Nile, yellow fever, Clostridium difficile, as well as smallpox vaccines for defence against bioterrorism. This speaks volumes for how the expansion of collaborative One Health principles would fast-forward drug and vaccine development worldwide!

All large companies separate these sectors physically and do not foster active collaborations. This is wasteful, since there are obvious cross-cutting concerns, overlapping expertise, and need for innovation in diseases that affect animals and humans including cancer, obesity, allergy, infectious diseases, and other areas.
How do you propose to increase awareness and which methods of dissemination have proved to be most useful thus far?

Educating political leaders and the public about One Health is absolutely essential for widespread support and adoption of the concept. Getting the word out takes time and patience. My colleagues and I have been reaching out to policy makers and the public, but it’s been a challenge because of many other competing issues. The economic recession certainly hasn’t helped, and healthcare reform has dominated the news in the U.S. One Health can have a potentially huge impact in preventing disease and ultimately cutting healthcare costs, but again, the challenge has been to get people to see beyond hospital and clinic walls. We have written newspaper Op Eds and letters-to-the-editor in newspapers and magazines, written papers in professional journals, and given One Health talks. We have colleagues at the Florida Department of Health who have a One Health Newsletter available for free online. All of these efforts must continue. A blockbuster One Health book and movie would certainly help!

Could you elaborate on the training and educational efforts that you are promoting between human medical, veterinary medical schools and schools of public health?

At one time, a number of schools of medicine and veterinary medicine shared classes during the first two years of study. This practice has largely disappeared as faculties have grown. Schools of veterinary medicine certainly see the relevance of a One Health approach, but there just aren’t that many of them to partner with the medical schools. In the U.S., there are only 28 schools of veterinary medicine compared to around 125 medical schools and only a handful of universities have veterinary and medical schools located in the same city. Globally, the ratio of veterinary and medical schools is about the same, so promoting increased communication and collaboration between them is a challenge from a logistical and geographic standpoint. Schools of public health could serve an important role as a common denominator, but not all physicians pursue additional education in public health. At the very least, medical schools should teach their students about zoonotic diseases and the importance of recognising veterinarians as important colleagues rather than merely as animal health technicians.

Ideally, there should be shared courses, electives, and clinical experiences between the two professions. Much could be learned from a comparative medicine approach to health.

Are there any particular cases that have proved to be a particular success thus far? Are there any areas in which you expect to make significant progress in the next few years?
There have been a number of successes. After U.S. officials recognised the important contributions that veterinarians made during the 1999 West Nile virus outbreak, the CDC established the National Center for Zoonotic, Vector-borne, and Enteric Diseases headed by a veterinarian, Dr Lonnie King. They also set up ARBOnet which is a West Nile virus surveillance system for humans, birds, mosquitoes, and other species. For the first time, scientists could watch the spread of a virus rocket across the U.S. in just a few years.

Another success has been avian influenza (H5N1). After a slow start, the World Health Organization, The Food and Agriculture Organization, and the World Organization for Animal Health recognised the impact of zoonotic diseases on human health and have been working hard to increase their communicative and collaborative efforts.

Furthermore, the Initiative is a keen advocate of collaboration to encourage progress. Who are the key collaborators and what has their inclusion brought to your work?

There have been a number of important advocates for One Health whom we have worked with. In Europe, Dr Jakob Zinsstag, a veterinarian at the Swiss Tropical Institute in Basel, Switzerland has been a tireless One Health advocate for many years. He has been studying the health of African pastoralists and their livestock. Dr Peter Rabinowitz, a physician at Yale University in New Haven, Connecticut, and Dr Lisa Conti, a veterinarian with the Florida Department of Health, recently published a landmark book titled ‘Human-Animal Medicine. Clinical Approaches to Zoonoses, Toxicants and Other Shared Health Risks’. This is the first book of its kind co-edited by a physician and veterinarian.

Drs Kaplan, Monath, and I developed, wrote and edited copy for a One Health monograph published by Veterinaria Italiana in which many physicians, veterinarians, and others discussed why the One Health approach is so important in their work. (http://www.izs.it/vet_italiana/2009/45_1/45_1.htm).

In November 2009, the American Society of Tropical Medicine and Hygiene co-sponsored a One Health forum for the first time with the Society for Tropical Veterinary Medicine at the ASTMH’s annual convention in Washington, D.C (USA).

The 1st International One Health Congress is being planned and scheduled for February 2011 in Victoria, Australia; it is entitled ‘Human Health, Animal Health, the Environment, and Global Survival’.

And, as previously mentioned, the National One Health Commission had a summit last fall and is engaged in implementing One Health efforts in the U.S. and globally.

These efforts illustrate that there is much interest in One Health and the concept is diffusing outward. The challenge will be to implement and institutionalise it in government, academic, and industry settings. Some foundations are beginning to recognise the importance of this approach. For example, the Rockefeller Foundation has supported the One Health Commission. It’s an important step.

How do you see the role and activities of the initiative changing in the future? Will climate change and overpopulation increase the need for multidisciplinary, collaborative programmes?

Much of the role and activities of the One Health Initiative concerns outreach and advocacy efforts. The One Health Initiative website has been serving as an important source of information on news, events, and publications relevant to One Health. I am currently looking to start a One Health journal and am seeking partners in establishing an academic forum for this new field. Climate change and increasing human populations will definitely increase the need for multidisciplinary, collaborative programmes. As the Earth’s resources are strained with increasing demands for energy, food, shelter, and water, we must anticipate that a sustainable future will require a holistic approach to human, animal, and ecosystem health. A One Health approach will be critical if we hope to meet the challenges of the 21st Century and beyond.

www.onehealthinitiative.com
The Jenner Vaccine Foundation was founded in 2005. Could you offer an insight into its background and its overall aims and objectives?

BG: The Jenner Vaccine Foundation’s mission is to support the development of innovative vaccines against major infectious diseases of man and animals, with the objectives to:

- Develop new vaccines for globally important human and veterinary diseases. This is done by providing support to the Jenner Institute, a partnership between the University of Oxford and the Institute for Animal Health (IAH).
- Enhance training in vaccinology to ensure that there is sufficient capacity to develop and deploy a new generation of vaccines that save lives and enhance food security.
- Undertake advocacy activities to ensure that the benefits and importance of vaccines and vaccination, as hugely cost-effective public health strategies, are widely understood and appreciated.

What are the benefits of a dual approach, combatting both human and livestock diseases?

AH: There were several reasons for this union of human and veterinary vaccine researchers. Firstly, there was the realisation that vaccinologists are facing common technological challenges in designing a new generation of vaccines for difficult human and veterinary diseases and that there are clear advantages in tackling these together. Human vaccine research tends to be better funded but veterinary vaccines progress faster. Large animals such as cattle can be far better predictors of human immunogenicity than laboratory mice, and microbial challenge studies are more often justifiable in animals than humans. Also, increasing public awareness that many of the greatest epidemic threats to humans come from animal pathogens has made the traditional cultural separation of these disciplines increasingly unwarranted.

One important aspect of the Foundation is to produce rapid translational research. How quickly are you able to employ new vaccinations in field studies after their conception?

AH: Rapid assessment of new vaccine technologies in humans and livestock is a major goal of the Jenner Institute. There have been too many exciting new vaccine technologies that looked superb in mice but failed badly in clinical trials, such as DNA vaccines. The Jenner Institute’s strategy is to undertake testing of
The Jenner Vaccine Foundation is a collaborative enterprise which supports vaccination against infectious diseases in humans and animals. In this interview four key figures from the initiative offer their perspective on this ambitious goal.

How do you propose to optimise vaccination regimes to increase the effectiveness and longevity of vaccines for malaria and TB?

AH: The major strategy for a malaria vaccine is to develop a multi-antigen, multi-stage vaccine. So far, single component vaccines have struggled to achieve high efficacy, but several potential components of a multi-stage vaccine are now showing some efficacy in humans. The Jenner Institute has been at the forefront of developing new vectored vaccines that induce particularly strong cellular immunity and lend themselves to the inclusion of multiple antigens. The most recent advance has been to assess chimpanzee viral vectors as vaccines for humans with impressive safety, immunogenicity and efficacy.

How is the Jenner Vaccine Foundation working to promote enhanced links with the pharmaceutical industry? Would this be particularly beneficial for cost reduction and increasing drug distribution?

AH: The Jenner Vaccine Foundation works closely with the pharmaceutical industry in many ways. Some industrialists serve as non-executive members of the Foundation’s Board, and several clinical trials are partnered with or funded by industry. However, the majority of the Jenner Institute’s work is supported by public and private funders who fund bench to early stage clinical testing of new vaccine concepts and designs. This is particularly beneficial to the pharmaceutical industry which prefers to buy into a vaccine candidate after phase I/II trials are completed successfully, when the likelihood of reaching licensure is enhanced. Providing a viable candidate with a low risk of failure is even more important for developing country diseases where, because of lower returns, industry can afford to take less risk with earlier stage candidates.

Looking to the future, will global events induced by climate change have a substantial impact on the prevalence and potency of infectious diseases?

MS: Infectious diseases emerge and re-emerge with changing agriculture and farming practices, including changes in regulation that prohibit the use of antimicrobial substances, and are ‘predictably unpredictable’ in their occurrence. There is now, however, general agreement that the introduction of vector-borne pathogens in to previously ‘free’ areas of the world is becoming more common and that the trend is set to continue significantly faster and further. Currently, almost half of the world’s population is infected by vector-borne pathogens, with the greatest impact in developing countries within tropical and subtropical areas. However, the impacts of climate change and global warming are increasing and the survival and spread of bluetongue virus into northern Europe provides a disturbing example of how an ‘exotic’ vector-borne livestock pathogen can quickly become established in new geographical regions and present new and significant risks to livestock production.
Infectious diseases transcend the direct impacts on individual human and animal health, and have the potential to create serious social and economic disasters. The Jenner Vaccine Foundation is addressing these problems by supporting the development of innovative vaccines to combat major diseases.

**AN ESTIMATED 1.8 million people died from tuberculosis (TB) in 2008, with the highest number of deaths occurring in South Asia and the greatest mortality rate in Africa. This is an alarming statistic, but one that does not include the large numbers of domestic cattle that were affected by the condition in the same year, hiding the true impact of this disease.** There has been an emphasis on controlling human infectious diseases before attending to those which affect livestock. This is an issue which the Jenner Vaccine Foundation is addressing, recognising the importance of a comprehensive approach to both human and animal infections.

**UNIQUE APPROACH**

The Jenner Vaccine Foundation is the successor to the Edward Jenner Institute for Vaccine Research, and was founded in 2005 as a unique partnership between the University of Oxford and the Institute for Animal Health. This collaborative effort and dual focus on animal and human health is pivotal to successful research, as Chairman of the Jenner Vaccine Foundation, Professor Brian Greenwood, asserts: "This encourages the development of innovative vaccines through parallel work on both humans and animals. In this framework, animals become beneficiaries of vaccine development and not just models for human disease."

The Jenner Institute was established by the Jenner Vaccine Foundation, as a multi-site institute which supports vaccine research and development. It is home to 25 Jenner Institute Investigators who are collaborating in keeping with the One Medicine One Health agenda. In addition to its unique focus on both human and livestock diseases, it places heavy emphasis on translational research and the swift development and evaluation of new vaccines in clinical trials. The Institute has developed the Clinical Biomanufacturing Facility (CBF), at the University of Oxford, which provides a key interface between research and clinical medicine, enabling the production of gene-based products for use in clinical trials. This provision is an essential part of the Jenner remit, as Institute Director Professor Adrian Hill describes: "This allows the expanding programmes of translational research in the medical school cost-effective access to a state-of-the-art manufacturing facility for new types of vaccines."

The Jenner Vaccine Foundation’s main role has been to provide support to the scientists at the University of Oxford and the Institute for Animal Health, and to encourage the exchange of ideas and sharing of resources between the two institutions, thus assisting in the development of vaccines for humans and livestock.

**THE INSTITUTE FOR ANIMAL HEALTH**

The Institute for Animal Health (IAH) is a world-leading centre of excellence for research into infectious diseases, based in the UK and situated on two campuses - the Compton and Pirbright Laboratories. The IAH has a wealth of knowledge regarding fundamental, strategic and applied science focused on infectious animal diseases, and now works in collaboration with the Jenner Vaccine Foundation to investigate methods for disease prevention, control and eradication, with particular emphasis on rinderpest, foot-and-mouth, bluetongue disease and bovine pneumonia. **THE UNIVERSITY OF OXFORD**

The University of Oxford has world-leading strengths in the basic sciences, and together with its more recent dramatic expansion in clinical sciences, this provides new avenues for translational medicine and the opportunity for the Medical Sciences Division to establish itself as one of the best centres for such research in the world. Within one institution, Oxford combines clinical understanding of human infectious diseases, the basic research necessary to discover target antigens, expertise in constructing vaccines, and extensive experience in designing and implementing clinical trials. It is unique among universities in developing vaccines for challenging human infectious diseases and taking them all the way to trials in the field. Several of Oxford’s leading infectious disease researchers are Jenner Institute Investigators and work within the multi-site Jenner Institute with colleagues from the Institute for Animal Health in the search for innovative vaccine candidates.

**ONE MEDICINE ONE HEALTH**

Many diseases that affect domestic animals also possess the potential to spread to humans, and TB is a particularly pertinent example where the collaborative effort employed in this research comes to the fore. A test and slaughter policy for cattle has been the frontline defence against the spread of TB in the UK but has not stopped the incidence rate rising, causing the overall cost of bovine TB control to escalate from £25 million in 1998/9 to over £99 million in 2005/6. The Jenner consortium’s studies into TB have yielded some promising results and have led to the creation of a new TB vaccine, MVA85A. This new vaccine is designed to be used in conjunction with the traditional BCG vaccine, and produces higher levels of cellular immunity with increased longevity. It is the first new TB vaccine to enter a large proof-of-concept trial, which will involve around 2,800 BCG-vaccinated South African infants divided equally into those receiving MVA85A or a placebo. The infants will be monitored for two years and the results should be available early in 2012. The team is conducting a study to ascertain the effects of MVA85A on TB in cattle, as well as a major efficacy trial in HIV-infected adults.

**RESEARCH INNOVATIONS**

A pioneering force in vaccine development, Jenner Institute Investigators have led the development of new prime-boost approaches to inducing strong cellular immunity against major infectious diseases such as HIV/AIDS, malaria and TB. Recently, the malaria vaccine programme at the University of Oxford, a clinical trials programme linked to strong pre-clinical vaccine research, has been targeting the induction of high level T-cell responses against multiple parasite antigens, with encouraging efficacy results in phase II trials. The
novel malaria vaccines must be temperature resistant to have the greatest impact in the worst affected regions. Very few areas in the developing world have adequate refrigeration capacity for all the new vaccines required. As Hill points out, the consequences of this shortage can be disastrous: "Every year about $200 million is spent on trying to maintain a ‘cold chain’ for vaccines that provides refrigeration in even the remote rural areas of poor developing countries," he states. "This often fails so vaccines are lost, children are not immunised and in consequence lives are lost." Encouragingly, as Hill goes on to explain, recently published work by the collaborators has led to a breakthrough, which bodes well for the future success of a vaccination programme in developing countries: "The trick here was to mix a known sugar stabiliser, trehalose, with the vaccine and dry it onto a simple filter membrane allowing the vaccine to form a stable glass that re-dissolves readily to allow vaccination. The challenge now for vaccine stabilisation is probably more logistic and organisational than scientific”.

TRAINING

The Jenner Vaccine Foundation supports training of vaccinologists; in particular, it plays an important role in creating an exciting and engaging environment for PhD students in this field, thereby providing a valuable link between education and practical experience. Training activities are designed to emphasise the importance of assisting and offering guidance to scientists working in developing countries in the field of vaccinology. In addition to training opportunities, a new vaccinology course, the Oxford Vaccinology Programme, has been created by researchers from the Jenner Institute with collaborators from industry and is being run at the University of Oxford. The short course offers a state-of-the-art approach to both human and veterinary vaccinology and has a particular focus on translational research, providing the students with insights into recent developments from both academic and industrial perspectives.

LOOKING AHEAD

The Jenner Vaccine Foundation is working to accelerate the development of vaccines for the prevention of major human and animal diseases to help deliver better public health and food security. Specific goals are to enhance the standing of vaccinology in the UK and Europe, and to disseminate the importance of the field and the value of disease prevention to political decision makers and the general public. As transparency and the credibility of advice become increasingly important, the Jenner Vaccine Foundation aims to become a trusted independent source of vaccinology knowledge and resources of translational research so that more vaccines enter clinical trials and become a leading source for vaccine-related information.

OBJECTIVES

- To support the development of new vaccines for globally important human and veterinary diseases by providing resources for vaccinology research programmes, training, and advocacy
- To accelerate the rate of vaccine development and improve the level of translational research so that more vaccines enter clinical trials
- To create a network of investigators to increase the availability of vaccinology knowledge and resources
- To enhance the recognition of the importance of vaccinology

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PROFESSOR BRIAN GREENWOOD qualified in medicine at the University of Cambridge, UK in 1962. He is the Manson Professor of Clinical Tropical Medicine at the London School of Hygiene and Tropical Medicine. In 2008, he became director of a new capacity development initiative supported by the Wellcome Trust and the Bill and Melinda Gates Foundation, the Malaria Capacity Development Consortium (MCDC), which operates a postgraduate malaria training programme in five countries in sub-Saharan Africa, and he also directs a new consortium (MenAfriCar) established with support from the Wellcome Trust and the Bill and Melinda Gates Foundation to study meningococcal carriage in Africa. He currently holds the position of Chairman of the Jenner Vaccine Foundation.

PROFESSOR MARTIN SHIRLEY is an avian parasitologist by training and is the author of over 150 scientific papers on coccidial parasites of poultry. Shirley led the team that produced the unique Paracox vaccine for the control of the disease, which now sells around 1000 million doses worldwide each year. In 1989, he received the Tom Newman International Award for Poultry Science and in 2004 he was awarded a Research Medal from the Royal Agricultural Society of England for his services. He is currently the Director of the Institute for Animal Health and a member of the Jenner Vaccine Foundation Board.

PROFESSOR ADRIAN HILL trained in medicine at Trinity College Dublin and the University of Oxford, qualifying in 1982. He has been a Wellcome Trust Principal Research Fellowship at Oxford University since 1995 and in 1996 was awarded the title of Professor of Human Genetics. He participated in the founding of the Wellcome Trust Centre for Human Genetics in 1994, and in 2003 co-founded the Oxford Centre for Clinical Vaccinology and Tropical Medicine, which he now chairs. He has led the development of new malaria vaccines at Oxford and has undertaken over 30 clinical trials of new vaccines. In 2005 he was appointed Director of the new Jenner Institute.