A quarterly newsletter highlighting the interconnectedness of animal and human health

**Fall 2009** 



This newsletter is dedicated to enhancing the integration of animal, human, and environmental health for the benefit of all by demonstrating One Health in practice.

#### nd health profesn the following Host Switching – a critical area for research

### Martyn Jeggo, B. Vet. Med., Phd and Deborah Middleton, BVetSc (Hons), PhD

#### Introduction

Pathogens, by definition, cause unwanted effects in their hosts which can range from mild disease to death. Critical to the outcome is not only the ability of the pathogen to infect a host, but the resources available to the host to withstand a pathogen assault that will result in disease. Many pathogens are unselective in their host, e.g. most Gram positive bacteria, whilst others are highly selective and limited to particular species or groups of living organisms, e.g. African Horse Sickness virus only affects equines. What controls host specificity is poorly understood and the more selective the pathogen the less is known [1]

That a pathogen can invade more than one host species would seem a clear advantage to survival for the pathogen, but many survive well in a single species host in apparently stable ecological relationships. Nevertheless, examples abound of pathogens that adopt a new host [2]. This phenomenon is particularly common for viral pathogens and there is plenty of evidence that it is on the increase – often with devastating effects for the " n ew " host [3]. A striking example is the jump to humans by the monkey immune deficiency virus in the late 1950 ' s to cause the now globally occurring HIV-AIDS. But there are many recent examples including the clear and alarming discovery in 2008 of Ebola Reston virus in pigs in the Philippines.

#### What is "host switching "?

The term "host switching" is used here to describe emergence of a pathogen in a new host

in which there had been no previous discernable evidence of the pathogen. After such emergence events, the source species of the disease agent or "natural reservoir" from which the switch has

occurred may be identified following active surveillance programs. Focusing on viral pathogens, recent examples could include Nipah virus infection of pigs in Malaysia [3], Nipah virus in humans in Bangladesh, Hendra virus in horses and Menangle virus in pigs in Australia, and SARS in civets in China [4]. For other emergent pathogens, such as Ebola virus, identification of the reservoir has proved more elusive. Whilst there are many examples outside of these, what also characterises this group is that each were previously asymptomatic infections in bats. What makes this particularly intriguing is the obvious fact that these " p athogens" were apparently comfortably existing with bats over many years without the need to find new hosts [5]. Dissecting the bat 's immune system may well assist in understanding how this adaptation system works. But of equal importance is the ecological advantage that underpins the

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Coming Events: .....page 27 switching to a new host and in doing so creating disease in the new host – on the surface a somewhat self limiting process for the virus!

#### Why is host switching important?

New and emerging diseases pose significant risks both to man and animals, and for man, some 70% of all new diseases emerge from animals. The switch of an organism from a symbiotic or even pathogenic existence in one host group to a new group of hosts occurs because an ecological opportunity has arisen that permits this to occur [6]. If we are to manage the risks posed by new and emerging diseases and develop effective mitigating strategies, we must first understand these underlying ecological mechanisms, including the molecular basis of host susceptibility to infection and disease.

#### What do we need to know?

The explanation for host switching should be considered within the framework of the Darwinian theory of evolution. Based on random mutation, a new version of the pathogen will contain a characteristic that enables it to invade and survive in a new host. In this context, many viruses are ideally suited with their very high rate of propagation and ability to continually mutate and re-assort. Based on the quasispecies theory of viral populations, those with a new characteristic that enhances survival will dominate in the "soup" of viral mutants [7]. Other non-viral based factors will provide opportunity for a pathogen to interact with a new host as has been shown for the bat -derived diseases. Intensive farming practices might further assist this evolution through providing alternative hosts in very high numbers, thus increasing the opportunity for a mutation characteristic that enhances survival in the host and, ultimately, transmission between new host members. As an example, the

replication of the SARS virus in the civet cat allowed for rapid adaptation of the virus to

the human SARS receptor, with a coincidental enhancement in pathogenesis.

Many key questions remain. Do some viruses have more defined processes that enhance this ability to develop new characteristics such as new host cell attachment proteins that will ultimately enable host switching – and is this a characteristic of all virus or specific viral groups? What are those underlying interactions that limit the host range for a virus? Not only must a host cell invasion process succeed, but there is a complex series of virus-cell interactions that must be overcome before the host switch can realistically occur. A viral selective process based on an adaptation that overcomes host protective mechanisms should succeed as a favourable adaptation and will enhance the survival of that particular mutant virus [8]. Clearly though, the process is not open ended. Foot and Mouth virus is a highly mutating virus that continually evolves to invade the host's immune response yet it remains confined to even-toed ungulates – what controls this? Importantly, and perhaps most intriguingly, what determines virulence? So long as Ro>1 the pathogen can continue to evolve, with virulence being little more than an epiphenomenon.

#### Some workable approaches

Whilst there are many examples that could be used to study host switching, answers for contemporary cases that have posed high risk to the host will likely be of particular interest. Further advantage would be gained in using examples where the pathogen has moved from a symbiotic to a pathogenic relationship. Clearly other factors play a part, and having a model that has recently been influenced by climate or anthropomorphic change would seem useful. Finally, understanding of the process will un-

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If we can unravel the underlying processes that drive disease emergence, we have a realistic chance of developing risk mitigation strategies. doubtedly be gained though unravelling the underlying molecular and genetic changes that occur, and current advances incorporating whole virus sequencing and metagenomics place this within our grasp. Using examples where this exquisite detail can be readily sought would seem essential. Based on the above, focusing on new bat-derived viral infections that have currently evolved in a number of species, including man, would seem a plausible approach.

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#### And the outcomes might be?

New and emerging diseases are a reality of our current lives as clearly witnessed in the recent response to the swine-derived human influenza outbreak this year, and the costs associated with the SARS outbreak in 2003. If we can unravel the underlying processes that drive this emergence, we have a realistic chance of developing risk mitigation strategies. Without understanding what drives host switching, and the subsequent application of disease management controls, we continue to risk a human disease catastrophe.

#### References

http://www.doh.state.fl.us/Environment/medicine/One\_Health/HostSwitching\_References.pdf

Dr. Martyn Jeggo is Director of the Australian Animal Health Laboratory, Geelong, Australia and as such, oversees many services and research activities involving both animal and human health interactions. He is Chairman of the Organising Committee of the 1st International Congress on "One Health" taking place in Melbourne in November 2010.

Dr. Deborah Middleton is the research Director at the Australian Animal Health Laboratory with an extensive program of research dealing with zoonotic disease, with an underlying focus on their pathology including many aspects of "host switching."



## Marine Mammals as Sentinels for Oceans and Human Health

Gregory D. Bossart, VMD, PhD

#### Introduction

Concern is being raised about the health of the Earth's aquatic ecosystems due to many factors including anthropogenic impacts and global climate change. The concept of marine sentinel organisms provides one approach to evaluating aquatic ecosystem health. Such sentinels provide indications of current or potential negative trends and impacts on individual and population health. In turn, such indicators will permit the characterization and potential management of environmental impacts associated with our oceans that ultimately affect human and animal health<sup>1</sup>.

Marine mammals are sentinels for oceans and human health because many species have long life spans, are often long-term coastal residents, feed at a high trophic level, and have unique fat stores that can serve as depots for anthropogenic toxins. Additionally, marine mammals are charismatic megafauna that typically stimulate a human behavioral response and are thus more likely to be observed<sup>2</sup>. Similarly, diseases that impact these species may make humans more likely to pay attention to ocean health issues.

Without an understanding of what drives host switching we continue to risk a human disease catastrophe.

The concept of marine sentinel organisms provides one approach to evaluating aquatic ecosystem health.

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#### Infectious and Neoplastic Disease

Newly documented diseases involving emerging infectious and neoplastic components are being reported in some marine mammal species.

Data suggest that interactions occur among genes, anthropogenic toxins, immunologic factors and/or emerging viruses in these marine mammals that share a coastal environment with humans.

Toxoplasmosis is a major cause of mortality among southern sea otters and is a serious infectious disease in humans.

These diseases may provide important information on aquatic ecosystem health. Newly documented complex diseases involving emerging infectious and neoplastic components are being reported in some marine mammal species. In turn, these diseases may provide important information on aquatic ecosystem health. For example, approximately 20% of sexually mature stranded California sea lions have a newly described urogenital cancer, which is associated with a novel herpesvirus, as well as exposure to anthropogenic contaminants such as PCBs and DDTs that persist in the sea lion's feeding grounds<sup>3, 4</sup>. Genetically inbred sea lions, and those with a specific MHC genotype, are more likely to develop urogenital cancer.

Recently, orogenital papillomatosis that occasionally undergoes transformation to metastatic squamous cell carcinoma was found to be associated with another novel herpesvirus and a papillomavirus in Atlantic bottlenose dolphins (Figure 1)<sup>5,6,7</sup>. The dolphin disease is associated with immunologic perturbations that may have an environmental basis<sup>6</sup>. Additionally, cutaneous viral papillomatosis with concurrent immunologic suppression was recently documented in endangered Florida manatees <sup>8,9</sup>. These data suggest that interactions occur among genes, anthropogenic toxins, immunologic factors and/or emerging viruses in these marine mammals that share a coastal environment with humans<sup>10</sup>.

Toxoplasmosis is a major cause of mortality among southern sea otters and is a serious infectious disease in humans, particularly in the congenital form. A recent analysis of seroprevalence or antibodies to *Toxoplasma gondii* showed evidence of prior infection in 52% of beachcast sea otters, and 38% of live sea otters sampled along the California coast. As coastal predators, otters serve as sentinels of the distribution of marine ecosystem pathogenic protozoans since they share the same environment as humans. Investigations of the pathogenesis of sea otter *T. gondii* infection is providing important information about terrestrial parasite flow and the emergence of disease at the boundary between wildlife, domestic animals, and humans<sup>1,11</sup>.

We recently reported the emergence of lobomycosis in a free-ranging Florida bottlenose dolphin health assessment study along Florida's Atlantic coast (Figure 2)<sup>12</sup>. Lobomycosis is a rare chronic mycotic disease of the skin and subcutaneous tissues caused by a yeast-like organism known as *Lacazia loboi* (formerly *Loboa loboi*).

Dolphins and humans are the only species known to be naturally susceptible to infection with *Lacazia loboi*. The reasons for the emergence of this rare disorder are unclear, but our data indicate that the disease in some dolphins is associated with humoral and cell-mediated immunosuppression of suspected environmental origin<sup>13</sup>. Limited evidence exists to suggest that lobomycosis may be transferred from infected animals to people. However, the high prevalence of lobomycosis in the dolphin population of this Florida coastal region, which is used extensively for recreational purposes, raises concerns for zoonotic or common source transmission.

#### Anthropogenic Toxins

Bottlenose dolphins reside in ocean, coastal, and estuarine communities and are exposed to a variety of persistent organic and inorganic pollutants. High levels of mercury have been reported in dolphins from the eastern U.S. coast and the Gulf of Mexico<sup>14,15</sup>. Additionally, elevated organohalogen compounds have been found in dolphins from this region including PCBs and organochlorine pesticides and polybrominated diphenyl ethers (PBDEs) in blubber and perfluoro alkyl compounds (PFCs) in

Dolphins and humans are the only species known to be naturally susceptible to infection with Lacazia loboi.

The high prevalence of lobomycosis in the dolphins of the Florida coastal waters, which are used extensively for human recreational purposes, raises concerns for zoonotic or common source transmission.

#### Anthropogenic

toxins present in coastal waters raises concerns for both dolphin populations and humans.

Marine mammals appear to be good sentinels for the ecosystem and public health effects of HABs. liver<sup>16</sup>. The high concentrations of PFCs and PBDEs are of concern in these dolphin populations as well as in the coastal human populations that are exposed to the same toxins.

#### Harmful Algal Blooms

Harmful algal blooms (HABs) and the potent neurotoxins they produce are associated with mass mortalities of dolphins, sea lions and manatees. The range of biotoxins produced by HABs is extensive and these toxins directly or indirectly impact human health. Biotoxins associated with HABs include: brevetoxins, the cause of neurotoxic shellfish poisoning; saxitoxins, the cause of paralytic shellfish poisoning; okadaic acid, the cause of diarrhetic shellfish poisoning; and others. The HAB problem is significant, growing globally, and posing a major threat to human and ecosystem health. Marine mammals appear to be good sentinels for the ecosystem and public health effects of HABs<sup>1</sup>.

Recent often unprecedented Florida manatee and Atlantic bottlenose dolphin epizootics have been associated with potent marine neurotoxins known as brevetoxins, which are produced by the 'red tide' dinoflagellate *Karenia brevis*<sup>17</sup>. Brevetoxins are known to kill large numbers of fish and cause illness in humans who ingest toxic filterfeeding shellfish or inhale toxic aerosols. The pathogenesis of brevetoxicosis is suspected to involve direct inhalation of toxins (in manatees) or ingestion of toxins in food sources (in manatees and dolphins). New data indicate that brevetoxin vectors such as seagrasses and fish can result in delayed or remote exposure causing intoxication in the absence of toxin-producing dinoflagellates<sup>18</sup>. Manatee mortality resulting from brevetoxicosis may not necessarily be acute but occur after chronic inhalation and/or ingestion and involve the release of inflammatory mediators that result in fatal toxic shock<sup>17</sup>. The inhalational route of brevetoxin exposure in manatees is shared with humans. Increases in human pulmonary emergency room diagnoses are temporally related to 'red tide' occurrences, which may be increasing in frequency along Florida coastlines.

#### Conclusion

Marine mammals are proving to be good sentinels for oceans and human health due to their many unique natural attributes. New opportunities for interdisciplinary and multi-institutional projects are emerging for utilizing marine mammal sentinel species. Additionally, these novel sentinel projects will provide important information in the One Health worldwide strategy for expanding interdisciplinary collaborations and communications in all aspects of health.

#### References

http://www.doh.state.fl.us/Environment/medicine/One\_Health/ MarineMammals\_References.pdf

**Acknowledgments:** Tissues from free-ranging dolphins were collected under National Marine Fisheries Service Scientific Research Permit No.998–1678 issued to G. Bossart as part of the Health and Risk Assessment of Bottlenose Dolphin Project (HERA) conducted in the Indian River Lagoon, Florida, and the coastal waters of Charleston, S.C. Excerpts are reprinted with permission from the North American Veterinary Conference.

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The One Health Commission (OHC) was officially established on June 29, 2009.

Top priorities for the OHC include developing a three year strategic business plan and soliciting major sustaining financial support.

#### Update on the One Health Commission

#### Carina Blackmore, DVM, PhD

The effort that started with Dr. Roger Mahr's vision and the work of the AVMA One Health Initiative Taskforce has come to an end. The One Health Commission (OHC) was officially established on June 29, 2009. We have reported on this project in several issues of the One Health Newsletter. The Board of Directors consists of 8 members representing the not-for-profit, non-government charter organizations that spearheaded the formation of the interim One Health Initiative Joint Steering Committee. These members are: Albert J. Osbahr, III, MD, American Medical Association, Susan Polan, PhD, American Public Health Association, Ronald M. Atlas, PhD, American Society for Microbiology, Michael Cates, DVM, MPH, American Veterinary Medical Association, Elizabeth Bishop, Association of Academic Health Centers, Wile Souba, MD, BSc, MBA, Association of Medical Colleges, James Fox, DVM, MS, Association of American Veterinary Medical Colleges, and John Fischer, DVM, PhD, Association of Fish and Wildlife Agencies. The first organizational meeting of the OHC BOD was held on August 14 in Washington, D.C. The OHC Bylaws were approved at the meeting.

Officers were also elected. Dr. Ron Atlas agreed to serve as the Chair of the OHC. Other officers include Dr. Al Osbahr (Vice-Chair), Mike Cates (Secretary-Treasurer) and Roger Mahr (Chief Executive Officer).

Top priorities for the OHC include developing a three-year strategic business plan and soliciting major sustaining financial support for that plan. The OHC will also continue the work towards a National Academies One Health study in 2010, and a national Summit later this fall. You may access the OHC web site at <u>www.onehealthcommission.org</u>. A copy of the press release announcing the formation of the OHC can be accessed at http://www.onehealthinitiative.com/publications/SCI\_OneHealth.pdf

Dr. Carina Blackmore is a member of the One Health Newsletter editorial board, and Florida's State Public Health Veterinarian.

#### Immuno Valley addresses "One Health" in the Netherlands

#### Arno Vermeulen, PhD and Liana Steeghs, PhD

The One Health initiative is rapidly spreading over the entire globe, creating awareness of the global issues the world is facing, especially where animal and human health are concerned. An increasing population on a global scale, an ageing population in more developed countries, a strong competition for agricultural land, a changing climate and anticipated shortage of fossil energy and drinking water are major concerns, which need to be addressed by every nation and the world as a whole.

Immuno Valley is a consortium of 30 partners from industry, institutions, universities, and central and local government.

Its mission is to bring science into society...

.....by striving to reinforce economic activity in the field of health and life sciences. On the forefront of these challenges, immediate threats originate from lifethreatening emerging infectious diseases. Pandemic H1N1 flu is the most recent example but other diseases such as chikungunya, Rift Valley Fever, West Nile Virus and even Tuberculosis and MRSA are also rapidly spreading around the world, the latter due to increasing resistance to antibiotic drugs. In fact, more than 60% of emerging pathogens are zoonoses meaning that they infect both animals and man. The spread of these diseases have major economic and societal impacts including high treatment costs, disruption of societal structures, and reduced availability of the workforce. Timely anticipation of these threats is a major global objective.

In the Netherlands, the Immuno Valley research institutions and businesses are working closely together to use their synergies to combat infectious diseases of animals and man.

#### **Innovation Network**

Immuno Valley is a consortium of 30 partners (>1000 FTE in the field ) comprisinternationally renowned life science institutions (Utrecht and Amsterdam), the tional Institute for Public Health and Environment, the National Vaccine Institute, the Central Veterinary Institute, Sanquin Blood Supply Foundation, and several small and multinational enterprises in the fields of human and animal pharmaceuticals, cofinanced by the Dutch Ministry of Economic Affairs. The universities are top ranking in Europe and the veterinary faculty of Utrecht are ranked as 3<sup>rd</sup> of the world. Multinational human and veterinary pharma have large R&D facilities based in the Netherlands and partner the Immuno Valley consortium. Spin-offs complete the cluster organization. Dr. Roger Mahr, former president of the American Veterinary Medical Association, spoke at the Immuno Valley kick-off meeting in June 2008, addressing the One Health approach in his video-message, which was greatly appreciated by conference participants.

#### Mission:

Immuno Valley strives to become a network of excellence in infectious disease detection and control.

Immuno Valley creates innovative scientific opportunities supporting a "One Health" proach by treating animal and human health as a single field of study.

Immuno Valley stimulates entrepreneurship by IP consolidation and start-up initiatives.

Immuno Valley promotes cooperation, innovative strength, and commercialization awareness as a prerequisite for acting as an open, results-oriented Life Sciences Network.

#### Focus areas

The Immuno Valley consortium has adopted four focus areas to direct and streamline the research and its commercialization.

<u>Virus discovery</u> as a basis for the surveillance and detection of new diseases. <u>Emerging pathogens</u> to develop the epidemiological tools to study their biology <u>Antibiotic resistance</u> as the cause for re-emergence of bacterial pathogens Vaccine technology as the toolbox to develop sustainable solutions

#### True partnership

The Netherlands have created a unique collaboration structure in the form of public-private partnerships. This means that costs and risks are shared between all stakeholders of innovative research including industry, science institutions and government.

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The final and common goal is faster development of products that serve the health of society in a sustainable manner. This can only be reached by mutual trust and collaboration driven by technological innovations.

#### ALTANT

One Health in Action !

The Immuno Valley research institutions and businesses are working closely together to use their synergies to combat infectious diseases of animals and man.

# The costs and risks are shared between all stakeholders.

The goal is faster development of products that serve the health of society in a sustainable manner.

"By keeping our animals healthy we will create a healthy society and environment that will finally be shown to be sustainable." Antibiotic resistance is a major issue for society as is obvious from the problems in treating Methicillin Resistant *Staphylococcus aureus* (MRSA). The use of antibiotics in livestock is considered a major cause of this widely increasingly occurring resistance and farmers are nowadays held in isolation when they are hospitalized to prevent any possible risk of spreading resistant bacteria inside the clinic.

Immuno Valley has initiated a new research program financed by the Ministry of Agriculture, Nature and Food Safety, in order to develop alternatives to the use of antibiotics in livestock. This research program is named "ALTernatives to ANTibiotics " (ALTANT). The program now runs four different projects each covering a different line of research, from phage therapy, to anti-microbial peptides, phytochemical drugs, and vaccine development. The major pathogens associated with antibiotics use are the target of the program including *Streptococcus suis*, MRSA, coccidiosis, and *E. coli*. With this program, Immuno Valley models the One Health approach, since all of these projects deal with zoonotic pathogens and aim for solutions that on one hand will relieve the pressure on resistance, and on the other hand even be applicable for human use.

This unique collaborative partnership exemplifies the research and innovation climate in the Netherlands and of Immuno Valley in particular.

#### One Health products

Apart from the government and academic institutions, pharma industry also endorses the One Health initiative. The use of vaccines against *Salmonella* in chickens has demonstrated a major reduction of the problem of salmonellosis in man (R. Aerts, Intervet/SPAH). There is also a lot to learn from veterinary vaccine technology when developing products for human use, as has been addressed by Dr. R. Nordgren from Merial Ltd, speaking at the Immuno Valley Biobusiness event in June 2009. Platform technology can be applied in both fields since safety and efficacy profiles of veterinary vaccines reach very high quality standards.

It is therefore predicted that new technological entries will result in products that will solve the threats of emerging diseases. Broader protection against flu strains, easily administered vaccines, and alternative products for antibiotic use in livestock are knocking at the door. By keeping our animals healthy we will create a healthy society and environment that will finally be shown to be sustainable.

#### Join our consortium

The Immuno Valley consortium is open for partnerships and collaboration with other nations ' institutes and industry in order to enhance research and development of these urgently needed products.

Dr. Arno Vermeulen (<u>a.vermeulen@immunovalley.nl</u>) is General Manager and Dr. Liana Steeghs (<u>l.steeghs@immunovalley.nl</u>) is Research Program Manager at Immuno Valley (<u>www.immunovalley.nl</u>). Veterinary and human orthopaedic surgeons share the same problems when it comes to joint arthroplasty therefore the solutions are most likely the same for both physicians and veterinarians.

A multi-disciplinary team of health professionals – veterinarians, physicians, and bioengineers – was assembled to attack this problem from a "one medicine" approach.

The successful use of cells, matrices, and osteochondral allografts for treatment of focal articular defects provided the impetus to expand the concept to complete resurfacing of osteoarthritic joint surfaces.

## Biologic joint replacement strategies for humans and hounds

James L. Cook<sup>1,2</sup>, DVM, PhD; B. Sonny Bal<sup>1,2</sup>, MD, MBA; Eric Lima<sup>3</sup>, PhD; Prakash Jayabalan<sup>1</sup>, MD; Kevin Marberry<sup>1,2</sup>, MD; Matt Smith<sup>2</sup>, MD; Ferris Pfeiffer<sup>1</sup>, PhD; Cristi R. Cook<sup>1</sup>, DVM, MS; Keiichi Kuroki<sup>1</sup>, DVM, PhD; Derek B. Fox<sup>1</sup>, DVM, PhD; Aaron M. Stoker<sup>1</sup>, PhD; Gerard Ateshian<sup>3</sup>, PhD; and Clark T. Hung<sup>3</sup>, PhD

<sup>1</sup>Comparative Orthopaedic Laboratory and <sup>2</sup>Department of Orthopaedic Surgery, University of Missouri, Columbia, MO USA and <sup>3</sup>Cellular Engineering Laboratory, Columbia University, New York, NY USA

Osteoarthritis (OA) is the foremost disability in the world. This pervasive disease negatively affects millions and millions of people and animals worldwide. The costs of OA to the public are in the hundreds of billions of dollars annually. The majority of currently available treatments for OA are palliative at best. While total joint arthroplasty is often considered an optimal treatment for OA as it has very high success rates for pain relief and functional outcomes in the hips of dogs and man, this procedure still cannot be considered ideal based on level of function, potential complications, and longevity of the synthetic implants. In addition, outcomes associated with total joint arthroplasty for shoulders, elbows, knees, and ankles are far from optimal for either species. The major problems that human and veterinary orthopaedic surgeons face in this arena include implant failure, implant-associated inflammatory, immune, and neoplastic reactions, and need for removal or revision. Importantly, these problems, and therefore likely the solutions, are the same for both veterinarians and physicians. As such, we developed a multi-disciplinary team of health professionals - veterinarians, physicians, and bioengineers - to attack this problem from a "one medicine" approach to most broadly and efficiently develop solutions for this major problem.

The concept of "biologic joint replacement" stems from the successful use of cells, matrices, and osteochondral allografts for treatment of focal articular defects. Various methodologies in this category have proven effective for functional replacement of cartilage defects in various joints of dogs, horses, and humans. Incorporation of these biologic implants resulting in long-term preservation of cartilage integrity in the absence of rejection or other detrimental side effects, provided the impetus for us to consider expanding the concept to complete resurfacing of osteoarthritic joint surfaces.

Through a series of collaborative studies, we have been optimizing tissue processing, chondrocyte culture, tissue loading, construct composition, and implantation strategies for creation of patient-specific tissue engineered osteochondral implants for resurfacing shoulders, hips, and knees of dogs and humans.

Our current methodology involves computed tomographic or magnetic resonance imaging of the affected joint in order to create computer-assisted design renderings of molds, which are subsequently fabricated for tissue engineering the construct. Once the mold is created, allogeneic chondrocytes from an "organ donor" are loaded into it in a three-dimensional agarose gel. This chondral gel layer is integrated with an osteo-layer and the construct is cultured in a specific medium while dynamically loaded in the mold in our bioreactor. The biochemical and biomechanical properties of the osteochondral construct can then be optimized prior to implantation into the harsh environment of the osteoarthritic joint.

## One Health in Action !

Patient-specific tissue engineered osteochondral implants for resurfacing hips, knees and shoulders of dogs and humans. In this series of studies, our team has shown that both juvenile and mature chondrocytes can be stimulated using specific culture media and dynamic *in vitro* load-ing protocols to produce engineered cartilage tissue with mechanical properties and composition similar to healthy cartilage; that multiple types of clinically-relevant scaffolds can be used to create functional osteochondral constructs; and that these constructs can be successfully implanted into dogs' knees using currently available surgical techniques and instrumentation with safe and effective short-term outcomes.

Based on this initial success, we are moving this technology forward in the hopes of providing a "one medicine" solution for treatment of end-stage osteoarthritis in humans and hounds.

Dr. James L. Cook is the William C. Allen Endowed Scholar for Orthopaedic Surgery and Director of Comparative Orthopaedic Laboratory at the University of Missouri

Dr. Sonny Bal is an associate professor of orthopedic surgery at the University of Missouri School of Medicine.



## Safety and Health Topics for Workers in the Horseracing Industry

#### Kitty J. Hendricks, MA and John D. Gibbins, DVM, MPH

Horse racing is a popular spectator sport in the United States, with over 125 thoroughbred race tracks found in more than half of the States. Concerns about potential work-related hazards for jockeys and other employees in the horse racing industry were raised at a 2005 hearing by the U.S. House Energy and Commerce Subcommittee on Oversight and Investigations. As a result of these hearings, the Subcommittee Chairman requested that the National Institute for Occupational Safety and Health (NIOSH) evaluate these concerns and provide recommendations for preventing occupational injury and illness risks.

NIOSH provided the subcommittee with a summary report [ PDF 39 KB (7 pages )] of the available scientific literature and with safety and health recommendations. Additionally, NIOSH conducted on-site visits at two locations in Lexington, KY the Keeneland race track and the North American Racing Academy—to interview state racing officials, jockeys, and others, and to collect other information pertaining to safety and health issues. NIOSH also conducted a Fatality Assessment and Control Evaluation (FACE) research investigation of the death of a 63-year-old jockey.

Additionally, in May 2007, NIOSH held a public meeting, "Safety and Health in the Horse Racing Industry and Best Practices." This meeting brought together experts from many different areas of the horse racing industry to discuss safety and health issues. Using the knowledge gained through these efforts, NIOSH released "<u>An Over-view of Safety and Health for Workers in the Horse-Racing Industry</u>" DHHS (NIOSH) Publication No. 2009-128 (April 2009). This document is intended for all workers associated with the horse racing industry, including jockeys, other race track workers, horse and race track owners, and State racing commissions.

The National Institute for Occupational Safety and Health (NIOSH) was asked to evaluate safety and injury concerns in the horse racing industry.

The NIOSH team included a physician, veterinarian, and safety specialists working together on an issue that impacts both human and equine health.

The evaluation and resulting document exemplifies "**One Health**" in practice.

US Navy Fourth Fleet Commander, Rear Admiral Joseph D. Kernan asked the Alliance for Rabies Control to assist in the **USNS Comfort's** medical outreach mission to Latin America. The document provides background information on the horse racing industry in the United States and the inherent safety concerns of working with race horses, data analyses of reported fatal and nonfatal injuries, and known and potential adverse health effects due to exposures and behaviors reported primarily among jockeys.

The document also compares safety equipment requirements for nine states selected based on their prominence in the industry and/or unique features in their regulations. Finally, we make recommendations for areas of future research, and recommend steps that industry representatives (race tracks, racing commissions, and horse owners), jockeys, professional organizations, and others can take to improve the safety and health of employees in the horse racing industry.

This evaluation and document exemplifies **"One Health"** in practice, as the original authors included a physician, veterinarian, and safety specialists working together on an issue that impacts both human and equine health.

*Ms. Kitty J. Hendricks is a research epidemiologist at the National Institute for Occupational Safety and Health, Division of Safety Research in Morgantown, WV.* 

Dr. John D. Gibbins is a veterinary epidemiologist at the National Institute for Occupational Safety and Health, Division of Surveillance, Hazard Evaluations and Field Studies in Cincin- nati, OH

### Global Alliance for Rabies Control as a One Health Program Model

Deborah J. Briggs, MS, PhD, Peter J. Costa, MPH, CHES, and Bruce Kaplan, DVM

As professionals in the field of public health, we are sometimes presented with unusual opportunities that can open doors of new possibilities for educating the students that are on their way to becoming the next generation of global public health professionals. This summer, the Alliance for Rabies Control had one of those rare opportunities and immediately called upon its Partner, the autonomous One Health team (Laura H. Kahn, MD, MPH, MPP, Bruce Kaplan, DVM, Thomas P. Monath, MD and Jack Woodall, PhD) that manages the One Health Initiative website, to determine if we could provide a lifetime training opportunity for a student working in the field of global public health.

It all began with an email contact in mid-February from a most unusual source, the Fourth Fleet of the U.S. Navy. The Alliance was contacted by the Fourth Fleet Commander, Rear Admiral Joseph D. Kernan with an inquiry as to whether we would be interested in joining them on the *USNS Comfort* as it traveled to and docked at several Latin American countries (including Colombia, El Salvador, Nicaragua, and Panama) in an effort to bring professionals in the field of human and veterinary medicine to those in greatest need. Our participation would include sharing rabies educational messages with medical professionals and the general public at every stop made along the voyage. Team members of the Alliance were thrilled to think what we could do with this opportunity but the challenge to organize everything before the ship left in early April was daunting!

After some moments of mental panic about what to do, we contacted Dr. Kaplan

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This was a unique opportunity to share rabies educational messages with medical professionals and the general public

The mission brought rabies educational messages to countries that continue to have a problem with both canine and vampire bat rabies.

The Global Alliance for Rabies Control hopes to find funding to continue their participation in the U.S. Navy outreach efforts. interested in working as a team to find an experienced veterinarian with a background in public health that could represent the Alliance on board of the *USNS Comfort*. After several teleconferences with Dr. Kaplan, we determined that perhaps the best solution at the time was to invite participation by a known veterinarian working toward a degree in the field of public health who may be interested in participating in an international field experience as part of their Masters of Public Health program. Within a very short time, Roberta L. Hughes, DVM, of Bradenton, Florida was offered the position and accepted. She was in the process of looking for an externship in the field of global health as a student at the University of South Florida 's College of Public Health. Plans were quickly put in place to secure the necessary travel vaccinations and malaria prophylaxis for Dr. Hughes.

Peter J. Costa, MPH, CHES, the Global Communications Coordinator for the Alliance contacted a number of our Partner organizations and secured a generous donation of educational material in Spanish from the Ministry of Health in Chili and from the American Veterinary Medical Association. Posters conveying messages about how to prevent human rabies were donated from Sanofi Pasteur and all educational material was quickly shipped to the *USNS Comfort* prior to its leaving port. Soon the mission was underway and through the joint efforts of our Partners, the Alliance was able to participate in bringing educational messages about rabies and other diseases to several Latin American countries.

In reviewing our own 'lessons learned' during the preparation and the actual mission of the *USNS Comfort*, we are confident that we were successful in bringing rabies educational messages to several countries that continue to have a problem with both canine and vampire bat rabies. Additionally, the trip itself served as an excellent training opportunity for our educational " a mbassador " veterinarian to learn about veterinary diseases not commonly, if ever, seen in the United States. For example, members of the ship's medical team were able to visit the screw worm eradication project in Panama and learn first hand about how the surveillance system to keep this disease from spreading was operational at the time.

The Alliance also learned some valuable lessons about how to better prepare for the next mission and sincerely hopes that we will be able to find financial support to continue to participate with the U.S. Navy and their continuing medical outreach throughout the world. In so doing, we hope to create a ripple effect that continues to influence the way we approach global health. The plan of establishing a long lasting educational strategy out of seemingly 'nowhere ' takes a bit of getting used to.

The concept of promoting rabies prevention and control plus that of other zoonotic diseases within the context of the One Health concept represents a paradigm shift that promises to be mutually advantageous, sustainable and synergistic.

#### References

http://www.doh.state.fl.us/Environment/medicine/One\_Health/ GlobalAllianceRabies\_References.pdf

Dr. Deborah J. Briggs is the Executive Director of the Global Alliance for Rabies Control. She is also Adjunct Professor, Diagnostic Medicine/Pathobiology and consultant to the Rabies laboratory at the College of Veterinary Medicine, Kansas State University, Manhattan, Kansas. <u>Dibriggs2004@yahoo.com</u>.

*Mr.* Peter J. Costa currently serves as the Global Communications Coordinator for the Rabies Alliance and its flagship initiative World Rabies Day Campaign.

Dr. Bruce Kaplan is the primary contents manager of the One Health Initiative website and serves on the One Health Newsletter's editorial board.

## **One Health in Action !**

Professionals from different backgrounds and areas of expertise collaborating to advance scientific knowledge for the benefit of all.

Veterinarian Sean Altekruse teamed up with fellow NCI researchers Katherine McGlynn and Marsha Reichman to analyze the increasing rate of hepatocellular carcinoma.

In recent years, the greatest increase in HCC incidence rates was seen among white, African American and Hispanic men between 50 and 59 years of age.

#### Liver Cancer Incidence Continues Steep Climb

Sean F. Altekruse, DVM, MPH, PhD, Katherine A. McGlynn, Ph.D., M.P.H. and Marsha E. Reichman, Ph.D., MS

A new National Cancer Institute (NCI) study in the March 2009 Journal of Clinical Oncology offers both good and bad news about the leading form of liver cancer, hepatocellular carcinoma (HCC), according to the study 's lead author, Sean Altekruse, a veterinary epidemiologist with NCI 's Division of Cancer Control and Population Sciences. Between 1975 and 2005 the research team found that HCC incidence rates tripled. However, between 1992 and 2005, HCC survival improved, with 1-year survival rates doubling.

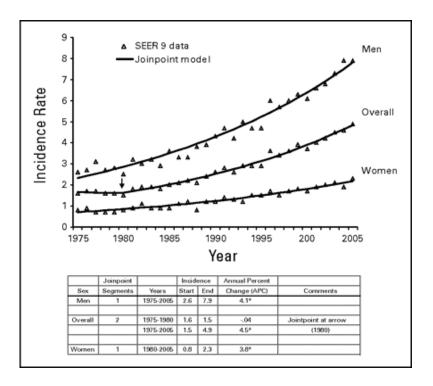


Fig 1. Annual age-adjusted incidence rates per 100,000 and trends, all hepatocellular carcinoma cases and by sex, 1975 to 2005 (Surveillance, Epidemiology, and End Results 9 [SEER9]). (\*) The overall join-point model had two segments, with a change point at 1980 (arrow).

The research team analyzed data from NCI 's Statistics, Epidemiology, and End Results (SEER) Registries. Overall, HCC incidence rates increased from 1.6 cases per 100,000 people in 1975 to 4.9 per 100,000 in 2005. Consistent with previous findings, HCC incidence rate among men were three times higher than among women. From 1992 to 2005, when more detailed racial information were available, the most significant increases in HCC incidence rates occurred among American Indians and Alaska Natives, followed by African Americans, whites, and Hispanics. While overall HCC incidence rates remained highest among Asians and Pacific Islanders, the increase in incidence trends for this race was relatively modest.

In recent years, from 2000 to 2006, the greatest increase in incidence rates was seen among white, African American and Hispanic men between 50 and 59 years of age. "Although the study could not determine why liver incidence rates are increasing, these trends may be partially attributable to an increase in chronic infections with hepatitis C virus, which together with hepatitis B virus is a major risk factor for liver

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There has been a steady increase in age-adjusted HCC incidence rates among men and women since 1975.

The 1-year overall

survival rates are

still below 50 per-

cent.

cancer, " said Katherine McGlynn, PhD, senior author and a Principal Investigator with NCI 's Division of Cancer Epidemiology and Genetics. Several findings in this report suggest, however, that risk of HCC is likely to be driven by additional factors. The steady increase in age-adjusted HCC incidence rates among men and women since 1975 with increasing age-specific rates in each successive birth cohort between 1900 and 1959 are not consistent with the view that a hepatitis C virus epidemic in the 1960s alone is driving the increase in HCC. Etiologic studies of newly diagnosed HCC patients are needed to elucidate factors contributing to the ongoing increase in HCC incidence. Potential factors include weight, diabetes mellitus, cirrhosis, or iron storage diseases. "This research is vital to preventing HCC rates from rising further," said coauthor Marsha Reichman, Ph.D.

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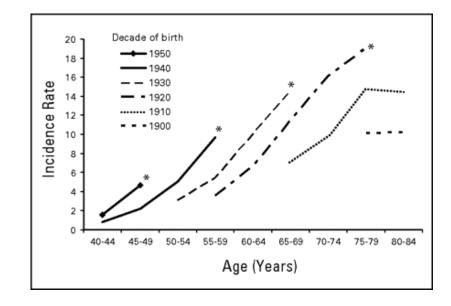


Fig 2. Age-specific hepatocellular carcinoma incidence rates per 100,000 by decade of birth (cohort), 1975 to 2005 (Surveillance, Epidemiology, and End Results 9).

The survival improvements may be due to tumors being diagnosed at earlier stages, when they are potentially curable. The study authors stressed that with 1-year overall survival rates still below 50 percent, there is much room for improvement. More screening of at-risk groups and treatment of localized-stage tumors may further increase HCC survival rates in the United States. The advent of targeted HCC therapies also holds promise for improvements in prognosis for patients with regional and distant-stage HCC. "This report provides reason for optimism that, with more HCC screening of high-risk groups and treatment of low-stage disease, the burden of HCC can be lessened, " the authors wrote.

#### **Reference:**

1. Altekruse SF, McGlynn KA, Reichman ME. Hepatocellular cancer incidence, mortality and survival trends in the United States from 1975 to 2005 J Clin Oncol 2009;27:1485-91

Dr. Sean Altekruse is an epidemiologist with the Cancer Statistics Branch, Division of Cancer Control and Population Sciences, National Cancer Institute.

Dr. Katherine McGlynn is a tenured Principal Investigator at NCI, internationally recognized as an expert in the field of hepatocellular carcinoma epidemiology.

Dr. Marsha Reichmann is Senior Advisor of the Biospecimens and Bioinformatics in the Division of Cancer Control and Population Sciences at the National Cancer Institute.

With more HCC screening of high-risk groups and treatment of low-stage disease, the burden of HCC can be lessened.

Although this article was originally prepared by the Florida Department of Agriculture and Consumer Services and the Florida Department of Health for veterinarians, it is a useful background piece for anyone interested in familiarizing themselves with the current spectrum of influenza viruses.

#### A Quick Guide to Influenza Viruses

#### Introduction

As the veterinarian is the only health care professional likely to see both people and their animals, they must have an awareness of the potential threat of zoonotic diseases. With the recent spread of novel H1N1 Influenza (Swine Flu) and the H5N1 Highly Pathogenic Avian Influenza, this responsibility has never been more important.

#### Influenza Virus

Influenza, commonly referred to as the flu, is an infectious disease caused by RNA viruses of the family Orthomyxoviridae, which affects birds and mammals. Influenzas are broadly divided into three types: A, B, and C. Influenza A viruses are found in many different animals and influenza B viruses circulate widely only in humans. Influenza C viruses are known to infect humans and swine, but are rarely encountered when compared to types A or B.

Influenza A viruses are divided into subtypes based on two proteins on the surface of the virus: the hemagglutinin (H) and the neuraminidase (N). There are 16 different hemagglutinin subtypes and 9 different neuraminidase subtypes, all of which have been found among influenza A viruses in wild birds. Wild birds are the primary natural reservoir for all subtypes of influenza A viruses and are thought to be the source of influenza A viruses in all other animals.

Typically, influenza is transmitted through the air by droplets containing the virus. Influenza can also be transmitted by bird droppings, saliva, nasal secretions, feces, and blood. Infection can also occur through contact with these body fluids or through contact with contaminated surfaces.

The influenza virus is easily killed by disinfectants commonly used in veterinary facilities, such as quaternary ammonium compounds and bleach solutions. Animals showing signs of influenza infection should be isolated. Clothing, equipment, surfaces, and hands should be cleaned and disinfected after exposure to these animals.

#### Canine Influenza

The first recognized outbreak of canine influenza is believed to have occurred in racing greyhounds in January 2004 at a track in Florida. The canine influenza virus is closely related to the virus that causes equine influenza and it is thought that the equine influenza virus mutated to produce the canine influenza virus.

Canine influenza virus causes clinical disease that mimics kennel cough. As a result, infection with the virus is frequently mistaken for infections caused by the *Bordetella bronchiseptical* parainfluenza virus complex. Two clinical syndromes have been reported—a mild form of the disease and a more severe form that is accompanied by pneumonia. Fatal cases of pneumonia resulting from infection with canine influenza virus have been reported in dogs, but the fatality rate ( 5 % to 8%) has been low. There is no evidence of transmission of canine influenza virus from dogs to

Canine Influenza, first recognized in racing greyhounds in January 2004 at a track in Florida, is thought to have jumped species from the equine influenza virus (H3N8).

On-going concerns about the H5N1 virus and the recent spread of novel H1N1 virus (Swine Flu) have brought influenza into the limelight.

humans or other animal species.

A canine influenza H3N8 vaccine received conditional approval from the USDA in May, 2009.

Young foals lacking adequate maternal antibodies are at particular risk of developing a rapidly fatal viral pneumonia from equine Influenza.

Wild birds are the natural hosts of avian influenza viruses.

Avian influenza is broadly divided into highly pathogenic (HPAI) and low pathogenic (LPAI) strains based on its ability to cause disease in poultry. A canine influenza H3N8 vaccine manufactured by Intervet/Schering Plough received conditional approval from the USDA in May. The vaccine has been available to veterinarians since June. While this vaccine does not induce sterilizing immunity, it does significantly reduce virus replication and associated pathology in the lungs, the severity and duration of clinical disease, and the amount and duration of virus shedding. This means that vaccinated dogs that become infected are less likely to have severe symptoms and are not as contagious to other dogs. The kennel cough (*Bordetella bronchiseptica* /canine parainfluenza complex ) vaccine does not provide protection against canine influenza.

#### **Equine Influenza**

Equine influenza affects horses, donkeys, mules, and other equidae. The virus is widespread with only Iceland, New Zealand, and Australia considered to be free of the virus.

Equine influenza virus causes clinical disease of the upper respiratory tract. The virus spreads rapidly, and naïve or immunocompromised horses are at higher risk of developing disease. Colic and edema of the legs and scrotum have also been observed with influenza infection. In the absence of secondary complications, healthy, adult horses usually recover within one to two weeks; however, coughing may persist for a longer period. Young foals lacking adequate maternal antibodies are at risk of developing a rapidly fatal viral pneumonia.

There is evidence that equine influenza can be transmitted to humans, but this occurrence is rare. Inactivated intramuscular and intranasal vaccines are commercially available for prevention of influenza in equids.

#### Avian Influenza

Avian influenza has appeared periodically in regions all over the world, including the United States. The virus spreads easily among wild birds, which are the natural hosts of avian influenza viruses, but certain strains can also infect domesticated birds.

Avian influenza is broadly divided into highly pathogenic (HPAI) and low pathogenic (LPAI) strains based on its ability to cause disease in poultry. Low pathogenic avian influenza is a natural infection of waterfowl that may cause few, if any, signs of disease in domestic poultry and wild birds. Highly pathogenic avian influenza is rarely found in waterfowl, but causes severe disease in domestic poultry with a high case fatality rate.

Clinical signs include diarrhea, sneezing, gasping for air, nasal discharge, coughing, lack of energy and appetite, swelling of tissues around eyes and in neck, purple discoloration of wattles, combs, and legs, depression, muscular tremors, drooping wings, twisting of head and neck, incoordination, complete paralysis, and sudden death.

Avian influenza is found in secretions from the nares, mouth, and eyes of infected birds and is also excreted in their feces. It is most often spread by direct contact between infected and healthy birds. It may also be spread indirectly through contact with contaminated equipment, materials or feces.

H5N1 Highly Pathogenic Avian Influenza (H5N1 HPAI) has infected birds in Asia, Europe, and Africa since the end of 2003.

To date, H5N1 HPAI has not been found in birds in North America, including the United States.

Outbreaks of swine influenza are most commonly associated with commercial herds during the introduction of new animals.

The risk of contracting avian flu is not particularly high for pet birds in the United States. Pet birds should not be allowed to interact or have contact with wild birds or their feces.

Some strains of avian influenza have infected humans and a variety of other mammals. Avian influenza vaccines are available and used primarily in commercial flocks.

#### H5N1 Highly Pathogenic Avian Influenza (Asian strain)

H5N1 Highly Pathogenic Avian Influenza (H5N1 HPAI) has infected birds in Asia, Europe, and Africa since the end of 2003. This particular form of avian influenza is deadly to most domestic poultry and some wild birds, and can spread rapidly in flocks.

To date, H5N1 HPAI has not been found in birds in North America, including the United States. However, if H5N1 HPAI is identified in North America, everyone, including veterinarians and pet owners, should be aware of the potential of H5N1 HPAI to cause disease and death in animals and humans.

H5N1 HPAI can infect wild and domestic birds and poultry, humans, domestic cats, and dogs. Swine, palm civets, cynomolgus macaques, New Zealand white rabbits, stone martens, tigers, leopards, and rats can also become infected with the H5N1 HPAI virus. Ferrets are very susceptible to H5N1 HPAI infection, as well as other human influenza viruses. Cats are not usually susceptible to avian influenza viruses; however, a research study published in September 2004 demonstrated that domestic cats can become infected with the H5N1 HPAI virus and are capable of transmitting the virus to other cats. Like cats, dogs are not usually susceptible to avian influenza viruses; however, an unpublished study performed in 2005 by the National Institute of Animal Health in Bangkok indicated that dogs could be infected with the virus. No clinical disease was detected in association with that study. This limited information is insufficient to determine how susceptible dogs are to the virus. Pet birds are susceptible to infection with avian influenza viruses, however, because the H5N1 HPAI virus has not yet been identified in the United States, risk of infection for pet birds is very low.

Humans are susceptible to H5N1 HPAI infection. There are no commercial vaccines for H5N1 HPAI in birds and animals available in the United States.

#### Swine Influenza

Swine influenza is a respiratory disease that regularly causes illness in swine. It is generally found in North and South America, Asia, and Europe and has been reported in Africa.

Outbreaks of swine influenza are most commonly associated with commercial herds during the introduction of new animals. Most affected swine will recover within five to seven days in the absence of complications. Severe bronchopneumonia may develop as a secondary complication, and is a high risk factor for mortality. Once introduced, the swine influenza virus may become endemic in herds. Annual outbreaks may be observed, primarily during the colder months of the year. Young, naive pigs are at increased risk of infection.

Some strains of swine influenza have infected humans; however, reports are infrequent and infections are typically not spread from person to person. Virus transmission has been documented in public settings such as fairs and exhibitions. People can also transmit human influenza to swine.

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Pet swine can be protected by getting them vaccinated against the most commonly encountered strains of swine influenza.....

....and by keeping them away from other swine that are suspected to have a swine influenza infection and away from humans suspected to have human influenza.

Properly prepared pork poses no threat of H1N1 virus transmission from swine food products to humans. Clients with pet swine should take precautions to protect their pet against any strain of influenza that is known to affect swine. These precautions may include having the pet vaccinated against swine influenza and keeping the pet away from other swine that are suspected to have a swine influenza infection and humans suspected to have human influenza. Commercial vaccines are available against the most commonly encountered strains of swine influenza.

#### Novel H1N1 Influenza (Swine Flu)

While called "swine flu," the novel H1N1 influenza virus appears to at some point in the past have jumped from swine to people and evolved into a human disease. This virus readily spreads from person to person. When the human outbreak was first detected in April 2009, the virus had never been isolated from swine.

Cooperative State/Federal novel H1N1 swine influenza surveillance procedures have been established for swine in the United States. To date, no infections have been reported in swine in the United States. Due to the low number of domestic swine in Florida, and the fact that most are not raised in commercial confinement operations but in backyard herds, the risk of introduction and spread of the novel H1N1 virus in Florida swine is small. There have been a few cases reported in other countries which produced a mild to moderate illness in swine. Swine that recover from the illness are no longer infectious. Novel H1N1 swine influenza testing is available at the Kissimmee Animal Disease Diagnostic Laboratory and national USDA laboratories.

Properly prepared pork poses no threat of virus transmission from swine food products to humans. At this time, there is no commercially available vaccine for the novel H1N1 influenza virus in swine.

The novel H1N1 influenza virus is continuing to spread in the human population. The virus has shown no change in virulence and remains predominantly in the 5-24 and 25-49 year old age groups. When the vaccine becomes available, vaccinations will be voluntary. There has been no suggestion of mandatory vaccinations for any age group.

#### Conclusion

Influenza viruses, particularly avian and swine influenza viruses, have been shown to be transmissible between species with animal-to-people and people-to-animal transmission possible. Veterinarians should take safeguards to prevent disease passage to themselves and their staff and take steps to reduce human and animal exposure. The use of gloves, protective clothing, masks, and eyewear by their staff when warranted and limiting human and animal exposure to affected people and affected animals are recommended. For more information, please visit: <a href="http://www.nasphv.org/Documents/VeterinaryPrecautions.pdf">http://www.nasphv.org/Documents/VeterinaryPrecautions.pdf</a>.

Avian Influenza is a reportable animal disease in Florida. Although not a reportable animal disease, any suspected novel H1N1 influenza infection in swine should be reported as well. Any veterinarian with questions regarding these animal diseases or their public health significance should contact the Florida Department of Agriculture and Consumer Services, Division of Animal Industry (State Veterinarian, ) at (850) 410-0900 or the Florida Department of Health (State Public Health Veterinarian ) at (850) 245-4299. The goal is to prevent the spread of this novel virus or any other influenza (flu) virus from people to pigs and from pigs to people. CDC Interim Guidance for People who have Close Contact with Pigs in Non-Commercial Settings: Preventing the Spread of Influenza A Viruses, Including the Novel Influenza A (H1N1) Virus August 5, 2009 5:00 PM ET http://www.cdc.gov/h1n1flu/guidelines\_pig\_workers.htm

This document has been updated in accordance with the CDC Recommendations for the Amount of Time Persons with Influenza-Like Illness Should be Away from Others. This document provides interim guidance and will be updated as needed.

As of June 26, 2009, the novel influenza A (H1N1) virus has not been found in any pigs within the United States, but has been detected in pigs on a farm in Alberta, Canada. This interim guidance is issued with the goal of preventing the spread of this novel virus or any other influenza (flu) virus from people to pigs and from pigs to people.

The following interim recommendations are based on what are deemed **minimal** precautions for protecting people exposed to **pigs known or suspected to have influenza** on premises not used for commercial production (e.g. small backyard or hobby farms, zoo settings including petting zoos, homes with pet pigs) AND for protecting pigs from people with influenza.

#### Recognizing the signs of flu in pigs

Flu viruses are thought to spread from infected people and pigs to other people and pigs mostly through coughing or sneezing, and through contact with surfaces contaminated by flu viruses. To prevent flu viruses from spreading between people and pigs, it is important for people working with pigs to recognize the signs of flu in pigs. Typically a combination of signs will occur together in infected pigs. Signs of flu in pigs can include any of the following:

- sudden onset of fever
- lethargy, lack of alertness
- going off feed (poor appetite)
- coughing (barking)
- discharge from the nose or eyes, eye redness, or inflammation
- sneezing
- breathing difficulties

If a pig is showing these signs, even mildly, you should call your veterinarian. Do not allow sick pigs to enter your farm or facility and do not move sick pigs off your property.

#### Recognizing the signs of flu in people

To prevent spread of flu viruses from people to pigs, you should also be aware of the signs of flu in people. Flu-like symptoms in people can include any of the following:

- fever
- cough
- sore throat

It is important for people working with pigs to be able to recognize the signs of flu in pigs....

.....and in people.

- runny or stuffy nose
- body aches
- headache
- chills
- fatigue
- possibly vomiting or diarrhea

#### Preventing spread of flu viruses from pigs to people

If possible, people should avoid getting close (within 6 feet) to pigs known or suspected to be infected and/or their environment. However, if you must come in contact with pigs known or suspected to be infected, or their environment, you should use appropriate protective measures and practice good personal hygiene.

When entering barns or areas where sick pigs are present, wear protective clothing. This can include disposable coveralls or barn clothes that are laundered after each use and shoes or boots that can be disinfected. This will limit your chances of getting flu from the pigs and from spreading flu virus to other people or pigs. Barn clothes should ideally be laundered at the barn. If clothes must be taken home they should be placed in a plastic bag and laundered separately from non-work family clothing. When working around sick pigs, you should avoid touching or rubbing your eyes, nose, and mouth. Ideally, you should wear goggles and a disposable NIOSH-certified N-95 (or greater) filtering face-piece respirator. Disposable gloves or gloves that can be disinfected after use should be worn. Disposable gloves should be taken off by turning them inside out over the hand and placed in the trash after use.

Hands should be washed after contact with animals or their environments, equipment and surfaces that are possibly contaminated, and after removing gloves and/ or contaminated clothing. Hands should be washed thoroughly for 20 seconds with soap and running water after gloves are removed. Use <u>alcohol-based gel hand cleaners\*</u> if soap and water are not available.

Commonly used disinfectants, such as quaternary ammonium compounds and 10% bleach solutions, will kill flu viruses. Equipment and surfaces that have been in contact with sick pigs should be thoroughly cleaned and disinfected with products registered for use against flu viruses. More information on disinfectant use can be found at: http://www.epa.gov/oppad001/influenza-disinfectants.html.

#### Steps to take if you develop flu-like symptoms

If you become ill with flu-like symptoms you should take the following steps:

- Seek medical care or advice. Your healthcare provider will decide if testing or treatment is needed. Be sure to tell your healthcare provider if you were in contact with pigs.
- Keep away from others as much as possible. This is to keep from making others sick.
- Stay home for at least 24 hours after your fever is gone except to get medical care or for other necessities. (Your fever should be gone without the use of a fever-reducing medicine).
- Practice good personal hygiene, such as covering your nose and mouth with a tissue when you cough or sneeze. If tissues are not available, cough or sneeze into your upper sleeve. Wash your hands often with soap and warm water. Alcohol-based gel hand cleaners are also effective\*.

Use appropriate protective measures and practice good personal hygiene if you must come in contact with pigs that may have influenza.

Wash your hands after coming in contact with animals, their environments, or equipment and surfaces that could be contaminated. Persons at increased risk for having severe illness from influenza and household contacts of these persons should get seasonal flu vaccine every year.

If your pig became

ill two weeks before

or after contacting a

person with flu-like symptoms, notify

your veterinarian.

Persons at higher risk for complications from flu

Certain groups of people are at increased risk of becoming severely ill with influenza. These groups include children younger than 5 years, persons 65 years and older, and pregnant women. Also included are persons of any age who have certain medical conditions (including those immunosuppressed because of medications or HIV). Individuals in these groups may choose to avoid direct animal contact. Persons at increased risk for having severe illness from influenza and household contacts of these persons should get seasonal flu vaccine every year (see <u>http://www.cdc.gov/flu/</u> protect/vaccine/index.htm).

#### Preventing spread of flu virus from people to pigs

Influenza is occasionally transmitted from people to pigs. If you have been diagnosed with flu or if you develop flu-like symptoms, take the steps listed above: seek medical care, limit your contact with others, and practice good personal hygiene. In addition to limiting your contact with people, you should avoid contact with pigs. You should also contact your veterinarian if you note signs of flu in a pig. Notify your veterinarian if the pig became ill two weeks before or after contacting a person with flu-like symptoms.

#### Additional resources

- •CDC H1N1 Flu website
- •USDA Website
- •National Pork Board 🖻



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#### The Case For A "One Health" Paradigm Shift

Bruce Kaplan, DVM and Mary Echols, DVM, MPH

#### The One Health concept calls for a merging of perspectives from within human and veterinary medical disciplines.

A public health emergency declared due to the newly emerged "swine flu" virus (H1N1) was recently classified as a worldwide pandemic. This is definitely an indication of impending similar, serious "brewing storms". Since 1998, public health officials and scientists have been speculating about this with the avian flu (H5N1) virus strain. Fortunately, this has not evolved yet and may never do so. But, make no mistake; we are on the precipice of unpleasant health and health care threats that need to be addressed.

These influenza events, plus the fact that approximately 75% of recently emerging infectious diseases affecting humans are diseases of animal origin, strongly suggest the need for a paradigm change on how public health approaches these phenomena called "zoonotic diseases", i.e. diseases transmissible from animals to man.

Today, many institutional, geographic, and financial barriers often prohibit meaningful interactions among experts. The result is that surveillance, research,

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Effectively combating zoonoses as well as chronic illnesses that affect humans and animals will require a "One Health" approach.

Scientists and health professionals from all disciplines must work together without regard to "turf" barriers.

Peter Doherty (veterinarian) and Rolf Zinkernagel (physician) received the 1996 Nobel Prize for their discovery of how the immune system recognizes virus-infected cells.

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prevention, and control measures for cross-species infections like influenza and dangerous bacteria emerging from antibiotic resistance, like those demonstrated by methicillinresistant *Staphylococcus aureus* (MRSA) between pigs and people, have been short changed. This deficit must be rectified in order to pursue an enlightened course of modern health and health care for this generation and for generations to come.

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The 1918-1919 influenza pandemic killed 50 to 100 million people worldwide. Emerging influenza viruses have been isolated from a variety of animals, including humans, pigs, horses, wild and domestic birds, and sea mammals. The recent events caused by swine flu came to light only when human cases occurred. The interval between cross-species spread and the declaration of a public health emergency was extremely brief, a matter of days. It is reasonable to ask: could surveillance for the emergence of new strains of flu be more effective if targeted at animals—the " mixing pot " of flu virus evolution? Could we develop more effective tools to identify strains with potential to spill over from animals to humans?

Besides influenza, other animal diseases are transmissible to humans. Hantaviruses exist in various rodent reservoirs where the hosts are persistently infected without disease symptoms. Specific hantaviruses transmitted from the contaminated urine and feces of infected rodents cause two important human diseases, hemorrhagic fever with renal syndrome (HFRS) and hantavirus-pulmonary syndrome (HPS). Nipah virus is a newly discovered virus of fruit bats responsible for encephalitis outbreaks in southeast Asia. West Nile, a virus of birds, invaded the U.S. in 1999 and is now endemic. Emerging bacterial disease agents can be transmitted by food animals including E. coli 0157:H7, various Salmonella species, Campylobacter species, and Streptococcus iniae (from farmed fish). Leptospirosis is the most common rattransmitted disease in the United States.

Combating zoonoses effectively will require a "One Health" approach—an interdisciplinary collaborative model for prevention and control of infectious disease epidemics, as well as chronic illnesses (e.g. cancer, obesity, orthopedic prosthetics, genetics, and others) that affect humans and animals. Physicians, veterinarians, ecologists, environmental scientists, laboratory animal specialists, and other health science-related disciplines must work together, equally without regard to "turf" barriers.

#### ACHIEVEMENTS THROUGH INTEGRATION

The One Health concept promotes the integration of human, animal, and environmental health by communication and collaboration among multiple disciplines. Successful One Health examples during the late 19th century and 20th century include:

*Yellow Fever* - In 1893, Theobald Smith ( physician ) and Frederick L. Kilborne ( veterinarian ) published a seminal paper on Texas cattle fever transmitted by ticks that set the stage for Walter Reed 's discovery of yellow fever transmission via mosquitoes.

*Anthrax* - In 1903, John McFadyean (veterinarian with a degree in veterinary medicine and medicine) published a paper on "McFadyean methylene-blue reaction in anthrax", still referred to and recognized in microbiology texts.<sup>2,3</sup> It is currently noted as "the ideal method for demonstration of the [anthrax] capsule."<sup>4</sup> McFadyean is regarded as the founder of modern veterinary research.

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Karl Johnson and Fred Murphy's long term collaboration on zoonotic viruses truly exemplifies the concept of One World, One Medicine, One Health.

Drs. Cook and Bal collaborate on efforts to provide a "one medicine" solution for the treatment of end-stage osteoarthritis in humans and hounds. *Tuberculosis* - In 1921, Albert Calmette ( physician ) and Jean-Marie Camille Guerin ( veterinarian ) collaborations resulted in the "BCG" Tuberculosis vaccine that, along with the use of streptomycin, was credited with a dramatic reduction in the human toll from Tuberculosis caused by Mycobacterium bovis contracted by contact from infected cattle.

*Immune System* - In 1996, Rolf M. Zinkernagel (physician) and Peter C. Doherty (veterinarian) won the Nobel Prize for discovering how the body 's immune system distinguishes normal cells from virus-infected cells.<sup>5,6</sup>

#### ONE HEALTH COLLABORATIONS ADVANCE SCIENCE

In 1976, Frederick A. Murphy (veterinarian) and Karl M. Johnson (physician) worked closely together (along with others) to help unravel the mystery surrounding the initial outbreak of Ebola hemorrhagic fever and discovered its etiologic agent, Ebola virus<sup>5,6</sup>

Karl M. Johnson, MD is Past Director, Middle America Research Unit - NIAID, NIH Founding Chief -Special Pathogens Branch, CDC (retired). Commenting on their work together, Johnson noted, "Fred Murphy and I collaborated on zoonotic viruses, their pathogenesis, epidemiology, and ecology; initially at great distance but later in daily contact at CDC. Although Ebola virus was perhaps the most notable project, our work over many years truly exemplifies the concept of One World, One Medicine, One Health. My prayer is that support, both scientific and financial, for the marriage of human and veterinary medicine will grow at an ever expanding rate. The earth requires it. "

Fred Murphy, DVM, PhD, University of Texas Medical Branch, Department of Pathology, reflected on the work of some of the pioneers. He stated, "My recent delving into the foundations of medical and veterinary virology has provided much evidence of common roots and incredible early interplay, much more than we see today. For example, Walter Reed and his colleagues, the discoverers of the first human virus, yellow fever virus, acknowledged the influence of Friedrich Loeffler and Paul Frosch, who had discovered the first virus, foot-and-mouth disease virus, a few years earlier.

"From my reading, it was Sir William Osler, the founder of modern human medicine and of veterinary pathology, who in the late 1800s coined the term 'O ne Medicine'. Calvin Schwabe, the inspiring veterinary epidemiologist from UC Davis, has been credited with revitalizing the concept, and now it seems that the concept is gaining new breadth and depth, thanks to the efforts of the One Health Initiative. As others have noted, bringing substance to the concept, shaking up institutions and individuals, will require a difficult and long-term effort, especially as this applies to the interplay of physicians, veterinarians, and biological scientists in biomedical research and in the scholarly base for public health—but, as [golfer] Arnold Palmer said, "Never up, never in."

In an impressive One Health example in the 21st century, veterinarian James "Jimi" Cook, DVM, PhD, a University of Missouri-Columbia college of veterinary medicine Professor of Orthopedic Surgery, and physician B. Sonny Bal, MD, JD, MBA, Associate Professor of Orthopedic Surgery college of medicine have been investigating practicable clinical medicine betterment in the field of orthopedics—for humans and animals. Drs. Cook and Bal have collaborated for about seven years on efforts to create hip and knee replacements without using commonplace biomechanical metal and plastic materials. The technique being developed by Cook for dogs involves use of

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Ronald Davis, MD and Roger Mahr, DVM collaborated to establish a bond between the AMA and AVMA.

The One Health concept is expanding globally within public health and academic circles.

However, it is not widely known among practicing physicians, veterinarians, news media, or the general public.

There in lies the next challenge.....

laboratory grown tissue (cartilage) that can be molded into replicas of joints that require replacement. Bal and Cook are jointly developing a process whereby a similar process can be adapted for humans.<sup>7</sup>

Following a June 2009 story in the Missourian where both men were recognized for their important biomedical research, Dr. Bal commented, "Jimi Cook and I have worked alongside a team of specialists from medicine, veterinary medicine, and engineering for seven years now. Our current focus is to develop replacement joints that mimic the natural process of cartilage and bone formation as they grow and develop. This kind of collaboration is essential to the creation of better options for the replacement of failing hips and other joints. By working with specialists in the veterinary field, we are able to evaluate our technology more rapidly, and that means that we will be able to develop these alternatives for humans sooner than if we worked alone."

#### **ONGOING EFFORTS**

The early 21st century physician and former President of the American Medical Association, Ronald Davis, MD [now deceased] collaborated with the former President of the American Veterinary Medical Association, Roger K. Mahr, DVM helping to establish a bond between the AMA and AVMA. Davis skillfully shepherded an historic One Health supportive resolution through to adoption by the AMA membership—a major milestone in the progress of this modern day One Health movement.

In July 2007, Dr. Davis said, "I'm delighted that the AMA House of Delegates has approved a resolution calling for increased collaboration between the human and veterinary medical communities and I look forward to seeing a stronger partnership between physicians and veterinarians. Emerging infectious diseases, with the threats of cross-species transmission and pandemics, represent one of many reasons why the human and veterinary medical professions must work more closely together ".

A large number of North American professional organizations have endorsed the One Health concept. Among these are the American Medical Association; American Veterinary Medical Association; American Society for Tropical Medicine and Hygiene; Association of American Medical Colleges; and American Association of Veterinary Medical Colleges. Globally, One Health has been recognized by the Immuno Valley Consortium in The Netherlands; the Indian Veterinary Public Health Association; The Institute for Preventive Veterinary Medicine and Food Safety, Lazio and Tuscany Regions, Italy; the Italian Society of Preventive Medicine; the Corporation Red SPVet, Bogota, Colombia; and others.

A recent One Health monograph—containing 13 diverse essays—was published in the European Journal, *Veterinaria Italiana*. It provides a strong scientific international case for implementing the One Health model worldwide. It is the product of 53 prominent interdisciplinary professionals (physicians, veterinarians, and health scientists) from twelve countries<sup>1</sup>.

#### CONCLUSION

The One Health concept is a global strategy that is expanding within public health and academic circles. However, it is not widely known among practicing physicians, veterinarians, news media, or the general public. Once implemented, the synergism achieved will advance health care for the 21st century and beyond by accelerating biomedical research discoveries, enhancing public health efficacy,

expeditiously expanding the scientific knowledge base, and improving medical education and clinical care. Seeking essential practicable "out of the box" scientific knowledge will most likely require a mind merging of various perspectives from within human and veterinary medical disciplines as well as others.

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Dr. Bruce Kaplan is the primary contents manager of the One Health Initiative website and serves on the One Health Newsletter's editorial board.

Dr. Mary Echols is an Environmental Consultant with the Palm Beach County Health Department and is the Editor of the One Health Newsletter.

## **Recent and Pending One Health Books:**

Who's In Charge? Leadership during Epidemics, Bioterror Attacks, and Other Public Health Crises By Laura H. Kahn, Praeger Publishers, 9/3/2009

**Description:** An imminent threat to the public health, such as the swine flu outbreak, is no time for a muddled chain of command and contradictory decision making. Who's In Charge? Leadership during Epidemics, Bioterror Attacks, and Other Public Health Crises explores the crucial relationships between political leaders, public health officials, journalists, and others to see why leadership confusion develops.

http://www.greenwood.com/catalog/C9485.aspx

HUMAN-ANIMAL MEDICINE: Clinical Approaches to Zoonoses and Other Shared Health Risks Editors: Rabinowitz, Peter, Conti, Lisa Release Date: December 2009

**Description:** This evidence-based practice manual is designed to help you manage a wide range of clinical problems at the intersection of human and animal health, with practical steps for implementing the concept of "One Health" in daily practice of human and veterinary medicine and public health.

http://www.elsevier.com/wps/find/bookbibliographicinfo.cws\_home/720333/ description

**One Man, One Medicine, One Health: The James H. Steele Story** By Craig Nash Carter – BookSurge Publishing, 2009

**Description:** This is the story of Jim Steele's life, in and outside the allied health professions. He is a true pioneer in the evolving philosophy of One Medicine, One Health, One World. He has been called by many of his colleagues, The Father of Veterinary Public Health.

http://www.amazon.com/One-Man-Medicine-Health-Steele/dp/1439240043/ ref=sr 1 1?ie=UTF8&s=books&gid=1246048712&sr=8-1



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## **Recent One Health Publications:**

 'One Health' – the Rosetta stone for 21<sup>st</sup> century health and health providers, Veterinaria Italiana 2009 – Volume 45(3), July-September

http://www.izs.it/vet italiana/2009/45 3/377.htm

MORE SOPHISTICATED, BETTER COORDINATED GLOBAL SYSTEM NEEDED TO EFFECTIVELY PREVENT, DETECT, RESPOND TO ZOONOTIC INFECTIOUS DISEASES, National Academies Press 2009 Gerald T. Keusch, Marguerite Pappaioanou, Mila Gonzalez, Kimberly A. Scott, and Peggy Tsai, Editors

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Emerging Infections: A Tribute to the One Medicine, One Health Concept, Zoonoses and Public Health, Volume 56, pages 407-428. R. E. Kahn, D. F. Clouser and J. A. Richt

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"From one medicine to one health and systemic approaches to health and well-being" 2009 Published by the 12th IVEE Conference in Durban, South Africa J. Zinsstag, E. Schelling, D. Waltner-Toews, M. Tanner

<u> Abstract Print http://www.isvee.co.za/dynamic/users/abstractPrint ...</u>

For other One Health publications visit the One Health Initiative website.



http://www.onehealthinitiative.com/publications.php



## **Coming Events:**

## **Contributors:**

William D. Hueston, DVM, PhD Global Initiative for Food System Leadership University of Minnesota

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James Steele, DVM, MPH Professor Emeritus University of Texas

Ana Viamonte Ros, MD, MPH Surgeon General Florida Department of Health

Jedd D. Wolchok, MD, PhD Memorial Sloan-Kettering Cancer Center

John (Jack) Woodall, MA, PhD Director (retd.) Nucleus for the Investigation of Emerging Infectious Diseases Institute of Medical Biochemistry Federal University Rio de Janeiro, Brazil 2009 ISAZ / HAI International Conference

1st Conference for The Research Center for Human-Animal Interaction (HAI)

Kansas City, MO USA

October 21-25, 2009

http://rechai.missouria.edu/

#### American Society of Tropical Medicine and Hygiene (ASTMH) and the Society of Veterinary Tropical Medicine (SVTM)

Joint One Health Symposium at the ASTMH 58th Annual Meeting "One World - One Health and Intercontinental Invaders"

> Washington, DC, USA November 21, 2009 at 3:45 p.m.

> > www.astmh.org

### Seventh Annual "One Medicine" Symposium

Humans & Birds & Pigs - Oh My! A One Medicine Approach to Emerging Influenzae

> Durham, North Carolina December 9, 2009

www.onemedicinenc.org



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