One Health Newsletter

A quarterly newsletter highlighting the interconnectedness of animal and human health

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In This Issue

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This newsletter was created to lend support to the One Health Initiative and is dedicated to enhancing the integration of animal, human, and environmental health for the benefit of all.

The *One Health* Community - A Paradigm for Developing Countries

Nigel D. Brown, BVSc, MSc, MRCVS, MACVSc

'An investment in knowledge pays the best interest' - Benjamin Franklin

Overview

This paper considers the promotion of One Health *concepts in developing countries, many with endemic zoonoses having massive pandemic potential but severely handicapped health services. It proposes a new paradigm to increase professional knowledge, founded on a moral commitment to universal health by committed colleagues.*

Developing Nations Today

Pathogen control within developing countries is weak, with local conditions limiting effective application of global advances in scientific knowledge.

More advanced countries possess mature health services with reasonable funding, support staff and a culture of analysis and improvement for individuals and the system. Novel disciplines such as epidemiology and risk analysis have emerged, linking disease development and control, while valuable management concepts (e.g. HACCP and audit systems) have been imported from industry, the military and other spheres of life. Remuneration for veterinarians and doctors has increased - financially and in terms of community respect - but with regulatory control over qualification standards, continuing professional development (CPD) and professional conduct.

As a result, changing Western technical and administrative training reflects vast increases in knowledge and the subsequent specialization required by populations with high expectations.

Dr. Nigel Brown

Unfortunately many of these features are missing in developing countries. Their models of veterinary and medical care are generally inadequate and may be loosely described as an ineffective blend of understaffed government services, diverse aid projects and free-enterprise facilities, hindered by unregulated drug supplies and governed by ineffective bureaucracies that are influenced by the favouritisms of feudal society.

To become a potent force for world health, *One Health* should not be content to merely promote an alliance between disciplines in the western world

which already possess collaborative organizations to mobilize resources. Its real thrust must be pro-active, addressing fundamental issues in developing countries where many pandemics originate.

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With today's freedom of international moment, trying to prevent entry of novel diseases in the continued absence of effective endemic control merely allows spread to other nations with inadequate systems, increasing the diversity of epidemiologically dangerous foci. That's a bit like trying to prevent consumers contracting *E.coli* O157 from lettuces by always washing them but without stopping farmers from using dangerous slurry fertilizers.

Appraising medical and veterinary services in most developing nations reveals major problems dependent upon a few core structural and educational weaknesses including:

- poor management systems
- inadequate service resources – technical skills, manpower and consumables
- flawed undergraduate education
- limited access to quality continuing professional development
- weaknesses in codes of professional conduct and regulatory mechanisms

Royal Flying Doctor Service emergency airstrip
(Courtesy Hossen 27)

Unique problems require novel solutions…….. e.g. Australia's Royal Flying Doctor Service.

Their Infra-Structure and Management

Political, geographical and cultural diversity should indicate that some conventional mechanisms are potentially unsuited to local application but frequently, such structures remain.

Unique problems require novel solutions – e.g. Australia's Royal Flying Doctor Service.

A Royal Flying Doctor Service Beech KingAir on a remote airstrip in Queensland, Australia. (Courtesy Peter Schuller)

Improper disposal of waste from slaughterhouses and the lack of basic food safety practices illustrate a need for a One Health approach to environmental services in developing countries.

Because power ensures survival and wealth, empire-building within organizations frequently hinders progress. At the same time, a dearth of practical experience and business management training among decision-makers often reflects a flawed, societal belief that leaders do not require training (or anything that minions might perceive as training).

As a result, many out-dated concepts, long superseded elsewhere, are retained. Inadequate legislation, standards, procedural guides and cross-disciplinary ventures create far too many 'grey areas' outside the remit of a particular organization. The resulting, often dangerous, inaction is compounded by

the almost total absence of any independent scrutiny or audit.

Consider the horrors of livestock waste disposal. Blood, offal, bones and intestinal contents leave slaughterhouses into diverse locations – water courses, fishponds, animal feed, public landfill sites and local scavengers. High percentages of pathological material removed during meat production (frequently 100%) are inadequately treated and viable pathogens re-enter an infection cycle (personal observations; *Livestock and Slaughter Waste Management*, 2008, World Bank study in preparation). Veterinary services generally inspect animals and carcasses, municipalities are responsible for waste disposal (despite inadequate staff with relevant knowledge) and environmental services are in their infancy. Medical services have little involvement in quantifying or correcting this epidemiological headache.

Slaughtered goats in Pakistan
(Courtesy Robyn Hepburn)

Blood, offal, bones and intestinal contents removed during meat production are inadequately treated and viable pathogens re-enter an infection cycle.

One apparently simple, yet ultimately complex, example exemplifies the need for basic *One Health* principles.

Livestock and human habitation on an unfenced municipal dump
(Courtesy Robyn Hepburn)

Offal for sale – Egypt
(Courtesy Robyn Hepburn)

"Without doubt, the most beneficial service the fledgling One Health can provide is a reliable source of knowledge, training and support for colleagues in developing countries."

Human Resources

Serious shortages of qualified professionals and support staff are widely identified. However, official figures do not indicate another phenomenon – global variation in standards. Undergraduate selection criteria and teaching techniques have qualified many who are ignorant of basic facts and weak in applying rote-learned data to practical scenarios.

Aggravating these educational flaws is the widespread absence of worthwhile post-graduate training to ameliorate their weaknesses. Individuals frequently remain stuck in the time-warp of their own university instruction. Any tuition available is frequently misdirected, with colleagues in more remote areas missing rare opportunities, even for workshops. Many valuable but frustrated nationals enter a brain-drain.

In another perspective, oil-rich Middle East countries have few indigenous health professionals. Consequently, public and private services are commonly staffed from other developing countries, e.g. Sudan, Egypt and India, with Western-trained expatriates in the minority because of cost. In this region,

immigrants are often poorly-suited to providing strategic advice and locals frequently unwilling to accept guidance.

Committed One Health members helping colleagues in developing countries offers immense potential.

Added to these poor levels of knowledge, inadequate professional registration mechanisms, codes of conduct and ethical standards are stifling progress within some developing nations. Sadly, little importance can be placed on the integrity of 'certification' where powerful, corrupting influences predominate. The resulting misplaced confidence in official decisions severely handicaps disease control.

The CDC staff had to use a small air craft to reach the outbreak area in a remote part of western Uganda. (Courtesy CDC)

With this background and few progressive ideas entering relatively closed communities, *One Health* has a magnificent opportunity to deliver vital information and key messages to cross-pollinate disciplines.

The Future for Developing Nations

"We are what we repeatedly do. Excellence, then, is not an act, but a habit.

Durant, after Aristotle.

Without doubt, the most beneficial service the fledgling *One Health* can provide is a reliable source of knowledge, training and support for colleagues in developing countries. This will enhance their individual skills and collective ability to control disease.

In 2007 scientists from the CDC deployed to the Democratic Republic of the Congo to support efforts to control an outbreak of Ebola in a remote in a remote part of western Uganda.

Such a concept for collaboration with developing countries can either drift into professional awareness or proactively soar into prominence. The former will disappear beneath stronger influences so it requires a powerful '*One Health* awareness package'. This needs a meaningful tool which allows results to do the talking rather than glossy promos. Vital components should be a basic manual, carefully-targeted with fundamental principles, and a subsidized distance-education program. Widespread adoption of both will provide immense benefits to our professional colleagues and support staff, their Services and, ultimately, world health.

CDC scientists from Atlanta help the Ugandan health ministry and medical relief organizations track and monitor the family and friends of Ebola victims in the outbreak zone of Bundibugyo. (Courtesy CDC)

With worthwhile CPD systems unavailable to most professionals, this *One Health* mechanism should help as many people as possible by advancing modern concepts and narrowing the education gap between developing and more advanced nations. For best effect, an active mentoring system would pay unexplored dividends.

Committed *One Health* members helping colleagues in developing countries offers immense potential. Those experienced in modern learning techniques can offer support in private and group correspondence, visits and other ways that are potentially lifelong support-lines. And such activities are not all one-way traffic.

Revealing new ideas and concepts to impressionable young undergraduates seems an especially vital influence – stimulating habits which will become routine for the rest of their careers. Twinning Faculties for student

communication may be a useful concept.

Until rank and file health professionals have adequate knowledge, there is little chance of national Services raising their standards. The Golden Horde of Genghis Khan only achieved success because of the outstanding training of his soldiers and the generals who rose through their ranks.

A One Health Structure for Countries in Transition

A triad of mutually-supportive approaches is suggested -

- awareness and training of individuals (vets, medics, pharmacists, administrators and others)
- international promotion through official organizations, universities, etc
- monitoring penetration of *One Health* philosophy and education

For more information, please visit:
www.doh.state.fl.us/Environment/community/One_Health/OH_countries_Fall2008.pdf

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CDC scientist works with samples in HHS/CDC's mobile field laboratory in Luebo, Democratic Republic of the Congo. (Courtesy Chris Black, World Health

The "Other" One Medicine uses the mantra of……

"One Gene, One Disease, One Medicine."

THE "OTHER" ONE MEDICINE

Robert D. Cardiff, MD, PhD

The One Medicine/One Health Movement has, quite correctly, called attention to the relationship between man and his animals encouraging renewal of cooperation between the medical and veterinary professions. Borne from the era of globalization with its increasing threats of bioterrorism and emerging new infectious diseases, the focus has been on infectious disease, public health and epidemiology. However, another "One Medicine" exists that profoundly effects modern medicine and implementation of One Health. The "Other" One Medicine uses the mantra of "One Gene, One Disease, One Medicine." Society will be best served by recognizing the two movements and encouraging their convergence.

(Photos courtesy of Center for Genomic Pathology)

Sequencing of hundreds of genomes has lead to the realization of a closer relationship between all animals than previously imagined and provide medicine with powerful new insights.

The Other One Medicine grows out of molecular biology and genomics. The sequencing of hundreds of genomes, including mouse and human, has confirmed a remarkable similarity between all mammalian species and traced highly conserved genetic sequences down evolutionary trees to invertebrates. These discoveries bring the realization of a closer relationship between all animals than previously imagined and provide medicine with powerful new insights.

For example, most of the cancer-causing genes (oncogenes) identified in humans were initially identified in chickens or rodents. The most common oncogene found in human breast cancer is HER2. This gene is also "human ERBB2" and was first identified as an oncogene in avian erythroblastic leukemia, hence, the name ERB. The cancer-associated Wnt genes are named after "Wingless" developmental genes from fruit flies. One of the most common cancer-associated genes, MYC, was first identified in and named after avian

myelocytomatosis. The SRC gene, that merited the 1989 Nobel Prize for Varmus and Bishop, came from Peyton Rous's 1916 discovery of an infectious agent in chickens (a 1966 Nobel Laureate). In all four cases, the genes are highly conserved from species to species.

The list of cancer-associated genes first discovered in other species is extensive. More importantly, these cancer-causing oncogenes cause the same disease (cancer) in all species. In fact, genetic engineering of mice has become the standard technique for determining the oncogenic potential of any suspected oncogene. Investigators suspecting that a gene is associated with cancer can test their hypothesis by inserting or deleting the gene in mice. Genetically engineered mice (GEM) not only develop cancers but in many cases, the cancers are exact molecular and morphological copies of the human cancers. Knocking-out a cell adhesion gene (E-Cadherin) in the mouse mammary gland results in mammary tumors that are microscopically indistinguishable from human lobular breast carcinoma that also has lost E-Cadherin. One gene results in the same disease in the same organ in both species fulfilling the one gene, one disease premise.

Genetically engineered mice (GEM) not only develop cancers but in many cases, the cancers are exact molecular and morphological copies of the human cancers.

If one gene initiates one disease, it makes sense that treatments that cure disease in one species will cure the same disease in other species.

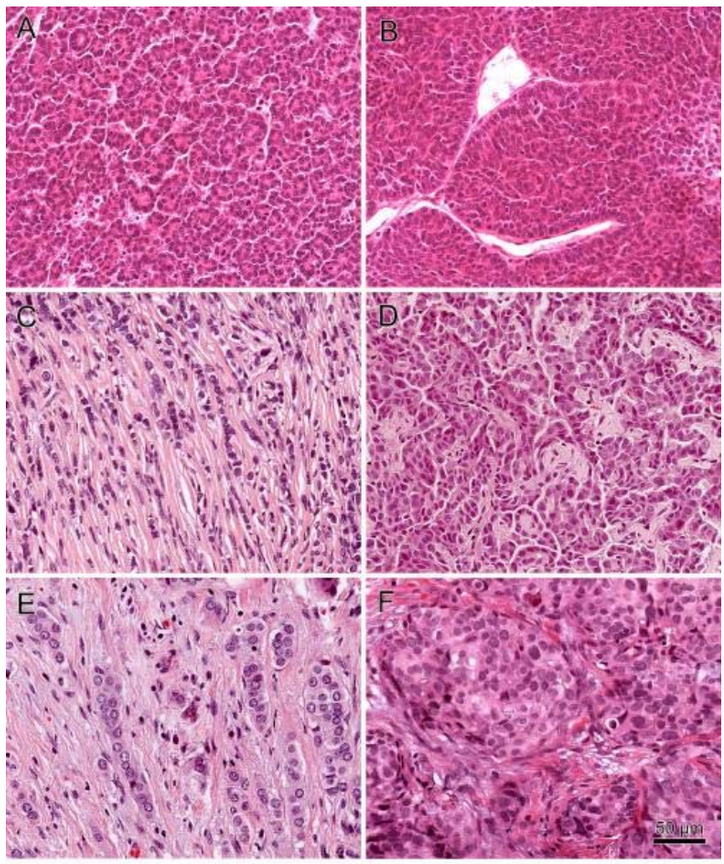

FIG. 1 Mouse-Human Comparisons
Axiom: Genetically Engineered Mouse (GEM) tumors are unique. The microscopic patterns of classical MMTV-induced mouse mammary tumors (Fig. 1A and 1B) are structurally different from the histological patterns of GEM tumors (Fig. 1C and 1D). Remarkably, the GEM tumors more closely resemble human breast cancer (Fig. 1E and 1F) than the virus-induced tumors (Fig. 1A and 1B).

For a detailed discussion of Figure 1, please go to:
www.doh.state.fl.us/Environment/community/One_Health/OH_mousehuman_Fall2008.pdf

If one gene initiates one disease, it makes sense that treatments that cure disease in one species will cure the same disease in other species. Preclinical

trials in GEM cancer models provide proof-of-principle. Various molecular-targeted therapies have proven effective in these mice. For example, tumors initiated by genes using the mTOR pathway, that controls cell growth, are effectively treated with drugs that interfere with the pathway, i.e. Rapamycin. This provides an ideal proving ground for molecular-based medicine which aims to target specific molecular abnormalities. Homologs of Rapamycin are being used in various clinical trials. As predicted: One Gene, One Disease, *One Medicine*.

Ironically, the barrier to translating one medicine into human medicine is that we know much more about the molecular basis of the mouse's disease than we know about the individual patient's disease. Human diversity is also daunting. However, clinical scientists are working to overcome the heterogeneity barrier with personalized, or genomic, medicine. As our technology and understanding improves, genome-based personalized medicine will become feasible.

While mouse models of cancer provide excellent examples of one gene, one disease, one medicine, the GEM have been equally useful in studies of autoimmune, metabolic, infectious and other diseases.

While mouse models of cancer provide excellent examples of one gene, one disease, one medicine, the GEM have been equally useful in studies of autoimmune, metabolic, infectious and other diseases. These observations lead to the ultimate realization that the human genome project will come through the mouse. The sequencing of the human genome tells us very little about the function of most of our 20,000+ genes. Their functions will be determined by phenotyping them in the mouse.

The post-genomic effort to characterize the genome has been initiated by the international community that has started a massive knockout mouse project (KOMP) designed to knockout each gene in the mouse. Between 20,000 and 200,000 new strains of mice will be created over the next ten years. Although many mouse gene knockouts will result in embryonic lethality, each strain requires phenotyping. This massive undertaking is justifiable to realize the benefits of sequencing the human genome.

The scientific community will also need a new type of comparative pathologists, the genomic pathologists, who know mouse and human pathology as well as genomic biology.

Our mouse houses are already overflowing with mice as more and more molecular biologists use the GEM to characterize their favorite genes. Now that mouse geneticists have created KOMP to complete their own mission, science will need professionals devoted to lab animal husbandry and health. The scientific community will also need a new type of comparative pathologists, the genomic pathologists, who know mouse and human pathology as well as genomic biology. This workforce will be required to maintain, characterize and validate the models of disease that emerge from the KOMP and other programs. Unfortunately, the leadership has forged ahead without recognizing the need for comparative medicine.

The resources for creating and training the post-genomic workforce are neither in place, nor planned. The need must be recognized by mouse geneticists, basic scientists and the veterinary and medical communities. The Center for Genomic Pathology has developed an educational program designed to close the gap between genotype and phenotype by providing online training for all levels of need. Hopefully, this and other programs will prepare medical and veterinary scientists for the future of One Health.

It will take our combined efforts to train the workforce needed to realize the benefits of one gene, one disease, one medicine, and the genomic revolution.

It will take our combined efforts to train the workforce needed to realize the benefits of one gene, one disease, one medicine, and the genomic revolution. The One Medicine-One Health Movement is salutary in its efforts to enhance and re-invigorate the traditional connection between the Health Sciences but we need to include the *other one medicine* into our thinking and programmatic planning if we are to benefit from the genomics.

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Biological Warfare Involves Animal Diseases

Patrick Ryan, DVM, MPH

The majority of emerging infectious diseases, including those caused by bioterrorist agents, are zoonoses.

Animal diseases, particularly zoonoses, are likely to be employed in biological warfare. The Centers for Disease Control and Prevention (CDC) currently classifies bioterrorism diseases/agents most likely to be used into categories A, B, and C, with A having the highest priority. Of the infectious diseases in CDC's classification system, the majority are zoonoses. Of the category A diseases, more than 80% are zoonoses. The only disease that does not involve animals in category A is smallpox, which was eliminated by a worldwide vaccination program. Category C includes emerging diseases, of which about 75% are zoonoses.

Consequently the human medical and veterinary communities should work closely together to improve prevention and control strategies.

The World Health Organization (WHO) officially declared smallpox eradicated in 1979. Elimination was possible because there was no animal reservoir. The global eradication of smallpox was a tremendous achievement made possible by the development of an effective vaccine. As a result, routine vaccination of the general population is no longer recommended. Stocks of smallpox still exist in two secure laboratories. There was concern that the threat of smallpox could be used as a bioterrorist weapon, which in 2002 led to a vaccination campaign in U.S. military and civilian health-care workers and first responders.

Edward Jenner
(Courtesy The Jenner Museum)

Edward Jenner developed a vaccine against a devastating human disease (smallpox) from a milder zoonosis (cowpox).

Venezuelan equine encephalitis (VEE) is a mosquito-borne alphavirus that causes disease in both horses and humans.

A horse displaying symptoms of VEE (Courtesy CDC)

Horses with VEE develop a sufficient level of viremia to act as a reservoir or as amplifying hosts.

Interestingly, the control of smallpox began with the observation that people exposed to cowpox, a zoonosis, were later immune to smallpox. Effective control of smallpox began in the late 16th century when Dr. Edward Jenner, an English physician, became intrigued with farmers' reports that people who caught cowpox did not develop smallpox afterwards. He used an animal pox virus (cowpox) to immunize people against the smallpox virus. Jenner published his research in 1798; however, great opposition arose in the medical community and in the general public to using cowpox to provide immunity to smallpox. His initial report to the Royal Society was rejected as the concept conflicted with established knowledge. With time, his research was accepted and Jenner spent much of the rest of his life traveling the world to demonstrate his technique and distribute cowpox material to others.

Cowpox is a mild infection of cows that causes weeping ulcers on their mammary glands but little discomfort. People in close contact with milking herds may become infected, developing a fever and lesions on the hands, arms, or face. Although once common in cattle, cowpox is now rare. Jenner concluded that cowpox not only protected against smallpox but could be transmitted from one person to another as a deliberate mechanism of protection.

Zoonoses Impacted Military Campaigns Throughout History

Since recorded time, there have been examples of animal diseases that affect people being used in biological warfare. The attack of the Tatars on the city of Caffa, a well-fortified port, was recorded during the Middle Ages. Soldiers catapulted plague cadavers into the city. The tactic of hurling bodies of dead plague victims over city walls occurred in other conflicts and was also reportedly used by Russian troops battling Swedish forces in 1710.

The British Army used smallpox as a biological weapon in 1763 when they provided American Indians loyal to the French with blankets and handkerchiefs from their "Smallpox Hospital". The French and Indian War (1754-1763) was the last and most important conflict in North America before the Revolutionary War in America. The "white man's disease" had a high mortality rate on non-immune populations.

The Japanese began one of history's most notorious bioweapons programs in 1932, and numerous human experiments were conducted at the infamous Unit 731 throughout World War II. Located in Manchuria, Unit 731 sprawled across 150 buildings and five satellite camps, and had a staff of more than 3,000 scientists and technicians. Unit 731 allegedly experimented with biological agents on at least 3,000 prisoners of war. More than 1,000 prisoners were estimated to have died following experiments using such zoonoses as anthrax, botulism, brucellosis, and plague. These allegations were supported during a military tribunal held in the former Soviet Union in December 1949.

Exotic Sleeping Sickness Outbreak

In the United States during 1971, an outbreak of Venezuelan equine encephalomeningitis (VEE) suddenly occurred. The disease had a high fatality rate (>50%) in horses and was debilitating in humans, producing flu-like symptoms

During the 1971 VEE outbreak, a vaccine developed to protect humans in biological warfare was released for use on horses to halt the spread of the zoonosis around the U.S.

Mandatory vaccination of horses was required to halt the spread of VEE and protect both horses and humans.

These illustrations are just some examples of how collaboration between human and veterinary medicine can advance both human and animal health.

with a case fatality rate of about 1%. Four hundred thousand horses were quarantined in Texas in an attempt to halt expansion of the outbreak. The epizootic was an extension of an epidemic that involved thousands of humans and equids, which appeared to have begun in 1969 at the Peru-Ecuador border.

In July 1971, the Agriculture Secretary declared a national emergency to fight the sleeping sickness epidemic. In most equine arboviruses, the horse is not an efficient amplification host. The significance of infected horses in maintaining epizootic VEE, however, is illustrated by the observation that human disease has never been demonstrated in the absence of equine disease. Horses with VEE develop a sufficient level of viremia to act as a reservoir or amplifying hosts and are considered the most important species for amplification of virus in VEE epizootics.

The U.S. Army released stockpiles of an attenuated live-strain vaccine, TC-83, developed to protect soldiers in biological warfare. Mandatory vaccination of horses was required in the southern-border states (Alabama, Arizona, California, Georgia, Florida, and Mississippi) to create a wall of immunity to halt the northward spread of the outbreak. Some horse owners were reluctant to use their animals as "guinea pigs" for the vaccine untried in animals. However, since it was compulsory they unenthusiastically complied.

In this situation, a vaccine developed for use in humans was released for use on horses to halt the spread of the zoonosis around the U.S. The declaration of a national emergency, the release of a biowarfare vaccine, and the mandatory vaccination of horses created panic in the nation, and various local and state governments were put on alert. However, with the use of the vaccine, the outbreak was quickly resolved.

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Avian Flu and the One Health Initiative

Robert Kahn, PhD

"There is already an influenza pandemic among chickens; and there is going to be an influenza pandemic among humans, but no one knows when……."

The science is clear: There is already an influenza pandemic among chickens; and there is going to be an influenza pandemic among humans, but no one knows when the human pandemic will begin or how lethal and contagious the virus will be. It is this ambiguity about both timing and severity that makes the link between science and policy, as well as human and veterinary medicine, so challenging. The stakes are high. Between a third and a half of the population of the world is likely to become ill, with many millions of deaths, some 95% of which will be in the developing world (See the Sydney-based Lowy Institute for

The carrier who will probably establish the pandemic will not be a chicken, but a person in a plane, as happened with SARS in 2002.

Civet cats were recognized as a host for the SARS coronavirus and later Chinese Horseshoe bats were implicated as the original reservoir of the virus.

(Courtesy S. Kruskop)
http://zmmu.msu.ru/bats/rbgrhp/ewelc.html

International Policy's report *Global Macroeconomic Consequences of Pandemic Influenza* by Warwick J. McKibbon and Alexandra A. Sidorenko on line at: www.lowyinstitute.org/Publication.asp?pid=345).

The present number of human casualties is small. Fewer than 250 laboratory-confirmed deaths have occurred since this highly virulent H5N1 form of influenza killed a three-year-old boy and five others in Hong Kong in 1997 before Margaret Chan, then Hong Kong Director of Health (now Director-General of the World Health Organization—WHO) ordered the killing of more than 1 million chickens in Hong Kong. Furthermore, since 2003, according to WHO data, 80% of the victims have been in five countries—Indonesia (108), Viet Nam (52), Egypt (22), China (20) and Thailand (17) (Regular WHO updates are on line at: www.who.int/csr/disease/avian_influenza). However, H5N1 influenza threatens the entire world, although those who have died so far have been people with close contact with chickens, or within the same family. The carrier who will probably establish the pandemic will not be a chicken, but a person in a plane, as happened in 2002 with Severe Acute Respiratory Syndrome (SARS) that began in Southern China and then came to Hong Kong and Canada, eventually killing nearly 900 people.

The animal reservoir for SARS was found—civet cats that transferred the disease to those who were killing and eating them, as documented by Assistant Professor Yi Guan of the Department of Microbiology, University of Hong Kong. The story of how scientists, veterinarians, hospital administrators, doctors and journalists worked together and just managed to stop SARS is brilliantly told by Karo Taro Greenfeld in *China Syndrome: The True Story of the 21st Century's First Great Epidemic* (Penguin Books, 2006). As Greenfeld explains in reflecting on future viruses: "If the virus is there today, it will be here tomorrow. We are as vulnerable as the weakest immune system at the farthest link of the human chain" (p. 292).

The primary reservoir for H5N1 influenza is within the domestic ducks, geese and rice paddies of southern China, as set out by Marcus Gilbert and Jan Slingenbergh and their colleagues at: www.fao.org/newsroom/en/news/2008/1000817/index.html, 26 March 2008). Ducks and geese have passed their non-virulent form of flu to chickens and turkeys for which H5N1 is lethal. As Deborah MacKenzie has pointed out in *New Scientist,* avian flu has already become "the biggest outbreak of an animal disease ever recorded" (17 January 2006). Several hundred million chickens have died or been slaughtered to present further spread. However, with 50 billion ducks, geese and swans migrating throughout the world, the reservoir cannot be eliminated. Furthermore, the infected poultry pass the H5N1 virus back to the water birds, in a deadly mix of viruses.

The veterinary challenge is compounded by human interaction with chickens. Throughout Asia, chickens are raised in backyards, traded alive in markets and consumed in growing numbers from immense poultry farms. In *Bird Flu: A Virus of Our Own Hatching*, Michael Greger, MD casts the blame for the spread of H5N1 firmly on commercial poultry farms. (See the book, free on line at: www.birdflubook.com.) This study by the Director of Public Health

and Animal Agriculture at the Humane Society of the United States is possibly the best single book to read to clarify the origins and transmission pathways of H5N1, especially the capability of the virus to jump species. As the British virologist, John Oxford, wrote in *Nature*, Greger has balanced "a scientific exposition about influenza with a cry from the heart about industrialized farming" (Vol 444, 21/28 December 2006, pp.1007-1008).

Chickens for sale in a wet market (Courtesy AP)

Solutions will not be easy. Regular monthly cleansing of the wet markets where chickens are sold will help; education about not eating undercooked chicken can save lives; and improved hygiene at (and eventual closing of) commercial poultry farming is essential. Understanding the possibility of global and personal action is helpful, as set out in websites such as those of the Minneapolis-based Center for Infectious Disease Research & Policy (CIDRAP), especially the award-winning articles by Marilyn McKenna on delays in producing a pandemic vaccine (at: www.cidrap.umn.edu/cidrap/content/influenza/panflu/news/oct2507panvax1.html), Bob and Julie Butler's Survive the Flu (at: www.survivetheflu.com) and Laura Kahn's recent article in Bulletin of the Atomic Scientists, "Children: The Bioterrorists We Love" (at: http://thebulletin.org/columns/laura-kahn/20070917.html). However, possibly the single most important long-term "solution" is the interdisciplinary integration of human and veterinary medicine in environmentally-aware analysis, education and action. Only when One Health is recognized as a respected way forward for medicine will we begin to tackle effectively the causes and consequences of H5N1 influenza in all species.

"Only when One Health is recognized as a respected way forward for medicine will we begin to tackle effectively the causes and consequences of H5N1 influenza in all species."

Dr. Robert Kahn is Coordinator of Avian Flu Action, an educational website at: www.avianfluaction.org, and lives in Warrington, Great Britain.

The following article is chapter from the soon to be released book Human-Animal Medicine: Clinical Guide to Toxic, Zoonotic and Other Shared Health Risks, Elsevier (Spring 2009)

Immunocompromised Individuals *

Lisa Conti, DVM, MPH, Dipl ACVPM and Peter M. Rabinowitz, MD, MPH

1. Introduction

Available evidence continues to suggest that the psychosocial support value of companion animals - particularly for the elderly or infirm- [1,2,3] outweighs the risk of acquiring a serious infection from such animals. Nevertheless, issues regarding hygiene and common sense practices must be addressed to support a healthy human-animal bond, especially among immunocompromised people or pets.

A large proportion of American households include pets [4] and millions of people in this country are living with less than a robust immune system. Immunosuppression can result from a number of etiologies, either, rarely, from a primary/genetic malfunction, or, commonly, as a result of a secondary or acquired factor such as human immunodeficiency virus (HIV) in people or feline leukemia

"Millions of people in this country are living with less than a robust immune system."

* Immunocompromised Individuals: ©2008 Lisa Conti DVM MPH and Peter Rabinowitz MD MPH Gary Patronek/Anne Justice Allen edits LC Fin 1

Armed with complete and accurate information, patients and their care providers can weigh these risks against the often substantial benefits of love, touch, social support, and companionship that accrue to pet owners.

Zoonotic disease prevention is a shared responsibility among human and veterinary and public health professionals.

virus (FeLV) in cats, or immunosuppressive chemotherapy. In general, defects in humoral immunity (B cell lines) can lead to increased susceptibility to bacterial infections; cell-mediated immunity (T cell lines) defects to viral, fungal or protozoal infections, and defects of phagocytosis or the complement system to disseminated infections. Pet ownership among immunocompromised persons is common. For example, studies of patients with HIV infection have reported rates of pet ownership similar to that of the general population with about half owning or living with pets.[5] In addition, on a global level, the HIV/AIDS pandemic has created large populations of individuals with compromised immune systems, many of whom may also be exposed to zoonotic diseases.[6, 7] Human and veterinary clinicians are quite likely to encounter situations where they may provide appropriate guidance for reducing animal sources of infectious diseases for humans and vice versa, by educating themselves and staff to provide the best available information.

Table 1: **Etiologies of inability to mount an effective immune response (immunocompromised state)** is available at: www.doh.state.fl.us/Environment/community/One_Health/Immuno_Table1_Fall2008.pdf

2. Impact of human immunodeficiency states on animal-human disease transmission.

There are at least three possible effects of human immunodeficiency on animal- human disease transmission:

1. An immunocompromised host is more susceptible to infection with opportunistic disease.
2. An immunocompormised host may transmit opportunistic disease to others.
3. A disease may be more severe in an immunocompromised host. (An example is toxoplasmosis, which causes asymptomatic or mild disease in most immunocompetent patients, but can cause severe and even fatal systemic disease in immunocompromised individuals.)

The knowledge level among immunocompromised persons and their health care providers about the risk of acquiring infections from pets could be increased with an appropriate educational strategy. In one study in which over 400 AIDS patients were interviewed -- half of whom owned pets -- only about 10 percent who were living with pets were given any information about zoonotic diseases from their health care provider and one-quarter of this information was incorrect or misunderstood (e.g., “fleas can give you rabies,” “cats can give you AIDS”).[11] Because pet ownership is as common (and understanding of zoonoses as likely uncommon) among persons living with AIDS as in the general population, human health care providers must be prepared to discuss with immunocompromised patients the risks of living with pets. Overly conservative approaches, including physician recommendations for their patients to relinquish pets have largely been unheeded as owners often have strong bonds with their animals.[12] Armed with complete and accurate information, patients and their care providers can weigh these risks against the often substantial benefits of love, touch, social support, and companionship that accrue to pet owners. Zoonotic disease prevention is a shared responsibility among human and veterinary and public health professionals. Improving communication among these persons will enhance zoonotic disease prevention.[13]

"Hand and food hygiene is vital!"

Unequivocally, immunocompromised individuals should avoid raw meat and eggs, and unpasteurized dairy products.

While cats are the definitive host for Toxoplasma gondii, undercooked meat (<165°F) and inadequately washed, contaminated fruits and vegetables are the most likely the source for infection.

3. Human Health Setting

Pet-owning human health practitioners must be vigilant regarding nosocomial zoonoses, particularly if they are working with immunocompromised patients. In one situation, a common yeast pathogen of canine otitis externa was introduced into a neonatal intensive care unit by a dog-owning health care worker, causing colonization in infants, some with serious infection.[14, 15] In another case, a cat on a geriatric ward was the likely suspect of staphylococcal infections.[16]

4. General Guidelines for the Prevention of Zoonotic Disease in Immunocompromised Patients

Guidance from Both Human Health and Veterinary Providers

- Hand and food hygiene is vital. Pets are not likely the most common source of zoonotic disease infection. More likely, contact with raw or undercooked meat, or from an environmental infectious source are implicated in transmission. Unequivocally, immunocompromised individuals should avoid raw meat and eggs, and unpasteurized dairy products. For example, while cats are the definitive host for *Toxoplasma gondii*, it is undercooked meat (<165°F) and inadequately washed, contaminated fruits and vegetables that are likely the source for infection. (Links to United States Department of Agriculture [USDA] food safety fact sheets http://www.fsis.usda.gov/Factsheets/Keep_Food_Safe_Food_Safety_Basics/index.asp and http://www.fsis.usda.gov/Factsheets/At_Risk_&_Underserved_Fact_Sheets/index.asp
- Serologic or fecal evaluation of healthy cats for toxoplasma infection is not recommended. Oocysts are shed transiently and are easily missed and serologic evaluation does not predict cats shedding oocysts. Instead, prevention of transmission of toxoplasma directly from cats should focus on the husbandry recommendations stated below.
- Pets should not be given prophylactic antibiotics without clinical signs of infection (e.g., salmonella carriage in reptiles cannot be eliminated. Use of antibiotics for this purpose has been unsuccessful and may favor development of antibiotic resistant bacteria).[17]
- Any bite or wound from an animal should be flushed with copious amounts of soap and water, and a health care provider contacted for wound management, including assessment for appropriate antibiotics, tetanus and possible rabies post exposure prophylaxis.

Risk Reduction Recommendations:

When selecting a pet, choose one with a documented veterinary health history and current vaccinations.

Select healthy, well mannered, dogs or cats 6 months or older.

Avoid exotic or wild animals to reduce the likelihood of exposure to emerging infections.

Sulfur crested cockatoo

- Review guidance to reducing exposure to selected opportunistic diseases among persons with HIV (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5108a1.htm).
- Encourage questions about healthy living with pets.
- Pet vaccines, including live attenuated strains, should be recommended as they are not thought to cause a human health hazard.[18]

Occupational or Recreational Risk Reduction

- Avoid contact with wild animals to reduce the risk of enteric disease such as acquiring cryptosporidium from wild birds
- NEVER touch the feces of any animal
- Avoid farm animals and petting zoos to decrease exposure to *E. coli* in ruminants, *Bordatella bronchioseptica* in swine, and salmonella in chicks and ducks, for example.
- Occupational health providers working with high risk workers such as veterinarians, veterinary staff, zookeepers and pet shop workers should counsel immunocompromised workers about the risk of occupational zoonotic disease infection, and consider work restrictions to reduce risk for workers with significant impairment of immunity.

Animal Selection Recommendations for Immunocompromised Persons

- Select healthy, well mannered, dogs or cats 6 months or older to decrease the likelihood of exposure to enteric diseases and *Bartonella* from kittens.
- Avoid petting or handling free-roaming animals; when selecting a pet, choose one with a documented veterinary health history and current vaccinations.
- Avoid exotic or wild animals to reduce the likelihood of exposure to emerging infections (i.e., monkeypox in rodents) and known diseases such as herpes B infection from macaque monkeys and salmonella from reptiles.
- Cockatoos, like pigeons, may shed *Cryptococcus* in their feces, and transmission of this infection was documented from a cockatoo to its owner who was chronically immunocompromised because of a renal transplant.[19] Therefore, some authors have recommended that immunocompromised patients not own cockatoos.[20]

Nodular cutaneous cryptococcosis on the back of the neck of an HIV+ cockatoo owner. (Rosen T. Jablon J. Infectious threats from exotic pets: dermatological implications. Dermatologic Clinics. 21(2):229-36, 2003 ©Elsevier)

Immunocompromised individuals (as well as pregnant women) should avoid having contact with wild or pet rodents.

Keep pets indoors or walk them on a leash.

Keep animals and litter boxes out of food preparation areas.

Have a non-immunocompromised household member remove and dispose of pets' solid waste.

Avoid rough play with the pet that could result in being bitten or scratched.

- A fatal outbreak of lymphochoriomeningitis virus (LCMV) in solid organ transplant recipients was traced back to a pet hamster acquired by the organ donor 17 days before organ donation. The prevalence of this virus in rodent populations has led to recommendations that immunocompromised individuals (as well as pregnant women) should avoid owning pet rodents or having contact with wild or pet rodents.[21]
- Have a veterinarian conduct a physical examination and fecal analysis on the new pet

Animal Husbandry Guidance for Immunocompromised Persons

- Seek veterinary care early in the course of clinical disease of pets to limit chances for zoonotic disease exposure.
- Keep pets indoors or on leashed walks to decrease the likelihood of engagement with other animals.
- Because of occasional cases of *Bordatella bronchioseptica* among immunocompromised persons[22], avoid exposing dogs or owners to situations in which dogs are congregated such as boarding kennels, grooming parlors, off leash dog parks, or dog shows.
- Do not allow pets to hunt or scavenge or eat feces to reduce the likelihood of exposure to enteric infections.
- Do not feed pets raw meat or egg diets or provide unpastuerized dairy products to limit exposure to enteric infections.
- Do not allow your pet to drink from the toilet.
- Keep animals and litter boxes out of food preparation areas.
- Avoid exposure to pet's urine, feces, saliva (don't allow your pet to lick your face or open lesions).
- Have a non-immunocompromised household member remove pets' solid waste and dispose daily by flushing down a toilet, discarding in the garbage or in a compost area (not to be spread on fruits or vegetables).
- Avoid animals with diarrhea; have an immunocompetent household member clean soiled areas in the house of organic debris, followed by a 1:10 household bleach solution.
- Avoid rough play with the pet that could result in being bitten or scratched, keep pet's nails trimmed short.
- Remove and dispose of bird cage linings daily and use "wet" cleaning for the cage and utensils on a weekly basis. Wear gloves when handling items that are contaminated with bird droppings.
- Have an assistant clean the fish tank, or wear disposable gloves during such activities, washing hands thoroughly with running water and soap afterwards.
- If assistance is required to care for your pet, contact local volunteer groups who may be willing to provide exercise, food or foster care (e.g., during hospitalization).

Veterinarians may be best qualified to advise pet owners and persons in high risk professions about zoonotic risks.

They can address immunocompromised individuals' risks during routine discussions about zoonotic disease diagnosis, control and prevention.

Veterinarians should also emphasize to their staff the need for strict confidentiality about a pet owner's health status.

5. U.S. Public Health Service Guidelines for HIV positive individuals:

While any zoonotic disease that occurs in immunocompetent individuals can also affect immunocompromised patients, the U.S. Public Health Service has highlighted a number of animal-agents that pose a significant risk to HIV-infected persons. These include causes of enteritis, (especially campylobacter, salmonella, and cryptosporidium), and *Bartonella*, toxoplasma, histoplasma, and *Mycobacterium marinum*.

The evidence-based recommendations of the U.S. Public Health Service and the Infectious Diseases Society of America are listed in Table 2.

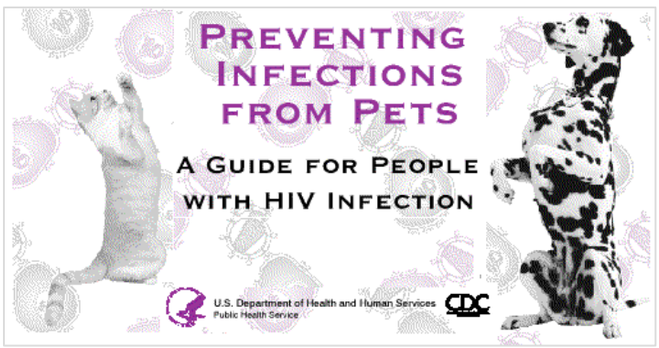

Table 2: Guidelines for Preventing Opportunistic Infections among HIV-Infected Persons can be found at**::**

www.doh.state.fl.us/Environment/community/One_Health/Immuno_Table2_Fall2008.pdf

While these guidelines recommend that human health care providers perform such counseling, surveys of physicians have indicated that many feel that veterinarians are best equipped to provide such counseling and should therefore be involved in patient education of immunocompromised individuals. [23] Some authorities have stated that veterinarians are more qualified than physicians to advise pet owners and persons in high risk professions about zoonotic risks. [24]

6. Public Health Role of the Veterinarian: Safer Pet Ownership for Immunocompromised Persons and Care of Immunocompromised Pets

In the veterinary setting, pet owners may be more willing to request information regarding safer pet ownership for immunocompromised persons if there are, for example, posters and handouts encouraging such client education, or information in practice newsletters. Veterinarians can address general high risk humans during general discussions about zoonotic disease diagnosis, control and prevention. Veterinarians should also emphasize among their staff the need for strict confidentiality regarding any personal information an animal owner happens to disclose about their own medical status (it is not recommended, for example, to document human medical information in the veterinary record).

Care for Pets of Immunocompromised Owners

- Gonadectomize the pet Provide strict adherence to strategic deworming protocols and maintenance of appropriate vaccinations.
- Be prepared to discuss end of life planning for the pet's continued care (http://www.hsus.org/pets/pet_care/guidelines_for_finding_a_responsible_home_for_a_pet.html)

Protecting the Immunodeficient pet:

- *Do not use live virus vaccines*
- *Keep the animal indoors*
- *Wash hands before and after handling the pet*
- Avoid exposure to other ill animals
- Manage secondary and opportunistic infections
- Provide supportive care

Care for Immunodeficient animals

- Do not administer modified live virus vaccines
- Manage secondary and opportunistic infections
- Provide supportive care

Guidance for owners of immunodeficient animals

- Animals with primary immunodeficiency disorders should not be bred
- Cats with FIV or FeLV can spread the viruses to other cats typically via bite wounds or close contact (FeLV). Therefore, separate household contacts that are FIV/FeLV negative. (All cats with unknown FIV/FeLV status presenting with a bite wound should be tested for these viruses at the time of presentation and again 60 days later.)
- Keep these animals indoors, do not allow pets to hunt or scavenge, consume raw meat or egg diets, or unpasteurized dairy products.
- Wash hands before and after handling the pet.
- Provide appropriate endo- and ectoparasite control
- Avoid exposure to other ill animals

References can be found at:
www.doh.state.fl.us/Environment/community/One_Health/Immunorefs_Fall2008.pdf

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Bicol, Philippines

UC Davis, California, USA
(Courtesy Rachel Kaplan)

World Rabies Day Initiative: One Health-One Medicine in Action

Cathleen A. Hanlon, VMD, PhD, DACVPM

Rabies awareness and prevention is necessary no matter what business we are in or where we live. The risk of rabies is global - because humans travel, animals are translocated, and due to the importance of bats in rabies transmission, their widespread distribution, and ability to fly. Even though human rabies is 100% preventable, more than 55,000 people die each year, mostly in areas of the world which still have the "dog-to-dog" type of rabies. Responsible animal stewardship and dog vaccination campaigns can control and even eliminate this type of rabies. Rabies control in dogs leads to better health for both dogs and humans - a perfect example of the One Health-One Medicine approach.

The World Rabies Day initiative advocates for improving the health of the whole population, human and animal, by raising awareness about the need to control rabies in the main global reservoir, the dog, and to prevent human rabies through education and medical prophylaxis. The initiative arose from a small group of rabies professionals who formed the Alliance for Rabies Control and built

St. Georges University, Grenada (Courtesy Allison Alchemy)

Zambia (Courtesy Dr Perfecto Buyamba Kabanshi)

Thailand (Courtesy Molecular Biology Center for Neurological Diseases, Chulalongkorn University Hospital)

partnerships with the Student American Veterinary Medical Association (AVMA), World Organization for Animal Health (OIE), Centers for Disease Control and Prevention, World Health Organization, and many others.

As part of a World Rabies Day One Health Challenge series, the Student AVMA Chapters staged events at 24 North American Veterinary schools during the inaugural World Rabies Day 2007. The funds that they raised and donated to the initiative through the Alliance for Rabies Control were matched by Veterinarians Without Borders /Veterinaires Sans Frontieres, Canada. At least 45 proposals from around the world are now competing for this funding. These activities and donations led to an additional donation from a private donor - we are calling this part of the campaign "Dr. Bob's Patron for Prevention" - to enhance this years' funding of community level rabies prevention projects and secure resources for next seasons' campaign.

Presently, the World Rabies Day team has responded to inquiries from individuals in at least 180 countries throughout the world. We expect that this initiative will to help reduce inequities and neglect that lead to human rabies cases and uncontrolled dog-to-dog transmission of rabies, produce measurable results, and catalyze increased momentum, scale, and sustainability of change, through collaborations with government, philanthropic, private-sector, and not-for-profit partners.

As Professor Dzikwi from Ahmadu Bello University said,

"Together we can Make Rabies History."

Dr. Cathleen A. Hanlon is the Director of the Rabies Laboratory at Kansas State University.

New 'One Health' website to be unveiled soon…

Bruce Kaplan, DVM

Dr. Bruce Kaplan

The pro bono "One Health" team of Laura H. Kahn, MD, MPH, MPP, Bruce Kaplan, DVM, and Thomas P. Monath, MD has announced that an autonomous free access 'One Health' website is under construction and will shortly be available online at www.onehealthinitiative.com . This has been under consideration for many months. Over the past months inquiries about such a venture have been received from individuals in the U.S. and other countries. The most common comment heard has been "a One Health website is not only important but a must…as soon as possible!"

The developers envision this website as a method of providing worldwide 'One Health' Initiative information for the general public, political and governmental leaders, news media and all 'One Health' professionals, advocates and supporters. As the 'One Health' movement evolves via the American Veterinary Medical Association (AVMA) 'One Health' task force Steering committee/National One Health Commission, it is hoped that this website will eventually be transitioned/merged under their auspices.

The 'One Health Newsletter' and its links will be prominently featured on the site as a major 'One Health' international educational online publication. In addition, there

will be links to the AVMA 'One Health' task force recommendations published in the Journal of the AVMA (JAVMA) and other pertinent 'One Health' publications.

Drs. Kahn and Monath serve as contributors to the Newsletter and Dr. Kaplan serves on the editorial board. All three have been closely allied with the Newsletter since its inception. It should be noted that Dr. Monath served as a member of the AVMA 'One Health' task force.

"All stakeholder organizations, their leaders and individual advocates are requested to notify the website of any suggested corrections, changes or additions (such as news items, publications and future 'One Health' symposia or events). Contact will be via Dr. Kaplan at brucekaplandvm@onehealthinitiative.com . Thank you for your valued participation and assistance."

The One Health concept is a worldwide strategy for expanding interdisciplinary collaborations and communications in all aspects of health care for humans and animals. 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. When properly implemented, it will help protect and save untold millions of lives.

Dr. Bruce Kaplan is a retired veterinarian, who formerly worked as a CDC Epidemic Intelligence officer, staff officer and regional public affairs specialist for USDA-FSIS and has been a columnist writer/editor. Dr. Kaplan promotes "One Health" collaboratively with Laura H. Kahn, MD, MPH, MPP and Thomas P. Monath, MD.

Recent One Health News and Publications:

- **The Global Initiative for Food Systems Leadership** released its inaugural update **"One to One"** promoting global food chain leadership.

http://www.cvm.umn.edu/cahfs/globalinitiative/onetoone/1/index.html

- Dairy Herd Management, September 8, 2008, **Food-animal veterinarians and One Health**
http://www.dairyherd.com/special_reports.asp?pgID=295&ed_id=7635

- JAVMA News , October 1, 2008, **Public Health, One-health wonders,**
http://www.avma.org/onlnews/javma/oct08/081001h.asp

An interview with Barbara Natterson Horowitz, MD, a cardiology professor at the University of California-Los Angeles and the director of imaging (electrophysiology) for the Cardiology Division at the David Geffen School of Medicine at UCLA, who has provided imaging and consultative services to the veterinarians at the Los Angeles Zoo.

One Health Newsletter

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Coming Events:

- **International EcoHealth Forum 2008**

  "EcoHealth: Healthy Environments, Healthy People"

  Mérida, México

  December 1– 5, 2008

  www.ecohealth2008.org

- **Sixth Annual "One Medicine" Symposium**

  Durham, North Carolina

  December 10-11, 2008

  www.onemedicinenc.org or call 919-966-4032

  "Earth, Wind, and Fire:
  A One Medicine Approach to Climate Change"

- **The International Meeting on Emerging Diseases and Surveillance (IMED 2009)**

  Vienna, Austria

  February 13-16, 2009, Hotel Hilton

  http://imed.isid.org/