One Health Newsletter

A quarterly newsletter highlighting the interconnectedness of animal and human health

Summer 2009 **Volume 2 Issue 3**

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.

An Academic Commitment to One Health

Cheryl Scott, DVM, MPVM, Bennie Osburn, DVM, PhD, and Rance LeFebvre, PhD

Today's global health issues increasingly require the expertise of the veterinary profession. Bioterrorism, emerging infectious diseases, food- and waterborne contaminants, environmental degradation, and ecological disturbances are all issues that veterinary medicine can help address. But historically, few veterinarians have been trained in the One Health approach. Most veterinary curricula emphasize small-animal or food-production-animal clinical care. There is often little integration with other fields such as ecology, policy making, or public health, leaving the One Health role of the veterinarian constrained by the lack of a broader educational background.

The University of California, Davis, which houses schools of medicine, veterinary medicine, nursing, and law, as well as colleges of agricultural and environmental sciences, is uniquely positioned to galvanize such multidisciplinary education. The **Calvin Schwabe One Health Project (CSOHP),** at the UC Davis School of Veterinary Medicine, was established to advance the School's commitment to the One World-One Health movement in the education of graduating veterinarians. These practitioners of the future will contribute unique skills toward the common goals of uniting animal and public health with ecosystem protection.

Clearly, to address current global health issues, we must train veterinary students in One Health. But veterinary education is already lengthy and expensive. Asking students to attend additional years of schooling at additional cost is unlikely to be met with enthusiasm unless students are made vividly aware of the need for veterinarians in this area. Even then, students need to feel assured that there are career opportunities awaiting them in One Health.

One solution is to support and create expanded educational avenues outside the traditional clinical path. The Calvin Schwabe One Health Project provides opportunities that will produce veterinary graduates who are prepared to step immediately into non-clinical positions in support of One Health objectives. CSOHP creates internships, externships, fellowships, post-doctoral positions, and graduate degrees in pertinent fields, and offers intense but broad-reaching, practical, comprehensive training. With these efforts, CSOHP ensures that future practitioners are well prepared to monitor and provide optimum healthcare for humans, animals, and the ecosystems in which they live. At a time when California is experiencing cuts to higher education budgets, programs such as

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- Palm Beach County Health Department
- Florida Department of Health
- University of Florida
- Kahn/Kaplan/Monath One Health Team

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In This Issue

Articles:

Calvin Schwabe One Health Project make relevant and lasting contributions to society by wisely using financial resources to train students to solve real-world problems that affect everyone.

Students participating in CSOHP are already making valuable contributions to global health concerns. Davis veterinarian Marcia Merryman, for her MPVM (Masters of Preventive Veterinary Medicine, the only such program in the country), conducted the project, "Veterinarians' preparedness to respond to a foreign animal disease or bioterrorism event." The results of this study suggest that veterinary practitioners are inadequately prepared to identify "red flag" clinical presentations of potential public-health threats that warrant immediate notification of animal regulatory authorities. This study sets up an important needs-assessment question and warrants further queries. Another ongoing project, "Migratory waterfowl and their role in emerging zoonotic infectious disease transmission," being conducted by veterinarian Juliana Milani, is exploring how Tundra Swans may be implicated in the overlap of animal and human health as the swans migrate and settle near populated areas.

The Calvin Schwabe One Health Project is producing a new generation of veterinarians who will be ready to lead a collaborative, transdisciplinary, multi-species effort to improve global health. With expertise in biohazard events, food and water safety, vector-borne diseases, established and emerging zoonotic diseases, herd health, foreign animal risks, and public health issues such as antimicrobial resistance, these graduates will be positioned as true One Health advocates and practitioners of the future.

For more information, please visit the Calvin Schwabe One Health Project website at http://www.vetmed.ucdavis.edu/onehealth/.

Dr. Cheryl Scott is the Director of the Calvin Schwabe One Health Project at the University of California, School of Veterinary Medicine.

Dr. Bennie Osburn is the Dean of the School of Veterinary Medicine at the University of California Davis.

Dr. Rance LeFebvre is associate dean of student affairs at the University of California Davis, School of Veterinary Medicine.

One Health concept: *mirabile dictu*

Bruce Kaplan, DVM

"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 in our present and future generations." The previous statement is indeed *mirabile dictu*, i.e. Latin for 'wonderful to relate' … and the original language was derived from the One Health Initiative website (http://www.onehealthinitiative.com).

The One Health concept is a worldwide strategy for expanding interdisciplinary collaborations and communications in all aspects of health care for humans and animals.

As most One Health advocates/supporters know, there have been various altruistic One Health physician, veterinarian, and health scientist leaders in the past including the father of **cellular** pathology, Rudolf Virchow; the father of modern medicine, Sir William Osler; Calvin Schwabe, the veterinarian-parasitologist who coined the "One Medicine" term, now called "One Health"; the past President of the American Medical Association, Ronald Davis; the former JAVMA Editor-in-Chief, Janis Audin, and the Nobel Laureate, Joshua Lederberg.

I dare say some living One Health altruists are CDC veterinarians, Lonnie King, Director-National Center for Zoonotic, Vector-Borne and Enteric Diseases, and James H. Steele (the founder of the veterinary public health division); Kansas State University veterinary medical college Dean Ralph Richardson; Princeton physician Laura H. Kahn; physician virologist Thomas P. Monath; Yale physician Peter Rabinowitz; virologist and ProMED-mail co-founder, Jack Woodall; and prominent international public health leader, Michael Osterholm. Of course, there are many others, too numerous to name in the USA and globally.

Mirabile dictu, i.e. Latin for 'wonderful to relate.'

A critically important national (USA) One Health Commission is expected to be operational by July 1, 2009 with the charge to promote implementation and institutionalization of One Health in the USA and internationally. Several prominent, influential individuals will serve on this commission and represent various organizational constituencies and stakeholders. Efficacy here will be essential and crucial for the blossoming of the One Health movement.

The Pulitzer Prize winning military historian of the 20th century, John Toland, has said, "…it is human nature that repeats itself, not history". In our noble pursuit of the benefits that One Health will inevitably provide for human and animal health, we must strive for perfection, not mediocrity. The following articles—their authors and co-authors— in this One Health Newsletter Summer Issue are prime examples of *mirabile dictu.*

Dr. Bruce Kaplan, a retired veterinarian, currently co-manages the One Health Initiative website (http://www.onehealthinitiative.com), and serves on the editorial board of this One Health Newsletter.

One Health Joint Steering Committee Update

Carina Blackmore, DVM, PhD

A critically important national (USA) One Health Commission is expected to be operational by July 1, 2009.

The One Health Joint Steering Committee held its 3rd meeting in Washington DC on May 6, 2009. As I have mentioned in previous Newsletter updates, the main purpose of this Committee is to create a One Health Commission (OHC). The Commission will complete the implementation of the recommendations of the One Health Initiative Taskforce (http://www.avma.org/onehealth/recommendations.pdf) over a three-to-five year period. The Taskforce report was discussed in detail in our July, 2008 edition of the Newsletter (www.doh.state.fl.us/Environment/community/One_Health/OneHealth.html).

The work of the One Health Joint Steering Committee is coming to an end and the Committee is transitioning to the One Health Commission(OHC) in July 2009.

The work of the One Health Joint Steering Committee is coming to an end and the Committee is transitioning to the OHC in July 2009. The draft by-laws of the new not-for-profit 501(c)(3) organization were reviewed and edited during the meeting. One appointed representative each from the American Medical Association, American Veterinary Medical Association, American Society for Tropical Medicine and Hygiene, American Association of Medical Health Center, American Public Health Association, American Association of Medical Colleges, American Association of Veterinary Medical Colleges, Association of Fish and Wildlife Agencies, and American Society of Microbiology will make up the membership of the OHC. The Commission will also be able to add additional ad hoc Ex Officio members as needed. It is anticipated that the OHC also will form a One Health Advisory Council with members from additional One Health stakeholder groups including governmental agencies and associated interest organizations.

Work is currently underway to support an Institute of Medicine report on One Health.

Representatives from the One Health Steering Committee met with the representatives from the Institute of Medicine (www.iom.edu) on May 5th to discuss our interest in supporting an Institute of Medicine report on One Health. Such reports are written by experts in the field and intended to guide policy and other leaders as they attempt to write or implement One Health science and public health policies or ideas. The first meeting was a success and discussions will be continuing over the summer to define the scope and goal of the study. The first phase of the project, the fund raising phase, will get underway later this fall. The one-day One Health Summit will be held in Washington DC in conjunction with this event.

Dr. Carina Blackmore is Chair of the One Health Initiative Steering Committee's communications workgroup, a member of the One Health Newsletter editorial board, and Florida's State Public Health Veterinarian.

Of Mice & Men (and DOGS!): One Health Realized through Xenogeneic DNA Vaccines for Cancer

Philip J. Bergman DVM, PhD, DACVIM-Onc & Jedd D. Wolchok MD, PhD

Melanoma is the most common oral malignancy in the dog.

Melanoma is the most common oral malignancy in the dog.[1] Oral and/or mucosal melanoma is generally considered an extremely malignant tumor with a high degree of local invasiveness and metastatic propensity. Dogs with malignant melanoma in anatomic sites predicted to have a moderate to high metastatic propensity (oral, digit, foot pad, etc.), or dogs with cutaneous histologically aggressive melanoma, require the use of systemic therapies. Unfortunately, response rates with chemotherapy are poor.[2, 3] Two recent studies suggest that chemotherapy plays an insignificant role in the adjuvant treatment of canine malignant melanoma (CMM), similar to human melanoma (HM). It is clear that new approaches to the systemic treatment of this disease are desperately needed.

Recent studies suggest that chemotherapy plays an insignificant role in the adjuvant treatment of canine melanoma, similar to human melanoma.

Immunotherapy represents one potential logical systemic therapeutic strategy for melanoma. A variety of immunotherapeutic strategies for the treatment of human melanoma have been reported previously, with typically poor outcomes due to a lack of breaking tolerance. Immunotherapy strategies to date in canine melanoma have also used a variety of approaches.[4-8] Although these approaches have produced some clinical anti-tumor responses, the methodologies for the generation of these products are expensive, time consuming, sometimes dependent on patient tumor samples being established into cell lines and fraught with the difficulties of consistency, reproducibility, and other quality control issues.

The advent of DNA vaccination circumvents many of the previously encountered hurdles in vaccine development. DNA is relatively inexpensive and simple to purify in large quantities. Although DNA vaccines have induced immune responses to viral proteins, vaccinating against tissue specific self-proteins on cancer cells is clearly a more difficult problem. One way to induce immunity against a tissue specific differentiation antigen on cancer cells is to vaccinate with xenogeneic (different species) antigen or DNA that is homologous to the cancer antigen.[9]

Immunotherapy offers an alternate approach.

Vaccination with DNA encoding cancer differentiation antigens is ineffective when self-DNA is used, but tumor immunity can be induced by orthologous DNA from another species.[10]

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We have chosen to target defined melanoma differentiation antigens of the tyrosinase family. Tyrosinase is a melanosomal glycoprotein, essential in melanin synthesis. Immunization with xenogeneic human DNA encoding tyrosinase family proteins induced antibodies and cytotoxic T-cells against syngeneic B16 melanoma cells in C57BL/6 mice, but immunization with mouse tyrosinase-related DNA did not induce detectable immunity.[11] In particular, xenogeneic DNA vaccination induced tumor protection from syngeneic melanoma challenge and autoimmune hypopigmentation. Thus, xenogeneic DNA vaccination could break tolerance against a self-tumor differentiation antigen, inducing antibody, T-cell, and anti-tumor responses.

This study targeted defined melanoma differentiation antigens of the tyrosinase family.

From April 2000 to June 2007, approximately 500 dogs with previously histologically confirmed spontaneous malignant melanoma were treated at the Animal Medical Center with xenogeneic DNA vaccinations. All dogs were clinically staged according to the WHO staging system of stage I (tumor < 2 cm diameter), II (tumors 2-4 cm diameter, negative nodes), stage III (tumor > 4 cm and/or positive nodes), or stage IV (distant metastatic disease). Dogs with WHO stage II, III, or IV histologically confirmed malignant melanoma were allowed entrance into the studies due to the lack of effective available systemic treatments. Due to a strong safety profile, dogs with stage I melanoma were allowed inclusion from 2005 on. Written consent for entry onto this trial was obtained from each dog's owner prior to entry into the study; this consent included request for necropsy upon death due to any reason. These studies were performed under Animal Medical Center IRB approval.[12]

Human tyrosinase cDNA was inserted in the pING plasmid vector that contained both a cytomegalovirus promoter and a kanamycin resistance selection marker.

No toxicity was seen in any dogs receiving the aforementioned vaccines with the exception of minimal to mild pain responses at vaccination, one muGP75 dog experienced mild aural depigmentation, and one muTyr dog experienced moderate foot pad vitiligo. The Kaplan-Meier Median Survival Time (KM MST) for dogs which received any melanoma vaccine (ie HuTyr, MuTyr and MuGP75) for stage I, II, III and IV CMM was > 939 days (median not reached with 92.8% survival), > 908 days (median not reached, 79% alive at 1 year, 63% alive at 2 years), > 1646 days (median not reached, 77%, 65%, 57% alive at 1, 2, 3 years), and 239 days (40.5% and 18.8% alive at 1 and 2 years), respectively. The results from dogs vaccinated with huTyr were published in 2003.[13] We have investigated the antigen-specific immune responses of dogs receiving HuTyr as a potential explanation for the long term survivals seen in some of the dogs on this study.[14, 15]

The HuTyr-based canine melanoma vaccine became commercially available in June, 2007…….. This represents the first US-government approved vaccine for the treatment of cancer.

The results of these trials demonstrate that xenogeneic DNA vaccination in CMM is: 1) safe, 2) develops specific anti-tyrosinase immune responses, 3) potentially therapeutic with particularly exciting results in stage II/III local-regional controlled disease, and 4) an attractive candidate for further evaluation in an adjuvant, minimal residual disease Phase II setting for CMM. A safety and efficacy USDA licensure multi-institutional trial investigating HuTyr in dogs with locally controlled stage II/III oral melanoma was initiated in April 2006 across five sites. Human trials of xenogeneic tyrosinase DNA vaccination have initiated and are ongoing with promising initial clinical and immunologic assay results (Wolchok et al, 2007; Perales et al, 2008).[16, 17] In late March 2007, we received conditional licensure from the USDA for the HuTyr-based canine melanoma vaccine, and it became commercially available in June 2007. This represents the first US-government approved vaccine for the treatment of cancer. Approximately 2500 dogs with malignant melanoma have received the conditionally licensed Merial, Ltd. HuTyr canine melanoma vaccine, and approximately 1200 dogs are entered into the internet-based Merial melanoma vaccine follow-up database (personal communication, Dr. Robert Menardi, Merial Ltd.).

Human trials of xenogeneic tyrosinase DNA vaccination have initiated and are ongoing with promising initial clinical and immunologic assay results.

In summary, CMM is a more clinically faithful therapeutic model for HM when compared to more traditional mouse systems, as both human and canine diseases are chemoresistant, radioresistant, share similar metastatic phenotypes/site selectivity, and occur spontaneously in an outbred, immuno-competent scenario. In addition, this work also shows that veterinary cancer centers and human cancer centers can work productively together to benefit veterinary and human patients afflicted with cancer. It is hoped in the future that this same vaccine may also play roles in the treatment of melanoma in other species (e.g. horses, cats, humans, etc.) due to its xenogeneic origins, and in melanoma prevention once the genetic determinants of melanoma risk in dogs are further defined. It is easy to see how the veterinary oncology profession is uniquely able to greatly contribute to advances for both canine as well as human melanoma, in addition to many other cancers with similar comparative aspects across species. These authors believe that the xenogeneic DNA vaccine platform holds promise with other antigen targets and have Phase I and Phase II studies initiating soon utilizing murine CD20 and rat HER2 across the BrightHeart Veterinary Centers network.

Veterinary cancer centers and human cancer centers can work productively together to benefit veterinary and human patients afflicted with cancer.

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References:

http://www.doh.state.fl.us/Environment/medicine/One_Health/OfMiceandMen_References.pdf

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Dr. Jedd D. Wolchok is the Director of Immunotherapy Clinical Trials, Associate Attending Physician on the Melanoma-Sarcoma Oncology Service, and Associate Director of the Ludwig Center for Cancer Immunotherapy at Memorial Sloan-Kettering Cancer Center.

Dengue Research by the University of Florida in South America

Phil Lounibos, PhD, Jorge Rey, PhD & Harish Padmanabha

Dengue fever (DF) is currently the most important arboviral disease of humans, infecting an estimated 50 million persons annually. Originally an Old World zoonosis, DF has emerged in recent decades as a cosmotropical malady now maintained in most endemic areas by human-vector contacts, especially with the domestic and anthropophilic mosquito *Aedes aegypti.* The current health burden of dengue is immense, especially in tropical cities around the globe, and the problem is greatly magnified by the increasing frequency of co-circulation of multiple dengue serotypes, which is linked to the occurrence of the more dangerous and potentially fatal dengue hemorrhagic fever (DHF).

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In the Americas, where most countries from Mexico to Argentina suffer endemic transmission, four factors contribute to the present-day dengue burden. First is the abundance and expanded range throughout the Neotropics of *A. aegypti*, following the failed eradication program against this species in the Americas in the 1950s and 60s. Related to dengue's spread is urbanization and unplanned population growth, which concentrates susceptible humans, particularly children and rural immigrants, in close proximity to *A. aegypti* populations that proliferate in containers maintained or discarded in the vicinity of homes. A third contributor is globalization and increased movement of human hosts who transport new genotypes and serotypes of the virus between cities, countries, and continents. Finally, vector abatement is the only available method of disease control, yet has proven challenging to implement because of difficulties in identifying and reducing mosquito production from the varied and arcane larval habitats utilized by domestic *A. aegypti*.

Urbanization and unplanned population growth concentrates susceptible humans in close proximity to A. aegypti populations.

University of Florida researchers collaborated with counterparts in Colombia and Brazil to investigate sociological, entomological, ecological, and virological factors contributing to the dengue problem.

The rapid rise in importance of dengue in the Americas has outpaced research devoted to understanding the complex interrelationships of the sociological, entomological, ecological, and virological factors which contribute to this problem. Here we briefly describe the goals and preliminary achievements of two ongoing projects of University of Florida (UF) researchers conducted collaboratively with counterparts in Colombia and Brazil.

In the Andean nation of Colombia, dengue is endemic in cities located from sea level to approximately 1,700 m ASL, above which average daily temperatures become too cold for propagation of dengue viruses in mosquito vectors. Colombia's Integrated National Adaptation Project (INAP) supports the design and implementation of an integrated dengue surveillance and control system carried out through that country's National Institute of Health (INS). As the principal investigator of the dengue component of INAP, UF Ph.D. student Harish Padmanabha has worked with Colombian colleagues to acquire and analyze preliminary data that support a series of hypotheses about interrelationships between human behaviors, housing density, socioeconomic status, weather (especially temperature), dengue transmission and maintenance, and *A. aegypti* production.

Most vector production in the vicinity of Colombian houses comes from vessels used to store water, but when premises are large, containers discarded in yards also become important. Studying water storage vessels in three cities, we observed a strong relationship between frequency of container emptying and vector production, frequent emptying inhibiting the successful completion of mosquito development. Demographic data from national censuses and dengue incidence data from INS were analyzed for relationships between housing density, socioeconomic status (SES), and average age at first infection. Results showed that lower SES and higher housing densities were associated with younger ages of first infection. Further, urban census and dengue incidence data indicated that maintenance of dengue transmission requires a minimum population size of approximately 100,000 inhabitants, suggesting that epidemics in smaller cities are probably instigated through re-introductions of the virus.

Ongoing research in Colombia on vector production, dispersal and longevity, household behaviors favorable for *A. aegypti*, host age structure, social contact patterns, SES, and dengue infection rates is being integrated by the development, parameterization, and validation of two, complementary discrete-time models: (a) a model of temperature-dependent development of *A. aegypti* immature stages in water-containing vessels in urban residential areas; (b) a composite model of dengue transmission and propagation across houses and neighborhoods along interacting networks of vector dispersal and human movement.

An independent dengue research project is being conducted with colleagues at the Oswaldo Cruz Institute (IOC) in Rio de Janeiro, the Brazilian city which suffered in 2008 an astounding 125,512 official cases, with 159 deaths

attributable to DHF. The comparatively narrower focus of this project is to evaluate the impact of larval competition, which is correlated with smaller vector body size, on dengue infection in DF hot-spots in Rio. This research is predicated on the Ph.D. thesis of recent UF/FMEL graduate Barry Alto who demonstrated through laboratory experiments that intense larval competition among and between *A. aegypti* and the secondary dengue vector *A. albopictus*, leads to smaller adult females which succumb to higher rates of infection and dissemination of the virus. Although it has been known that larval competition is common in nature, especially in the nutrient-poor water containers occupied by immatures of these species, Alto's novel results demonstrated how competition could transcend its effects on the aquatic stages to impact disease transmission.

Both A. aegypti and A. albopictus are locally abundant in Florida…..

Supported by a three-year grant from NIH's Fogarty Center, Phil Lounibos of UF, Steve Juliano of Illinois State University, and IOC collaborators are investigating whether the aforementioned competition-vector competence relationship can be detected in dengue-endemic Rio de Janeiro. The principle objectives of this project are to demonstrate: (1) the presence and intensity of larval competition in containers occupied by vectors in Rio; and (2) that smaller mosquitoes have higher infection rates. To accomplish the latter, more than 3,000 adult mosquitoes were collected in 2008 during periods of high DF incidence by power aspiration of resting adults in dengue hot spots. These mosquitoes will be analyzed individually at IOC in 2009 for dengue infection, and body size correlated with dengue incidence, to test our hypothesis.

……So although dengue epidemics have not occurred in the state since the 1920s, the possibility of autochthonous local transmission of virus introduced by travelers or immigrants is very real.

Although dengue epidemics have not occurred in Florida since the 1920s, both *A. aegypti* and *A. albopictus* are locally abundant in Florida, so the possibility of autochthonous local transmission of virus introduced by travelers or immigrants should not be discounted. Ongoing research in Colombia, Brazil, and other dengue-endemic areas is dedicated to improving our understanding and, hence, capacity to control, this emergent disease.

Dr. Phil Lounibos and Dr. Jorge Rey are Professors at the Florida Medical Entomology Laboratory of the University of Florida, Vero Beach.

Harish Padmanabha is a Ph.D. candidate at the Florida Medical Entomology Laboratory of the University of Florida.

The One Health Concept in Comparative Orthopaedics

James L. Cook, DVM, PhD; Steven P. Arnoczky, DVM

The concept of comparative medicine is almost as old as medicine itself. The ancient Greeks understood that information about the process of life could be gained by dissecting and studying animals (1). From the comparative anatomical and physiological studies of Galen and William Harvey to the discovery of insulin by Frederick Banting and Charles Best, the careful and detailed studies performed on animals were often responsible for significant advances in human medicine (2). The musculoskeletal system is especially well-suited to comparative studies, as humans suffer from a variety of acute and chronic disorders of bone and joints that have similar counterparts in animals (1). Therefore, information gained from one

The concept of comparative medicine is almost as old as medicine itself.

Information gained from one species can often be directly translated to another.

species can often be directly translated to another, thus accelerating advancements in the diagnosis and treatment of musculoskeletal disorders in both man and animals. Because of this, comparative orthopaedic research has served as one of the cornerstones of the "one health" concept for decades.

As early as the 1930s, the concept of comparative orthopaedics was beginning to evolve. Otto Stader, a small animal veterinarian, took a comparative approach to fracture fixation in dogs. After studying the work of Swiss surgeon Gadvilli, Stader developed the first form of external skeletal fixation, the Stader splint, for fracture stabilization in dogs. His work was subsequently translated back to human application by Navy surgeons looking for improved methods of fracture treatment for sailors in World War II. In the 40s and 50s, various methods for intra-medullary pinning were being investigated in parallel by physicians and veterinarians. Jacques Jenny, a veterinarian surgeon in this era, performed one of the first intra-medullary pinning procedures in animals and significantly advanced the field of comparative orthopaedics by helping to develop successful strategies for fracture repair in horses and humans.

Jacques Jenny, a veterinarian surgeon, helped to develop successful strategies for fracture repair in horses and humans.

In the 50s and 60s, veterinarians were also involved in the development of Sir John Charnley's total hip replacement system for humans using a canine model, and participated in the development of internal fixation techniques and instrumentation through collaborations in the AO/ASIF organization. In 1966, Sten-Erik Olsson VMD, MD and John L. Marshall DVM, MD, both of whom had degrees in veterinary medicine as well as human medicine, founded the first laboratory dedicated to comparative orthopaedic research at the Hospital for Special Surgery in New York City. These innovative pioneers have helped to develop, define, and advance the role of comparative orthopaedic research in the "one-health" concept. In addition, they have inspired new generations of comparative orthopaedic researchers around the world.

Today, "one health" comparative orthopaedic laboratories are located throughout the world and typically employ both a comparative and translational research approach in an effort to improve diagnostics, develop preventative and therapeutic strategies, and advance our understanding of disease mechanisms.

While comparative research focuses on common pathological and regenerative pathways across species, translational research refers to studies that attempt to extend basic science discoveries into practical clinical applications.

Careful and detailed studies performed on animals were often responsible for significant advances in human medicine.

An example of a translational research study would be to determine if a drug's ability to increase cartilage cell metabolism could be translated into a clinical treatment of arthritis. Such translational studies are usually carried out in the animal species deemed most appropriate by comparative research investigations and are the "pre-clinical" foundations on which clinical applications in humans are based. Indeed, many of the current, standard-of-care, orthopaedic procedures associated with meniscal repair and replacement, articular cartilage repair and regeneration, ligament and tendon repair and replacement, and fracture repair have been the products of comparative and translational orthopaedic research studies.

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The comparative and translational avenues of "one-health" research should be considered "two-way bridges".

The multidisciplinary collaborations will continue to yield significant advances in the quality of orthopaedic healthcare for both animals and man.

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Importantly, the comparative and translational avenues of "one-health" research must always be considered *"two-way bridges".* While the knowledge gained and the technologies developed through comparative orthopaedic research are often initially focused on human applications, many of these advancements can be (and have been) brought back to the animal species in which they were originally studied in for veterinary clinical application. Because the majority of comparative orthopaedic research laboratories are directed by veterinarians who have had extensive clinical, as well as research training, such clinical applications are becoming more common. Advances in total joint replacement, fracture fixation, and cartilage repair are but a few examples of how knowledge flows in both directions on the *"two-way bridge"* of comparative and translational orthopaedic research (Figure 2).

Comparative orthopaedic research is an excellent example of the evolving paradigm of the "one health" concept. The multidisciplinary collaborations between physicians, veterinarians, physical therapists, engineers, molecular biologists, and a host of other scientific disciplines have yielded, and will continue to yield, significant advancements in the quality of orthopaedic healthcare in both animals and man.

References

1. Olsson, S-E; Comparative Orthopaedics, *Clin Orthop Related Res* 62: 3-5, 1969.
2. Lyons, AS, Petrucelli RJ: Medicine: An Illustrated History. Abradale Press, New York, 1978.

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Monitoring Animal Diseases & Their Impact on Public Health in Wyoming

Karl Musgrave, DVM, MPH and Emily Thorp, MS

Dr. Tim Graham drove his pickup loaded with trash down the dusty dirt road and through the entrance gate to the Big Horn County Landfill. He looked forward to seeing and talking to Connie Stolk, the landfill manager, as they had known each other for most of Tim's 57 years. Tim had been Connie's veterinarian for many of those years.

As Tim pulled up to the tiny shack where Connie collected the landfill fees, he immediately noticed the troubled look on Connie's face.

"Hey Tim, what is causing all the sheep deaths?" Connie asked. "We have buried probably ten sheep brought in by ranchers over the past week.

This incident illustrates one of the unexpected sources of animal disease information that has been discovered during the beginning years of a pioneering surveillance program at the Wyoming Department of Health (WDH). The program, initiated in 2004, collects information on zoonotic diseases and adverse health events in animals that may potentially affect humans. A zoonotic disease is one that can be transmitted from vertebrate animal to humans.

The Wyoming Department of Health established a surveillance program to collect information on zoonotic diseases and adverse health events in animals that may potentially affect humans.

The surveillance activity is accomplished through the use of seven regional veterinary public health coordinators (RVPHCs), who collect information from veterinary clinics and other sources each week. Dr. Tim Graham is one of the RVPHCs. The information is then forwarded to the State Public Health Veterinarian, who compiles a summary report that is distributed widely throughout both the public health and animal health communities.

In the landfill incident described above, the cause of the sheep deaths was not known for several days, though two zoonotic diseases were suspected. Anthrax was considered because many of the sheep were found dead without any previous illness observed by the rancher. Sudden deaths are often seen with anthrax. The other, less well known, zoonotic disease considered was Orf, or contagious ecthyma. Orf is caused by a *parapoxvirus* and causes lesions on the lips and mouth of sheep and goats. Most of the sheep at the landfill had oral lesions.

The outbreak, which occurred in the summer of 2007, was determined to be caused by Bluetongue disease. Also known as Catarrhal fever, Bluetongue is not a zoonotic disease and did not represent a danger to public health. It is caused by a virus transmitted through the bite of an infected fly, primarily to livestock such as sheep, cattle, goats, and to some wildlife including buffalo, deer, and antelope. When Dr. Graham alerted authorities to the outbreak, fewer than 25 sheep had died. However, those sheep came from several separate ranches, and even though a quarantine preventing movement of sheep in the area was instituted, the disease eventually spread to more than 900 sheep and caused the deaths of about 300. Dr. Graham's early discovery was instrumental in controlling what could have been a much larger outbreak.

After the September 11, 2001 terrorist attacks, Wyoming designated veterinarians to monitor and report animal disease activity in their areas.

Wyoming started designating veterinarians to monitor and report animal disease activity in their regions after the September 11, 2001, terrorist attacks. Because most of the biological agents that could be used as weapons against human populations are zoonotic, illness or death in animals could be early indicators of the release of a biological agent during a bioterrorism event. The state wanted to avert potential acts of agroterrorism that could negatively affect the Wyoming livestock industry. The directors of the Wyoming Office of Homeland Security, Wyoming Livestock Board, and the Wyoming Department of Health collaborated to initiate the program, which is supported through funds from the Wyoming Public Health and Emergency Preparedness Program. In the early stages of the program, the seven veterinarians, originally referred to as regional veterinary coordinators (RVCs), focused on preparedness activities related to a potential bioterrorism and agroterrorism incident. Disease monitoring was passive—the RVCs periodically informed area veterinarians, ranchers, and others that they were available to respond to suspected or confirmed outbreaks.

Each week, seven regional veterinary public health coordinators (RVPHCs) collect information from veterinary clinics and other sources.

The Bluetongue outbreak pointed out an unfortunate side effect of the passive approach. Investigators learned that a veterinarian suspected the disease on one ranch but withheld the information out of concern that the flock would be quarantined, economically harming the rancher. Because of an apparent reluctance of veterinarians, ranchers, and others to report diseases to their RVCs during the first two years, a confidential, active surveillance system was implemented in September 2007. The RVCs were encouraged to build good working relationships with source veterinarians and the general public by ensuring their confidentiality and discussing the importance of such a system for the safety of their livestock and public health.

Under the new surveillance system, RVCs are now referred to as regional veterinary public health coordinators (RVPHCs) to better reflect their public health role, and are required to spend at least two hours a week actively contacting their reporting sources. Each week, they report their findings to the State Public Health Veterinarian.

The information is then forwarded to the State Public Health Veterinarian, who compiles a summary report that is distributed widely throughout both the public health and animal health communities.

The type of contact between source and RVPHC varies. Some use e-mail while others contact their sources by phone and request reports by fax. A few RVPHCs meet in person each week with critical sources, such as the owner of the busiest veterinary clinic in their region. It is hoped that this active surveillance system will identify problems early, as reporting sources are now directly asked about animal diseases seen over the previous week.

A preliminary data analysis shows that, from September 2007 to October 2008, the system received 589 reports, 488 of which were confirmed or suspected zoonotic diseases. It showed 228 reports of animal bites or rabies-related incidents, including 20 confirmed cases of animal rabies, 63 cases of animals being confined and observed after biting a human, 7 cases of animals being quarantined after exposure to wild animals potentially infected with rabies, and 16 animals euthanized and tested for rabies. Among the confirmed or suspected zoonotic diseases, campylobacteriosis and salmonellosis were most common, with 35 and 15 reports respectively.

The information flows both way. Some of the zoonotic disease events were initially reported by the health department as human cases.

The information flows both ways. Some were initially reported by the health department as human cases where laboratory or epidemiological evidence pointed to an animal source of the illness. These included, in addition to the salmonellosis and campylobacteriosis cases, 12 poisonings, 9 wild animal die-offs, 15 undiagnosed illness syndromes, and a surprisingly high number of rattlesnake bites (14).

This surveillance system has numerous strengths. First, it has the ability to collect animal disease information that was missed by previous reporting mechanisms, including diseases diagnosed through private laboratories or those seen by non-traditional reporting sources such as landfill operators. Second, although Wyoming has an animal reportable disease list that includes major zoonotic diseases, it omitted many zoonotic pathogens such as *Campylobacter* and *Salmonella* species. Third, the program is inexpensive. The annual operating budget is $83,000, which includes the RVPHC contracts ($800 per month).

There are limitations to this surveillance system. In order to promote timely investigations and communication, veterinarians are encouraged to report suspected zoonotic diseases. However, further diagnostics may never be performed to determine if the veterinarian's suspicions are correct, and it can be difficult to determine the true incidence. Since the program is funded through a cooperative agreement from a federal agency, the long-term sustainability is susceptible to federal budget pressures. Furthermore, the voluntary nature of the program, as opposed to legally mandated reporting, makes it dependent on the willingness of individual veterinarians to participate. Currently, about half of the 70–80 veterinary clinics in Wyoming report information to the RVPHCs. The applicability of this program to other geographical areas where there are many more veterinary clinics may be limited; as the RVPHCs had met most, if not all, of the limited number of veterinarians in their regions before the program began. Nevertheless, the system provides a model of how an active surveillance system can be implemented at a modest cost. Efforts are underway to increase the number of reporting veterinary clinics as well as to recruit reporting from other sources such as animal control organizations.

Wyoming's surveillance system provides a model of how an active surveillance system can be implemented at a modest cost.

Resources

Heryford AG, Seys SA. Cattle and campylobacter risk factors in rural environments. *Northwest Public Health* 2003; 20(1): 10–11.

Zoonoses and Communi-cable Diseases Common to Man and Animals. 3rd edition, PN Acha, B Szyfres (Pan American Health Organization, Washington, DC, 2001, 2003).

Dr. Karl Musgrave is the State Public Health Veterinarian at the Wyoming Department of Health. Emily Thorp is a Surveillance Epidemiologist at the Wyoming Department of Health.

Lymphocytic Choriomeningitis Vrus (LCMV) – A Forgotten Microorganism of Man

R. Anthony Stidham, D.H.Sc., M.P.H.

Etiology and Epidemiology of Lymphoctytic choriomeningitis

The house mouse, Mus musculus, is the natural reservoir. Infected mice are often asymptomatic and may chronically shed the virus.

What image does one conjure up when one thinks of a mouthful of a word, Lymphocytic choriomeningitis virus (LCMV)? It's difficult to say, but the verdict probably wouldn't be good. A neglected pathogen of man, LCMV is a single-stranded RNA virus of the family Arenaviridae. [1] The first arenavirus, LCMV was discovered and coined by a Public Health Service physician, Charles Armstrong, during a study of an epidemic in St. Louis in 1933.[2,3] Although not the cause of the outbreak, LCMV was found to be a cause of non-bacterial or aseptic meningitis. His discovery of the virus demonstrated the veracity of the maxim "chance favors the prepared mind" exquisitely because he encountered a virus that was quite distinct from the virus strains he was isolating at the time of the 1933 epidemic of St. Louis encephalitis.

In addition, laboratory mice and colonized golden hamsters can be chronically infected and can be sources of human infection.

The infected house mouse, *Mus musculus*, is the natural reservoir and females transmit the infection to the offspring, which are often infected asymptomatically and chronically shed the virus in urine and other secretions. In addition, laboratory mice and colonized golden hamsters can be chronically infected and can be sources of human infection. Transmission to humans occurs through oral or respiratory contact with virus-laden excreta, or by ingestion of dust or food contaminated with the virus from the urine, feces, blood, saliva, droppings, nesting materials, or nasopharyngeal secretions of infected rodents.[4]

Person-to-person transmission does not usually occur, with the exception of direct transmission from an infected mother to fetus or patients who receive an organ transplant from an infected donor.[5] In May 2005, reports of the deaths of at least three organ transplant patients in the US were linked to the virus. Also, while the virus normally has little effect on healthy people, it can be deadly for people whose immune system has been weakened. In addition, handling articles contaminated by naturally infected mice may place individuals at high risk of infection.

Clinical Signs and Symptoms of LCMV

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Some people infected with LCMV do not become ill. For infected persons who do become ill, onset of symptoms usually occurs 6-13 days after being exposed to the virus.[4,11] A characteristic biphasic febrile illness then follows. The initial phase, which may last as long as a week, typically begins with any or all of the following symptoms: fever, malaise, lack of appetite, muscle aches, headache, nausea, and vomiting.[4] Other symptoms that appear less frequently include sore throat, cough, joint pain, chest pain, testicular pain, and parotid (salivary gland) pain. Following a few days of recovery, the second phase of the disease occurs, consisting of symptoms of meningitis (for example, fever, headache, and a stiff neck) or characteristics of encephalitis (for example, drowsiness, confusion, sensory disturbances, and/or motor abnormalities, such as paralysis).[1,4,11]

Although LCMV infection in humans with normal immune systems is usually either asymptomatic or a mild, self-limited illness, it can affect the nervous system, testes, heart, or joints

Pathophysiology

After transmission of LCMV via inhalation, consumption, cutaneous or mucosal exposure, or organ transplantation, the initial viremia of LCMV infection (phase 1) extensively seeds extra-CNS tissue. The secondary viremia (phase 2) infects the meninges and, less commonly, the cortical tissue. The leptomeninges are infiltrated mainly by lymphocytes and histiocytes, with few neutrophils. In LCMV encephalitis, the same type of inflammatory cells is observed in the perivascular response to the infected cells produces the various manifestations of this disease.

Natural killer (NK) cells are first to respond, followed by the production of interferon by cytotoxic T cells. In addition, LCMV can suppress the production of acetylcholine neuronal cells in cell culture. [6,7,8,9]

LCMV may affect the autonomic nervous system, various sensory modalities, and cranial nerves. Some cases of LCMV become chronic, potentially resulting in hydrocephalus. Other organs, especially the testes, heart, and joints, may be involved. Orchitis is usually unilateral. Cardiac involvement is typical of viral myocarditis. The metacarpal phalangeal joint and the proximal interphalangeal joint are the most common sites of arthritis caused by LCMV. The objective swelling, redness, and pain resolve within a few weeks.[8,9] Congenital LCMV infection is typically much more serious than the acquired disease. It mimics toxoplasmosis and cytomegalovirus (CMV) congenital infection. As in acquired infection, congenital disease is thought to result from T-cell and B-cell–mediated injury to the fetal host.

Frequency of LCMV in the United States

The exact incidence of LCMV infection is unknown, although the seroprevalence is approximately 5%.[10] Local variations in the frequency of LCMV infection depend on the rodent populations.

Infection of the human fetus during the early stages of pregnancy can cause severe illness or developmental defects in the fetus.

LCMV Mortality/Morbidity

LCMV is usually not fatal. In general, mortality is less than 1%.[10] Previous observations have shown that most patients who develop aseptic meningitis or encephalitis due to LCMV recover completely. No chronic infection has been described in humans, and after the acute phase of illness, the virus is cleared. However, as in all infections of the central nervous system, particularly encephalitis, temporary or permanent neurological damage is possible. Nerve deafness and arthritis have been reported.[10] Infection of the human fetus during the early states of pregnancy may lead to developmental deficits that are permanent.

There is no specific treatment for LCMV infection. Aseptic meningitis, encephalitis, or meningoencephalitis requires hospitalization and supportive treatment based on severity. Anti-inflammatory drugs, such as corticosteroids, may be considered under specific circumstances. Previous observations have shown that most patients who develop aseptic meningitis or encephalitis due to LCMV recover completely. No chronic infection has been described in humans, and after the acute phase of illness, the virus is cleared. However, as in all infections of the central nervous system, particularly encephalitis, temporary or permanent neurological damage is possible. Infection of the human fetus during the early stages of

pregnancy can cause severe illness or developmental defects in the fetus, including hydrocephalus (abnormal accumulation of cerebrospinal fluid or interference with normal flow of CSF caused by an increased secretion of fluid), psychomotor retardation, blindness, and fetal death.[12]

LCMV infection can be prevented by avoiding contact with house mice and taking precautions when handling pet rodents (i.e. mice, hamsters, or guinea pigs). Although rare, pet rodents may become infected with LCMV from wild rodents. Breeders, pet stores, and pet owners should take measures to prevent infestations of wild rodents. Pet rodents should not come into contact with wild rodents. If an individual has a pet rodent, he or she should wash their hands with soap and water (or waterless alcohol-based hand rubs when soap is not available and hands are not visibly soiled) after handling rodents or their cages and bedding.

If an individual has a pet rodent, he or she should wash their hands with soap and water after handling rodents or their cages and bedding.

Differential Diagnosis to Consider for LCMV

• **Amebic Menigoencepahlitis**	• **Meningococcal Infection**
• **Blastomycosis**	• **Mononucleosis and Epstien-Barr Virus Infections**
• **Coccidioidomycosis**	• **Mumps**
• **Cytomegalovirus Infection**	• **Mycoplasma Infection**
• **Dengue**	• **Parvovirus B19 Infection**
• **Enteroviral Infections**	• **Poliomyelitis**
• **Herpes Simplex Virus Infection**	• **Rabies**
• **Histoplasmosis**	• **Rickettsial Infection**
• **Influenza**	• **Rubella**
• **Leptospriosis**	• **Scrub Typhus**
• **Lymphadenopathy**	• **Toxoplasmosis**
• **Meningitis, Aseptic or Bacterial**	• **Viral Hemorrhagic Fevers**

Understanding the epidemiology of LCMV infections will help to further delineate risk factors for infection and in the development of effective preventive strategies.

Understanding the epidemiology of LCMV infections will help to further delineate risk factors for infection and develop effective preventive strategies. Increasing physician awareness will improve disease recognition and reporting, which may lead to better characterization of the natural history and the underlying immunopathological mechanisms of disease, and stimulate future therapeutic research and development.

References:

http://www.doh.state.fl.us/Environment/medicine/One_Health/LCMV_References.pdf

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Preventing human rabies during supply limitations of biologicals

Despite having the highest case fatality rate of any infectious disease, human rabies is completely preventable.

Heather Henderson, DVM, MPH

Rabies is a significant viral zoonosis worldwide, claiming an estimated 55,000 human lives annually. Despite having the highest case fatality rate of any infectious disease, human rabies is completely preventable by avoiding exposure to infected animals or, after exposure, by prompt wound care and administration of rabies vaccine and human rabies immune globulin (HRIG). Unfortunately, interruptions in the availability of human rabies biologicals for pre- (PreP) or post-exposure prophylaxis (PEP) are not unusual. Rabies is a multi-host zoonotic disease, and incidence of animal disease and human exposure varies with local population dynamics. This natural variation complicates the production and maintenance of adequate supplies of biologicals. With only two producers of human rabies vaccine (Novartis and Sanofi Pasteur) and two producers of HRIG (Sanofi Pasteur and Talecris) in the United States, any change in production or processing may affect the market supply.

Recently, the supply of human rabies vaccine in the United States has been less than ideal.

Recently, the supply of human rabies vaccine in the United States has been less than ideal. In June 2007, Sanofi Pasteur began renovating its production facility in France to maintain compliance with regulatory requirements. Before beginning these renovations, the company established an inventory based on historical and projected sales. The updated facility is scheduled to be operational by late 2009. Until then, Sanofi has a limited amount of vaccine. After Sanofi's renovations began, Novartis was unable to meet its projected rabies vaccine supplies. In early 2008, Novartis began supplying vaccine for post-exposure use only. Consequently, Sanofi had to supply most of the market for rabies vaccine, and the increase in demand quickly depleted its inventory.

A true shortage was narrowly avoided by close collaboration between local, state, and federal public health agencies, industry, and professional organizations.

The problem was compounded when an unexpected increase in potential rabies exposures and resulting need for PEP occurred during the summer of 2008. During this time, for a variety of reasons, either one vaccine manufacturer or the other was out of the market for most of the season. A pass code system was put in place requiring providers to consult with public health officials before ordering vaccine. Also, vaccine for PreP was limited to those individuals whose jobs are essential for the control and diagnosis of rabies (e.g. diagnostic lab workers, veterinarians, and animal control workers) as approved by state health officials, and was later suspended entirely when supplies became critically low. The situation has since improved, but is still not optimal. In October 2008, Novartis began providing vaccine for PEP use without restrictions and for PreP use in the highest risk groups. As of April 2009, Novartis has been able to provide vaccine for PreP use without restrictions. Sanofi has continued supplying vaccine only for PEP use after consultation with public health officials. A true shortage, defined as products being unavailable for PEP use in exposed persons, was narrowly avoided by close

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collaboration between stakeholders (local, state, and federal public health agencies, industry, and professional organizations) and intensive outreach efforts.

The majority of rabies exposures are avoidable.

Enhanced public health efforts can minimize the impact of shortages and maximize use of limited supplies. Health communications and basic rabies prevention principles are critical to conserve biologicals while still protecting public health. Most rabies exposures are avoidable with animal bite prevention, avoidance of contact with wildlife, and responsible pet ownership. The need for PEP after animal contact can be obviated in many cases with awareness of how the virus is transmitted as well as proper management and testing of biting animals.

Outreach efforts should stress animal bite prevention, avoidance of contact with wildlife, and responsible pet ownership.

Healthy dogs, cats, and ferrets should be observed for 10 days after a bite.

State agencies should provide outreach to local public health, veterinary medical, and animal control professionals, focusing on prevention of the most common types of exposures, situations where PEP is unnecessary, and the highest risk groups. Emphasis should be placed on not initiating PEP until the exposure is evaluated with the help of public health officials. Local agencies should maintain effective animal control and vaccination programs. Healthy dogs, cats, and ferrets should be observed for 10 days after a bite, and PEP should not be administered if the animal remains healthy. Biting wild carnivores and bats should be submitted for rabies testing. Management decisions for other animal species depend on the species involved, the local epidemiology of rabies, circumstances of the bite, and animal disposition, health, and vaccination status. Health communications should supply information and support for informed decision making; provide timely, consistent, credible, and easily accessible information; address rumors and inaccuracies; coordinate communication efforts across sectors; and educate the public to reduce exposures as well as the importance of observation or testing of an animal after an exposure.

An estimated 40,000 people receive PEP each year in the US. Human rabies exposure and PEP are not reportable. Therefore, it is not possible to track incidence and trends or to identify unusual or questionable exposures. Improved surveillance of vaccine use is needed for better management of supplies. It is unknown what types of exposures most often lead to PEP (e.g. bite vs. non-bite; domestic vs. wild animals), how often PEP could be avoided by adherence to basic guidelines like observation or testing of animals, or how many cases are for non-exposures (e.g. seeing a bat, touching a rabid animal, or being scratched by a small rodent).

The recent vaccine supply limitation should serve as a wake-up call for the need of a multi-disciplinary, one health approach to zoonotic disease prevention.

The experience of the recent vaccine supply limitation is a reminder that the availability of biologicals cannot be relied upon to guide the practice of human rabies prevention. No crisis occurred, yet a tremendous coordinated effort was required to manage supplies. The experience should serve as a wake-up call for preparedness and the need for a one-health, multi-disciplinary approach to zoonotic disease prevention.

Dr. Heather Henderson is Lead Epidemiologist for District 4 Health Services, Georgia Division of Public Health.

MRSA in people and pets… a shared problem?

Jorge Pinto Ferreira, DVM, MS

Zoonotic bacteria and antibiotic resistance are currently significant global public health threats. Methicillin-resistant *Staphylococcus aureus* (MRSA) is a microorganism that combines both characteristics and that has been increasingly reported as an emerging public health problem worldwide, both in human and veterinary fields. It is one of the most prevalent pathogens that cause nosocomial infections, and infection with MRSA is associated with increased mortality, morbidity, and hospitalization time. It has been estimated that antimicrobial resistance results in an annual cost of $100 million to $30 billion, as a consequence of poor response to treatment, longer hospitalization, and use of more expensive treatments.[1,2] Klevens *et al*[3] recently showed that deaths from MRSA infections in the US have overtaken those from other infectious diseases, including HIV/AIDS.

Methicillin-resistant *Staphylococcus aureus* (MRSA) has been increasingly reported as an emerging, worldwide public health problem both in human and veterinary fields.

Methicillin resistance (in human isolates) was reported for the first time in 1961 by Jevons, but the possibility that dogs and cats could act as a source for zoonotic staphylococcal infections was suggested even before that, in 1959.[4] From animals, the first isolations were in milk from mastitic cows.[5]

MRSA strains are resistant to β-lactam antibiotics, including all penicillinase-stable β-lactams, with resistance most commonly mediated by the *mec*A gene. This gene resides on a large mobile genetic element called the Staphylococcal chromosomal cassette *mec* (SCC *mec*) and encodes for a penicillin-binding protein (PBP 2a) which is expressed in the bacterial cell wall and has a low affinity for β-lactam antibiotics. Thus, the β-lactam antibiotics are ineffective against bacteria expressing this gene. In addition, most MRSA isolates are resistant to many other antimicrobial classes.

There are no universal definitions on MRSA classification. However, based upon epidemiological and molecular characteristics, MRSA strains are usually divided in:

- Hospital-acquired (HA-MRSA): defined as a positive MRSA blood culture obtained more than 48 hours after admission in a medical unit.
- Community-associated (CA-MRSA): one that occurs within 48 to 72 hours of hospitalization, unless it is clear that it was acquired during a previous hospitalization. The majority carries genes encoding Panton-Valentine leucocidin (PVL, a toxin that interacts with white blood cells), and SCC*mec* IV (a smaller cassette type, that might therefore be more easily transferred).
- Non-typable (NT-MRSA): those that are resistant to digestion with the restriction enzyme *Sma*I, a restriction enzyme used in routine typing of MRSA isolates. These isolates are, however, typeable with other molecular techniques such as Multi Locus Sequence Typing (MLST).

Indistinguishable MRSA isolates have been identified in humans and in different animals including livestock, pets, and captive elephants.

Recently, several reports have identified identical or undistinguishable MRSA isolates in humans and in different animal species like pets,[6-11] cows,[14] pigs,[15,16] horses,[17,18] or even elephants.[19]

Detecting similar MRSA isolates in both animals and humans does not establish causality, but it is highly suggestive of trans-infection between species.

It should be emphasized that detecting similar MRSA isolates both in animals and humans does not establish causality, but it is highly suggestive of trans-infection between species. This leaves clinicians and researchers faced with a very challenging question: "How can we find out who infects whom?"

The relationship between pets and their guardians has changed over the years.

The link between pets and humans seems to me of even more particular interest because about 60% of American households have pets and the relationship between pets and their guardians has changed over he last years. Instead of being kept in the outside of households, pets are ncreasingly seen and treated as family members, and allowed a high degree and frequency of contact with humans.[20]

The effect of this routine contact with household pets on the global epidemiology of MRSA is still unknown.[21] There are few answers to key questions such as prevalence and persistence of colonization and infection in animals, ease of transmission between animals and humans, efficacy of decolonization procedures in animals and on MRSA colonization rates in non-clinically affected dogs.[22] In summary, the significance of pets as a MRSA reservoir is unclear at present.

Pets are increasingly being seen and treated as family members.

Partnerships between human and veterinary medicine are essential to answer this question. Knowing its answer will allow public policy makers to know if changes are necessary regarding this topic. For example, the international movement and trade of pets has increased significantly over the last years…does it make sense to spend millions of dollars controlling the spread of MRSA from and to hospitals…and allow pets to come in this country only under a normal physical appearance and (Title 42 Code of Federal Regulations, 2007) proof of rabies vaccination? On the other hand, the use of some antibiotics has for a long time been restricted in food animal practice…is this true when we think about small animal practice? Can it be assumed that the inappropriate use of antibiotics will create resistance in animals… and that this will be transferred to humans?

This leaves clinicians and researchers faced with a very challenging question: "How can we find out who infects whom?"

MRSA demands a global approach and must be viewed from an integrated "One Medicine" perspective, combining human and veterinary public health. It represents a challenge for the scientific community, which should not ignore that its epidemiology is rapidly changing, even in small geographical areas.[23] It is the responsibility of the "One Medicine" scientific community to prevent MRSA from becoming a threatening epidemic.

MRSA demands an integrated, global One Health approach.

References:

http://www.doh.state.fl.us/Environment/medicine/One_Health/MRSA_References.pdf

Dr. Jorge Pinto Ferreira is a graduate student at North Carolina State University, CBS PhD program, Population Medicine & Veterinary Public Health concentration area, working with Drs. Maria Correa and Kevin Anderson.

One Health in Action !

The Vermont Chapter of the American Academy of Pediatrics and the Vermont Chapter of the American Academy of Family Physicians invited Vermont Veterinary Medical Association members to attend their joint spring meeting

Vermont Physicians and Veterinarians Talk 'One Health' while attending Joint Spring Meeting

J. Clyde Johnson, VMD

The Vermont Chapter of the American Academy of Pediatrics and the Vermont Chapter of the American Academy of Family Physicians invited Vermont Veterinary Medical Association members to attend their joint spring meeting in Rutland, VT on April 30, 2009.

Dr. Joan Hendricks, Dean of the University of Pennsylvania's school of veterinary medicine, was the keynote speaker.

Joan Hendricks, DVM, PhD, Dean of the University of Pennsylvania's school of veterinary medicine was invited to give the keynote presentation on the One Health Initiative from the veterinary medical perspective. In addition, Dr. Hendricks had been invited to present her description of the One Health concept at Pediatric Grand Rounds to students, residents, and staff at the University of Vermont medical school the day before. Drs. Hendricks, Charles D. Newton, DVM, MS, and Arthur Ribenstein, MBBCh (MD) recently published a comprehensive article in the *Veterinaria Italiana* One Health monograph entitled 'One Medicine-One Health' at the School of Veterinary Medicine of the University of Pennsylvania – the first 125 years (http://www.izs.it/vet_italiana/2009/45_1/183.htm).

The University of Pennsylvania's school of veterinary medicine was started 125 years ago by the physician faculty of their medical school. In 1807, Benjamin Rush, MD postulated that "By extending our knowledge of the causes of the diseases of domestic animals, we may add greatly to the certainty and usefulness of the profession of medicine, as far as it relates to the human species". From 1884 until the 1960's, students at Penn studying human and animal medicine took the basic science courses (e.g., physiology, pathology, microbiology, etc.) together…further evidence that One Health really does have a long and rich history at Penn.

Veterinary and human medical professionals collaborate in food safety, environmental health issues, biomedical research, and emergency medical response for the benefit of both human and animal health.

Dr. Hendricks discussed One Health in the context of how the veterinary and human medical professionals collaborate in biomedical research, food safety, environmental health issues, and emergency medical response for the benefit of both human and animal health. The Human-Animal Bond phenomenon was mentioned using companion animals (pets) and horses in therapy, learning, and helping "at risk" humans at every level. The use of household pets as sentinels for domestic abuse and prognostication of that possibility in the future was discussed.

A bright future was painted for One Health: developing closer "in the trenches" communication between local physicians/veterinarians/nurses and other health care personnel; increasing numbers of physicians, veterinarians, and nurses adding a PhD to their resume; encouraging state boards to recognize continuing education credits when licensees attend courses advanced by either medical or veterinary medical organizations.

Joann M. Lindenmayer, DVM, MPH, an associate professor in the Department of Environmental and Population Health at Tufts Cummings School of Veterinary Medicine and a prominent One Health supporter, presented a short synopsis of Tufts

A bright future was envisioned for One Health, including the development of closer "in the trenches" communication between physicians, veterinarians, and other health care personnel.

innovative programs involving human and animal medicine. Tufts veterinary medical program was founded 30 years ago on "One Health" principles promoted by University President Jean Mayer, a human nutritionist. Early on, Tufts veterinary medical students attended pre-clinical classes side-by-side with Tufts medical students. Dr. Lindenmayer joined Dr. Hendricks for an informative question, answer and comment session.

Dr. J. Clyde Johnson is Past President of the American Association of Equine Practitioners (AAEP).

Dr. Echols Honored As FVMA Gold Star Award Recipient

Amber Smith

Dr. Echols created the One Health Newsletter to provide an enjoyable forum for One Health supporters from all professions and nations to express their views and showcase their One Health activities and accomplishments.

Her hope is to generate further support and momentum for the One Health concept.

Dr. Mary Echols is the epitome of the “gentle doctor.’’ Her colleagues describe her as humble, hard working, visionary and extremely effective. Dr. Echols, an Environmental Consultant with the Palm Beach County Health Department, was nominated for the Florida Veterinary Medical Association’s 2009 Gold Star Award by Dr. Lisa Conti, Director of the DOH’s Division of Environmental Health. The award is given to a veterinarian who has contributed much of his or her time and energy to the FVMA and/or a local veterinary association, as well as promoting the advancement of veterinary medicine and the profession. The recipient must also be a member in good standing of the FVMA. In addition to her work for the Palm Beach County Health Department, Dr. Echols is also the editor of the One Health newsletter published by the Florida Department of Health. She brought together the resources and cooperation of the FVMA, the state Department of Health and the veterinary community in general, to launch the state’s One Health initiative.

“Dr. Echols is the driving force behind the One Health initiative,’’ said Dr. Conti. “She began the One Health Newsletter to reach a wide audience of veterinarians, human health workers and public health professionals to collaborate on protecting and promoting the health of all species.’’ Dr. Echols has successfully published four quarterly issues of the newsletter and has received national recognition for her efforts, as well as accolades for the high-quality publication. “We are very proud to have Dr. Mary Echols representing the FVMA so favorably,’’ said Dr. Conti.

FVMA Executive Director Philip J. Hinkle said it was an easy decision for the FVMA awards committee to make in selecting Dr. Echols as a Gold Star Award recipient. “Dr. Echols truly represents all the criteria of the Gold Star Award. She has done an excellent job in promoting veterinary medicine and is an outstanding example of the profession,’’ Hinkle said.

Amber L. Smith is Director of Communications and Public Relations at the Florida Veterinary Medical Association.

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Recent One Health Publications:

- **Infection Prevention and Control Best Practices For Small Animal Veterinary Clinics,** August 2008

  Sponsored by The Canadian Committee on Antibiotic Resistance

  http://w ww.wormsandgermsblog.com/uploads/file/CCAR%20Guidelines%20Final(2).pdf

- **In partnership with the U.S. Navy, the Alliance for Rabies Control has joined the United States Naval Ship (USNS) Comfort in providing humanitarian aid throughout Central America.**

  One Health advocate, Robin Hughes, DVM is on board the USNS Comfort representing the Alliance for Rabies Control…The following is a link to her Blog.

  http://www.rabiescontrol.net/EN/Programs/Projects-Overview/USNS_Comfort.html.

- **Compendium of Measures to Prevent Disease Associated with Animals in Public Settings, 2009**

  CDC - MMWR May 1, 2009/58(RR05); 1-15

  http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5805a1.htm

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

  http://www.amazon.com/One-Man-Medicine-Health-Steele/dp/1439240043/ref=sr_1_1?ie=UTF8&s=books&qid=1246048712&sr=8-1

- **AVIAN Influenza Toolkit -** The Australian Government Department of Agriculture Fisheries & Forestry (DAFF)

  http://www.aitoolkit.org/Default.aspx

- **ACIP votes to recommend reduced rabies vaccination series**

  At the June 24, 2009 Advisory Committee on Immunization Practices (ACIP) meeting, the rabies working group presented evidence in support of a recommendation to reduce the number of vaccine doses in the human rabies postexposure prophylaxis (PEP) series from 5 to 4 doses.

  http://www.cdc.gov/rabies/news/2009-06-24_ACIPvote.html

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

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

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Coming Events:

The American Veterinary Medical Association 145th Annual Convention

Seattle, Washington

July 11-14, 2009

http://avmaconvention.org/

The International Society for Veterinary Epidemiology and Economics (ISVEE)

Durban, South Africa

August 10-14, 2009

"Epidemiology Unplugged – Providing power for better health"

http://www.isvee12.co.za/default.php

2nd INTERNATIONAL BERLIN BAT MEETING: BAT BIOLOGY AND INFECTIOUS DISEASES

Berlin, Germany

February 19-21, 2010

The aim of this symposium is to foster an exchange of ideas among international specialists from many disciplines. Topics will include emerging infectious diseases in bats, bats and rabies, and bat diseases and the public.

http://www.izw-berlin.de/

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