One Health Newsletter

A quarterly newsletter highlighting the interconnectedness of animal and human health

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

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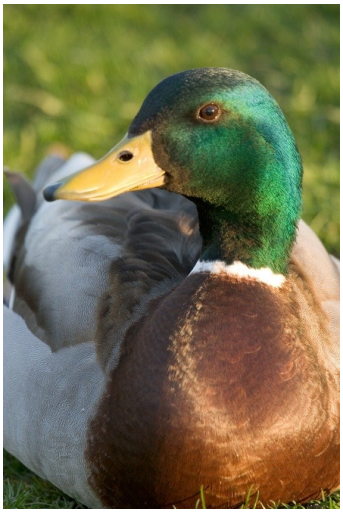
This newsletter is dedicated to enhancing the integration of animal, human, and environmental health for the benefit of all by demonstrating One Health in practice.

A provocative example of One Health principles: emergence of antiviral resistance due to unintended exposure of an animal reservoir of influenza to a human drug

[Posted on One Health Initiative website September 26, 2011]

Thomas P. Monath, MD



A recent study provides a provocative confluence of One Health issues. In an issue of PLoS One (2011;6(9): e24742) http://www.onehealthinitiative.com/publications/Oseltamivir%20resitance%20H1N1%20mallards%20PLoS%20ONE%2012Sep2011.pdf, Järhult et al. report the induction of a mutation (H274Y) in the influenza A neuraminidase gene by infecting mallard ducks with influenza A/H1N1 virus and then exposing them to oseltamivir (Tamiflu) in a pool of water, the only source of water available to the animals. The H274Y mutation is responsible for resistance to oseltamivir, a neuraminidase inhibitor widely used for the prophylaxis and treatment of influenza A, and a mainstay antiviral drug stockpiled for emergency use in the event of an influenza pandemic. During the 2008-2009 flu season the H274Y mutation and resistance to the antiviral drug spread rapidly worldwide. As pointed out by the authors, the spread of H274Y resistant strains did not correlate with usage of oseltamivir in the human population, suggesting that other factors may have put selective pressure on the virus.

The concentration of oseltamivir in water fed to the mallards in the experiment that induced the resistance mutation was as low as 1 g/mL, but not at 80 ng/mL. Ducks were infected and exposed to the drug in ten generations of 5five days each, with new ducks being introduced every third day allowing transfer of virus to the new ducks for two days before the preceding generation was removed. Mutated virus was detected as early as eight days (second generation).

In This Issue

What lessons derive from this experiment? It is clear that resistance to oseltamivir can be induced rapidly in ducks after experimental exposure to water containing low concentrations of the drug. Ducks are a primary reservoir of influenza A viruses, and a source of introduction of the virus to the human population. They also move long distances, both by local and long-distance migrations, and by being moved in human conveyances to market. The central questions, not answered by this study, are whether natural exposure of wild and domesticated ducks (and other aquatic birds) to oseltamivir occurs in the environment, how widespread such environmental contamination is, and what concentrations are present.

Oseltamivir is actually a prodrug since the active form is not readily bioavailable from the gastrointestinal tract. The prodrug (oseltamivir phosphate) is metabolized to the active form (oseltamivir carboxylate). The latter is excreted in the urine unchanged, and thus could find its way from human patients to sewage plants and the environment. Multiple studies cited in the paper have demonstrated that oseltamivir carboxylate is stable in sewage and it has been detected in waste water, rivers, and sewage effluent. However, levels reported from samples taken in nature ranged from 58-293 ng/mL, below the 1 g/mL that induced resistance experimentally. However, the high end of this range was not tested in the experiments performed, and environmental levels could reach higher concentrations in focal areas or with high usage of the drug in the human population during a pandemic.

If oseltamivir contamination of aquatic environments—an unintended treatment of the zoonotic reservoir host of influenza A viruses—are factors in the emergence and spread of antiviral resistance, this would appear to be a difficult problem to control. It would also be an unprecedented and unique mechanism in

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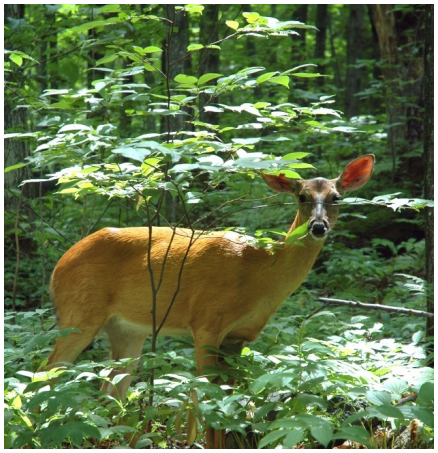
disease emergence. The closest analogy is the use of antibiotics in animal feed in the evolution of antibiotic resistant bacteria, but for oseltamivir the exposure is unintended. The implications for One Health are clear and impressive, involving a human drug, environmental contamination, and the emergence of a zoonotic infection with a new virulence factor.

Dr. Thomas Monath, a medical virologist and physician, is a partner in the Pandemic and Biodefense Fund, Kleiner Perkins Caufield & Byers, and also Adjunct Professor, Harvard School of Public Health. Between 1992 and 2006, he was Chief Scientific Officer and Executive Director of Acambis (a publicly traded biopharmaceutical company) where he directed R & D on vaccines against dengue, Japanese encephalitis, West Nile, yellow fever, Clostridium difficile, as well as smallpox vaccines for defense against bioterrorism.

UF research in vector-borne diseases demonstrates the importance of One Health collaborations

A. Rick Alleman, DVM, PhD

Aside from being a nuisance, ticks can transmit pathogens that can infect many mammalian species including humans, dogs, and horses.



If you frequent any of the wooded areas in North Central Florida, such as nature trails, state parks, camp grounds or hunting grounds, it is only a matter of time until you encounter one of the various tick species that inhabit the brush. Two of the tick species, the Lone Star Tick (*Amblyomma americanum*) and the Deer Tick (*Ixodes scapularis*) are present in alarming numbers. Ticks can be found in Florida year round, but begin to be most active as early as late February, throughout the spring and summer and extending into the milder winter months. Aside from being a nuisance, ticks can transmit pathogens that can infect many mammalian species including humans, dogs, and horses. *A. americanum* is the primary vector for *Ehrlichia chaffeensis* (Human Monocytic Ehrlichiosis), *E. ewingii* (Human granulocytic Ehrlichiosis) and a newly recognized agent, the Panola Mountain Ehrlichia. *I. scapularis* is the primary vector for *Borrelia burgdorferi* (Lyme Disease) and *Anaplasma phagocytophilum* (Human Granulocytic Anaplasmosis). All of these agents cause zoonotic infections, causing disease in humans as well as other mammalian species.

A research group at the University of Florida College of Veterinary Medicine has recently noticed an increase in the number of people and pets being diagnosed with infections from these zoonotic pathogens.

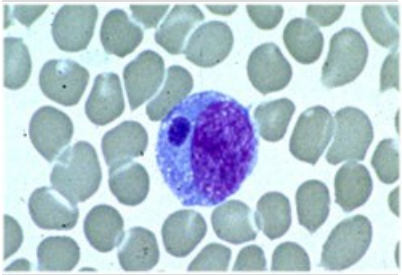
Dr. Tony Barbet and his group of researchers focus on evaluating diagnostic techniques used to identify infected animals and ticks and the understanding of genetic mechanisms used by the organisms to evade the immune system and persist in the mammalian host.

Our research group is focused on the study of these vector-borne pathogens and we have recently noticed an increase in the number of people and pets being diagnosed with infections from these zoonotic pathogens. For example, between the years 2000 – 2007 there were on average 47 cases per year of Lyme disease in Florida, reported to the CDC. From 2008 to 2010, there was an average of 78 cases of Lyme reported annually in the state of Florida. Similar trends have been documented for other tick-borne infections in both animals and people. In a recent, multi-institutional study that evaluated 733 dogs from Florida, we found that 3.7% of the animals tested had antibodies to one or more *Ehrlichia* species, most of which were *E. ewingii* and *E. chaffeensis*. Expanding tick populations may be one contributing factor to the upward trend of vector-borne diseases. However, white-tailed deer, which serve as a major wildlife reservoir for many of these agents, are also present in ever increasing numbers and in more concentrated areas due to a number of ecological factors. In the mammalian hosts, vector-borne agents can result in non-specific clinical findings sometimes described in people as flu-like symptoms of general malaise, muscle and/or joint pain, and fever. If left undiagnosed, more serious illness can result, with some cases resulting in mortality.

Our research group at the University of Florida, College of Veterinary Medicine has been involved with research with vector-borne pathogens for over two decades. Dr. Tony Barbet, a professor in the Department of Infectious Disease and Pathology, leads our group of researchers. We focus on evaluating diagnostic techniques used to identify infected animals and ticks and the understanding of genetic mechanisms used by the organisms to evade the immune system and persist in the mammalian host. Using experimental inoculations in sheep and dogs, we have evaluated mechanisms of antigenic variability in *A. phagocytophilum* infection, demonstrating variations in gene expression in subsequent parasitemic cycles in a single infection. We have documented chronic carrier states of infection for over one year in experimentally inoculated dogs, without expression of clinical disease. In the animals where chronic infection was established, cur-

In the animals where chronic infection was established, currently accepted antimicrobial therapy was ineffective in clearing the agent.

We hope to have a better appreciation for the prevalence of vector-borne agents in different geographic regions of Florida.



Courtesy CDC—Morulae detected in a monocyte on a peripheral blood smear, associated with *E. chaffeensis*

rently accepted antimicrobial therapy was ineffective in clearing the agent. We suspect that chronic persistent infections are also established in the wildlife reservoir for these agents, namely the white-tailed deer. If this is the case, it could potentiate an ever increasing number of infected carrier animals providing a source of infection for ticks that might eventually feed on people and/or pets.

Our current research involves evaluating tick and deer populations for evidence of exposure to these various vector-borne pathogens. Katherine Sayler, a PhD student in our lab, has spent the last two summers trapping ticks in various state parks in North Central Florida and is in the process of determining the prevalence of these pathogens in the *Amblyomma* tick population (Figure). In addition, we have worked cooperatively with the Florida Wildlife Commission, and with their assistance have obtained *Amblyoma* and *Ixodes* ticks and blood samples from deer from various counties around the state. By evaluating these samples using PCR analyses and serological assays, we hope to have a better appreciation for the prevalence of vector-borne agents in different geographic regions of the state. Our goal is to quantify the prevalence of these vector-borne pathogens in North Central Florida and further develop diagnostic measures for evaluating infection.

Figure. *Amblyomma americanum* ticks: adult female (left), adult male (right), and nymph (center). (Photograph courtesy of Katherine A. Sayler, University of Florida, College of Veterinary Medicine)

Ms. Sayler is also conducting investigations on a newly recognized *Ehrlichia* species, the Panola Mountain Ehrlichia (PME). A better understanding of this pathogen is important for a number of reasons, one of which is its close genetic relationship to another *Ehrlichia*, *E. ruminantium*, the causative agent of Heartwater. *E. ruminantium* is not found in the United States, but is a threat to Florida because of its presence in the Caribbean Islands and the migratory birds that travel between the islands and Florida. If introduced into the US, it could have devastating effects on the ruminant animal population. Katherine is inter-

ested in determining if the PME agent, which is only mildly pathogenic, might serve as a barrier to the spread of Heartwater by providing cross-protective immunity to *E. ruminantium*. In addition, further evaluation of the less pathogenic PME agent may aid in better understanding of the pathogenic Ehrlichias that presently cause disease in people and pets in Florida and other parts of the country where *A. americanum* is found.

Dr. Rick Alleman

The cooperative roles of the veterinarian and the physician in combating these infections cannot be underestimated.

Heightened awareness of these infections, improved diagnostics, and a better understanding of how these pathogens persist in carrier animals is critical in recognizing, treating, and controlling these diseases. The cooperative roles of the veterinarian and the physician in combating these infections cannot be underestimated. Current methods of diagnosis allow veterinarians to have access to rapid, point-of-care testing for exposure to multiple vector-borne diseases in the dog. Often, pets and their owners are exposed to the same environment where tick populations are present. Although transmission from pet to owner is unlikely, exposure of the pet to these infections should alert owners to the risk of disease transmission from infected ticks and warrant investigation in the event of recurrent or unexplained illnesses in patients exposed to ticks.

Dr. Rick Alleman is a professor of clinical pathology at the University of Florida College of Veterinary Medicine.

The dotSkapes project: One Health research on the cloud

Nicholas D. Preston, PhD

THE NELSON INSTITUTE FOR ENVIRONMENTAL STUDIES
University of Wisconsin-Madison
TOGETHER. FOR THE PLANET.

The dotSkapes Project reduces barriers to collaboration, thereby making it easier to find, analyze, tag, and share global public health research.

One Health research often transcends disciplines and geographic regions. This presents challenges for collaborating and integrating information from disparate sources. Among the potential solutions, we believe that cloud computing holds promise for accelerating global public health research. "Cloud computing," in this context, refers to interacting with a web-based application—rather than locally installed software—and moving data processing and storage to a shared and networked cyber-infrastructure.

The dotSkapes Project, based at the University of Wisconsin-Madison (UW) and EcoHealth Alliance, is developing a cloud application for One Health research. The dotSkapes virtual lab leverages recent advances in web technology to reduce barriers to collaboration, thereby making it easier to find, analyze, tag, and share research. The platform is designed to quickly connect users with relevant resources (e.g., people, data, and analytical tools) via search engines trained on the scientific literature (Figure 1). We employ an interactive geographic user interface to visualize complex datasets, a function well-suited to the inherently spatial nature of disease.

A researcher with a specific interest in Ebola could subset content from the shared dotSkapes platform via disease, region, or discipline.

Tools for analysis and visualization can be developed collaboratively in dotSkapes.

DotSkapes users will be encouraged to contribute data and analyses to the network.

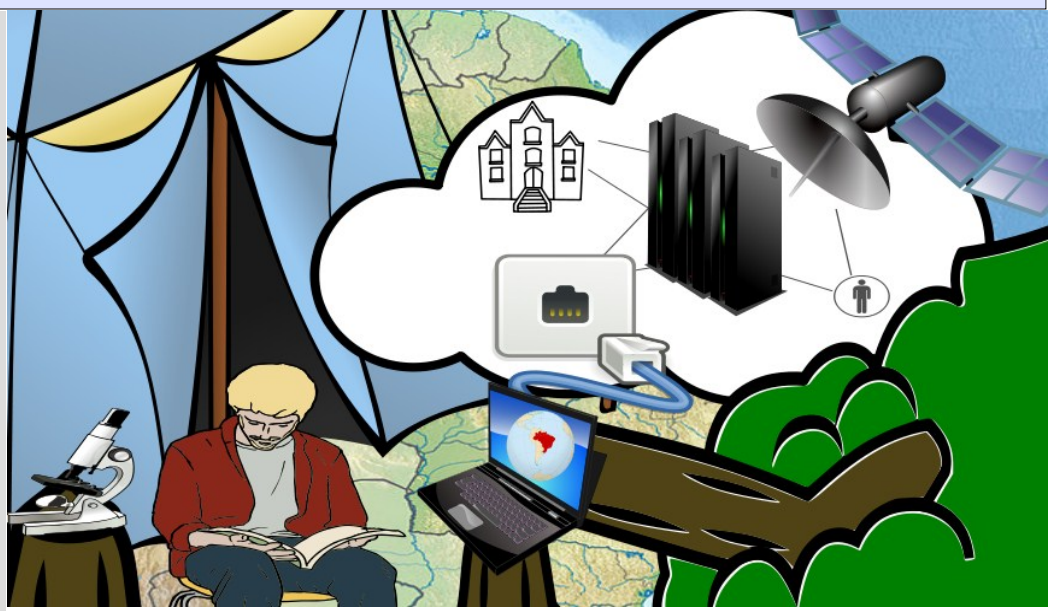


Figure 1. dotSkapes will be able to connect researchers to a variety of available data and resources on a particular topic or region, making the research more contextual and relevant (images:OpenClipArt/Wikimedia Commons).

The prototype ("Healthscapes") was supported by Jonathan Patz, Director of the UW Global Health Institute, and developed at the UW Center for Sustainability and the Global Environment. The project was re-branded "dotSkapes" to leverage "dot" subdomains to filter content. For instance, a researcher with a specific interest in Ebola could subset content from the shared dotSkapes platform via disease, region, or discipline, e.g., ebola.Skapes, congo.Skapes, or vet.Skapes. Users will be encouraged to customize the content of these subdomains to build recursive communities of collaborators.

Tools for analysis and visualization can be developed collaboratively in dotSkapes. The challenge is to allow users to harness powerful analytical tools without compromising the security of the servers and data, the privacy of other users, or the user experience on shared processing resources. To this end, we have developed a virtualization prototype that supports analysis in Python and R, while providing a balance between flexibility and security.

Distributed web platforms help lower barriers by pooling computing capacity regardless of resource availability. With dotSkapes, we have attempted to overcome additional technological barriers such as data formats, computation time, and search relevance, while promoting transparent methods. Whenever possible, we have plugged into open-source programming communities and adopted open web and data standards. Indeed, Free and Open Source Software (FOSS) communities developed many of the core components of dotSkapes infrastructure.

DotSkapes users will be encouraged to contribute data and analyses to the network. However, there are instances where this is not possible for privacy or professional reasons. Hence, we are developing private workspaces for users and groups, as well as a distributed network to interconnect data repositories.

Dot Skapes is in the final phase of internal testing and will be available for public testing in 2012.

The next generation of dotSkapes is being designed to support field workers using low-cost devices via fieldSkapes, bringing the field and laboratory closer together, and pushing the power of cloud applications to the front lines of One Health research.

There are considerable data in the public domain that can be difficult to integrate, yet are particularly relevant to historic analyses. We strive to facilitate finding these resources and provide incentives to share them such as storage, projection, processing, formatting, and integration with our analytical resources and datasets. This open model has the potential to lower technical barriers to data exploration, encourage best practices, and reduce redundancy by helping the research community adapt pre-existing tools to new questions.

DotSkapes is in the final phase of internal testing and will be available for public testing in 2012. Persistent challenges include issues of privacy, security, and data ownership. We are also experimenting with the balance between the desktop and cloud computing, as well as approaches to integrating reproducible analyses with scientific publications, wikis, and blogs. The next generation of dotSkapes is being designed to support field workers using low-cost devices via fieldSkapes, bringing the field and laboratory closer together, and pushing the power of cloud applications to the front lines of One Health research. We look forward to the day when we can call down the latest satellite imagery and solicit input from colleagues while collecting specimens in the wild.

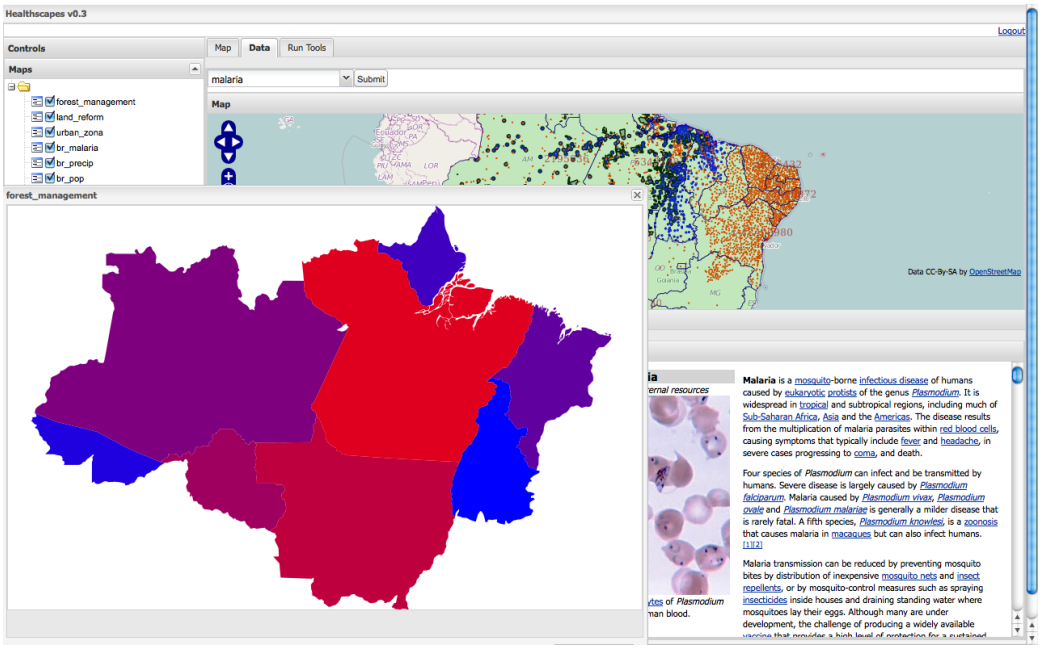


Figure 2. A researcher looking for relevant data on malaria could access environmental data, previous studies, existing sampling locations, and updated information on malaria within the study region. Here we show an example screen shot of what the dotSkapes interface could provide.

How would our platform be useful to a One Health researcher?

A search term such as “malaria” would identify resources such as analytical tools for meteorology, mosquito trap data, vegetation imagery, or a map of prior studies (Figure 2). The relationships between resources and the search term are mined from the scientific literature, while the resources themselves are harvested from the web, user contributions, expert case studies, or external repositories. The user could then apply our analytical tools or create new tools to share with collaborators. Lastly, a user could then link this reproducible analysis to the

Dr. Nicholas D. Preston

resulting study. The dotSkapes knowledge repository will improve with use, as resources are tagged, uploaded, linked, or recommended—a community approach to tackling global One Health challenges.

Nicholas D. Preston is a postdoctoral scientist at the UW-Madison Center for Sustainability and the Global Environment (SAGE). His research focuses on the intersection of the environment, computing, and health.
To access dotSkapes, visit http://dot.skapes.org

Texas A&M center confronts antibiotic crisis with potential new bacterial treatment

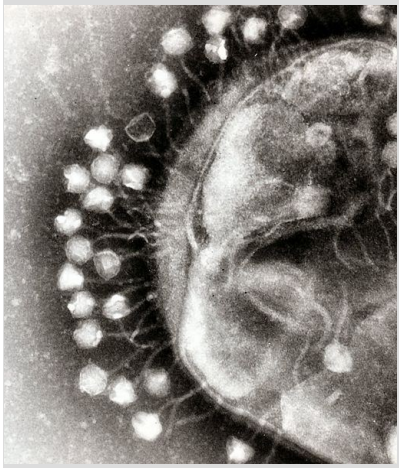
[Reprinted with permission by AgriLife Today, November 3, 2011]

Kathleen Phillips

Dr. Ryland Young, director of the Texas A&M University Center for Phage Technology (Texas AgriLife Research photo by Kathleen Phillips)

COLLEGE STATION – It's been called "the trots," "Montezuma's Revenge," "the runs" and worse. But no matter the name, when it strikes, victims wish for a medicine that could go straight to the offending bacteria to quickly knock it dead. That wish will ultimately come true if work by Texas A&M University scientists stays on target at the Center for Phage Technology in College Station.

A "medicine that grows" is how the phage concept was described by Dr. Ryland Young, a professor of biochemistry and biophysics who was instrumental in establishing the center. "Phage is a word that simply means viruses that grow on bacteria," Young said. "They are harmless to humans, harmless to animals, harmless to plants. The only things they attack are bacteria. And every kind of bacteria that are involved in the disease process has bacteria phages that will attack them. So if you are a bacterial cell, your enemy is the bacterial virus."



An electron micrograph of bacteriophages attached to a bacterial cell.

Young said new technology to fight bacterial diseases – of which there are many in addition to "the trots" — is critically important because people and animals have become increasingly resistant to antibiotics currently on the market. And yet, he said, there is no major U.S. pharmaceutical company currently trying to develop new antibiotics.

"There is not enough money in it," he said. "You can't blame them. They are companies and they are there to make money. They can make a lot more money making pain drugs and lifestyle drugs. Antibiotics are not a particularly attractive investment."

When antibiotics work, he explained, people get well and don't need drugs any more. Yet bacterial illnesses at a minimum cause lost productivity in the workplace and schools, and some bacteria, such one commonly called MRSA, or methicillin-resistant Staphylococcus aureus, can be deadly. "There is kind of a worldwide crisis right now in human medicine because for some bacteria such as MRSA, we are down to only one antibiotic that works," Young said. "Bacteria have this very pronounced characteristic of being able to very rapidly become

drug-resistant. And that's a problem. There is a need for alternatives to antibiotics."

So serious is the issue, that the Interagency Task Force on Antimicrobial Resistance was initiated in 1999 following a congressional hearing on the topic, according to the Center for Disease Control and Prevention. Ten federal agencies are participating in the effort. A transatlantic effort on the topic was formed between the U.S. and Europe in 2009. "People infected with antimicrobial-resistant organisms are more likely to have longer, more expensive hospital stays, and may be more likely to die as a result of the infection," the CDC notes on its website.

Phage, short for bacteriophage, is a word that simply means viruses that grow on bacteria. They are harmless to humans, animals, and plants.

Phages are not new to science. They were first described in 1915, before what Young called "modern biology." Years after the phage discovery, scientists began exploring molecular biology and the intricacies of DNA. What researchers now know is that the phage, or bacterial virus, encounters a bacterial cell, absorbs to it, injects its DNA into it and "typically 30 minutes later, the bacteria cell explodes," Young explained. Several hundred new virus particles then continue on to eliminate other targeted bacterial cells, if any. So, almost 100 years after their discovery, scientists can isolate bacteria phages, sequence their DNA and engineer them to be more effective against certain types of bacteria, he said.

Dr. Joel Berry handles an experiment at the Texas A&M University Center for Phage Technology. (Texas AgriLife Research, photo by Kathleen Phillips)

Scientists can isolate phages, sequence their DNA, and engineer them to be more effective against certain types of bacteria.

"They are relatively cheap to produce," Young said. "All you need to grow them is a culture of the bacteria that you want to kill. You throw one bacterial phage particle in there, come back in a few hours and you have trillions of the bacteria phages, and the bacteria cells have all been killed. Phages grow themselves, that's the beauty of them."

However, regulation will play a role in future development, he noted, because U.S. Food and Drug Administration policies currently subject phage technology to the same criteria as chemical drugs. "If I give you a chemical drug, that drug is likely to penetrate every tissue of your body — your ears, your eyes, your nose, your heart, your kidneys. And a chemical can have a different effect on every organ," Young explained. "And that is why drug testing is so important. I would not advocate lowering the barriers for chemical drugs at all.

"But bacteriophages are not going to go to your eyes, your ears, your brain. And even if they did, they can't do anything," Young said. "They're not capable of even recognizing human cells, and even if they could, the way genes are set up in bacteria phages are completely different than the way they are in humans, so they would not be recognized as genes." The researcher said part of the

center's plan is to educate policy makers so that the rules can be changed for approving phage-based medications for humans without subjecting them to the same type of requirements for chemical pharmaceuticals.

He said phages will likely first be used in veterinary medicine because the barriers for testing for animal use are a lot lower. Veterinary applications could be in use within 10 years, Young believes. "Once we are successful in veterinary applications, there will be a lot of pressure to get phage therapeutics approved for humans," he said.

Dr. Jason Gill, program director, Center for Phage Technology, examines lab work in progress. (Texas AgriLife Research photo by Kathleen Phillips)

Young said the center is midway through its five-year development plan and is hiring faculty with phage expertise to conduct research and assist other scientists with projects where phage technology might be introduced. Young expects the phage center to eventually have 15 scientists developing different phages to target different needs. "This is translational research," he said, "which means taking the basic research and translating it to practical applications as into commercial products. And we're the first such entity in the world."

"In the long run, we'd like bacteria phages to be exploited to their fullest for human, animal husbandry, and veterinary antibacterial uses," Young said.

Kathleen Phillips is Media Relations Manager at Texas A&M AgriLife Communications. To access the original article, please visit http://agrilife.org/today/2011/11/03/phages-confront-antibiotic-crisis/

USU research professor studies 'pasture pharmacy'

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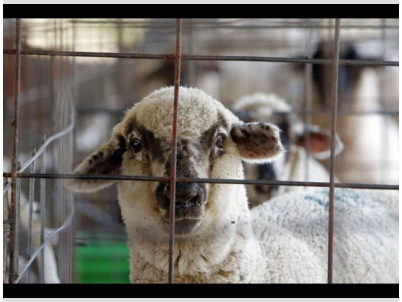
Keith McCord



A research professor at Utah State University is conducting experiments that may help farm animals live a more healthy life, which is something the agriculture industry is keeping a close eye on. But what makes this study different: the animals will basically treat themselves.

USU research professor Juan Villalba has been studying sheep and goat behavior for several years, in an effort to reduce certain diseases that affect those animals. "Parasites are one of the big problems -- health problems of livestock animals," Villalba said.

Parasites are one of the big health problems of livestock animals.

Not only can parasites kill animals, but they can also cause other detrimental health effects and can affect the taste of meat. Conventional farming methods of treating diseases -- using antibiotics and other chemicals -- has created parasites that are becoming resistant to drugs, which is a concern worldwide. So, in the lab, as well as in a controlled nine-acre pasture environment at Utah State, Villalba has been testing various plants that have certain medicinal properties that kill internal parasites.

Starting with the barrels of feed, Villalba planted test patches in the field, mixing alfalfa and plants with medicinal compounds, which basically was a medicine cabinet for the sheep. When microscopic tissue samples showed animals infected with a parasite, Villalba noticed the sick animals would migrate from the basic alfalfa field to the mix of plants that made them feel better. No chemicals at work here, just nature.

Sick animals would migrate from the basic alfalfa field to the mix of plants that made them feel better.

Dr. Juan Villalba of Utah State University points out different food options for sheep at the Pasture Research Facility of the Utah Agricultural Experiment Station in Lewiston, Utah.

Dr. Juan Villalba works in the lab where fecal matter from sheep is analyzed to check for parasites

"So, by the animals selecting these compounds by themselves, then that reduces the problem of resistance, because only the animals who are sick are going to seek the particular plant products," Villalba said. And as animals started feeling better, Villalba said he noticed the sheep went back to eating their normal diet.

In the future, Villalba said, instead of traditional chemicals and medicines, treating certain animal diseases may be just a matter of planting a "pasture pharmacy," letting animals decide when they need a prescription. Villalba said studies like his will continue, and perhaps expand to other types of crops that other animals, such as beef cattle, graze on.

Keith McCord is a reporter and anchor for KSL-TV (NBC) in Salt Lake City, Utah.

The online version of Dr. Villalba's article "Selection of tannins by sheep in response to gastrointestinal nematode infection," is located at: http://jas.fass.org/content/88/6/2189.full

Cleaning cows from the inside Out

[Reprinted with permission from the Nov/Dec 2011 issue of *Agricultural Research*]

Rosalie Marion Bliss

Millions of Americans become ill each year due to foodborne pathogenic bacteria.

Who knew? Those thick, sharp-tasting orange peels that people would never dream of eating are "snack heaven" for cows. Not only does the cow get good roughage and vitamins, but it also gets an antimicrobial boost from the peel's essential oils. That's partly because the peel contains a compound called "d -limonene," which is used in many cleaning products as an antimicrobial agent. And since adult cows can have one trillion or more microbes in one ounce of rumen fluid, there are lots to mop up!

Although experts consider the U.S. food supply to be very safe, millions of Americans become ill each year due to foodborne pathogenic bacteria. *Salmonella enterica* is a common foodborne pathogenic bacterium that is among the spectrum of microbes found inside the intestines of cattle, swine, and poultry. Transient or harmless organisms, as well as beneficial ones, are also among those intestinal microbes. Because pathogenic *Salmonella* can be found in the live food animal, reducing its populations in the gastrointestinal tract could potentially improve food safety because fewer pathogenic bacteria would be present during slaughter and processing.

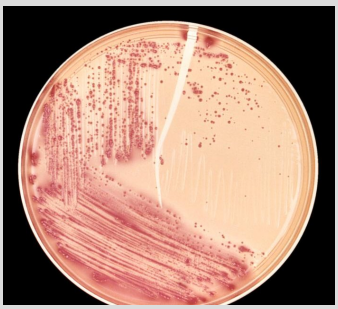
Reducing pathogenic Salmonella in the gastrointestinal tract of cattle, swine, and poultry could potentially improve food safety because fewer pathogenic bacteria would be present during slaughter and processing.

Cows seem to enjoy orange peel and pulp. But these citrus byproducts are more than just tasty and nutritious; they also have an antimicrobial effect in the cow's gut.

Several naturally occurring plant chemicals have shown promise as antibacterials in a variety of applications. Citrus essential oils, for example, have been part of the human diet for hundreds of years, and their effects on bacterial growth and survival are well studied. Citrus oils have been known to kill *Staphylococcus aureus, Pseudomonas, Salmonella,* and *Escherichia coli.*

An Unlikely Cleanser

A team of researchers recognized the potential of citrus byproducts as a possible food safety intervention and has been experimenting with them since 1999. The team consists of Agricultural Research Service microbiologist Todd R. Callaway and animal scientist Tom S. Edrington, with the Food and Feed Safety Research Unit in College Station, Texas; ARS animal scientist and research leader Jeffery Carroll with the Livestock Issues Research Unit in Lubbock, Texas; and John Arthington at the University of Florida in Ona. "While foodborne pathogens are found in the gut of food animals, non-antibiotic methods to reduce such pathogens in the live animal are important to improving food safety," says Callaway.



Colonies of Gram-negative *Escherichia coli* bacteria growing on a MacConkey agar culture plate (Courtesy CDC)

Initial laboratory results published in 2005 indicated that citrus products included in ruminant rations decreased pregastric gut and lower-gut populations

Citrus oils have been known to kill Staphylococcus aureus, Pseudomonas, Salmonella, and Escherichia coli.

of *E. coli* O157:H7 and a variant of *S. enterica, S.* Typhimurium, without causing a significant change in fermentation end products. These end products include acetate, which is a volatile fatty acid. Certain beneficial bacteria in the cow's gut produce these acids, which are absorbed by the animal to provide energy.
"Cows have evolved to depend on volatile fatty acids—or VFAs—for nearly all their energy needs," says Callaway. "Absorption of VFAs is necessary, and if there is a large disruption in VFA absorption, then there is also a disruption to the animal's efficiency, productivity, and health."

Callaway's early data showed the feasibility of using orange pulp as a feed source to provide antipathogenic activity in cattle. He also showed that citrus byproducts (orange peel and pulp) are compatible with current production practices, are palatable to the animals, and can be a "green" solution. Another plus—citrus byproducts are also economically feasible and readily available.

While citrus byproducts are fed to cattle because of their high nutritive value and low cost, Callaway has been shedding more light on how to exploit the essential oils inside the peel and pulp that are natural antimicrobials. Collaborations with University of Arkansas-Fayetteville researchers Steven Ricke and Philip Crandall have identified specific essential oils that kill pathogenic bacteria.

In other laboratory tests, Callaway's research group has demonstrated that the addition of a small amount of orange peel and pulp to a mixture of laboratory ruminal fluid fermentations reduced populations of *E. coli* O157:H7 and *S.* Typhimurium. The amount given was considered similar to a realistic amount ingested on a farm. The 2008 study, which was coauthored with Carroll, Arthington, and University of Arkansas researchers, was published in *Foodborne Pathogens and Disease*.

Callaway's further studies demonstrated that feeding orange peel and pulp reduced intestinal populations of diarrhea-causing *E. coli* in weaned swine. That study, also led by Carroll and coauthored with Callaway, was published in 2010 in the *Journal of Animal and Veterinary Advances*.

From Heavy Peels to Pellets

From the time Callaway began studying citrus as an animal gut cleanser, he also recognized that citrus peel can be heavy and expensive to ship long distances. "Even as compost, citrus peels are difficult to transport," he says.

Thus, Callaway's latest studies investigated the use of processed orange peel pellets. The team fed the pellets to sheep as a model for cows for 8 days. They found a 10-fold reduction in *Salmonella* and *E. coli* O157:H7 in the animals' intestinal contents. Callaway received a grant from the National Cattlemen's Beef Association (Beef Checkoff funds) to help fund the work. These studies were accepted for publication in 2011 in the *Journal of Food Protection* and *Foodborne Pathogens and Disease*.

"When approaching preharvest food safety, we take a 'multiple hurdle' approach," says Callaway. "These studies have the potential to lead to one more

These studies have the potential to lead to one more in a series of hurdles set up to prevent spread of foodborne pathogens.

in a series of hurdles set up to prevent the spread of foodborne pathogens." Processing plants, for example, depend on multiple hurdles for keeping pathogens at bay. A method of reducing the presence of pathogens in live animals before they enter processing plants could possibly be a key hurdle to add to their list. Callaway is now preparing upcoming field trials of citrus byproducts with collaborators at ARS, the University of Arkansas, and the University of Florida.

This research is part of Food Safety, an ARS national program (#108) described at www.nps.ars.usda.gov.

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Study finds "minimal" health impacts on canine 9/11 rescuers

[Reprinted with permission from the September 7, 2011 digital edition of the Philadelphia Inquirer]

Amy Worden

A study conducted by the University of Pennsylvania School of Veterinary Medicine found that canine rescuers at the World Trade Center site have shown only minimal health setbacks.

A new study shows that ten years after the 9/11 attacks, K-9 rescuers at World Trade Center site and elsewhere have shown only "minimal" health setbacks compared to their human counterparts. The study, conducted by the University of Pennsylvania School of Veterinary Medicine, monitored the long-term health effects of working at Ground Zero and the Pentagon and found that canines did not show the same level of respiratory problems found in human rescuers.

Tony Zintsmaster and Kaiser, and Indiana Task Force One search-and-rescue dog team, were deployed to Ground Zero immediately following the 9/11 attack on the World Trade Center. The pair continue search-and-rescue efforts.

"The most striking thing is that many of the humans that responded have developed reactive airway diseases, such as asthma, sinusitis, or other chronic infections in their nasal sinuses. The dogs on the other hand have fared

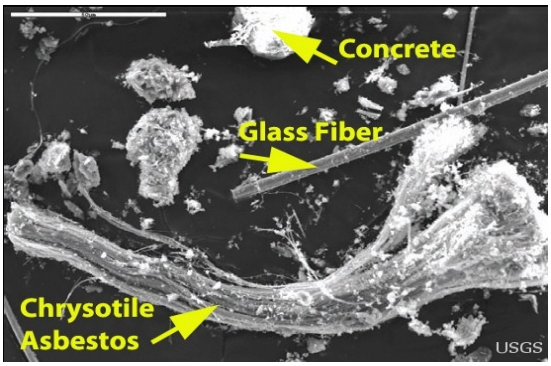
SAR (Search and Rescue) dog at World Trade Center, New York, USA on 9/11/2001 (Courtesy Joel Meyerowitz)

Future research could center on learning why the search-and-rescue dogs were able to endure the challenging conditions with minimal respiratory complications.

Amy Worden

extremely well," explained Dr. Cynthia Otto, the study's lead researcher and an associate professor at PennVet. "They're not developing any problems with their lungs or sinuses. That is a real surprise."

The study was supported by a $500,000 grant from the American Kennel Club's Canine Health Foundation (CHF). Otto said the vast majority of canines suffered only minor cuts and scrapes despite not wearing protective gear. Kaiser, now a 12-year-old German shepherd, was one of only four dogs in the study that required stitches while working at Ground Zero.



Electron micrograph of the microscopic particles found in the dust and debris from the fallen World Trade Center towers (Courtesy USGS)

"On our second day there, Kaiser sliced a pad on the pile," said Tony Zintsmaster, Kaiser's trainer and a charter member of Indiana Task Force One. "Once he was stitched up and felt better, Kaiser went back to work. He was quite amazing. He was able to adapt to the situation and showed great agility. He seemed happiest when he was on the pile working." Zintsmaster, along with other handlers who participated in the study, submitted annual X-rays, blood samples, and surveys on their dog's health and behavior to researchers.

The study also found that the average lifespan of deployed dogs was 12.5 years, while non-deployed search-and-rescue dogs lived an average 11.8 years. Today, at least 13 deployed search-and-rescue dogs that were part of the study are still alive.

"These dogs are a national resource and it's remarkable to know how well they were able to endure such harsh conditions," said Terry Warren, CHF chief executive officer and general counsel.

Because canine and human genomes are similar and most canine diseases also occur in humans, future research could center on learning why the search-and-rescue dogs were able to endure the challenging conditions with minimal respiratory complications. Identifying respiratory genetic markers in canines could lead to the development of treatments of respiratory ailments in humans. "The findings may open our eyes to the difference between dogs and people that makes them so resilient," Otto said. "If we could tap into that, we might actually help move human health forward."

Amy Worden is a politics and government reporter for the Inquirer. In that capacity she has explored a range of animal issues from dog kennel law improvements and horse slaughter to the comeback of peregrine falcons and pigeon hunts.

National League of Cities adopts One Health resolution at 2011 Congress of Cities

The National League of Cities (NLC) is a network of state municipal leagues and direct member cities from across the country that is dedicated to helping city leaders build better communities. Working in partnership with the 49 state municipal leagues, NLC serves as a resource to and an advocate for the more than 19,000 cities, villages and towns it represents. It promotes cities and towns through an aggressive media and communications program that draws attention to city issues and strengthens the voice of local government in the nation's capital.

At the 2011 Congress of Cities held in November in Phoenix, Arizona, the National League of Cities adopted the following One Health resolution that *"supports integrated decision-making in the context of the One Health Initiative, and calls on the federal government to adopt legislation and practices that address human health, animal health, and ecological health in an integrated fashion and support local efforts to advance sustainability goals."*

NLC Resolution #2012-17: One Health Initiative

WHEREAS, cities depend on the health and vitality of their inhabitants, reliable access to sufficient quantities of wholesome food and clean water, clean air, and the ecosystem services that support them; and

WHEREAS, government plays an important role in coordinating efforts to preserve and maintain those resources; and

WHEREAS, policymakers are challenged to make sense of complex interrelationships among human health, animal health, and ecological health, and pressed to conform with decision-making models that often isolate those critical connections and shorten planning horizons; and

WHEREAS, cities' economic, social, and environmental well-being—the triple bottom line – whereon environmental stewardship, economic prosperity, and social responsibility intersect—depends on our ability to integrate diverse interests through unified long-range planning, and to engage and inform policymakers and practitioners about critical interdependent needs; and

WHEREAS, the *One Health Initiative 4* is the collaborative objective of multiple disciplines, including the American Medical Association (AMA), U.S. Centers for Disease Control and Prevention (CDC), American Veterinary Medical Association (AVMA), their international counterparts, and environmental organizations, working locally, nationally, and globally to disseminate information about human health, animal health, and environmental health; and

WHEREAS, leaders in local government are ideally suited as partners in that responsibility; and

WHEREAS, successful adoption and implementation of the *One Health Initiative* will be predicated on the leadership, communication skills, and cooperation of its advocates; and

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WHEREAS, *One Health* topics that pertain to local government include the costs and organizational structure of public health services; pandemic preparedness; health education; adaptation to climate change; animal control and vaccination requirements; transportation and land use planning affecting public wellness; water quality protection; waste management; energy choices; food safety and regional food systems; ecological protection, restoration, and monitoring; homeland security and bioterrorism; measures of economic trends and workforce preparedness relative to sustainable practices; health, healthcare costs, and absenteeism of personnel; and

WHEREAS, facilitating communication among increasingly specialized experts will improve health outcomes for communities through increased awareness of connections between climate variability, food production, and infectious diseases; cross-species contagion (zoonoses), and human and animal health conditions; and demands on municipal infrastructure and services; and

WHEREAS, climate change will affect energy costs, the frequency and severity of floods, fires, wind events, heat waves, and other extreme weather conditions; coastal development and building standards; incidence vector-borne illnesses; crop production; habitat loss; endangerment and extinction of species; and human illness; and

WHEREAS, cities can only thrive if they remain attractive and livable, with sufficient quantities of clean water, clean air, efficient, affordable buildings, healthful food choices, healthy food animals, and leaders who are committed to cooperative long range planning for a sustainable future.

NOW, THEREFORE, BE IT RESOLVED that the National League of Cities supports integrated decision-making in the context of the *One Health Initiative*, and calls on the federal government to adopt legislation and practices that address human health, animal health, and ecological health in an integrated fashion and support local efforts to advance sustainability goals.

The One Health Newsletter is interested in publishing articles from a variety of view points and perspectives, and thus any opinions or statements made in the Newsletter's articles belong solely to the respective author(s), not the Editor, Editorial Board, or Newsletter Contributors.

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Coming Events

International Conference on Emerging Infectious Diseases (ICEID)

Atlanta, Georgia, USA

March 12 -14, 2012

http://www.iceid.org/index.php/registration

15th International Congress on Infectious Diseases (ICID)

Bangkok, Thailand

June 13-16, 2012

http://www.isid.org/icid/index.shtml

13th ISVEE Conference, 2012

The International Society for Veterinary Epidemiology and Economics

"Building Bridges - Crossing Borders"

Maastricht, Netherlands

August 20-24, 2012

http://isvee13.org/

4th International EcoSummit

"Ecological Sustainability: Restoring the Planet's Ecosystem Services"

Columbus, OH, USA

September 30-October 5, 2012

http://www.ecosummit2012.org/

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Editorial Board:

Recent One Health Publications (continued)

Climate Change Boosts Lethal Hendra Virus. Nancy Bazilchuk and Daily Climate. ScientificAmerican.com. November 2011. http://www.scientificamerican.com/article.cfm?id=climate-change-boosts-lethal-hendra-virus

Americans Worried About Global Pandemics, Yet Lack Knowledge of Their Likely Source, Survey Shows. Lynn Peeples. December 2011. http://www.huffingtonpost.com/2011/12/14/global-pandemic-animals_n_1148284.html

Following the genes: a framework for animal modeling of psychiatric disorders. Kevin Mitchell, Z. Josh Huang, et al. BMC Biology. November 2011. http://www.biomedcentral.com/1741-7007/9/76

For other One Health publications, please visit the One Health Initiative website:

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