The term One Health has been defined as the collaborative efforts of multiple disciplines working locally, nationally, and globally, to attain optimal health for people, animals, and our environment.

...we need to adopt an integrated, holistic approach that reflects both our profound interdependence and the realization that we are part of a larger ecological system—exquisitely and elaborately connected.

– from the AVMA
Global Pathogens Laboratory

- 15 research personnel (2 DVM/PhDs, 1 DVM/MSc, 2 PhDs)
- 3000 sq.-ft of BSL2, BSL2+Ag, and BSL3 space
- 6 BSL3 suites
- Access to much more BSL3 animal space
- High throughput deep sequencing and other core facilities

http://gpl.phhp.ufl.edu/index.html

GPL International Research Collaborations

Often We Work with Veterinarians and Study Disease Transmission at the Human-Animal Nexus

Most Human Emerging Diseases are Zoonotic

Among 132 emerging human pathogens, 75% are considered zoonotic

Zoonotic pathogens are twice as likely to be associated with emerging diseases than non-zoonotic pathogens.

Taylor LH, Lehman SW, Weisshaar MC. Philosophical Transactions of the Royal Society B: Biological Sciences. 2001; 356:983-9
Human-Animal-Environmental Nexus is Ignored as a research or training area

- Most human disease studies involve clinical ill patients who first appear in medical facilities
- Most animal disease studies involve clinical diseases that are apparent to caretakers
- Most environmental health studies are developed in response to recognized illness in man or animals
- No major effort to anticipate the next emerging disease threat

Research

- Swine influenza
- Avian influenza
- Equine influenza
- Canine influenza
- Marine mammal influenza
- Human adenovirus
- Naegleria fowleri
- Naegleria gruberi
- Acanthamoeba spp.
- Balamuthia mandrillaris
- Porcine reproductive respiratory disease syndrome virus (PRRS)
- Porcine circovirus 2
- Bovine calf diarrhea
- Canine coronavirus
- Clinique virus
- Chikungunya virus
- Rift Valley fever virus
- Bovine RSV
- Bovine coronavirus
- Bovine rotavirus

- Cross-sectional studies
- Prospective studies
- Diagnostic test evaluations & development

Avian Influenza

Photo by Greg Gray (CEID), Cambodia, Dec 2006

Results Zoonotic Influenza Study: Avian Viruses

Gray GC, McCarthy T, Capuano AW, Setterquist SF, Alavanja MC, Lynch CF Evidence for Avian Influenza A Infections Iowa’s Agricultural Workers. Influenza & Resp Viruses 2008; available on line 4/07/08

Table 4: Odds ratios for a positive serologic response against avian influenza viruses among workers with fewer than 1000 turkeys using logistic regression.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Avian H9</th>
<th>Avian H5</th>
<th>Avian H1</th>
<th>Avian H10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age controls (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;12</td>
<td>0.90 (0.38-2.22)</td>
<td>1.09 (0.79-1.49)</td>
<td>1.08 (0.79-1.49)</td>
<td>1.09 (0.79-1.49)</td>
</tr>
<tr>
<td>12-15</td>
<td>0.90 (0.38-2.22)</td>
<td>1.09 (0.79-1.49)</td>
<td>1.08 (0.79-1.49)</td>
<td>1.09 (0.79-1.49)</td>
</tr>
<tr>
<td>&gt;15</td>
<td>0.90 (0.38-2.22)</td>
<td>1.09 (0.79-1.49)</td>
<td>1.08 (0.79-1.49)</td>
<td>1.09 (0.79-1.49)</td>
</tr>
<tr>
<td>Worked with poultry in Iowa 2003</td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.02 (0.61-1.71)</td>
<td>1.07 (0.79-1.49)</td>
<td>1.08 (0.79-1.49)</td>
<td>1.09 (0.79-1.49)</td>
</tr>
<tr>
<td>No</td>
<td>0.90 (0.38-2.22)</td>
<td>1.09 (0.79-1.49)</td>
<td>1.08 (0.79-1.49)</td>
<td>1.09 (0.79-1.49)</td>
</tr>
<tr>
<td>Household influenza infection (aap)</td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.02 (0.61-1.71)</td>
<td>1.07 (0.79-1.49)</td>
<td>1.08 (0.79-1.49)</td>
<td>1.09 (0.79-1.49)</td>
</tr>
<tr>
<td>No</td>
<td>0.90 (0.38-2.22)</td>
<td>1.09 (0.79-1.49)</td>
<td>1.08 (0.79-1.49)</td>
<td>1.09 (0.79-1.49)</td>
</tr>
<tr>
<td>Exposed to poultry diseases</td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.02 (0.61-1.71)</td>
<td>1.07 (0.79-1.49)</td>
<td>1.08 (0.79-1.49)</td>
<td>1.09 (0.79-1.49)</td>
</tr>
<tr>
<td>No</td>
<td>0.90 (0.38-2.22)</td>
<td>1.09 (0.79-1.49)</td>
<td>1.08 (0.79-1.49)</td>
<td>1.09 (0.79-1.49)</td>
</tr>
</tbody>
</table>

Example: Examining study participants for antibody against avian influenza


Table 4: Odds ratio for a positive serologic response against avian influenza virus by immunization against, or lack of antibody.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Avian H9</th>
<th>Avian H5</th>
<th>Avian H1</th>
<th>Avian H10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variations</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
</tr>
<tr>
<td>Age controls</td>
<td>127</td>
<td>128</td>
<td>127</td>
<td>127</td>
</tr>
<tr>
<td>Age exposed</td>
<td>127</td>
<td>128</td>
<td>127</td>
<td>127</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Married</td>
<td>Yes</td>
<td>87</td>
<td>93</td>
<td>87</td>
</tr>
<tr>
<td>Non-exposed</td>
<td>31</td>
<td>31</td>
<td>31</td>
<td>31</td>
</tr>
</tbody>
</table>

Normally only titers above 1:80 would be considered as evidence of avian influenza infection. However, the proportional odds model uses data across all titers and has more discriminating power.

Study Design: Surveillance Study

Cohort Subject Enrollment:
- Complete Enrollment Form & Informed Consent
- Collect blood sample

Weekly Follow-Up:
- Complete questionnaire

Annual Follow-Up:
- (12, 24 and 36 months)
  - Complete questionnaire
  - Collect blood sample

Cohort subject develops ILI (ILI Investigation):
- Complete questionnaire
- Collect blood & respiratory specimens
- Test for Flu A & B by real-time RT-PCR

Confirmed influenza A infection:
Initiate Family Transmission Study
Case Contact Subject Enrollment:
- Complete Enrollment Form & Informed Consent
- Collect blood sample
- Collect respiratory specimens (nasal & throat swabs) if the subject has ILI

Weekly Follow-Up:
- Complete questionnaire

During the 60 day follow-up period, collect nasal & throat swabs if the subject has ILI

At day 60, collect convalescent blood sample

Test for Flu A & B by real time RT-PCR

Family Farm

Swine influenza

The Role of Swine in the Generation of Novel Influenza Viruses

Swine Workers and Zoonotic Influenza • CID 2006:42 (1 January)
Putting Meat on the Table: Industrial Farm Animal Production, April 2008

...the continual cycling of swine influenza viruses and other animal pathogens in large herds or flocks provides increased opportunity for the generation of novel viruses through mutation or recombinant events that could result in more efficient human-to-human transmission of these viruses.

Evidence of Swine Influenza Virus Infection Among Swine Workers

- Controlled, cross-sectional seroprevalence studies among 111 farmers, 97 meat processing workers, 65 veterinarians, and 79 control subjects using serum samples collected during the period of 2002–2004.
- Serum samples were tested using a hemagglutination inhibition assay against 6 influenza A virus isolates collected recently from pigs and humans: A/Swine/WI/238/97 (H1N1), A/Swine/WI/R33F/01 (H1N2), A/Swine/Minnesota/593/99 (H3N2), A/New Caledonia/20/99 (H1N1), A/Panama/2007/99 (H3N2), and A/Nanchang/933/95 (H3N2).

Preventing Zoonotic Influenza Virus Infection

- 49 swine industry workers and 79 non-swine exposed controls enrolled in a seroprevalence study
- Examined for antibodies with hemagglutination inhibition assay to swine and human influenza viruses.

| Table 1. Adjusted odds ratios of antibody against swine influenza virus, proportional odds model. |
|-------------------------------------------------|-----------------|-----------------|
| Risk factors | Swine H1N1 | Swine H1N2 |
| Occupation   |            |                |
| Farmers/controls | 35.3 (7.7-161.3) | 13.8 (5.4-35.4) |
| Meat processing workers/controls | 6.5 (1.4-29.2) | 2.7 (1.1-6.7) |
| Veterinarian workers/controls | 17.8 (3.8-82.7) | 2.5 (3.6-24.6) |
| Age           | (1.1)      | (1.5)         |
| Gender        |            |                |
| Male/Female  | 2.9 (1.5-5.2) | 2.3 (1.4-3.7) |
| Antibody to human virus |            |                |
| H1N1          | 2.8 (1.6-5)  | 2.7 (1.6-5.5) |
Population-based Surveillance for Zoonotic Influenza A (NIAID R21)

- **Design** – 2-year prospective, controlled study of farmers who were occupationally exposed to swine or poultry (n=805); 29 counties in Iowa
- **Exposure questionnaires** – at enrollment, 12-months, and 24 months
- **Specimen collection** – Sera collection upon enrollment, at 12 months and 24 months; viral specimens and questionnaire when ill


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Table 3. Enrollment analyses of risk factors using proportional odds model, university controls as reference.

<table>
<thead>
<tr>
<th>Swine Influenza A(H1N1)</th>
<th>Swine Influenza A(H1N2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Swine exposure</strong></td>
<td></td>
</tr>
<tr>
<td>AHS - worked in swine production</td>
<td>701</td>
</tr>
<tr>
<td>AHS - Never worked in swine production</td>
<td>108</td>
</tr>
<tr>
<td>Non AHS - Controls</td>
<td>73</td>
</tr>
<tr>
<td><strong>Age continuous</strong></td>
<td>600</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>486</td>
</tr>
<tr>
<td>Female</td>
<td>314</td>
</tr>
<tr>
<td><strong>Received flu shot in the past 4 years</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>479</td>
</tr>
<tr>
<td>No/Unsure</td>
<td>387</td>
</tr>
<tr>
<td><strong>Human H1N1</strong></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>347</td>
</tr>
<tr>
<td>Negative</td>
<td>519</td>
</tr>
</tbody>
</table>


---

Swine Influenza & Swine Shows Design & Methods

- **Design**: Prospective cohort study (13 months) of children >7 yrs and adults who participate in swine shows (1 hr/wk pig exposure)
- **Methods**
  - Enroll up to 300 swine show participants informed consent, sera, questionnaire and swabs of 1 show pig (influenza A, MRSA)
  - Give participant ILI kit (questionnaire, swabs, thermometer) for workup of ILI (influenza A, MRSA) during 13 months

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Reassortment of Pandemic H1N12009 Influenza A Virus in Swine


The emergence of pandemic H1N12009 influenza demonstrated that pandemic viruses could be generated in nature. Subsequent reassortment of H1N12009 to swine has occurred in multiple countries. Through systematic surveillance of influenza viruses in swine from a Hong Kong abattoir, we characterized a reassortant progeny of H1N12009 with swine viruses. Swine experimentally infected with this reassortant developed mild illness and transmitted infection to contact animals. Continued reassortment of H1N1209 with swine influenza viruses could produce variants with transmissibility and altered virulence for humans. Global systematic surveillance of influenza viruses in swine is warranted.

1 State Key Laboratory of Emerging Infectious Diseases and Department of Microbiology, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China
2 International Institute of Influenza and Immunity, Shantou University Medical College, Shantou, Guangdong 515003, China
3 Hong Kong Department of Health Laboratories
4 School of Public Health, University of Hong Kong
5 Hong Kong West China Medical University, Hong Kong
6 University of Hong Kong

pH1N1 in pigs by country

Generated from OIE data available from World Animal Health Information Database & sequences deposited in GenBank, August 2010...Courtesy of Dr. Amy Vincent of National Animal Disease Center, Ames, IA
Equine Influenza

- EIV 2nd most important respiratory tract disease in adult horses
- EIV epizootics are common among equine species
- Equine mortality as high as 20%
- H7N7 and H3N8 viruses

HI and neutralizing antibodies to A/Equine-2/63 virus were found in human serum from individuals born between 1870 and 1900. Persons born about 1880 to 1890, however, exhibited higher levels and higher frequencies of antibody than did younger or older individuals.

### Seroprevalence of Equine Influenza Antibodies among Persons with Horse Exposures

- Cross-sectional 2005 study of Iowans
- 94 horse-exposed persons and 45 non-exposed controls
- Hemagglutination inhibition (HI) and microneutralization assays (MN) were used against 3 equine and 3 human influenza A viruses
- Participants did not report increased use of masks or gloves when working with ill horses.

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#### Table 2: Risk factor analysis of microneutralization results for A/Equine/Ches(03) (H3N8) with exact logistic regression

<table>
<thead>
<tr>
<th>Variables</th>
<th>n</th>
<th>Unadjusted Exact OR (95%)</th>
<th>Adjusted Exact OR (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.0 (0.97-1.03)</td>
<td>1.0 (0.96-1.06)</td>
</tr>
<tr>
<td>Antibody against human H1 Nanfang (&gt;1.40)</td>
<td>Yes</td>
<td>66</td>
<td>1.7 (0.32-10.99)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>40</td>
<td>reference</td>
</tr>
<tr>
<td>Vaccinated horses in the past 12 months</td>
<td>Yes</td>
<td>60</td>
<td>0.5 (1.39-infinity)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>40</td>
<td>reference</td>
</tr>
<tr>
<td>Exposed type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Veterinarians</td>
<td>8</td>
<td>21.1 (1.55-infinity)</td>
</tr>
<tr>
<td></td>
<td>Recreational use of horses</td>
<td>30</td>
<td>0.7 (1.51-infinity)</td>
</tr>
<tr>
<td></td>
<td>Other horse exposures</td>
<td>52</td>
<td>2.1 (1.96-infinity)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>45</td>
<td>reference</td>
</tr>
</tbody>
</table>


---

### Research Study: Human Exposure to Equine Influenza

Dr. Fiona Burnell

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**Identifying Risk Factors for Zoonotic Influenza Transmission, Mongolia**

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Summary

- Zoonotic infections are an important area for research study and they often require partnerships between human, animal, and environmental scientists
- We need professionals trained across disciplines to lead these research studies

Our One Health Vision

- To train professionals to conduct “one health” investigative and experimental research
- Three levels of training: Certificate, Master’s, PhD programs
- To attract outstanding US and international researchers to such a training program
One Health Training Elements (Tools)

- Environmental health
- Modern laboratory techniques
- Epidemiology
- Biostatistics
- Food safety
- Animal science
- Meat science
- Soil and water engineering

- Modern animal production
- Human and animal ecological studies
- Agriculture engineering
- Climate change
- Geographical information systems
- Zoonotic infections
- Toxicology

Emerging Pathogens Institute

Global Pathogens Laboratory
http://gpl.phhp.ufl.edu