Lessons in One Health in Context to Zoonotic Diseases

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One Health

- One Health is a new phrase, but an ancient concept - Environmental factors and human health - Hippocrates

- German physician and pathologist Rudolf Virchow (1821–1902) coined the term "zoonosis", and said "...between animal and human medicine there are no dividing lines – nor should there be".

- In 1947, James H. Steele, DVM, furthered the concept in the U.S. by establishing the field of veterinary public health at the CDC.

- "One Medicine" was developed and promoted by Dr. Calvin W. Schwabe (1927–2006), a UC Davis veterinary epidemiologist and parasitologist in "Veterinary Medicine and Human Health".
“One Health,” inspired the AAVMC’s recent 2014 Annual Conference on “One Health in Veterinary Medical Education,” attracted a record number of more than 300 attendees.

During more than 60 conference presentations from more than 90 presenters, registrants learned about compelling opportunities associated with the One Health approach:

- Interdisciplinary, often international, educational outreach and partnerships
- Innovative, interactive, cross-disciplinary teaching methodologies
- Integrated clinical experiences, research and medical technologies
- Innovations like an integrated human/animal advanced care clinical facility
- Strategies for curricular and professional change
- Urgent need for action and change

Recurrent conference themes focused on the importance of developing One Health competencies related to communication, problem-solving, strategic “systems” thinking, leadership, and collaboration.

See the program on-line at: http://www.aavmc.org/annualconference.aspx
Björn Sigurdsson (1913-1959)

Recognized as developing original concept of “slow” (lenti) virus infections by studying sheep diseases

Sigurdsson B. Rida, a chronic encephalitis of sheep: infections which develop slowly and some of their special characteristics.

Sigurdsson’s Institute for Experimental Pathology, Iceland
Ovine Lentivirus Associated Diseases

Interstitial Pneumonia “Chronic Lungers” and Lymphoid Hyperplasia
Concurrent events – AIDS is recognized with early opportunistic infections in California

CDC
June 5, 1981 / Vol. 30 / No.21

MMWR
MORBIDITY AND MORTALITY WEEKLY REPORT

Pneumocystis Pneumonia — Los Angeles

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed Pneumocystis carinii pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

Patient 1: A previously healthy 33-year-old man developed P. carinii pneumonia and oral mucosal candidiasis in March 1981 after a 2-month history of fever associated with elevated liver enzymes, leukopenia, and CMV viraemia. The serum complement-fixation CMV titer in October 1980 was 256; in May 1981 it was 32.* The patient's condition deteriorated despite courses of treatment with trimethoprim-sulfamethoxazole (TMP/SMX), pentamidine, and acyclovir. He died May 3, and postmortem examination showed residual P. carinii and CMV pneumonia, but no evidence of neoplasia.

Patient 2: A previously healthy 30-year-old man developed P. carinii pneumonia in April 1981 after 6-month history of fever each day and of elevated liver-function tests, CMV viraemia, and documented seroconversion to CMV, i.e., an acute-phase titer of 16 and a convalescent-phase titer of 28* in anticomplement immunofluorescence tests. Other features of his illness included leukopenia and mucosal candidiasis. His pneumonia responded to a course of intravenous TMP/SMX, but, as of the latest reports, he continues to have a fever each day.

Patient 3: A 30-year-old man was well until January 1981 when he developed esophageal and oral candidiasis that responded to Amphotericin B treatment. He was hospitalized in February 1981 for P. carinii pneumonia that responded to oral TMP/SMX. His esophageal candidiasis recurred after the pneumonia was diagnosed, paired specimens not run in parallel.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES / Public Health Service
Fred Murphy DVM, PhD

My Boss at CDC 1987-1990

Leadership role in viral pathogenesis and has articulated clearly the role of animal pathogens in new and emerging diseases

Significant contributions - research work on viruses impacting animals and humans and mentoring and teaching of young scholars

Previous appointments include dean and professor of virology at the University of California—Davis; director of the National Center for Infectious Diseases at the Center for Disease Control and Prevention; and associate dean of research at Colorado State University.
Human T- Lymphotropic Virus Type 1

- First human retrovirus identified

- Deltaretroviruses
  - HTLV-1, HTLV-2,
  - HTLV-3, HTLV-4
  - STLV-1
  - BLV

- Complex retrovirus

  *gag, pol* and *env* genes

  Additional open reading frames (ORFs)

  Regulatory proteins (Tax and Rex)

  Accessory proteins (*p12^I, p13^II/p30^II*)
Adult T-Cell Leukemia/lymphoma

Clinical Presentations

- Asymptomatic
- Pre-leukemic

- Chronic/ Smoldering
  Abnormal T cells, marrow involvement and skin lesions

- **Acute**: Aggressive form
  immunodeficiency, lytic bone lesions, lymphoadenopathy, hypercalcemia, hepatosplenomegaly, system involvement.
Masao Matsuoka & Kuan-Teh Jeang
R49 or Jurkat cells

1 x 10^7 cells/ml

Necropsy at Day 1, 3, 5, 7, 14, 21, and 56 days post infection

PBMCs, MLN, Spleen, GALT

Plasma
Western blot
Humoral response

Mononuclear leukocytes

genomic DNA
ex vivo culture

Real time PCR
p19 (MA) expression
Intracellular Tax expression
Viral load
Virus expression
Center for Retrovirus Research
Signature Program Model

- First commercial feline retrovirus vaccine → $14 million in royalties to the university (Leukocell®) licensed to Pfizer Animal Health

- NIH funded Program Project Grant based in CVM – resulting in $20 million in sponsored research 2003-2013
ONE HEALTH APPROACH

Complex Global Health Challenges
UC Davis One Health Institute

- Fosters the science, innovation, capacity building, education and leadership that these **centers and projects** provide to the UC Davis campus, the UC system, state and federal agencies, and worldwide partners.

**PREDICT**
- California Conservation
- Health for Animals and Livelihood Improvement

**Zoological Medicine Service**
- Avian Flu Research
- SeaDoc Society

**Diagnostic and Technology Development Laboratory**
- Curricular Development and Training

**Oiled Wildlife Care Network**
- Gorilla Doctors
- UC Global Health Institute Center
One Health at Interface

- Majority of emerging infectious diseases (EIDs) in people are of animal origin (zoonotic)
- 75% of emerging zoonoses have wildlife origins
- Human activities at the interface linked to EIDs (Nipah virus, SARS, Ebola)
- Annual population growth among highest in buffers to protected areas near wildlife
PREDICT Diagnostic Strategy

Targeted screening for different wildlife taxa

- **primates**
  - Retro, Filo, Flavi, Influenza, Paramyxvo, Henipa, Pox, Bunya, Herpes, Seadorna, Astro, Corona, Arena

- **bats**
  - Flavi, Corona, Henipa, Paramyxvo, Rhabdo, Arena, Filo, Reo, Influenza, Bunya, Seadorna, Astro

- **rodents**
  - Arena, Hanta, Pox, Alpha, Flavi, Reo, Paramyxvo, Influenza, Bunya, Seadorna, Astro

- **human**
  - Retro, Filo, Flavi, Influenza, Paramyxvo, Henipa, Pox, Bunya, Herpes, Seadorna, Astro, Corona, Arena, Hanta, Entero, Lyssa

- **birds**
  - Orthomyxo, Paramyxvo, Flavi

Refine with specific primers or sequencing
Advanced pathogen discovery

20 PCR protocols developed and going out to countries

Follow-up on-the-ground field investigations
develop diagnostics
screen local human cases
screen local wildlife

USAID | PREDICT
• Trained >2,000 field personnel, veterinarians, laboratory technicians, public health workers from 20 countries in 59 ministries
• Building capacity to test for viral families in 33 labs
• Collected samples from 50,000 animals
• Discovered >250 novel viruses in wildlife (e.g. corona, retro, adeno, rhabdo, herpes, boca)
• Documenting human pathogens in wildlife and animal-origin pathogens in humans
First Case
Detection/Reporting
Lab Confirmation
Response

Surveillance, Observations and Monitoring Information

Opportunity for control

CASES

DAY

Adapted from J. Davis, Climate Adaptation Workshop, Nov. 2003
Human Metapneumovirus Infection in Wild Mountain Gorillas, Rwanda


The genetic relatedness of mountain gorillas and humans has led to concerns about interspecies transmission of infectious agents. Human-to-gorilla transmission may explain human metapneumovirus in 2 wild mountain gorillas that died during a respiratory disease outbreak in Rwanda in 2009. Surveillance is needed to ensure survival of these critically endangered animals.
GIARDIA IN MOUNTAIN GORILLAS (GORILLA BERINGENI BERINGEI), FOREST BUFFALO (SYNCERUS CAFFER), AND DOMESTIC CATTLE IN VOLCANOES NATIONAL PARK, RWANDA

Jennifer N. Hogan,¹ Woutrina A. Miller,¹ Michael R. Cranfield,²,⁵ Jan Ramer,³,⁵ James Hassell,⁴ Jean Bosco Noheri,⁵ Patricia A. Conrad,³ and Kirsten V. K. Gilardi²,⁶

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² Gorilla Doctors, Wildlife Health Center, University of California, Davis, One Shields Avenue, Davis, California 95616, USA
³ Indianapolis Zoo, 1200 W. Washington Street, Indianapolis, Indiana 46222, USA
⁴ Royal Veterinary College, University of London, Royal College Street, London NW1 0TU, UK
⁵ Current address: Mountain Gorilla Veterinary Project, 1876 Mansion House Drive, Baltimore, Maryland 21217, USA
⁶ Corresponding author (email: kvgilardi@ucdavis.edu)
Extreme Conservation Leads to Recovery of the Virunga Mountain Gorillas

Martha M. Robbins¹*, Markye Gray², Katie A. Fawcett³, Felicia B. Nutter⁴, Prosper Uwingeli⁵, Innocent Mburanumwe⁶, Edwin Kagoda⁷, Augustin Basabose², Tara S. Stoinski³,⁸, Mike R. Cranfield⁴, James Byamukama², Lucy H. Spelman⁴, Andrew M. Robbins¹
The New York Times

The 1918 Flu Killed Millions. Does It Hold Clues for Today?

Doubt Cast on Stockpile of a Vaccine for Bird Flu

Health Experts Meet in Atlanta to Tackle the Deadly Animal-to-Human Link in Illness

Cull of the Wild

AI: Already a Disaster for Birds
Why focus on One Health education?

• The world is a global community, events in one nation → repercussions worldwide

• “Transboundary” diseases such as foot-and-mouth disease, pandemic zoonotic diseases, water toxicity due to pathogens, pesticides and chemicals, etc.

• World shared concerns - malnutrition, migration, access to health care, environmental illness, urbanization, and infectious diseases

• Unique skill sets of professionals trained in public health, infectious diseases, epidemiology, etc.

Conrad et al., Evolution of a transdisciplinary “One Medicine–One Health” approach to global health education at the University of California, Davis Preventive Veterinary Medicine 92:268–274, 2009
One Health In Action: From the Field to the Classroom
Mission Statement:

• Work across disciplinary boundaries, recognizing the interconnectedness of humans, animals and their environments, to solve problems in the community and globally through education and service.

Goals:

• Multi-disciplinary understanding of health issues

• Advocacy of one world, one medicine, one health

• Global and domestic health projects that impact communities, public health, and human-animal interactions as a whole
Knights Landing, CA
Community Clinic
The Hybrid Learning Interface
Innovations & Applications in One Health Teaching & Training
Interactive On-Line Case Studies

IVImeds

International One Health Cases:
• Novel Pathogen Outbreak – Congo
• Water Quality and Quantity – Kenya
• Wildlife Reservoirs for bTB – S. Africa
• Ecotourism – Uganda
• Participatory Research – Tanzania
• Zoonotic Diseases - Tanzania
• Indoor Air Pollution – Nicaragua
• Herd/Herder Health – Mongolia

Local One Health Cases
• Sea Otters as Sentinels – California
• Transboundary Diseases - California
• Vectorborne Diseases – California
• Plants in Peril – California

Clinical case library?
One Health and Distance Learning

The Mountain Gorilla Veterinary Project and Ecotourism Case Study

Brucellosis: A One Health Disease at a Global Scale

Sophia Papageorgiou, DVM, MPVM, PhD
School of Veterinary Medicine & UCGHI, One Health Center of Expertise
University of California, Davis
Spring 2013
To encourage life long learning and networking opportunities expand their involvement in global health
Cat parasite 'is killing otters'

By Paul Rincon
BBC News website science reporter, St Louis

A parasite carried by cats is killing off sea otters, a veterinary specialist has told a major US science conference.

The Californian researcher has called for owners to keep their cats indoors.

Cat faeces carrying *Toxoplasma* parasites wash into US waterways and then into the sea where they can infect otters, causing brain disease.

The parasite is familiar to medical researchers, as it can damage human foetuses when expectant mothers become infected while changing cat litter.

The most likely source of infection for sea otters is the parasite's tough egg-like stage, known as the oocyst, which is passed in the faeces of cats.

"We need to control the infections in sea otters and reduce the risk to humans by managing our cats more responsibly," said the study author Patricia Conrad of the Wildlife Health Center at the University of California, Davis.
Comparing infection and oocyst shedding

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>Managed</th>
<th>Unmanaged</th>
<th>Bobcats</th>
<th>Mountain Lions</th>
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<tbody>
<tr>
<td>Blood Samples</td>
<td>720</td>
<td>16</td>
<td>22</td>
<td>72</td>
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<tr>
<td>Infection</td>
<td>16.8%</td>
<td>81.3%</td>
<td>72.7%</td>
<td>80.6%</td>
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<tr>
<td>Fecal Samples</td>
<td>435</td>
<td>17</td>
<td>16</td>
<td>50</td>
</tr>
<tr>
<td>Shedding Prevalence</td>
<td>1.8%</td>
<td>11.8%</td>
<td>12.5%</td>
<td>3.9%</td>
</tr>
</tbody>
</table>
Toxoplasma gondii, Source to Sea: Higher Contribution of Domestic Felids to Terrestrial Parasite Loading Despite Lower Infection Prevalence

Elizabeth VanWormer,1 Patricia A. Conrad,1,2 Melissa A. Miller,1,3 Ann C. Melli,2 Tim E. Carpenter,4 and Jonna A. K. Mazet1
Veterinary Teaching, Research and Clinical Service Locations

California Animal Health and Food Safety Laboratory System (CAHFS) Sites

Oiled Wildlife Care Network Vet Med Extension

Serving California
BSE Identified in California Cow

• On April 24, 2012, the USDA announced the detection of atypical bovine spongiform encephalopathy (BSE) in a California dairy cow.

• Diagnosed in SVM California Animal Health and Food Safety Laboratory (Davis)

  -- atypical form of mad cow disease
  -- not associated with contaminated animal feed
  -- milk and beef remain safe to consume
  -- not transmitted through milk
  -- cow did not enter the food or feed supply
One Health in Translational and Clinical Research

Preclinical models:
- Small animal
- Beagle dog
- Non-human primate

Phase I human clinical trials
Phase II human clinical trials
Phase III human clinical trials

Tumour-bearing dog studies:
- Activity
- Toxicity
- Pharmacokinetics
- Pharmacodynamics

Tumour-bearing dog studies:
- Dose
- Regimen
- Schedule
- Biomarkers
- Responding histologies
- Combination therapies

New cancer drug

Nature Reviews | Cancer
Examples in One Health Approach to Translational Medicine and Surgery
Familial subvalvular aortic stenosis of Newfoundland dogs is associated with a single codon insertion in the PICALM gene.

Open=unaffected, Blackened=affected, ?=unknown, Striped=equivocal, Circles=females, Squares=males

*Stern JA, White SN, Meurs KM. Mamm Genome. 2013*
Small molecule inhibition of clathrin-mediated endocytosis affects outflow tract (OFT) development in *Xenopus laevis* embryos.
Xenogeneic Extracellular Matrix Scaffolds

- Need for improved replacement and repair
- Cardiovascular Structures (Vessel, Valve, Heart Muscle, Whole Heart)

Vascular Engineering Collaboration with UCD School of Veterinary Medicine, UCD School of Medicine, UCD Department of Biomedical Engineering and Travis Air Force Base
Glutaraldehyde-Fixed Carotid Patch

Tissue Engineered Vessel
Minimally Invasive and innovative techniques, collectively under the specialty of Interventional Radiology (IR) pioneered at UC Davis — expanding worldwide

IR techniques—specialized equipment e.g., guide wires, catheters, balloons, and stents to treat many diseases—diagnosis and treatment
- Near-infrared operative imaging
- Transarterial chemoembolization
- Stenting for malignant and benign disease
- Cryoablation of neoplasia
- Percutaneous shunts
- Advanced laparoscopic and thoracoscopic surgery
- Sentinel lymph node mapping
- Clinical trials with varying client financial incentives

Drs. Bill Culp and Michele Steffey faculty leaders
VMTH oral surgeons are now able to utilize 3-D printing to **create exact replicas** of their patients’ skulls

UC VMTH partnered with UC Davis Translating Engineering Advances to Medicine (TEAM) in the Department of Biomedical Engineering

- Exact, to-scale replica of a patient’s skull.
- Accurately determine the extent and location of an injury or mass
- Determine close vital structures
- Accurate sizing of the plates for the surgery
- Reduces time of surgeries → improves patient safety and outcome.
Questions?