Looking at Microphysiological Systems through the One Health Lens

Bernadette Dunham, D.V.M., Ph.D.

Advisor to the FDA One Health Initiative – U.S. Food and Drug Administration

Professorial Lecturer, Milken Institute School of Public Health

The George Washington University

for the

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Microphysiological Systems: Bridging Human and Animal Research

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The Concept of One Health

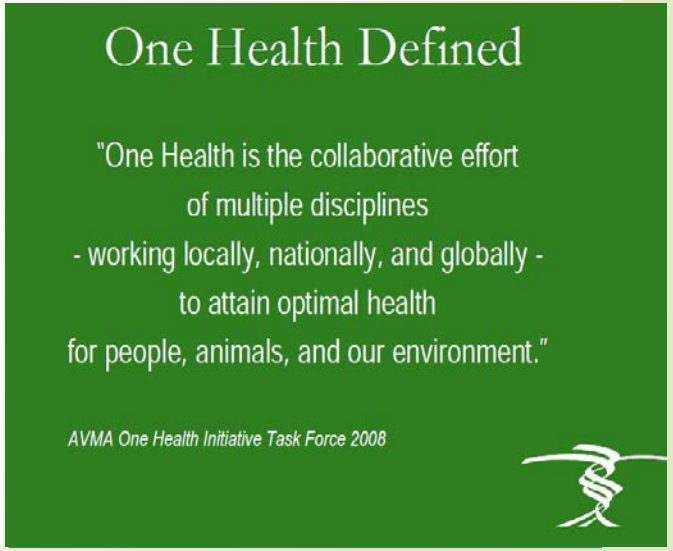
The concept of One Health is not really new, considering the fact that 2,500 years ago it was **Hippocrates** who

"urged physicians to consider…

- **where their patients lived,**
- **the foods they ate,**
- **the waters they drank,**
- **their lifestyles, and**
- **the seasons of the year."**

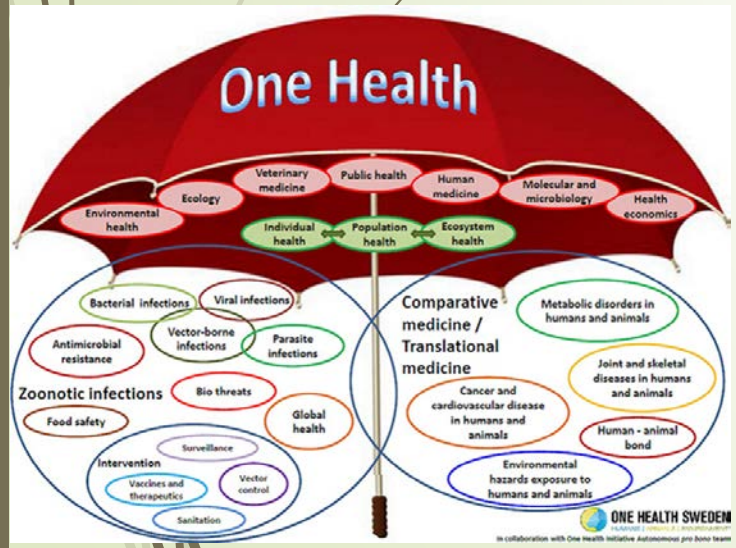
One Health is a collaborative, multisectoral, and transdisciplinary approach - working at the local, regional, national, and global levels - with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment.

https://www.cdc.gov/onehealth/basics/index.html



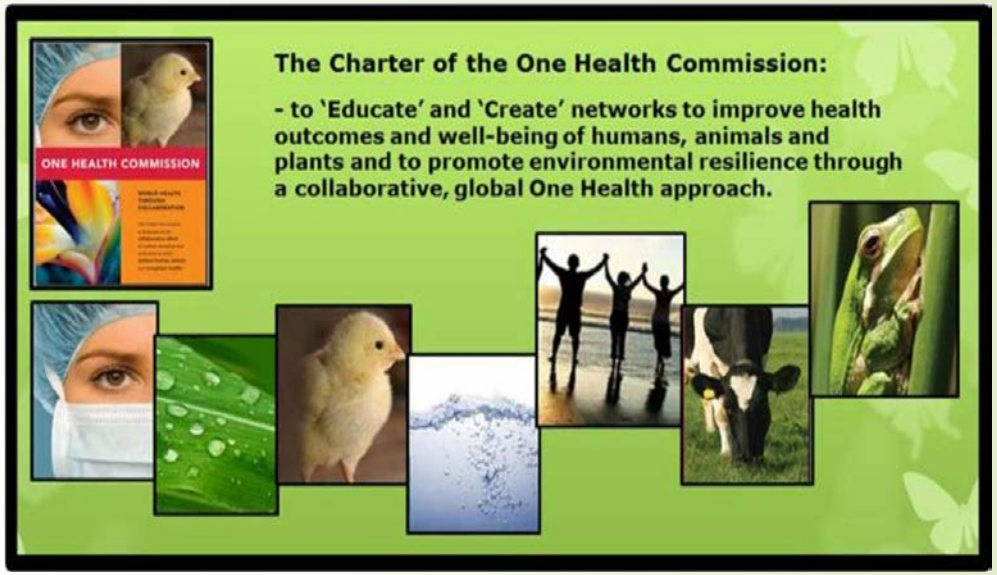
Mission Statement:
Recognizing that human health (including mental health via the human-animal bond phenomenon), animal health, and ecosystem health are inextricably linked, One Health seeks to promote, improve, and defend the health and well-being of all species by enhancing cooperation and collaboration between physicians, veterinarians, other scientific health and environmental professionals and by promoting strengths in leadership and management to achieve these goals.

One Health Initiative Website: https://onehealthinitiative.com



One Health Commission

https://www.onehealthcommission.org/en/news/covid19_and_one_health/

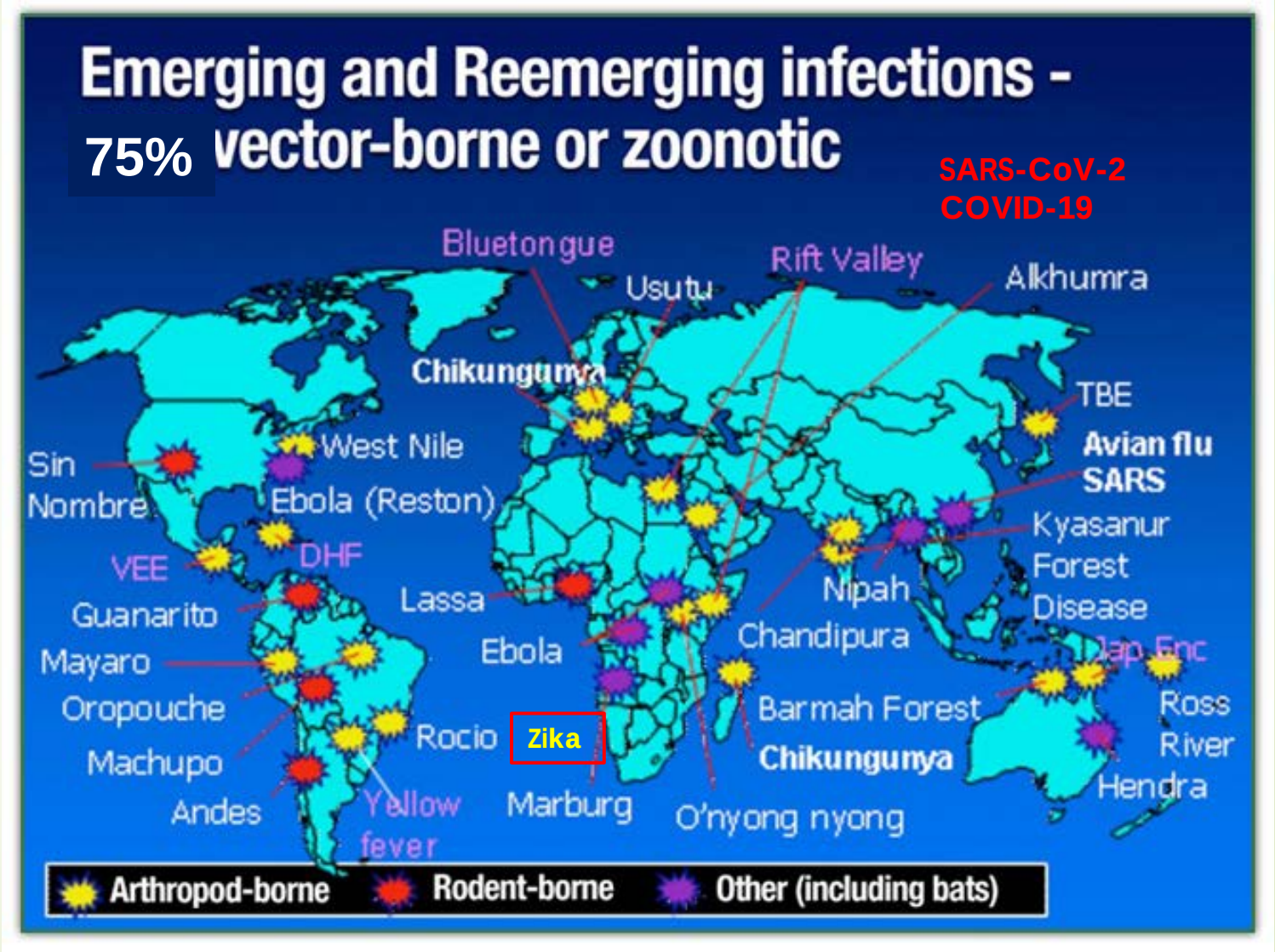


One Health Commission Website: https://www.onehealthcommission.org/

The One Health Platform website: http://onehealthplatform.com/

Three One Health Websites

Emerging & Re-emerging infections



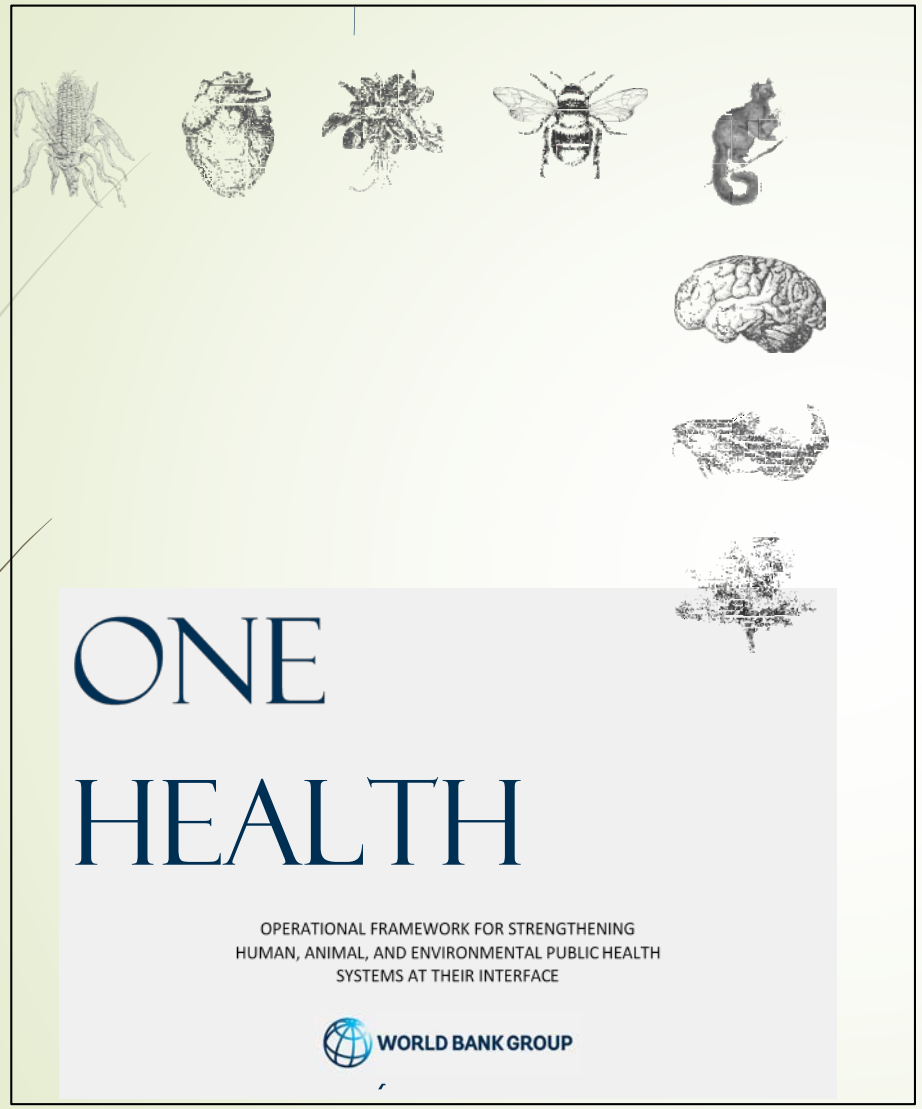
Created by Thomas P. Monath, MD for the One Health Initiative website. https://onehealthinitiative.com/

Transforming our world: The 2030 Agenda for Sustainable Development

'All countries and all stakeholders, acting in collaborative partnership, will implement this plan.'

Many of these United Nations goals demonstrate a <u>One Health approach</u>.

http://www.un.org/ga/search/view_doc.asp?symbol=A/RES/70/1&Lang=E



On 4/27/2018 the World Bank released their **"One Health Operational Framework for strengthening human, animal and environmental public health systems at their interface"**

The Operational Framework is intended as a guide for One Health operations, from project and program scoping and identification stages to design and implementation, including monitoring and evaluation, to help optimize investments.

http://documents.worldbank.org/curated/en/703711517234402168/Operational-framework-for-strengthening-human-animal-and-environmental-public-health-systems-at-their-interface

Senate Resolution 462 – Declares January as National One Health Awareness Month

116TH CONGRESS

1ST SESSION

S. RES. 462

Designating January 2020 as ‘‘National One Health Awareness Month’’ to promote awareness of organizations focused on public health, animal health, and environmental health collaboration throughout the United States and to recognize the critical contributions of those organizations to the future of the United States.

IN THE SENATE OF THE UNITED STATES

DECEMBER 19, 2019

Mrs. FEINSTEIN (for herself, Ms. MCSALLY, Ms. SMITH, Mr. BROWN, Mr. KING, Mr. CASEY, and Mr. PETERS) submitted the following resolution; which was considered and agreed to

Senate Resolution 462

Resolved, That the Senate designates January 2020 as ‘‘National One Health Awareness Month’’ to—

(1) promote awareness of organizations that focus on One Health efforts to improve the quality of life for people and animals;

(2) recognize the efforts made by such organizations in using a One Health approach to prevent epidemics; and

(3) recognize the importance of using the One Health approach to simultaneously protect the health of people, animals, plants, and the environment in the United States.

Tissue Chip and Organ-on-Chip for Drug Screening Benefits Human Medicine and Veterinary Medicine

- **Drug discovery** – preclinical modeling that is ultimately animal-free drug discovery (3Rs: Replacement, Reduction, Refinement)
- **Accurate models of structure and function of human and animal organs** – enables the prediction of whether, or not a candidate drug, vaccine or biologic is safe (*e.g.* 30% medications fail in human clinical trials due to toxicities that had not been shown by animal testing)
- **Expediency** - the process is faster and more cost-effective than traditional methods
- **Orphan diseases / Minor Species** – encourages studies and drug development opportunities that otherwise might not be pursued
- **Personalized medicine** – testing drugs on a patient's own Organ-on-Chip
- **Health care benefit to society** – efficiency, cost-savings, fewer drug failures, positive response to the 3Rs (replacement/reduction/refinement) regarding the use of animals in studies

Tissue Chip and Organ-on-Chip beyond the Pharmaceutical Industry

- **Food industry** – testing for allergenic components in food ingredients
- **Cosmetic industry** – testing for safety of products on skin or in eyes
- **Chemical industry** – testing for toxicity and impact on the environment
- **Defense industry** - threat assessment for biological or chemical weapons
- **Environmental Health** – testing for specific air (*e.g.* smoke, particulate matter) and water pollutants (*e.g.* toxic algal blooms) that lead to adverse health impacts in humans and animals and ecosystems.

Challenges Facing Adoption of Microphysiological Systems

Allwardt, V. *et.al*. Bioengineering 2020, 7, 112; doi:10.3390/bioengineering7030112

- **Scaling considerations** (physiological and metabolic)
- **Device development** (material selection, surface modifications)
- **Cellularization** (cell selection, cell sourcing, culture media)
- **Perfusion and Automation** (analytical readouts, closed loop control, connections, perfusion type and rates)
- **Validation** (quality, study design, response assessment)
- **Translation** (regulation, standardization, ease of use)

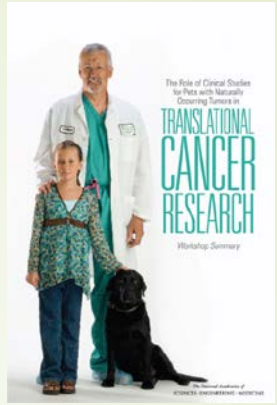
- **ADOPTION** 

Canine tumors share similarities with human cancers in histologic appearance, tumor genetics, biologic behavior, molecular targets, therapeutic response, heterogeneity, acquired resistance, recurrence, and metastasis.

Dr. Rodney Page, Director, Flint Animal Cancer Center
Colorado State University & NCI-COTC member;
partnership with the IOM Workshop 2015.

The Role of Clinical Studies for Pets with Naturally Occurring Tumors in Translational Cancer Research

- to examine the rationale and potential for an integrated comparative clinical trial approach to cancer drug development
- https://www.nap.edu/catalog/21830/the-role-of-clinical-studies-for-pets-with-naturally-occurring-tumors-in-translational-cancer-research



Human-femur osteosarcoma

The gene expression profiles for canine and human osteosarcoma are indistinguishable, suggesting that findings from clinical trials for dogs with that type of cancer would be informative for human patients with osteosarcoma.

Canine-radius & ulnar osteosarcoma

Scottish Terriers are 19 more times more likely to develop bladder cancer (Transitional Cell Carcinoma - BRAF gene mutation) than the average dog breed, accounts for 2% of all canine tumors and can affect up to 20,000 pets each year; this rate is similar to that seen in humans.

NCI Funded Canine Supplements

"The answer to cancer may be walking beside us…"

17 applications were received.

8 funded: scored in the Exceptional and Outstanding range. https://www.youtube.com/watch?v=02bYBJc_yK0 2 min

The 8 applications covered studies in all 6 canine tumors. https://www.youtube.com/watch?v=Raif_9STMYM 26 min

Institution(s)	Project Leader	Canine Cancer(s)	Title or Aims
Baylor College of Medicine/U. Florida Vet Med College/ Texas A&M/Tech U. Denmark	Jonathan Levitt, PhD/ Alan Herron, DVM	Bladder, Mammary, Melanoma	Mutational load and predicted neoantigens in canine tumors and characterization of immune infiltrate and the tumor microenvironment
U. Colorado/Colorado State U. Vet School	Jill Slansky, PhD/ Steven Dow, DVM, PhD	B-Cell Lymphoma	Immune profiling and neoantigen discovery in canine B cell lymphoma
DFCI-HCC/Tufts University Vet Med School	Katherine Janeway, MD/Cheryl London, DVM	Osteosarcoma	A multi-institutional approach to interrogate and improve immunotherapy outcomes in osteosarcoma
Purdue University/Duke University	Deborah Knapp, DVM/ H. Kim Lyerly, MD	Bladder	Advancing immunology in dogs with naturally-occurring invasive bladder cancer: a relevant model to improve immunotherapy across molecular cancer subtypes in humans
Roswell Park Cancer Inst. /Cornell U. Vet Med	Richard Koya, MD, PhD/Kristy Richards, PhD, MD	B-Cell Lymphoma	Immunogenic mutational load analysis for adoptive T cell therapy in canine B cell lymphoma
UC Davis/UC Davis School of Vet Med	Arta Monjazeb, MD, PhD	Glioma, Melanoma, Osteosarcoma	Evaluation of the tumor mutational landscape/neoantigens and immunophenotyping the tumor microenvironment in canine cancers
Ohio State U/OSU Vet Med School/TGEN	Peter Shields, MD/Jeffrey Trent, PhD	Melanoma, Osteosarcoma	Immunogenomic profiling of canine melanoma and osteosarcoma
MD Anderson CC/Texas A&M	Amy Heimberger, MD/ Jonathan Levine, DVM	Glioma	Genomic and immunological canine glioma characterization

https://deainfo.nci.nih.gov/advisory/ctac/1116/Att%2012.pdf Courtesy of Dr. Toby Hecht, NCI 11-02-2016

Embracing a One Health approach will help in the advancement and adoption of the various MPS technologies.

- Brings a multidisciplinary group of scientists together for open exchange of ideas, information, and expertise regarding MPS technology.
- Creates an open and coequal relationship between each profession that leads to better collaboration and teamwork.
- Addresses the many societal concerns regarding the use of conventional animal models for research and drug testing.
- Breaks down barriers in the translational biology process through the encouragement of collaborative innovation which in turn leads to delivery of effective treatments for the patient (human or animal).

Embracing a One Health approach will help in the advancement and adoption of the various MPS technologies.

- Lowers cost of drug development and time to approval by bridging the gap between preclinical testing and clinical trials courtesy of better predictive models and safety profiles.
- Stimulates discussion and awareness of the benefits of MPS amongst academia, industry, government, regulators, clinicians (physicians and veterinarians), health associations, environmental associations, and the general public.
- Utilizes social science to enhance communication and build trust in science within the public sector.
- Considers/realizes how diverse spheres of interest could collaborate to achieve policy outcomes (national/international).

Engaging in a Multidisciplinary One Health Approach

- **You** can be the agent of change…. first, seek to understand, then reach out to other disciplines to "bring the needed expertise to the table" in a collaborative effort to address the needs more efficiently, and often with an innovative approach not previously considered.

- Engage policy/law makers from your local community, state, and federal levels to embrace a One Health collaborative, multidisciplinary approach to issues of mutual concern. Tell the "story" and provide the examples.

- Work with granting agencies to develop cross disciplinary funding proposals that encourages collaboration and embraces these innovative technologies.

- Help facilitate introductions electronically, or by phone, or by in-person meetings… build relationships… engage in direct conversations… that lead to action items embracing a **Multidisciplinary One Health approach.**


Thank you!