

The brewing storm

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Summary

An eclectic collection of papers by physicians, veterinarians and other allied health medical scientists on the 'One Medicine – One Health' concept has been assembled in this monograph. The contributions include thirteen individual 'One Health' papers by fifty-three participants from twelve countries. The authors joined to confront various global health threats. In addition to the participating countries, individuals from twenty-six other nations have united as supporters of the 'One Health initiative'. Biomedical research, scientific knowledge, environmental health, public health, individual health and clinical health care will all be enhanced by implementing the 'One Medicine – One Health' concept which promotes co-equal, cross-disciplinary communication and collaboration. The scientific coalition that evolves through this collaborative effort will significantly enhance human and animal health for future generations.

Keywords

Biomedical research, Clinical care, Health, Health care, Knowledge, One Health, One Medicine, Physician, Public health, Science, Veterinarian.

Menti in fermento

Riassunto

La presente monografia è una raccolta di manoscritti di medici, veterinari e altri ricercatori interessati al concetto di "Una sola salute – Una sola medicina". Vengono proposti tredici contributi individuali realizzati da cinquantatré partecipanti di dodici paesi, che hanno unito le proprie conoscenze per affrontare svariate minacce alla salute globale. Ai paesi partecipanti si sono aggiunti altre ventisei nazioni per sostenere l'iniziativa "Una sola salute". La realizzazione del progetto "Una sola salute – Una sola medicina", che promuove la comunicazione e la collaborazione interdisciplinare a pari livello, concorrerà ad estendere le vaste conoscenze derivanti dalla ricerca biomedica e i progressi reali registrati sul fronte della salute ambientale, pubblica, individuale e clinico-assistenziale. La coalizione scientifica risultante da questo sforzo collaborativo porterà in futuro un miglioramento significativo della salute umana e animale.

Parole chiave

Assistenza clinica, Assistenza sanitaria, Conoscenze, Medico, Ricerca biomedica, Salute, Salute pubblica, Scienza, Una sola medicina, Una sola salute, Veterinario.

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Introduction

In 1946, Winston Churchill began writing his six volume history of World War II, beginning with *The Gathering Storm* (5). Horrible events related to this war began to emerge in the 1930s. By the late 20th century, the world knew most of the gruesome details. Towards the end of the last century, the concepts of 'emerging infections' and 'the coming plague' were put forward to describe a rising tide of threats from infectious diseases, many of which were diseases emanating from animals and transmissible to humans (zoonoses). This 'brewing storm' that developed from zoonotic disease threats, such as human immunodeficiency virus (HIV) and avian influenza, has the potential to inflict horrific consequences on millions of people. While, historically, efforts to understand and control zoonotic diseases began as early as the 18th century, strategies to advance scientific breakthroughs in an integrative fashion did not begin again until the early 21st century (10, 11, 12).

The 'One Medicine – One Health' concept recognises a unity of purpose, irrespective of anachronistic turf barriers and the impedances they impose. Co-equal by necessity, close collaboration and communication between the various disciplines of human and veterinary medicine, along with associated allied health scientists, represents a powerful facilitating strategy for today's and tomorrow's world. Among others, physicians, veterinarians, environmental scientists, public health professionals, wildlife experts and plant pathologists working together will offer extraordinary synergistic advantages whether the health challenges result from emerging infectious diseases, a myriad of systemic illnesses, antibiotic resistance, globalisation, natural disasters or climate change.

A strategic, comprehensive, interdisciplinary scientific approach will open new vistas for accelerated biomedical research discoveries, enhanced acquisition of essential basic biological/scientific knowledge and advanced public health effectiveness. Implementation will result in improved clinical care and the

management of perplexing disease problems, such as infectious disease ontogenesis, neoplasms, cardiovascular diseases, hypertension, endocrine disorders, obesity, orthopaedic problems, mental health (via the human-animal bond phenomenon) (13), metabolic diseases, biomechanical devices, genetics and others. Examples of current and previous collaborative benefits are included in this monograph.

Concept importance and expectations

Why is 'One Medicine – One Health' important and what are its expectations? This monograph proposes this introduction, twelve essays from a cross-section of scientific disciplines that will help elucidate these questions and answers and the eight '*One Health' in Action* series. A total of 53 participants are advocate representatives from Argentina, Australia, Bosnia and Herzegovina, Canada, Cote d'Ivoire, Croatia, France, Israel, Kyrgyzstan, Switzerland, the United Kingdom and the United States, as detailed below.

'One Medicine – One Health' interview with Ronald M. Davis MD, President of the American Medical Association, 14 May 2008 (L.H. Kahn)

This interview summarises the early 21st century background behind the unique and historic 'One Medicine – One Health' liaison between the American Medical Association (AMA) and the American Veterinary Medical Association (AVMA) as viewed by the past President of the AMA. This collaboration culminated in a groundbreaking 'One Health' resolution adopted by the AMA in June 2007. This joint intellectual pursuit evolved into the formation of an AVMA taskforce designed to develop strategies and tactics for eventual implementation of the concept and institutionalising it into society (see 'An implementation plan' below).

Ronald M. Davis passed away on 6 November 2008.

Human and animal sentinels for shared health risks

(P. Rabinowitz, M. Scotch & L. Conti)

This treatise cogently shows the high value of utilising and tracking sentinel health events (both animal and human) for more rapid detection and management of environmental and infectious disease risks to humans and animals. Examples cited include mercury and lead poisoning, anthrax and West Nile virus. Moreover, it points out the folly of past and present professional segregation stating: ‘The “us vs them” paradigm also leads to an under-appreciation of the fact that a better understanding and the more effective control of disease in the animal population (often through environmental management) may be required in order to truly reduce human risk’.

‘One World – One Health’ and the global challenge of epidemic diseases of viral aetiology

(E.P.J. Gibbs & T.C. Anderson)

This paper provides a virtual brief updated blueprint of the ‘why’s and wherefore’s’ for the critical need for rapid implementation of ‘One Health’. It complements an outstanding essay by Gibbs (7).

One Health – from science to policy: examples from the Israeli experience

(E. Klement, N. Shpigel, R.D. Balicer, G. Baneth, I. Grotto & N. Davidovitch)

This contribution presents three case studies from Israel. They demonstrate the successful scientific collaboration between physicians, veterinarians and a microbiologist who performed original research investigating Crohn’s disease in humans. Secondly, they present successful collaboration between veterinarians and physicians that led to the development of a post-exposure prophylaxis regime for tick-borne relapsing fever in humans. They conclude by demonstrating the necessity for and benefits from collaboration between veterinarians and physicians from different organisations and across state and political borders performing a joint avian influenza investigation.

Zoonoses and vector-borne diseases in Croatia – a multidisciplinary approach

(A. Markotić, L. Cvetko Krajinović, J. Margaletić, N. Turk, M. Miletić-Medved, L. Žmak, M. Janković, I.-C. Kurolt, S. Šoprek, O. Đaković Rode, Z. Milas, I. Puljiz, D. Ledina, M. Hukić & I. Kuzman)

The authors describe the long and beneficial tradition in collaboration between different experts and professionals (a ‘One Health’ approach) in the research of emerging infectious diseases in Croatia, including physician clinicians in infectious diseases, microbiologists, pathologists, veterinarians and animal scientists, ecologists, forestry experts, wildlife scientists, public health specialists, epidemiologists and laboratory scientists. The authors represent a broad spectrum of scientific disciplines.

Strategies for enhancing Australia’s capacity to respond to emerging infectious diseases

(S.J. Prowse, N. Perkins & H. Field)

This paper outlines Australia’s significant threats from emerging infectious diseases that involve wildlife vectors and the wildlife disease sources. The outbreak of Hendra virus in 2008 is highlighted. A ‘One Health’ strategy for improved management and essential sharing of biosecurity information, together with the development of an ideal laboratory infrastructure is described. ‘One Health’ collaborative research ventures are stressed with the establishment of the Australian Biosecurity Cooperative Research Centre for Emerging Infectious Disease; its aim has been and continues to be the improvement of Australia’s capacity to respond to emerging infectious disease outbreaks.

Healthy plants: necessary for a balanced ‘One Health’ concept

(J. Fletcher, D. Franz & J.E. LeClerc)

Recognising the basic fact that all humans and animals must eat to survive, it follows that since our food sources are all derived directly or indirectly from plants we must protect plant life on this earth. The authors offer proof that

the essence of 'One Health' requires access to healthy plants to maintain healthy humans and healthy animals. Thus, plant pathogens play a direct and indirect role in the ecological existence of human and animal species. We need human doctors (physicians) and animal doctors (veterinarians), as well as plant doctors (plant pathologists) – to work together for the common good of all species.

'One Toxicology', 'Ecosystem Health' and 'One Health'

(V. Beasley)

Quoting the author, 'This paper endeavours to illustrate how "Ecosystem Health", "One Health" and "One Toxicology" can better support one another. It illustrates how "One Toxicology" has existed and how it should evolve to do a far better job of controlling both direct and indirect toxicant-induced injury to human beings, other animals, and other components of biodiversity'. It does this in a comprehensive, scientific fashion by focusing 'on critically important chemically-mediated health problems and how they too are shared among humans, domestic animals and wildlife'.

How companion animals contribute to the fight against cancer in humans

(D. Thamm & S. Dow)

The authors describe similarities in tumour biology between humans and companion animals. It proposes that appropriately designed trials for novel therapeutics in companion animals may help evaluate and predict more accurately the degree of efficacy and toxicity in humans. The goals of predicting prolongation of life and survival of humans may also be achieved for animals. The comparative biology between companion animals, such as dogs, appears to be more similar to humans than does a comparison of similar data between rodents and humans.

Towards a 'One Health' research and application tool box

(J. Zinsstag, E. Schelling, B. Bonfoh, A.R. Fooks, J. Kasymbekov, D. Waltner-Toews & M. Tanner)

'What is required now is a radical paradigm shift in our approach to global public health with practical approaches and hands-on examples to facilitate its application and accelerating necessary leverage of "One Health"' The authors propose practical methodology for advancing mutually agreed upon cooperation between human and animal health professionals by integrating disease surveillance, joint animal/human epidemiological studies and health services development. It places special emphasis on developing countries.

Tuberculosis: a re-emerging disease in animals and humans

(C.O. Thoen, P.A. LoBue, D.A. Enarson, J.B. Kaneene & I.N. de Kantor)

This article is a testament to the historic period when the renowned scientist Robert Koch did not accept the idea of bovine tuberculosis as a significant disease entity by its transmission to humans via milk and milk products. The great 'One Health' veterinarian-physician John McFadaye, respectfully and successfully challenged Koch's erroneous conclusion. This piece elaborates in detail how tuberculosis continues to be an important disease of humans and animals worldwide. *Mycobacterium bovis* remains a small but significant disease entity that needs interdisciplinary synergistic scientific evaluation ('One Health' approach) to elucidate its management and future eradication.

'One Medicine – One Health' at the School of Veterinary Medicine of the University of Pennsylvania – the first 125 years

(J. Hendricks, C.D. Newton & A. Rubenstein)

This treatise explains how, in 1807, Benjamin Rush, a signatory to the Declaration of Independence, Philadelphia's most eminent physician and a member of the venerable Philadelphia Society for Promoting

Agriculture, in an introductory lecture to a medical school class, recognised and proposed the establishment in the University of a Veterinary Chair. Rush's lecture was entitled *An introductory lecture to a course of lectures, upon the institutes and practice of medicine... upon the duty and advantages of studying the diseases of domestic animals, and the remedies proper to remove them*. It further elaborates upon how, since its founding in 1884, the School of Veterinary Medicine integrated biomedical research and worked collaboratively with the school of medicine resulting in 'contributions to basic and clinical research by exemplifying One Medicine'. This is operational today and continues to expand.

'One Health in Action' Series: Nos 1-8 (L.H. Kahn, B. Kaplan & T.P. Monath)

This series of short articles was published in 2007 and distributed to the Kahn-Kaplan-Monath 'One Health' email distribution list. The articles are further examples of historical achievements obtained across numerous scientific disciplines, including human and veterinary medicine. Each article was written and developed with assistance from the Kahn-Kaplan-Monath 'One Health' team.

Global pandemic threat(s) linked to 'One Health' strategies

Approximately 75 years after the 1918-1919 influenza pandemic that killed 50 to 100 million people, Ferrara *et al.* (6) described what is now considered the basic pathogenesis of death from graft versus host disease (GVHD), i.e. the 'cytokine storm'. This cascade of 'out of control' immune system events precipitate death for patients suffering from avian influenza type A, subtype H5N1 and other infectious and non-infectious disease processes, including smallpox, yellow fever, dengue haemorrhagic fever, sepsis, adult respiratory distress syndrome (ARDS), systemic inflammatory response syndrome (SIRS) and GVHD (3, 8, 15, 16, 18).

Human patients infected with avian influenza A, subtype H5N1 and also probably the victims of the 1918-1919 avian influenza A,

subtype H1N1 pandemic ('Spanish flu') had vigorous, healthy immune systems. This subgroup of patients developed an exaggerated, uncontrolled reaction that stimulated T-cells and macrophages to produce the excessive release of over 150 mediators (cytokines, oxygen free radicals and coagulation factors) while fighting these pathogens. Essentially, flu patients die from ARDS with its resulting cytokine storm. Both anti-inflammatory (e.g. interleukin 10, and interleukin 1 receptor antagonist) and pro-inflammatory (e.g. tumor necrosis factor-alpha, interleukin 1 and interleukin-6 receptor antagonist) cytokines flood body tissues and organs – in the case of avian influenza, the lungs rapidly accumulate fluids and immune cells (e.g. infected macrophages) that eventually block airways. Adding insult to injury, the cytokines activate the body's T-cells and macrophages resulting in a feedback reaction with greater production of cytokines. This vicious cycle magnifies the likelihood of death from pulmonary oedema with fluids and macrophages accumulating in the lungs causing eventual airway blockage with multi-organ failure. A similar condition affects both humans and animals and laboratory animal models of cytokine storm are playing an essential role in dissecting the pathophysiology and intervention strategies.

The elucidation of the cytokine storm mechanism has involved input from a multidisciplinary mix of health scientists which is evidence of 'One Medicine – One Health' in action. Derivation of further knowledge regarding the pathogenesis and pathophysiology of this condition, together with efficacious prevention and therapeutic modalities will be expedited by the One Medicine – One Health strategy. Expanded attraction and utilisation of available veterinary medical and other basic science professional expertise is essential, including a greater inclusion of certified laboratory animal veterinarians who specialise in the field of laboratory animal medicine. Indeed, the pathogenesis and treatment of yellow fever was derived from animal model studies with macaques and hamsters.

Investigations on the epidemiology of avian influenza H5N1 and other highly pathogenic avian influenza type A viruses (including other potential pandemic threats from various pathogenic agents) are ongoing. The high risk of influenza type A viruses undergoing 'antigenic shift' resulting in greater transmissibility, lethality, immunological novelty is real and well documented historically (3).

Avian influenza prevention and control involves appropriate use of vaccines and antiviral agents to the extent available (to date and for the foreseeable future, the supply of both are limited). Other acceptable efforts include isolation and quarantine, exposure avoidance/social distancing, the simple highly valued practice of appropriate and frequent hand washing, use of masks by the general public and encouraging conventional respiratory etiquette by covering the mouth/nose when coughing/sneezing. In addition, development of an armamentarium of various specific therapeutic drugs and as yet undiscovered immunological and genetic therapies are needed.

In 2005, the global infectious disease public health infrastructure was challenged to prepare more vigorously for other pandemics (17). Recognising the global implications from ten previous pandemics of influenza A in the past 300 years, the risk of avian influenza H5N1 evolving in Asia was singled out. It was speculated upon as to whether or not this could rival the 1918 disaster or whether it would be a 'more muted' version, like the pandemics of 1957 and 1968. No one knew then and no one knows now.

No one knew the future of an emerging H5N1 in December 1997 (although experts predicted imminent scenarios with unabashed near certainty) when the United States Centers for Disease Control and Prevention (CDC) said *One of the most important aspects of the avian influenza investigation is to determine the source of the infection and mode of transmission* (9). The conundrum (of the course that H5N1 will take) continues. Paradoxically, while an influenza pandemic may or may not occur from the most likely candidate, avian influenza A, subtype

H5N1, it will most certainly happen in the future with some influenza subtype(s). The high probability is that the subtype(s) will be linked to animals. This fact demands the insight offered by veterinary medical basic science in conjunction with that of human medical science through One Medicine – One Health.

In November 2005, the second President's Award for Leadership in Health was presented at The University of Texas Health Science Center in Houston, Texas, to Klaus Stöhr, DVM, PhD, coordinator of the World Health Organization's Global Influenza Program. In his acceptance speech, Stöhr said *We believe that another influenza pandemic will occur. The severity is uncertain. The timing is unpredictable. But it will cause a global health emergency. We do have a window of opportunity if we act now to reduce death and disease, as well as social and economic disruption.* Stöhr was credited 'for awakening the world to the risk of avian influenza' (19). The economic disruption referred to by Stöhr reflects the tremendous financial losses expected from a potentially devastated poultry industry worldwide.

Significant and dangerous deficiencies in response capabilities exist to date even though the White House issued the National Strategy for Pandemic Influenza on 1 November 2005 that resulted in federal planning and response activities (20).

According to a Task Force for Mass Critical Care Summit Meeting held in January 2007 and published in 2008, the United States and Canada do not have sufficient surge capacity for critically ill patients or injured victims, e.g. in the event of an influenza pandemic or a successful terrorist detonation of a nuclear 'dirty bomb'. While reporting that 'great strides' had been made in preparation for disaster response, the task force generally conceded that there was inadequate availability of critical care staff, medical supplies/equipment and intensive care unit (ICU) space (4). Health care logistics are patently insufficient.

One of many prerequisites needed to cope with complications from a global influenza

pandemic would be positive pressure ventilators. The numbers needed have been predicted to be far in excess of the tens of thousands available in all the nations of the world that would suffer from widespread pulmonary disease manifestations.

It is important to note that the United States/Canadian task force members were primarily physicians, nurses, a pharmacist, a lawyer, an emergency medical technician professional – but no veterinarian. Considering the thousands of potentially available widely distributed and well equipped private practice small animal clinics and hospitals (plus veterinary medical institutions of higher learning) that might be used for emergency human services, not to mention the considerable medical expertise that doctors of veterinary medicine could provide to humans under these dire circumstances, it appears that a major vital health care resource was never considered.

In addition, in the United States alone, one-third of all hospitals are operating at a deficit. There are severe manpower shortages, especially in regard to nursing. About half of the emergency departments operate at capacity or over capacity. The number of intensive care unit beds is decreasing. Approximately 80% of essential supplies, including drugs, come from offshore suppliers that might not function during a pandemic (17).

A 'Manhattan-type' project required?

A repeat of a similar-type 1918 outbreak in the future could result in 1.7 million deaths in the United States and 180 to 360 million deaths globally (17). To stem the tide of expected disaster(s) from pandemics of the future, it is essential that all elements of the One Medicine – One Health concept be employed with speed and efficiency.

Avenues being pursued include the following:

- immunogenicity of influenza vaccines
- basic research on the ecology and biology of influenza viruses

- the epidemiological role of various animals and birds
- studies on early therapeutic interventions and risk assessment
- continued development of cell-culture technology for vaccine production
- enhancing worldwide industrial production capacity to ensure sufficient vaccine quantities
- detailed 12-24 month operational blueprints for a consistent public health approach
- health care delivery systems
- proactive public communication networks.

All things considered, the world is not adequately prepared (3) and the status quo seems to continue.

An implementation plan

A blueprint for implementation was published in the July 2008 issue of the *Journal of the American Veterinary Medical Association* (1). The guidelines developed by the AVMA 'One Health' Task Force have been identified but will need continuous nurturing for implementation.

Recommendations of the AVMA One Health Task Force 2008 are best explained and understood by viewing the final report (1) and executive summary (14). The quotes listed below highlight the task force deliberations.

'The purpose of the task force was to study the feasibility of an initiative that would facilitate collaboration and cooperation among health science professions, academic institutions, governmental agencies, and industries to help with the assessment, treatment, and prevention of cross-species disease transmission and mutually prevalent, but non-transmitted, human and animal diseases and medical conditions'.

'The convergence of people, animals, and our environment has created a new dynamic – one in which the health of each group is inextricably interconnected. The challenges associated with this dynamic are demanding, profound, and unprecedented. While the demand for animal-based protein is expected to increase by 50% by 2020, animal populations

are under heightened pressure to survive, and further loss of biodiversity is highly probable'.

'Compounding that is the fact that, of the 1461 diseases now recognized in humans, approximately 60% are due to multi-host pathogens characterized by their movement across species lines. And, over the last three decades, approximately 75% of new emerging human infectious diseases are defined as zoonotic. Our increasing interdependence with animals and their products may well be the single most critical risk factor to our own health and well-being with regard to infectious diseases'.

A One Health (United States) Steering Committee has evolved from the AVMA task force deliberations with several health oriented organisation representatives developing strategies for implementing One Health through the formation of a 'National One Health Commission' by late 2009. It is anticipated that the Commission will be representative of a broad spectrum of co-equal, all inclusive, interdisciplinary One Health stakeholders.

In addition, a One Health Initiative website has been operational since 1 October 2008 (2). This website is a repository for all relevant One Health news, publications and forthcoming events. At the time of writing, the website is being transferred from the Kahn-Kaplan-Monath One Health team to the auspices of the One Health (United States) Steering Committee.

Conclusions

The implementation of the One Medicine – One Health concept in the 21st century is critical to addressing life protecting/life saving measures against infectious zoonotic disease concerns (public health) including pandemics such as avian influenza, biomedical research endeavours regarding basic science discoveries and biosecurity, individual clinical health and health care relative to such conditions as cancer, diabetes, obesity, cardiovascular disease, biomechanical devices, such as orthopaedic joint replacements and vaccine development. These will all involve

collaborative efforts between schools/colleges of medicine, veterinary medicine and public health, along with government entities and private industry. The general public must be informed to enable their participation.

One Medicine – One Health extends across a plethora of health care concerns that afflict human and animal species. These are not mutually exclusive and include many different diseases and conditions. Practical scientific and political solutions to this challenge are crucial.

Many physicians, veterinarians, scientists and others within the health care scientific community have enthusiastically endorsed the One Medicine – One Health concept in addition to major United States and international organisations, as follows:

- American Association of Veterinary Laboratory Diagnosticians
- American Medical Association
- American Phytopathological Society
- American Society for Microbiology
- American Society of Tropical Medicine and Hygiene
- American Veterinary Medical Association
- Association of Academic Health Centers
- Association of American Medical Colleges
- Association of American Veterinary Medical Colleges
- Association of Schools of Public Health
- Corporation Red SPVet, Bogota, Colombia
- Council of State and Territorial Epidemiologists
- Croatian Society for Infectious Diseases
- Delta Society
- Immuno Valley Consortium in The Netherlands
- Indian Veterinary Public Health Association
- Italian Society of Preventive Medicine
- National Association of State Public Health Veterinarians
- National Environmental Health Association
- Nigerian Veterinary Medical Association
- Society for Tropical Veterinary Medicine
- State Environmental Health Directors
- The Global Alliance for Rabies Control
- The Institute for Preventive Veterinary Medicine and Food Safety, Lazio and Tuscany Regions, Italy

- Veterinarians without Borders/ Vétérinaires sans Frontières – Canada
- World Association of Veterinary Laboratory Diagnosticians.

The authors and co-authors of the articles in this issue advocate the earliest possible implementation of this concept. If implemented on a regional and global scale, 'One Medicine – One Health' would help to protect and save untold millions of lives.

The goal of this monograph is to demonstrate a clear emerging pattern of scientific advancement as told by an interdisciplinary broad spectrum group of health professionals. In addition, these papers are expected to comprehensively expand upon collaborative strategies similar to those described in the 'One Health' in Action series (eight stories) published

at the end of this treatise thereby offering a valuable ticket to fast-track action(s) for future human and animal health and health care.

Everyone must understand that this strategic concept is a tool for leapfrogging the status quo of nearly all health and health care endeavours.

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