Preventing the Next Pandemic: The Power of a Global Viral Surveillance Network

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Introduction

The ongoing COVID-19 pandemic has laid bare our collective weaknesses in being able to

effectively respond to the emergence of a highly contagious and lethal microbial threat.

Despite extraordinary advances over the past century in science and unprecedented

improvement in global health standards, as evidenced by the COVID-19 pandemic, we still live

in a world where the threat of an infectious agent can emerge anytime and any place without

warning and spread rapidly to every community and every household without regard to

national borders.

Importantly, COVID-19 is not the first pandemic of this century and is unlikely to be the last.

Over the last 20 years a number of high impact epidemics and pandemics have emerged or

reemerged. In this short period of time, we have had emergence of three new coronaviruses

(CoV), namely Severe Acute Respiratory Syndrome (SARS) in 2003; Middle East Respiratory

Syndrome (MERS) in 2012; and the ongoing COVID-19 pandemic caused by SARS-CoV-2, a

number of highly pathogenic influenza A viruses (e.g. H5N1 in 2003; H7N9 in 2013; and the

H1N1 pandemic of 2009), the Zika virus as a global health emergency in 2016, and the

continuing rise and spread of Ebola in West and Central Africa since 2013. All these epidemic

and pandemic viruses have jumped from wild animals, either directly into humans or indirectly

through domestic animals. Some of these viruses (e.g. avian influenza A, and MERS CoV), having

made the inter-species jump, tend to persist and evolve in animals systems presenting a

continuous danger to the global community.

Over the course of the remainder of this century, the likely frequency of epidemics and

pandemics will continue to increase, driven to a large extent by demographic trends, including

urbanization, and environmental degradation, climate change, persistent social and economic

inequalities, and globalized trade and travel (1,2,3)

While attempts at upgrading of the health security apparatus over the last decade has been

welcomed (4, 5), COVID-19 underscores that these processes and institutional arrangements

are not sufficient to responding to events such as those caused by SARS-COV-2. For example,

compliance with the International Health Regulations (4), that provide a normative framework

for surveillance, preparedness, notification and international support and coordination has also

been shown to be inadequate. The experience of the COVID-19 pandemic, yet again

underscores that new efforts need to be made to craft global strategies, policies and regulatory

frameworks that more directly address the multi-sectoral aspects of disease emergence in

order to improve our collective capacities to prevent, as well as rapidly detect and respond to

threats. Key is building a global surveillance system spanning wildlife, livestock and human

populations (6, 7, 8) that is able through the collection of detailed meta-data to further refine

the existing geographic "hot spots" (9, 10) where the risk of spill-over into human and livestock

populations is greatest, and to use this detailed understanding of "risk" to target surveillance to

those places for the early detection of spillover events in humans and livestock at a local level

(11) before they cause any serious outbreaks. Further, understanding where the threat of

spillover is greatest allows for the targeting of pre-emptive measures to disrupt spillovers.

Current efforts to address epidemics and pandemics after they have emerged, through the

traditional approaches such as quarantine, and drug and vaccine development are woefully

inadequate to contain a raging pandemic such as COVID-19.

Jones et al (9) created the first hot-spot maps based on comprehensive literature review of all

emerging and re-emerging infectious diseases in the last 60 years. This map was recently

updated (10). It shows that the tropical regions of Africa, Asia and South America are still

represented as high-risk ecological locations for majority of the zoonotic pathogens.

Creating a Global Viral Surveillance Atlas

In 2018 two papers were published (12,13) that proposed the Global Virome Project (GVP) with an ambitious global-scale 'big science' plan to develop an atlas of the majority of the planet's naturally-occurring zoonotic viral threats over a 10 year time frame, transforming the world of emerging diseases into a data-rich field. The GVP was established as a legal non-governmental entity in early 2020 with a planned launch of field operations in 2022. The expectation is that the GVP will transform our public health culture from one that responds to the latest disease outbreak, to one that is better able to detect pathogen spillover events early in human and livestock populations and quickly to pre-empt their spread, and support the scientific community far more effectively in generating biomedical countermeasures to respond to future outbreaks should they occur. This power to "prevent, detect, and respond" will protect against not only human infections but similarly protect domesticated animal populations which share our vulnerability to emerging viral threats, and by extension protect against the devastating effects of viral threats such as the recent emergence of the zoonotic H5N1 highly pathogenic avian influenza, and recent incursion and spread of African Swine fever in Asia causing serious concerns of food security and livelihoods of poor farming communities of the world (14,15,16,17).

The Need for a Global Viral Surveillance Network

The GVP will likely make substantive contributions during its planned 10 year life to enhancing the multi-sectoral capacities across countries for the collection and analysis of viral samples from the across wildlife (and under certain circumstance livestock and humans) and provide a baseline against which to monitor their evolution over time. What the GVP will not do is sustain

the kind of long-term surveillance that will be needed to monitor the critical biological and ecological changes among the "watch list" that could signal elevated risk to human and animal health.

While information and knowledge about hundreds of thousand of yet undiscovered viruses is essential, it is only a piece of a complex multifactorial reality. What is needed is a comprehensive viral surveillance system that will build on the country-level capacities developed by GVP and other on going initiatives such as IHR and GHSA (4, 5), and use the "watch list" to track genetic and ecologic evolution over time. This system should also look at the human side of the equation. Among the millions of viruses present in nature, only very few have the capacity to infect humans and even fewer have the capacity to spread. However, even if the likelihood of an effective spill over is very low, the impact can be disastrous and therefore specific investment in systems that can prevent such events is justified. Many of the epidemics with pandemic potential were discovered early through an unusual cluster of severe cases or deaths in humans. This is a weak signal, one that is often missed by the classical surveillance systems. In the future, to improve our capacity to detect early viruses with pandemic potential, it also critical that we strengthen the global capacity to pick-up unusual clusters of severe morbidities and mortalities for further investigation and response. This can be achieved by dual strategy of strengthening the existing health care systems and improving the surveillance and diagnostic capacities to detect above-mentioned viral watch list in hot spot regions. Such a multi-sectoral system will contribute to an enhanced capacity to forecast future threats and enable early intervention before they pose a threat.

Examples of Viral Surveillance Exist but Need to Be Broadened

There is precedent for establishing a global scope for the longitudinal monitoring of a select

pathogen. WHO's Global Influenza Surveillance and Response System (GISRS) for more than

half a century has been tasked with monitoring the evolution of influenza viruses for

development of the annual influenza vaccine, as well as serving as a global alert mechanism for

the emergence of influenza viruses with pandemic potential (18). The GISRS has grown into a

global partnership of 143 National Influenza Centers (NICs), 6 highly specialized Collaborating

Centres for Reference and Research on Influenza and 4 national licensing agencies or Essential

Regulatory Laboratories and 13 H5 Reference Laboratories. The NICs collect, identify and ana-

lyze influenza strains isolated from clinical specimens and forward representative or unusual

virus isolates to a WHO Collaborating Centres for detailed characterization. Although

individual-level epidemiological or clinical data are not collected, NICs provide weekly reports

to WHO of geographically-based influenza like activity using FluNet, a web-based electronic

interactive data reporting, query and mapping system (19).   The network has provided

information on circulating seasonal influenza viruses, as well as supporting response to the

influenza pandemics in 1957, 1968, and 2009, and to threats caused by animal influenza viruses

and by zoonotic transmission of coronaviruses.

Before the H1N1 2009 pandemic, WHO developed FluID, which is a global platform for data

sharing that links regional influenza epidemiological data into a single global database

(https://www.who.int/influenza/surveillance_monitoring/fluid/en/) to monitor the influenza

disease. It complements FLuNet by providing critical information of the impact of the viruses on

human health.

The 2009 H1N1 pandemic showed that only monitoring for viruses does not provide adequate

information for decision makers to respond to and mitigate the health impacts of an epidemic.

Information on the severity of the disease and the real time impact on populations' health are

essential. After the 2009 H1N1 pandemic most of the influenza surveillance systems in the

world started to include surveillance for respiratory symptoms with standardized case

definitions for Influenza Like Illnesses (ILI) and Severe Acute Respiratory Influenza (SARI), and

real time modelling into the existing viral surveillance. Similarly, OFFLU, the OIE/FAO Animal

Influenza Surveillance platform, established in 2005 to interface with the existing WHO

influenza network (20) routinely shares as well as promotes the collection, exchange and

characterization of animal influenza viruses, including selection of viruses for seasonal influenza

and deposition of sequence data in genome banks.

GISRS and OFFLU are excellent examples of a robust global surveillance system, however, they

are focused on influenzas. While it is important to maintain these surveillance systems, forging

the alliances essential for sustaining a multi-dimensional data base that encompasses virtually all

zoonotic viral families and spans the wildlife-livestock-human ecosystems will require an order

of magnitude higher level of political and institutional commitments of the key international

stakeholders, in particular WHO, FAO and OIE, and a buy-in from their membership and the

global development partners.

Fortunately, WHO, FAO and OIE, recognizing the need for enhanced multisectoral collaboration for effective strategies for improving national, regional and community level pandemic preparedness and response, have been strengthening their partnerships over the past decade. Through a formal 'tripartite' agreement (21, 22) these organizations have agreed to set up joint action to combat health threats emerging from interactions between humans, animals and the environment.

One example of a formalized monitoring and reporting platform for disease events involving the WHO, FAO and OIE is the Global Early Warning and Response System (GLEWS). Established in 2006, it aims to combine the strengths of three organizations to enhance a public and animal health early warning system intended to reduce incidence and impacts of emerging infectious diseases in animals and humans (23). Partners in GLEWS, which incorporates both animal and public health sectors, share information from all over the world on disease outbreaks in real time, conduct rapid cross-sectoral risk assessments, evaluate control and prevention options, and coordinate their responses.

GLEWS combines and coordinates the alert and response mechanisms of the OIE, FAO, and WHO to assist in prediction, prevention, and control of emerging infectious diseases. This international platform is among the most effective means by which these agencies currently collaborate. The scope of GLEWS, however, is focused on early detection of ongoing outbreaks and does not address monitoring for and detection of emerging pathogens in animals and humans before outbreaks occur, or support the "pre-event" surveillance of viruses in wildlife population enabled by the GVP.

The Time for Building a Sustained, Multi-sectoral Global Viral Surveillance Network is Now

While these surveillance platforms provide important examples of ongoing surveillance operations, nearly all of these are very much event based, or syndromic in nature. Most pathogens that are identified are from outbreaks. Apart from GISRS, all other multi-sectoral collaborations are focused on disease information sharing through their respective networks and country offices. There is no formal system that is in place in any country that routinely conducts active viral surveillance in humans and domestic animals combined with rapid clinical assessment for a list of priority emerging and re-emerging viral diseases. Identifying viral spillover events from wildlife to livestock and humans, well before they manifest in localised outbreaks, is a pre-requisite for pre-empting high consequence epidemics and pandemics. While such an approach under a global coordination mechanism has never been attempted the magnitude of the dual, health and socio-economic impact of current COVID-19 crisis, the benefits of such an approach can be easily justified.

Introduction of a formalized and sustained, longitudinal viral surveillance for detection of spill-over events at the interface of wild and domestic animals and humans of priority viruses in pre-defined hot-spot regions of the world is not without significant challenges. This approach is fundamentally different in scope and scale from syndromic, passive surveillance and require sustainable investment at the interface of multiple sectors. Dealing with high impact emerging and re-emerging infectious diseases is of international public good (24) and hence will require a strong buy-in and financing from national public, animal and environmental sectors, with

support from UN technical agencies (e.g. WHO, FAO and OIE), as well as numerous bilateral

donors, multi-lateral development partners and Foundations. The technical challenges in

designing sampling frames, availability of trained human resource, infrastructural support for

joint public health and animal health collection of biological samples, transportation and

laboratory testing are complex, particularly in the hot-spot regions. In addition, mechanism of

sharing information for rare spillover events that may occur in distant and remote places at

evolving interfaces, and in dynamic livestock and wild animal production systems and their value

chains, driven by a complex set of factors such as climate change, land use and demographic

changes cannot be under-estimated. Challenges of handling large volumes of data,

standardization, establishment of databases, multi-dimensional data analysis, and regulatory

and legislative framework for sharing information pose significant challenges.

Coordination among the United Nations and other international agencies, together with relevant

national and regional partners and financing institutions is needed urgently to discuss and plan

such a global venture and to develop a shared vision leading to a formal agreement on the

principle of the establishment of an active, targeted global, innovative one health surveillance

programme as an essential basis for preventing future pandemics. Ultimately the global

architecture for such a global surveillance network and the associated technical,policy and

regulatory framework will require the cooperation of stakeholders from the U.N system,

multinational organizations, governments and civil society. (21, 22).

The products of GVP will offer a unique opportunity to the global community for the first time in

providing information on the precise geographical location of the new high-risk viruses that are

being detected. New virus discovery will enable generation of multiplex diagnostic platforms

with appropriate pathogen specific molecular primers and probes for rapid and affordable

detection of these viruses through active virological surveillance. In addition, rapidly evolving

next generation or 'deep' DNA sequencing technologies and real time digital pathogen

surveillance allow a generic approach (non-specific method) to virus identification that does not

require *a priori* knowledge on the targeted pathogens but can deliver a species/strain specific

result (25, 26). Combining these technologies with associated bioinformatics tools can greatly

enhance the power of active viral surveillance programme for early spill over events of novel

viruses from wild life to domestic animals and humans.

The time for establishing such a long-term surveillance platform is not, however, at the end of

the GVP's ten-year lifespan. The projected discovery curves under the GVP for new viral threats

will be rapid (12). By year three of the GVP tens of thousands of new viruses are projected to

have been identified and the first "viral watch-lists" will have been generated. Given the time

sensitivity of the "baseline data" there will be an urgent need to begin the immediate

monitoring of this "list".   Current plans for the GVP have the first phase of its launch beginning

in 2022– a two year "incubation period" in a limited number of "start up" countries to test the

ability of the GVP to go to operational scale (both sampling and data management). The full

scale 10 year "steady-state" phase of the GVP will begin in 2024 – with an expected rapid

generation of viral data. The ongoing COVID-19 pandemic, the worst since the influenza

pandemic 100 years ago, has heightened the sensitivity of the global community to devastating

socio-political and economic damage to the planet. This is a significant opportunity to initiate a

high-level dialogue to embark on how to formalize and support a sustainable global surveillance

system for emerging pathogens to avert future epidemics and pandemics that continue to

emerge and re-emerge at increasing frequency from wild animals.

The global community has an opportunity over the next three years to partner with and build on

the knowledge and information that will be generated by the GVP to early detect and prevent

pandemics through longitudinal tracking of high risk viral threats –and contribute to the wider

global One Health efforts to better able to prevent the next pandemic.

Ultimately, multi-pronged approaches are needed to address the challenges of mitigating the

impacts of epidemics and pandemics of new viruses originating from wild animals. These should

include addressing the root causes of spill-overs and spread of new pathogens, reducing risky

practices, improving livestock food systems, enhancing biosecurity along the animal food chains

(27) and in parallel continuing with the development of innovative diagnostic, vaccines (28) and

chemotherapeutics.

Abbreviations

CDC: Centres for Disease Control, CoV: Coronavirus; COVID-19: Coronavirus Disease; FAO: Food

and Agriculture Organization; GISR: Global Influenza Surveillance; GLEWS: Global Early Warning

System; GVP: Global Virome Project; HPAI: Highly Pathogenic Influenza; ILI: Influenza like

Illnesses; MERS: Middle East Respiratory Syndrome; OFFLU: OIE/FAO; OIE: The World

Organization for Animal Health; SARI: Severe Acute Respiratory Infections; SARS: Severe Acute

Respiratory Syndrome; WHO: World Health Organization

14

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15

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