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Editorial

Planning for the Next Global Pandemic

A B S T R A C T

In order to mitigate human and financial losses as a result of future global pandemics, we must plan now. As the Ebola virus pandemic declines, we must reflect on how we have mismanaged this recent international crisis and how we can better prepare for the next global pandemic. Of great concern is the increasing frequency of pandemics occurring over the last few decades. Clearly, the window of opportunity to act is closing. This editorial discusses many issues including priority emerging and re-emerging infectious diseases; the challenges of meeting international health regulations; the strengthening of global health systems; global pandemic funding; and the One Health approach to future pandemic planning. We recommend that the global health community unites to urgently address these issues in order to avoid the next humanitarian crisis.

1. Introduction

The West African Ebola virus pandemic has shown us yet again that the world is ill prepared to respond to a global health emergency. This follows similar statements that were made after the H1N1 outbreak in 2009 that “The world is ill prepared to respond to a severe influenza pandemic or to any similar global, sustained and threatening public health emergency”. Our response to the Ebola zoonotic ‘spillover’ was delayed and as a result 11,158 people lost their lives in nine countries. The direct financial cost of the Ebola pandemic was estimated to be in the vicinity of six billion US dollars and global economic losses over 15 billion dollars. Clearly there are lessons to be learnt from the Ebola outbreak.

In 2005, following the Severe Acute Respiratory Syndrome (SARS) pandemic, the International Health Regulations (IHR) were modified. While two thirds of the 194 World Health Assembly countries have failed to comply with the regulations as of 2015, and for the one third who say they did, there are serious concerns about the reliability of their self-assessment. Now, with Liberia declared free of Ebola and declining incidence in Sierra Leone and Guinea, these same regulations are once again being revisited after more than a decade. Is this a futile exercise and should the IHRs be abandoned if they cannot be enforced by WHO and fulfilled by the World Health Assembly (WHA) member nations? The national health systems in West Africa, and for most low and middle income countries (LMICs), would not meet IHR standards (despite claims by some member WHA nations) and it is unlikely that following the Ebola pandemic much will change.

Many have stated that WHO failed to respond to the current Ebola epidemic in a timely manner but even if they did, would the outcome have been really that different? There were no drugs or vaccines available to treat and prevent the disease, thus quarantine, isolation and safe burials were the primary methods utilized to halt the spread of disease and were initiated by the afflicted nations themselves. It typically takes years if not decades to develop a vaccine or drug that will have public health impact. One only has to look at the countless billions that have been spent on trying to develop a vaccine for HIV, thus far without success. Moreover, weak, malnourished, immunosuppressed populations living in poverty with little or no hygiene, sanitation or running water will always be highly susceptible to new emerging or re-emerging infectious diseases. At ‘ground zero’ of the Ebola epidemic it was believed that in 2013, hungry children living in the remote Guinean village of Melianou killed and ate infected fruit bats. Thus, what can realistically be done to prevent and contain future national epidemics from becoming global pandemics? We discuss a number of issues that urgently need to be addressed in order to plan, and possibly prevent, the next global pandemic.

2. Emerging and Re-emerging Infectious Diseases

If one looks at the history of emerging or re-emerging infectious disease pandemics globally, on average they have appeared every decade but now, worryingly, the frequency between pandemics seems to be disturbingly shorter as evident with Severe Acute Respiratory Syndrome (SARS) in 2003, Influenza A H1N5 (bird flu) in 2007, H1N1 (swine flu) in 2009, Middle East Respiratory Syndrome (MERS) in 2012 and Ebola in 2014. Overpopulation and poverty are the primary contributing factors that have brought about this change and are strongly linked with global warming, environmental degradation, habitat destruction, and increased...
human/host/reservoir interaction. Weak malnourished populations in LMICs serve as the breeding grounds for future pandemics (Figure 1). For example, in metro Manila, the most densely populated city in the world, approximately six million people live in slums with no piped water or toilets. According to WHO, 137 million people in urban centres have no access to safe drinking water and over 600 million lack sanitation. The UN predicts that the world’s urban population will double to over six billion by 2050 and most of the increase in density will occur in LMICs. Population density is directly correlated with the rate of transmission of respiratory and faecal-oral pathogens (e.g. Mycobacterium tuberculosis, influenza, cholera, rotavirus, helminths).

Between 1940 and 2004 there were 335 emerging infectious disease (EID) origins reported globally. Figure 2 illustrates some of the most recent EID epidemics. EIDs are primarily zoonotic (60%), originating in wildlife populations (e.g. HIV, SARS, Ebola, West Nile Virus, Lyme Disease) but bacterial pathogens have become increasingly of concern due to antibiotic resistance especially in the developing world. Multidrug-resistance (MDR) to Mycobacterium tuberculosis, Streptococcus pneumoniae and Staphylococcus aureus are a global concern and gram-negative bacteria resistance to β-lactams is widespread. Drug resistance to enteropathogens has also become a major global health challenge. MDR Salmonella enterica Typhi and S. enterica Paratyphi are common in Asia and sub-Saharan Africa, and there are increasing reports of reduced susceptibility to fluoroquinolones. Campylobacter jejuni resistance to fluoroquinolones has become a concern in Southeast Asia, with rates of resistance of 80% reported from Thailand. Viral pathogens (e.g. Ebola, Makona variant (EBOV), MERS-CoV, H1N1) are also of concern due to their high rates of nucleotide substitution, poor mutation error-correction rate ability and capacity to quickly adapt to human hosts.

Table 1 displays some potentially pandemic pathogens that should be under active global surveillance. The current outbreak of MERS-CoV in South Korea is of grave concern given the case fatality rate is over 10%. Surveillance of zoonotic diseases is largely based on detecting illnesses in humans who often serve as the sentinel species and dead-end hosts. Apart from rabies, most national surveillance systems in the world do not monitor zoonotic diseases appearing in wildlife, yet 72% of zoonotic EIDs (e.g. Anthrax, Nipah virus, Hantavirus, type A influenza, SARS, MERS-CoV, Ebola) come from this source. Many RNA viruses have emerged and dispersed globally such as Chikungunya virus, West Nile virus and dengue virus. These three arboviruses alone have morbidity and mortality rates that far exceed those of the combined rates of SARS, Ebola and MERS-CoV. Thus, EID discovery efforts need to be directed toward reservoirs and vectors at the human-animal interface. The integration of human, veterinary, and agricultural medicine, as proposed by the ‘One Health’ approach, should result in earlier warning of EIDs and provide us with a better opportunity to respond to potential spill-over threats. Moreover, targeting surveillance to regional hotspots of EIDs provides an evidence-based rationale for more appropriate allocation of global resources.

### Table 1. Potential Pandemic Pathogens

| Pathogen                  | Sub-genus | Characteristics |
|---------------------------|-----------|-----------------|
| Mycobacterium tuberculosis|           | Zoonotic        |
| Streptococcus pneumoniae  |           | Zoonotic        |
| Staphylococcus aureus     |           | Zoonotic        |

### Figure 1. The breeding grounds for the next global pandemic: left panel illustrates slums in Metro-Manila, The Philippines; the middle panel shows slums in Dhaka, Bangladesh, and the right panel displays slums in Kibera, Kenya. Note photographs are available on public domain.

### Figure 2. Pandemic origins reported globally, 1940-2004.
4. Global Health System Strengthening

For most countries in the developing world it is difficult to improve their health systems to a standard that is similar to that of high-income countries. Moreover, as mentioned, most LMIC countries will not be able to establish core IHR capabilities without considerable donor support and international assistance for training, creating the necessary laboratory infrastructure for prompt diagnosis, and the technology required for ‘real-time’ reporting of epidemics. Point of care screening tests for use in community health posts are increasingly available for rapid diagnosis of emerging pathogens and will shorten the time from presentation to treatment. However improvements and access to diagnostic technologies will need to be supported by the capacity to interpret and act on the findings. Presently limited health-care dollars are spent on running tertiary national hospitals with little, or none, spent on preventive services, disease control or epidemic preparedness. However, most countries do have offices or departments for communicable disease control with the number of staff engaged in such full-time activities varying considerably. At the district/municipal level most developing countries have medical health officers and at the community level a considerable human resource of community health workers (CHWs).

Gostin and Friedman (2015) have proposed a new global health framework with robust national health systems at its foundation and an empowered WHO at its apex. However, WHO has failed to provide the necessary leadership to coordinate global health emergencies on the ground and adequately support WHO member nations to develop core IHR capacities. In September 2014, the UN assumed leadership of the Ebola response and created the UN Mission for Emergency Ebola Response (UNMEER), the first UN mission to respond to public health emergencies. In contrast with IHR recommendations, Security Council resolutions are legally binding for member countries. We now propose a new UN Centre for Disease Control (UN CDC), potentially based in New York, to serve at the apex of a new global health framework with a number of new and existing regional CDCs reporting directly to it (Figure 3). A proposed structure might be: National CDC departments reporting to their regional CDCs, and Provincial/District/Municipal CDC departments reporting to their National CDCs with Community Health Workers at local health centres reporting to their municipal health officers. In sum, at the apex of our proposed global health framework would sit a new UN CDC with Security Council authority and at the foundation, CHWs in local health centres. CHWs have transformed the health-care systems of many developing nations including Bangladesh, India, Ethiopia, and Malawi and are absolutely crucial for future global security.

5. Global Pandemic Funding

On October 10th 2014, World Bank President, Dr Jim Yong Kim, has proposed a new pandemic emergency facility (PEF). As stated on their website “The World Bank Group is playing a lead role in conceptualizing the facility, working in coordination with international organizations, including the WHO, the private sector and other development partners. PEF is a global financing facility that would channel funds swiftly to governments, multilateral agencies, NGOs and others, to finance efforts to contain dangerous epidemic outbreaks before they turn into pandemics. Financing from the PEF will be linked to strong country-level epidemic and pandemic emergency preparedness plans, thereby incentivizing recipient governments and the international community to introduce greater rigor and discipline into crisis preparedness and reduce the potential for moral hazard. The PEF is expected to cover a range of response activities such as: (i) rapid deployment of a trained and ready health care work force; (ii) medical equipment, pharmaceuticals and diagnostic supplies; (iii) logistics and food supplies; and (iv) coordination and communication. The PEF would
| Pathogen       | Areas of High Risk                  | Modes of Transmission                          | Incubation Period | Common Symptoms                                                                 | Vaccine                        | Treatment                                                                 |
|---------------|-------------------------------------|------------------------------------------------|-------------------|--------------------------------------------------------------------------------|--------------------------------|---------------------------------------------------------------------------|
| Influenza A   | Asia, South East Asia, Middle East  | Wild birds, poultry, pigs, humans (respiratory)| 1-4 days          | Productive cough, sore throat, fever, malaise, myalgia, rhinitis                | Fluvax®, inactivated split vision; LAIV, live attenuated nasal spray   | Oseltamivir (Tamiflu) 30-75mg twice daily for 5 days; Zanamivir (Relenza) 10mg inhaled every 12 hr for 5 days |
| e.g. H1N1, H5N1, H3N2 |                                    |                                                 |                   |                                                                                  |                                |                                                                           |
| MERS-CoV      | Middle East, Asia                   | Bats, camels, humans contact                    | 2-14 days         | As above                                                                         | No vaccine available           | No antiviral treatment                                                   |
| Ebola         | Central Africa, West Africa         | Bats, human body fluids                         | 2-21 days         | Haemorrhage, fever, sore throat, vomiting, diarrhoea, muscular pain, headache, rash | No vaccine available           | No antiviral treatment                                                   |
| Malaria       | South East Asia, East Africa        | Anopheles mosquito                              | 9-14 days         | Fever, headache, chills, vomiting                                               | No vaccine available           | ACTs¹ recommended                                                       |
| e.g. P. falciparum | South America                 |                                                 |                   |                                                                                  |                                | e.g. Artemether, 40 mg + lumefantrine, 240 mg twice a day for 3 days       |
| Chikungunya   | Africa, Southeast Asia, Asia,      | Aedes mosquito                                  | 2-12 days         | Biphasic fever, joint pain, maculopapular rash, uveitis, headache, vomiting, insomnia | No vaccine available           | No antiviral treatment                                                   |
|               | Caribbean, Venezuela, USA, France, |                                                 |                   |                                                                                  |                                |                                                                           |
|               | Italy, Australia                    |                                                 |                   |                                                                                  |                                |                                                                           |
| Campylobacteria| South Asia, South-east Asia        | Poultry, milk, drinking water                   | 1-4 days          | Acute watery diarrhea, fever                                                    | No vaccine available           | Azithromycin, 500 mg once a day for 3 days                                |
| Salmonella    | South Asia, Africa                 | Human contact, food, drinking water             | 5-14 days         | Fever, headache, malaise, abdominal pain, diarrhea                              | Attenuated strain Ty21a        | Ciproflaxacin, 20 mg/kg/day for 7 days; or Azithromycin, 20 mg/kg/day for 7 days |
| Serovar typhi | South East Asia, Oceania           | drinking water                                  |                   |                                                                                  | typhoid vaccine; Vi capsular polysaccharide typhoid vaccine; Killed whole-cell typhoid vaccine |                                                                           |
| Nontyphoidal  | Poultry, eggs, meat                |                                                 | 8-24 hr           |                                                                                  |                                |                                                                           |

Note: All figures were obtained from public domain. ¹ACT = Artemisinin-based Combination Therapy.
not cover pandemic preparedness or reconstruction efforts. A total of $1 billion is available for all of the 77 poorest countries through June 2017.\textsuperscript{22}

If the WHO contingency fund (100 million US dollars) and the World Bank pandemic emergency facility cannot be utilised to strengthen national health systems in LMICs in order to meet IHRs core capabilities, then how can this be achieved? A multi-billion US dollar International Health System fund has been proposed\textsuperscript{2} but considerable funding from both the private and public sector will need to be secured if the fund is to be successfully launched. The G20, the European Union, and philanthropic organizations will need to contribute. The implementation and monitoring of such funds at the national level will have to be carefully scrutinized and audited if the core capacities of the IHRs are to be achieved and maintained. Ultimately LMIC nations themselves will need to allocate health care dollars toward health prevention and epidemic planning. For many LMICs this is not a priority and they are ill prepared to respond to epidemics on their own soils. Building national capacity is the rate limiting step for global health security. If the international community fails to support this capacity-building initiative then this puts the world in a precarious situation with regard to future pandemics.

6. Conclusions

It is well known in management circles that ‘if one fails to plan then one should plan to fail’. With regard to pandemic planning, if we fail to build national epidemic capacities in LMICs then we should plan to deal with a global pandemic in the not too distant future. However, in order to build such national capacity it will take considerable international political will that at the moment seems to be lacking. Instead of allocating huge resources that ‘react’ to pandemics, funds must be earmarked to ‘prevent’ pandemics. This would include building national capacities of LMICs and smart surveillance of EIDs in identified hotspots in the tropical and subtropical world. What are the likely organisms to cause a future pandemic and where will they originate from? Zoonosis from wildlife represents the most significant global health threat of our time yet little funds are spent monitoring and identifying new zoonotic pathogens originating in wildlife. Clearly a ‘One Health’ approach is the way forward.

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