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Not to Be Sneezed at – The Threat From Infectious Disease
by Ross Campbell, Gen Re, London

The range of infectious diseases that cause distress, illness and death remains truly staggering. Malaria, pneumonia, HIV, meningitis, plague, yellow fever, cholera, influenza and most recently Ebola continue to influence not only individuals but the economic and social life within large regions of the world. Most countries have experienced epidemics of one form or another over the past decade. The majority has been contained, but the H1N1 influenza outbreak of 2009 briefly demonstrated the potential for global reach.

The Ebola Virus Disease (EVD) emergency underlined that infection can create unprecedented levels of sickness and mortality. Although centred in Western Africa where the hobbled efforts to contain it are well known, isolated cases emerged in more distant countries – a reminder that microbes can spread rapidly across borders. Anxiety about EVD spread was particularly marked in medically advanced countries that may regard themselves as largely immune to this kind of problem. Yet their very sophistication is creating drug-resistant bacteria capable of becoming significant threats in their own right. Because international cooperation is poor and hampered by budget cuts, awareness of the scale of new threats, through monitoring and reporting, remains weak.

Distress and disease

The psychology of disease outbreaks is of interest. As an outbreak occurs, anxiety rises in developed countries as the perceived threat to their economic activities grows. Forces to combat infection are mobilised only once the threat becomes significant, but they are usually too late for the people on the ground. Rumour and panic may spread faster than a virus. Action plans are developed, mock exercises take place and people may even be ostracised in a completely unreasonable manner.

As the epidemic dies away, any medical opportunities to develop countermeasures, such as vaccines, are shelved as interest moves on to the next threat. HIV is probably the exception that proves the rule as its effects were being felt in more developed countries. Treatments for HIV were relatively rapidly developed and advanced for use in the West, but the technology remains sparse elsewhere in the world.
The organisms responsible for infectious diseases are incredibly inventive in the ways they find to spread from person to person. On a day-to-day basis, we are most familiar with bacterial and viral infections that may be transmitted in body fluids, by direct contact with infected individuals or by touching surfaces that harbour germs. Waterborne cryptosporidium causes prolonged diarrhoeal illness. Haemorrhagic colitis and renal failure stem from food infected with (Escherichia) E. coli. Hantavirus pulmonary syndrome is transmitted from rodents. Zoonotic diseases, such as Severe Acute Respiratory Syndrome (SARS), influenza and Ebola, are infectious diseases of animals that can be transmitted to humans.

However devious these routes of transmission are, they require help from us. People are more vulnerable to infection when they are receiving medication to suppress their immune systems or when they are ill, very old or malnourished. Resurgent diseases, including cholera and tuberculosis, illustrate our vulnerability to microorganisms in a changing environment. The immense difficulties experienced during efforts to contain EVD serve to underline how much global cooperation and coordination is required when infectious disease spirals out of control. Worryingly, the transmission routes for EVD are extremely limited, and this raises questions about the potential international response to a fast-moving and more easily transmitted pathogen.

Antimicrobial resistance (AMR) – when a bacteria, fungus, virus or parasite can no longer be controlled with drugs – threatens to create a post-antibiotic era in which common infections can once again kill. Modern medicine risks being undermined by AMR as health systems have become reliant on antibiotics to reduce the risk of infection following most surgery and when patients require chemotherapy. Resistance of bacteria to treatment has been increasing in line with rising levels of antibiotic prescription and a slowing in the development of new drugs. Second- and third-generation antibiotics are expensive and less widely available but some strains of bacteria are resistant to them.

This short-term outlook means that outbreaks remain hard to predict, limiting the effectiveness of investigations, such as pathogen sequencing, to improve detection and surveillance. It remains equally difficult to predict when an outbreak will become a pandemic, meaning that control measures are only deployed once an outbreak is underway.

**Cause and response**

Infectious diseases are caused by pathogenic microorganisms – bacteria, viruses, fungi and parasites. The threat that these pose to human health and social cohesion is nothing new. Public health measures and the development of antibiotics led to expectations of control, or even eradication of infectious disease, but this has never materialised. New organisms emerge in response to the antibiotic challenge (e.g. malaria) and other organisms experience a resurgence by finding new hosts in which to reproduce. Health systems become distracted by other demands (e.g. tuberculosis). Novel infections can result from the evolution of existing organisms. Known diseases may spread to new geographic areas in response to social and economic change. Previously unrecognised infections may emerge in regions undergoing ecological change, which increases human exposure to animals and insects that host these agents.

<table>
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<th>Table 1 – Contributing factors to emerging infectious disease</th>
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In 2011 the World Health Organization (WHO) European Strategic Action Plan on Antibiotic Resistance called for better information sharing, more effective interventions to slow the development of AMR, and stimulation for new antimicrobial drugs development. In 2014, the World Health Assembly provided the WHO a mandate to produce a global action plan on AMR for approval in 2015.

Already, patients with infections caused by AMR are at increased risk of worse clinical outcomes and death. The results of new research show the considerable human and economic cost. Looking only at part of the impact of AMR, a continued rise in resistance by 2050 would lead to an extra 10 million people dying every year – more than die from cancer today – at a loss of 100 trillion USD of economic output.

Anticipation and forecast

A striking feature of the unfolding EVD outbreak – the “largest” to date – was the inaccuracy of statistical reporting. In a world used to real-time data, this seems an aberration. Knowing that the true numbers of infections and deaths were under-reported also calls into question those recorded for prior outbreaks when surveillance infrastructures were even less well-developed. Merely knowing the total numbers of infected and dead in a disease outbreak, however, does not help the public health agencies, researchers or the aid workers preparing for a future pandemic.

The WHO views predicting pandemics as akin to weather forecasting. There is a parallel between certain climatic conditions and disease incidence and spread; cold weather brings influenza while floods allow the spread of rodent and waterborne disease. To this end the agency reports working with the World Meteorological Organization to develop more effective forecasting tools. The “Supramap” initiative takes the analogy a step forward. It works by integrating knowledge of pathogen genomes with host biology and geographical information to reveal the aetiology of an epidemic. By overlaying genomic data and geospatial information on Google Earth, it can reveal how pathogens are spread from a geographical origin and host species, allowing infectious disease to be tracked. It is now possible to deploy real-time disease detection in the community – taking samples following clinical consultation and integrating this with geo-spatial information to see if a disease outbreak is occurring.

The Global Microbial Identifier (GMI) is a genomic epidemiological database that stores whole genome sequencing data of microorganisms, offers identification of relevant genes, and compares genomes to detect outbreaks and emerging pathogens. The GMI initiative seeks to harness genomic technology and informatics tools to improve global patient diagnostics, surveillance, research and public health response to make informed decisions on where and how to allocate resources to prepare for emerging diseases.

Biomedical informatics – collections of comparative genomic, phenotypic and geospatial information – are powerful tools but the outputs require careful interpretation if they are to be helpful in disease control. The context comes from phylogenetics – an analysis of the classification of organisms that traces their relationship and evolutionary trajectory over time. In phylogenetic analysis, similar strains of organisms are grouped into lineages. Information known about one lineage is used to predict the properties of another, including predicting which strains are capable of infecting humans, and which are pathogenic or resistant to drugs.

Prediction and control

There is no evidence that new business dwindles during epidemic activity – in fact, it likely prompts an increase in demand for life and health insurance – which prompts the question: Could the underwriting process be effective at selecting out those at risk during a sweeping pandemic? Traditional underwriting approaches are ill-equipped to recognise acute infectious disease risk. Instead, assessment protocols have been developed to be adept at exposing and assessing heart, circulatory, malignant and nervous diseases. Most life insurance application forms are restricted to requesting details of known chronic infection (e.g. Hepatitis or HIV). It seems unlikely that insurers would wish applicants to make disclosure of the mild symptoms of early infections or ask...
underwriters to expend energy investigating these because most are trivial. Questions about travel patterns and occupation serve to fill in the knowledge gaps about applicants’ risk of exposure to infection.

For underwriters, understanding the mortality threat from pathogenic microorganisms would assist them in selecting risks should the inevitable outbreak happen. For agencies and healthcare providers, the ability to anticipate outbreaks of epidemic-prone diseases would help them to prepare an orderly response to a pandemic. The Global Outbreak Alert and Response Network (GOARN) seeks to pool the human and technical resources of existing health agencies and charity networks in a bid to combat the international spread of disease outbreaks. The WHO outlines a vision of an integrated global alert and response system for epidemic emergencies with the capacity to mount an effective and coordinated international response.

From those in the front line fight to gain control of Ebola, much of this sounds like just that, a vision. Their request was not simply for the international community to construct isolation wards but to provide trained staff to run them and to do so without delay. Despite the presence of GOARN, the response was deemed slow and fractured.

During a pandemic, over-stretched local health services suffer a double blow with reductions in care because of the surge of newly-ill people leading to further compromising the care of existing patients as they cease to be treated with priority. Part of the difficulty in limiting the spread of EVD in West African countries stemmed from chronic under-funding in their national health systems. Put simply, too many patients for too few isolation beds.

**Conclusion**

Despite the advances in medical capabilities, the versatility of the organisms to adapt and exploit changes in human behaviour means infectious diseases remain a significant challenge. Despite its importance, the reporting and monitoring of infectious disease is slow and unreliable, with the detection of new threats undermined by ineffective international cooperation. Ensuring antibiotics are used less, and more responsibly, will take international commitment. To complicate matters, there are gaps in surveillance and standards for methodology, while data sharing and coordination are both lacking.

The quest to develop swift diagnostic tests and effective vaccines remains a future hope. The spread of pathogens across international borders may be the price of globalisation. The immense difficulties encountered by those tasked with managing and containing the Ebola outbreak underlines how poor administration coupled with a lack of infrastructure and interconnectivity can undermine already weak health systems. The WHO even found it hard to track the number of dead accurately – surely the most profound data available.

Harnessing the power of scientific research, creating effective disease models, collecting and managing data, coordinating national public health systems and mobilising an international crisis response with adequate funding is, unarguably, visionary. With limited resources for addressing EVD, it feels more likely the focus will be elsewhere – on diabetes, cancer and heart disease, for example, or the politically fraught areas of tobacco and alcohol control.

Perhaps this is precisely because the health systems of the developed countries are so adept at isolating and treating dread illnesses, even including EVD. Once EVD infections occurred in the U.S. and in Europe, the outcomes offered a stark contrast to those in Western Africa; the virus was contained and patients had a real chance of recovery. The problem is that the epicentres of future infection are again likely to be territories with low economic importance and poor health infrastructures, making tracking and limiting pathogen spread nigh impossible. This means long-term investments in the non-commercial projects, such as vaccine development, are less likely to happen.

Using microbial genomic data and informatics tools to monitor and manage outbreaks requires a coordinated infrastructure with excellent communication, data storage, analytics and real-time reporting. Once in place, accessing and sharing such data raises legal and ethical privacy issues. Investment in surveillance, laboratory research and training, and epidemiologic investigations with prevention and control efforts,
are needed. The Ebola crisis underlines the need for urgent solutions to these complex difficulties if the human and economic loss from infectious disease is to be mitigated.

Endnotes
6 https://supramap.renci.org/supramap/home.

About the Author
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