

Planning for the unexpected: Ebola virus, Zika virus, what's next?

Since 2000 we have witnessed global pandemics and public health emergencies of international concern. This review details which viruses are likely to caused further outbreaks and looks at the strategies and tools available to UK medical professionals to mitigate the threat posed.

The outbreak of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002–4, swine-origin, pandemic H1N1 influenza in 2009–10 and Middle East respiratory syndrome coronavirus (MERS-CoV) since 2012 highlights the threat that emerging viruses pose globally. None of the above outbreaks were as severe as initially feared as a result of a combination of the viruses being less easily transmitted from person to person, causing less severe disease or being inhibited by existing, approved drugs. However, there are a number of other threats against which we have no vaccines or antiviral drugs (World Health Organization, 2015; *Table 1*). Within the UK, travel-associated cases of emerging viruses are regularly identified but only very rarely lead to further, locally transmitted cases (*Figure 1*). The recent outbreak of Ebola virus in west Africa and the ongoing outbreak of Zika virus in the Americas have tested global and UK preparedness. The key question is what contingencies have been, or need to be, put in place to limit the potential harm these infections can cause?

Emerging viruses are going to be a continuing threat for a number of reasons. A growing global population and urban spread means that more people are living in closer proximity to the natural reservoirs of these viruses and each other. Greater mobility and connectivity allows these infections to spread more rapidly across the globe (Weiss and McMichael, 2004). As bat species are the reservoirs for a number of these viruses it would be very difficult, if not impossible, to eradicate the viruses from these hosts and stop the initial spillover events (Amman et al, 2014).

The scale of the Ebola outbreak in west Africa has been widely cited as unprecedented. The number of cases

exceeded 28 000 while the previous largest outbreak, in Uganda in 2000–1, had just 425 cases (To et al, 2015). These figures are unfortunately dwarfed by the estimated impact of emerging viruses over the last century – the 1918 pandemic influenza killed 50–100 million people (Johnson and Mueller, 2002), and HIV has claimed over 35 million lives (World Health Organization, 2016). The SARS-CoV outbreak cost an estimated USD\$40 billion. Lastly, pandemics in the 21st century are predicted to wipe USD\$6 trillion off the global economy (National Academy of Medicine, 2016).

In the UK, the number of cases underestimates the impact of emerging viruses as extensive efforts and resources are expended to prevent spread.

Mitigating the threat

Strategies for reducing the risk of outbreaks of emerging viruses occurring and the size of any outbreaks are well known: surveillance, early diagnosis, infection control and isolation, clinical care, contact tracing and community mobilization.

Surveillance

Within the UK, the multi-agency Human Animal Infections and Risk Surveillance (HAIRS) group undertakes horizon scanning (Human Animal Infections and Risk Surveillance, 2013) to identify, discuss and risk assess infections with potential for interspecies transfer (i.e. zoonotic infections). Human Animal Infections and Risk Surveillance publishes a monthly report of infections thought to be of potential significance (*Table 2*) as well as disease-specific risk assessments, most recently for Zika (Human Animal Infections and Risk Surveillance, 2016).

Pre-travel

NaTHNaC, the National Travel Health Network and Centre, provides travel health advice and guidance for health-care professionals and travellers (*Table 2*).

Control

The high quality of UK infrastructure (i.e. water, sanitation, housing), high standards of living, climate and universal infection control precautions within health care offers some protection against spread of infectious diseases in the UK.

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Table 1. (Re-)emerging virus threats to human health

Virus family	Species	Disease caused	Suggested treatment	Other information
<i>Filoviridae</i>	<i>Marburg marburgvirus</i> <i>Zaire ebolavirus</i>	Haemorrhagic fever	Supportive therapy. Some drugs and vaccines in early clinical testing	Viruses not reported in UK wildlife
<i>Coronaviridae</i>	MERS-CoV SARS-CoV	Significant respiratory disease	Supportive therapy. Evidence for use of repurposed drugs but no licensed vaccines	Viruses not reported in UK wildlife
<i>Flaviviridae</i> *	Dengue virus Zika virus	Varied, from asymptomatic to haemorrhagic fever	Licensed vaccines (e.g. Japanese encephalitis virus) but no licensed drugs. Supportive therapy or drug repurposing	Some mosquito vectors found in the UK but no local transmission of the viruses
<i>Orthomyxoviridae</i>	Influenza A virus	Respiratory disease	Licensed vaccines and drugs available	Cases of highly pathogenic avian influenza have been reported in UK wildlife
<i>Togaviridae</i>	Chikungunya virus	Rash, fever, polyarthrititis, encephalitis	Supportive therapy. No licensed drugs or human [†] vaccines	Virus or animal reservoir not found in UK
<i>Paramyxoviridae</i>	Hendra virus Nipah virus	Respiratory and encephalitic disease	Supportive therapy. No licensed drugs or human [†] vaccines	Viruses not reported in UK wildlife
<i>Bunyaviridae</i>	Crimean-Congo haemorrhagic fever virus Hantaan virus Rift Valley fever virus	Fever, rash, encephalitis, haemorrhaging	Supportive therapy. Only a few licensed vaccines available (e.g. Rift Valley fever virus and Hantaan virus) for use in Africa and Asia	Hantavirus already found in UK rodents. Some transmission vectors also present
<i>Rhabdoviridae</i>	Non-rabies lyssaviruses (European bat lyssavirus 2)	Delirium, partial paralysis and encephalitis	There are licensed vaccines and antiviral drugs for rabies virus that are partially effective against some non-rabies lyssaviruses in vitro	The UK is considered rabies free. However, it is important to note that European bat lyssavirus 2 has been found in UK bats
<i>Arenaviridae</i>	Lassa fever virus	Febrile illness, haemorrhaging	Supportive therapy. Generic antivirals and convalescent plasma therapy. Preclinical vaccines in development	Viruses not found in UK, but have been in other European countries. Some transmission vectors found in UK

*Specifically tick- or mosquito-borne, emerging flaviviruses. †Licensed animal vaccines available for some viruses. MERS-CoV = Middle Eastern respiratory syndrome virus; SARS-CoV = severe acute respiratory syndrome coronavirus.

This is highly effective for many imported infections (e.g. cholera, rabies virus, malaria). However, specific diseases require additional control measures.

On return from overseas travel, an early specific response is dependent on early recognition and thus clinicians asking about travel history is key. This was reinforced recently as part of both the Ebola and Zika responses.

Once the risk of an imported infection is identified, the initial support for clinicians comes from local infection services (microbiology, virology or infectious disease teams). Local health economies will have established systems for managing infectious diseases. Local infection consultants are supported by a wider national system. The imported fever service provides a clinical advisory and specialist diagnostic service for clinicians managing travellers who have returned to the UK and have presented with fever. Hospital doctors can contact the imported fever service after discussion with their local infection consultant (Table 2).

Local health protection teams of Public Health England and their equivalents in Scotland, Wales and Northern

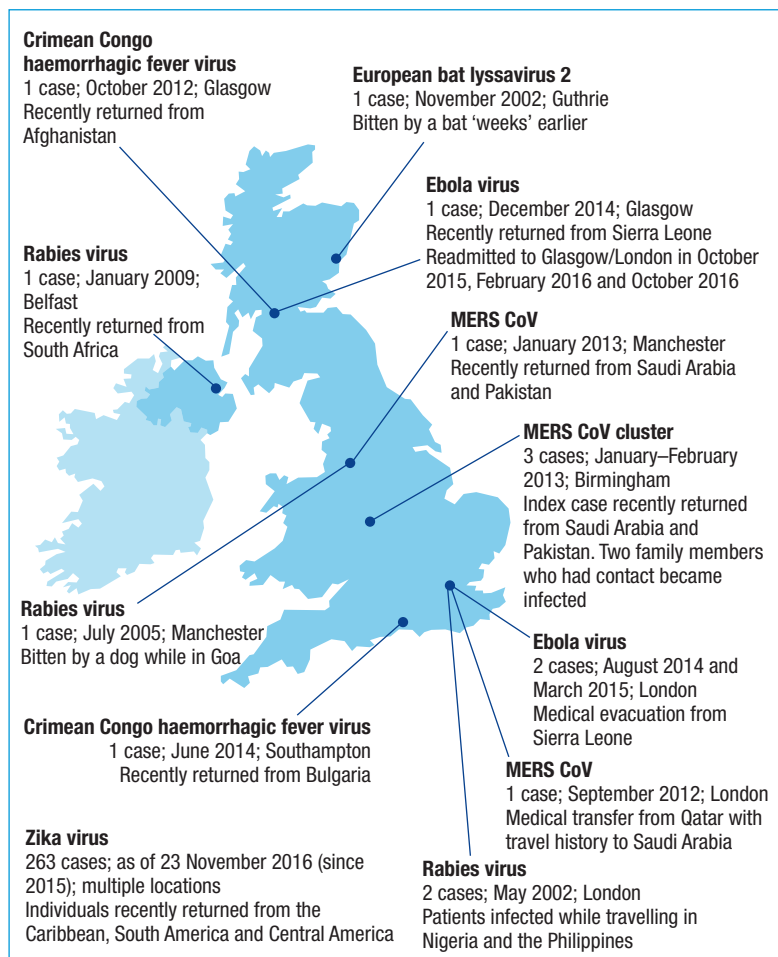
Ireland provide the initial public health risk assessment and response for any suspected cases (including contact tracing and management). For clinicians in England, the Public Health England website should be used to identify and contact the local health protection team, as detailed in Table 2.

Following the Ebola outbreak in West Africa, NHS England and Public Health England have established a High Consequence Infectious Diseases programme. This aims to 'develop an agreed approach to managing the end-to-end patient pathway for known and unknown HCID [High Consequence Infectious Diseases] (including suspected and confirmed cases)'. This programme includes early isolation of suspect cases, safe systems of work and access to appropriate infectious diseases facilities.

Public health and scientific research

The public health and clinical responses should be implemented hand in hand with scientific research and development programmes. These would include

Figure 1. (Re-)emerging virus infection cases in the UK since 2000.



fundamental research to improve our understanding of these viruses, disease-specific interventions and also technological platforms that could be used to target a variety of different viruses. Ongoing endeavours include:

1. Ensuring a more integrated global framework of public health bodies to counter infectious diseases. These would comprise strong national public health infrastructure that could be advised by effective global and regional bodies. Implementation of the International Health

Regulations (World Health Organization, 2005), and the Global Health Security Agenda (Table 2) will both contribute to this

2. A 'global biosecurity outbreak vaccine fund' has been proposed to develop vaccines and treatments through to phase II clinical trials (Hill, 2016). These could then be used initially to protect front-line workers against the threat of emerging viruses as they bear the major burden from these diseases
3. The World Health Organization (2015) is currently shortlisting platform technologies for diagnostic, antiviral drug and vaccine development that can be established immediately and readily adapted in an outbreak situation.

The combined cost for all of this? An estimated USD\$4.5 billion a year (National Academy of Medicine, 2016). This sounds a lot, but it needs to be balanced against the USD\$40 billion cost of SARS-CoV alone (National Academy of Medicine, 2016). **BJHM**

Conflict of interest: Dr W Welfare is employed by Public Health England and holds honorary positions at University of Manchester and University of Liverpool. Dr E Wright has received funding from the BBSRC, Wellcome Trust, Department for International Development and Innovate UK for studies on emerging viruses.

Amman BR, Nyakarahuka L, McElroy AK et al (2014) Marburgvirus resurgence in Kitaka Mine bat population after extermination attempts, Uganda. *Emerg Infect Dis* **20**(10): 1761–1764. <https://doi.org/10.3201/eid2010.140696>

Hill AVS (2016) Oxford London Lecture 2016: Vaccines for Ebola. www.ox.ac.uk/news-and-events/the-university-year/oxford-london-lecture (accessed 18 October 2016)

Human Animal Infections and Risk Surveillance (2013) The processes of risk assessments undertaken by the Human Animal Infections Risks and Surveillance Group. www.gov.uk/government/publications/hairs-risk-assessment-process (accessed 25 September 2016)

Human Animal Infections and Risk Surveillance (2016) Qualitative assessment of the risk that Zika virus presents to the UK population. www.gov.uk/government/uploads/system/uploads/attachment_data/file/540204/Zika_Virus_Risk_Assessment.pdf (accessed 25 September 2016)

Johnson NPAS, Mueller J (2002) Updating the accounts: global mortality of the 1918–1920 “Spanish” influenza pandemic. *Bull Hist Med* **76**(1): 105–115. <https://doi.org/10.1353/bhm.2002.0022>

National Academy of Medicine (2016) *The Neglected Dimension of Global Security: A Framework to Counter Infectious Disease*

Table 2. Links to infectious disease public health resources			
Resource	Published by	Web address	
Emerging infections: monthly summaries	Public Health England/Human Animal Infections and Risk Surveillance group	www.gov.uk/government/publications/emerging-infections-monthly-summaries	
Travel health guidance for health-care professionals advising travellers	National Travel Health Network and Centre	http://travelhealthpro.org.uk/	
Contact details for the imported fever service	Public Health England	www.gov.uk/guidance/imported-fever-service-ifs	
Contact details of the local health protection team	Public Health England	www.gov.uk/health-protection-team	
Global Health Security Agenda	A partnership of ~50 nations, organizations and stakeholders	https://ghsagenda.org/	

Crises. National Academies Press, Washington, D.C.. <https://doi.org/10.17226/21891>

To KKW, Chan JFW, Tsang AKL, Cheng VCC, Yuen K-Y (2015) Ebola virus disease: a highly fatal infectious disease reemerging in West Africa. *Microbes Infect* 17(2): 84–97. <https://doi.org/10.1016/j.micinf.2014.11.007>

Weiss RA, McMichael AJ (2004) Social and environmental risk factors in the emergence of infectious diseases. *Nature Med* 10(12s): S70–S76. <https://doi.org/10.1038/nm1150>

World Health Organization (2005) *International Health Regulations*. 3rd edn. World Health Organization, Geneva

World Health Organization (2015) Blueprint for R&D preparedness and response to public health emergencies due to highly infectious pathogens. www.who.int/csr/research-and-development/meeting-report-prioritization.pdf?ua=1 (accessed 25 September 2016)

World Health Organization (2016) Fact Sheet 2016. www.unaids.org/en/resources/fact-sheet (accessed 25 September 2016)

KEY POINTS

- Emerging viruses remain a threat to health globally and they can not be readily eradicated as their natural reservoir is wild animals.
- The threat posed mostly comes from known viruses that re-emerge intermittently or emerge in countries where the population has not been exposed before. However, viruses that have never been reported before can also appear.
- Individuals should seek health advice before overseas travel.
- Clinicians need to ask about travel history and know the local pathway and arrangements for managing imported fever.
- Public health surveillance and response is interlinked with the clinical response.
- Research and development is needed for vaccines, treatments and diagnostics to minimize the risk of infection and the size of outbreaks.

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