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PLANNING FOR THE UNEXPECTED - EBOLA VIRUS, ZIKA VIRUS...WHAT'S NEXT?

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Key points

1. Emerging viruses remain a threat to health globally and they can not be readily eradicated as their natural reservoir is wild animals.
2. 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.
3. Individuals should seek health advice before overseas travel.
4. Clinicians need to ask about travel history and know the local pathway/arrangements for managing imported fever.
5. Public health surveillance and response is interlinked with the clinical response.
6. Research and development is needed for vaccines, treatments and diagnostics to minimise the risk of infection and the size of outbreaks.

What is on the radar, why and what is the potential impact?

The outbreak of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002-2004, swine-origin, pandemic H1N1 influenza in 2009-2010 and Middle East respiratory syndrome coronavirus (MERS-CoV) since 2012 highlights the threat emerging viruses pose globally. None of the above were as severe as initially feared due to 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 Organisation 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 & McMichael 2004). As bat species are the reservoirs for a number of these viruses it would be very difficult, if not impossible, 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 2000-2001, had just 425 cases (To et al. 2015). These figures are unfortunately dwarfed by the estimated impact of emerging viruses over the last century - 1918 pandemic influenza killed 50-100 million people (Johnson & Mueller 2002), and HIV has claimed over 35 million lives (World Health Organisation 2016). The SARS-CoV outbreak cost an estimated USD\$40bn. Lastly, pandemics in the 21st century are predicted to wipe USD\$6tn off the global economy (Anon 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/isolation, clinical care, contact tracing and community mobilisation.

Surveillance

Within the UK, the multi-agency Human Animal Infections and Risk Surveillance (HAIRS) group undertakes horizon scanning (HAIRS 2013) to identify, discuss and risk assess infections with potential for interspecies transfer (*i.e.* zoonotic infections). HAIRS 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 (HAIRS 2016).

Pre-travel

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

Control

The high quality of UK infrastructure (water, sanitation, housing *etc.*), high standards of living, climate and universal infection control precautions within healthcare offers some protection against spread of infectious diseases in the UK. This is highly effective for many imported infections (cholera, rabies virus, malaria *etc.*). 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 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 (IFS) 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 IFS after discussion with their local infection consultant (Table 2).

Local Health Protection Teams (HPT) of Public Health England (PHE) and their equivalents in Scotland, Wales and Northern Ireland provide the initial public health risk assessment and response for any suspected cases. For clinicians in England, the website to identify and contact the local HPT is in Table 2.

Following the Ebola outbreak in West Africa NHS England and PHE have established a High Consequence Infectious Diseases (HCID) programme. This aims to “*develop an agreed approach to managing the end-to-end patient pathway for known and unknown HCID (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 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 (Anon 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 (Prof. Hill, Oxford London Lecture 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 WHO is currently shortlisting platform technologies for diagnostic, antiviral drug and vaccine development that can be established immediately and readily adapted in an outbreak situation (World Health Organisation 2015).

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

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> <i>MERS-CoV</i> <i>SARS-CoV</i>	Significant respiratory disease.	Supportive therapy. Evidence for use of repurposed drugs but no licensed vaccines.	Viruses not reported in UK wildlife.
<i>Flaviviridae</i> ¹ <i>Dengue virus</i> <i>Zika virus</i>	Varied. From asymptomatic to haemorrhagic fever.	Licensed vaccines (e.g. JEV) but no licensed drugs. Supportive therapy or drug repurposing.	Some mosquito vectors found in the UK but no local transmission of the virus.
<i>Orthomyxoviridae</i> <i>Influenza A virus (HPAI)</i>	Respiratory disease.	Licensed vaccines and drugs available.	Cases of HPAI have been reported in UK wildlife.
<i>Togaviridae</i> <i>Chikungunya virus</i>	Rash, fever polyarthrits, encephalitis.	Supportive therapy. No licensed drugs or human ² vaccines.	Virus or animal reservoir not found in UK.
<i>Paramyxoviridae</i> <i>Hendra virus</i> <i>Nipah virus</i>	Respiratory and encephalitic disease.	Supportive therapy. No licensed drugs or human ² vaccines.	Viruses not reported in UK wildlife.
<i>Bunyaviridae</i> <i>CCHFV</i> <i>Hantaan virus</i> <i>Rift Valley fever virus</i>	Fever, rash, encephalitis, haemorrhaging.	Supportive therapy. Only a few licensed vaccines available (e.g. RVFV and HTNV) for use in Africa and Asia.	Hantavirus already found in UK rodents. Some transmission vectors also present.
<i>Rhabdoviridae</i> <i>Non-rabies lyssaviruses</i> <i>(European bat lyssavirus 2)</i>	Delirium, partial paralysis and encephalitis	Licensed vaccines and antiviral drugs for rabies virus that are partially effective against some non-rabies lyssaviruses <i>in vitro</i> .	The UK is considered rabies free. However, it is important to note that EBLV-2 has been found in UK bats.
<i>Arenaviridae</i> <i>Lassa fever virus</i>	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.

¹ Specifically tick- or mosquito-borne, emerging flaviviruses.

² Licensed animal vaccines available for some viruses.

MERS-CoV = Middle Eastern respiratory syndrome virus; SARS-CoV = severe acute respiratory syndrome coronavirus; JEV = Japanese encephalitis virus; HPAI = highly pathogenic avian influenza; CCHFV = Crimean-Congo haemorrhagic fever virus; HTNV = Hantaan virus; EBLV-2 = European bat lyssavirus 2

Table 2: Links to infectious disease public health resources

Resource	Published by	Web address
Emerging infections: monthly summaries	PHE / HAIRS	https://www.gov.uk/government/publications/emerging-infections-monthly-summaries
Travel health guidance for healthcare professionals advising travellers	National Travel Health Network and Centre	http://travelhealthpro.org.uk/
Contact details for the imported fever service.	PHE	https://www.gov.uk/guidance/imported-fever-service-ifs
Contact details of the local health protection team	PHE	https://www.gov.uk/health-protection-team
Global Health Security Agenda	A partnership of ~50 nations, organizations and stakeholders	https://ghsagenda.org/

PHE = Public Health England; HAIRS = Human Animal Infections and Risk Surveillance group



Figure 1: Details of (re-)emerging virus infection cases in the UK since 2000.

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