Infectious Disease Surveillance and Monitoring for Animal and Human Health: summary of notable incidents of public health significance. November 2019

*Incident assessment:

<table>
<thead>
<tr>
<th>Deteriorating</th>
<th>No Change</th>
<th>Improving</th>
<th>Undetermined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident is deteriorating with increased implications for public health</td>
<td>Update does not alter current assessment of public health implications</td>
<td>Incident is improving with decreasing implications for public health</td>
<td>Insufficient information available to determine potential public health implications</td>
</tr>
</tbody>
</table>

Notable incidents of public health significance

**Ebola virus disease (EVD), Democratic Republic of Congo**

During November, EVD transmission further decreased with 39 confirmed cases, down from 76 in October. This was the lowest monthly total since the declaration of the outbreak in August 2018. As of 30 November 2019, there had been 3,195 confirmed and 118 probable cases across 3 provinces (North Kivu, Ituri and South Kivu), with 2,203 deaths (overall case fatality ratio 66%). Four health zones (of the 29 ever affected) reported cases in November, compared to 10 in October.

Military offensives resulted in retaliatory attacks and large protests by local populations. The increased insecurity in the region slowed response activities in certain health zones. Violent attacks against response activities also continued to occur, with destruction of health facilities and the death of four Ebola response workers.

A second EVD vaccine, (Johnson & Johnson), was introduced in two health areas in Goma, North Kivu, in the context of a large clinical trial. As of 30 November, 872 individuals had been vaccinated.

The Merck vaccine that has been used in the outbreak under the Monitored Emergency Use of Unregistered Interventions (MEURI) protocol, was granted market authorisation by the European Commission, and prequalification by WHO.

**Lassa fever imported into the Netherlands**

Two imported cases of Lassa fever were reported in The Netherlands. Both were Dutch healthcare workers working in the same rural hospital in Masanga, Sierra Leone (map) where they had undertaken surgical procedures on the presumed index case. Contact tracing activities, including amongst other workers at the same hospital, were carried out in the Netherlands, the United Kingdom, Sierra Leone, Germany, Denmark, Uganda and India. Some high risk contacts were medically evacuated to Europe.

Other incidents of interest

- **Spanish** authorities reported likely sexual transmission of dengue. The index case had travelled to Cuba and on his return had unprotected sex with his male partner, the secondary case. Semen samples from both individuals were PCR positive with
genetically identical viruses, similar to those circulating in Cuba. Local investigations did not detect *Aedes albopictus*, ruling out mosquito transmission. Sexual transmission of dengue has very rarely been reported previously. This is the first time that dengue in a non-endemic area was attributed to sexual transmission, and the first sexual transmission described between men who have sex with men

- two further locally-acquired dengue cases were reported in Florida, USA, bringing the 2019 total to 14. Affected counties are Miami-Dade (12 cases), Broward (1) and Hillsborough (1). This is Florida’s highest annual total since 2014
- polio due to vaccine-derived polioviruses continues to be reported from many countries, with at least 60 cases reported this month. Pakistan reported its first cVDPV2 cases (n=11) and Côte d’Ivoire had 2 environmental VDPV2 detections linked to an outbreak in Nigeria. As of 26 November 2019, 177 cVDPV cases had been reported in 2019. Polio responses have been detrimentally affected; the Taliban banned vaccination in Uruzgan, Afghanistan, and vaccination workers were victims of an armed ambush in the Philippines. WHO provided a update on outbreaks in recently affected countries in the African Region
- herpes B viruses occur naturally in macaques and can cause fatal encephalitis in humans. The first herpes B virus infection in Japan was confirmed in an employee of a pharmaceutical research and development company, said to have assisted with experiments involving monkeys although the route of acquisition is not known. This is the first documented infection anywhere in the world since the late 1990s
- the ongoing Rift Valley Fever outbreak in Sudan totalled 345 human cases as of 28 November - an increase of 97 in the last month, with no new states affected. No new areas reported livestock disease
- the first case of locally-acquired severe fever with thrombocytopenia syndrome (SFS) was identified in Taiwan, in an elderly man living in the north of the country. The virus was identified as being similar to Korean strains
- locally acquired yellow fever was confirmed in Venezuela, for the first time since 2005

### Publications of interest

- candidaemia has traditionally been associated with nosocomial infection. Population-based surveillance in 9 US states revealed that a significant proportion (10.7%) of candidaemia cases overall was associated with injection drug use (IDU) in 2017. In patients aged 19-44 the proportion was higher at 34.6%. In 4 states with multi-year data, there had been an increase from 6.9% in 2014 to 15.2% in 2017. IDU cases were significantly younger, had fewer typical healthcare-associated risk factors, and were more like to be community-associated than non-IDU cases. Infections were often polymicrobial suggesting that non-sterile practices may be contributory. A linked commentary provides an overview in the context of the ongoing US opioid epidemic
- a study of 2800 patients with cat scratch disease (CSD) in Israel characterised a unique syndrome, CSD-associated fever of unknown origin (CSD-FUO). This was identified in 66 (2.4%) patients over a 14 year period. Fever was prolonged (median 4 weeks), and the syndrome was characterised by its severity and multiorgan involvement. Malignancy was a common initial diagnosis
- a case report describes chronic dengue presenting with progressive dementia in a 45 year old in the US. Neutralising antibodies were detected at high titre using a phage-display assay, and dengue virus was detected in post mortem brain tissues by immunohistochemistry and molecular methods. The virus was also detected in pre-mortem brain biopsy sampled 33 months before the patient’s death. He had frequently travelled in dengue endemic countries, though had never had an acute encephalitis.
persistent neurological dengue infection appeared to have been in situ for several years

- **Wolbachia** species are bacterial endosymbionts of insects, that blocks transmission of dengue viruses when introduced into *Aedes aegypti* mosquitoes. New evidence indicates that the release of Wolbachia-infected mosquitoes has resulted in major decreases in dengue incidence at pilot sites in Australia (96% decrease), Indonesia (76%) and Brazil (70%). A study with a different Wolbachia sp in Malaysia showed that at the 6 intervention sites, human dengue incidence was reduced by an estimated 40.3%

- the **'Palm trial', a randomised, controlled trial of therapeutics for Ebola virus disease** was conducted in Ebola treatment centres in the DRC during 2018 and 2019, and 681 patients were enrolled. Of the 4 investigational therapies, both the single monoclonal antibody MAb114 and the triple monoclonal antibody REGN-EB3 were superior to standard care plus the triple monoclonal antibody ZMapp (the control group) in reducing EVD mortality. The effect was apparent with both low and high viral loads at presentation. The study also demonstrated the importance of early diagnosis and treatment; odds of death increased 11% for every day of symptoms prior to enrollment. It is unclear why mortality rates differed so much between ZMapp recipients in the PREVAIL II trial in West Africa (22%) and ZMapp recipients in the Palm trial (50%)

- in the UK, **65 individuals were exposed to a patient with EVD relapse in October 2015**. At that time, no licensed vaccine was available but the experimental vaccine rVSV-ZEBOV was offered as an emergency intervention. Of 45 individuals considered to have had possible direct skin contact with the case, 26 agreed to vaccination. None of the exposed developed EVD. A 1-year observational study showed that the vaccine was relatively well tolerated, even though 50% of recipients developed a temperature of $\geq 37.5^\circ C$ within the first 72 hours. This necessitated urgent clinical assessment and PCR testing. Half developed arthralgia, and this was persistent for at least 14 days in 4 individuals. All recipients seroconverted by 3 months. The authors attributed the high rate of side effects to “variation in genetic background and high levels of psychological stress”

- epidemiological evidence has long suggested that measles is associated with increases in morbidity and mortality attributed to other subsequent infections. A new study shows that **measles virus (MeV) infection can greatly diminish previously acquired immune memory**. The study was conducted during an outbreak in the Netherlands; 77 unvaccinated children were tested before and 2 months after natural measles, as well 119 controls. VirScan, a seroprofiling tool which detects a very diverse range of pathogen specific antibodies was used. After acute measles, antibody elimination ranged from 11 to 73%, an effect not seen amongst controls or recipients of MMR vaccine. The duration of the immune amnesia is potentially long-lived for months or years. These findings highlight the critical importance of continued MeV vaccination across the globe

- **human plague and animal exposures**. In the US between 1970-2017, a total of 482 human cases were identified, of which 76% were bubonic, 19% septicaemic, and 3% pneumonic. In over half (54%) there was a history of animal exposure(s) considered plausible for plague transmission, and a wide range of domestic (mostly cats and dogs) and wild animals (particularly rodents and lagomorphs) were implicated. The types of exposure were varied, including handling sick or dead animals, casual handling, skinning, and bite/scratch/lick or cough. Although rare (<1%), pneumonic plague was more frequent among patients with animal exposure, whereas proportions of bubonic and septicaemic plague were similar between patients with and without animal exposures
• probiotics are regularly given to patients in hospital for a variety of indications, though their use remains controversial. A study in 22,174 ICU patients found that those receiving *Lactobacillus rhamnosus* strain GG (LGG) probiotics had a significantly higher risk of developing *Lactobacillus* bacteraemia (6/522, 1.1% vs 2/21652, 0.009% in LGG non-recipients). Whole-genome analyses revealed that isolates from LGG-receiving patients and the LGG probiotic product were indistinguishable, and that diversity among blood isolates largely paralleled that in the probiotic product. While patients were seriously ill, they were not typical of those usually considered at risk of invasive *Lactobacillus* infections. The findings support a causal link between probiotics and *Lactobacillus* bacteraemia

• **Q fever outbreak associated with transport of pets in Spain**: there were 10 confirmed and 6 probable cases. Epidemiological and laboratory investigations identified Q fever in a quarter of the 180 investigated workers, and that two deliveries of miniature goats were the likely source. Dust samples collected from holding areas and throughout the premises were positive by PCR indicating extensive contamination. The genotype identified was that most commonly identified in goats and sheep in the Basque Country.

• **asymptomatic infection with severe fever with thrombocytopaenia syndrome (SFTS) virus** (SFTSV) was detected in a serological study in China. Blood samples from 1463 healthy individuals in a highly endemic area were tested by ELISA, PCR and virus isolation. SFTSV-specific IgG was detected in 10.46% (153/1463), 12 (0.82%) were IgM positive, and 6 of these also positive for SFTSV RNA. SFTSV was isolated from 5 of the 6 PCR positive samples. At one month follow-up, no IgM positive individual reported having had any symptoms compatible with SFTS. This is the first time that SFTSV has been isolated from otherwise healthy individuals; it is not yet known if such asymptomatic individuals can infect others

• despite widespread avian infections, few human infections with Usutu virus (USUV) have yet been reported. In Northern Italy, 1967 samples from suspected autochthonous arboviral infection collected during the annual West Nile virus (WNV) surveillance period in 2018 were tested for both WNV and USUV. There were 427 WNV and 8 USUV infections. Of these, 3 were PCR positive and 5 diagnosed by seroconversion and neutralising antibody detection. Six had a febrile illness, 1 had encephalitis, and 1 was a viraemic blood donor. In the 3 PCR positive individuals, USUV RNA persisted in blood and urine during the follow-up period (at least 30 days) Sequencing of two viruses showed over 99.9% sequence identity and clustering within the Europe 2 lineage

• **new UK yellow fever vaccine recommendations** to minimise risk in those with weakened immune systems, aged 60 years or older, or who have had thymus removal. These aim to ensure that only those at significant and unavoidable risk of yellow fever are offered vaccine, to avoid the risk of vaccine-associated viscerotropic and neurotropic disease