Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Overcoming the cost or logistical issues for the mass production of these vaccines is now urgent.

In conclusion, much progress has been made in control of meningococcal disease outbreaks in the meningitis belt of Africa. However, it is now evident that a monovalent conjugate vaccine is only a palliative solution and multivalent, protein conjugate or novel DNA vaccines are urgently needed in quantities that can be offered routinely to at least the most vulnerable people in this region. It is concerning that the clone that caused the recent outbreak of serogroup C disease originated from Nigeria, where poor vaccine acceptability for poliomyelitis has cost the world a great toll in eradication of this infection. It is prudent to pay particular attention now, given the size of the population at risk here, because without adequate control at this location we might have a cesspool for meningococcal genetic recombination for future outbreaks within the region.

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Zika virus and neurological disease—approaches to the unknown

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The early part of the 21st century has seen an unparalleled number of emerging infectious disease events: West Nile virus across the Americas, severe acute respiratory syndrome in China and beyond, chikungunya, avian influenza, Middle East respiratory syndrome coronavirus, Ebola virus. So many in fact that perhaps we should no longer consider them extraordinary.

The latest in this series of events is Zika virus (family Flaviviridae, genus Flavivirus), a mosquito-borne pathogen that was first isolated from a sentinel rhesus monkey in the Zika forest of Uganda in 1947, and identified in human beings in 1952. Since then there have been occasional reports of Zika virus infection in human beings in Africa and later in southeast Asia, characterised by the fever, arthralgia, and rash typical of many arthropod-borne viruses (arboviruses). Phylogenetic studies suggest the virus emerged in east Africa in the early part of the 20th century, later spreading to southeast Asia.[1] In 2007 there was a small outbreak in Yap, Federated States of Micronesia, and in 2013 a larger outbreak in French Polynesia, with 28 000 cases recorded in the first 4 months. Since the first reports of Zika virus infection in Brazil in early 2015,[2] its rapid and explosive spread has resulted in an estimated 1·5 million cases with 4 million predicted across the continent by the end of the year, and the declaration by WHO of a Public Health Emergency of International Concern.

Many mosquito-borne flaviviruses are zoonotic—for example, Japanese encephalitis virus and West Nile virus, being transmitted naturally among animals, with human beings coincidentally infected as dead end hosts. By contrast, Zika virus, like the four dengue viruses, is transmitted between human beings by mosquitoes. *Aedes aegypti* is the principle vector, although *Aedes albopictus* (the Asian tiger mosquito), which is also found in southern Europe and parts of the USA might play a part too. In Brazil the abundant numbers of *Aedes* spp mosquitoes and densely crowded populations of immunologically naive individuals have probably contributed to this unprecedented situation. Why an epidemic had not happened earlier, in the 60 years since Zika virus was first isolated, is unclear. It is probably simply because the virus had not arrived on the continent. Phylogenetic studies suggest the

Brazilian strain originated in the Pacific islands,[3] and a viraemic traveller to an international canoe racing event in 2014, which included Pacific nations as participants, is postulated to be the source.[3] For chikungunya virus, another arbovirus that has spread globally in recent years, the rapid spread was associated with a crucial change on the virus E2 envelope glycoprotein that increased its transmissibility by *A albopictus* mosquitoes enabling it to extend its range.[4] Preliminary data for Zika virus suggest South American isolates are almost identical to strains previously circulating in the Pacific region.

In the Polynesia Zika virus outbreak of 2013, an apparent increase in the incidence of Guillain-Barré syndrome was noted,[5] and this also seems to be the case in Brazil, although details are scant. It is important to distinguish this postinfectious or parainfectious syndrome from direct viral invasion of the anterior horn cells in the spinal cord, which causes a poliomyelitis-like flaccid paralysis that is usually irreversible.[6] The number of children reported born with microcephaly has also risen in Brazil, and Zika virus has been detected in amniotic fluid, placental, or fetal tissue in babies with nervous system malformations, including those stillborn or with microcephaly.[7] Abnormalities seen on CT scans include calcification in the periventricular parenchyma and thalamic areas, and ventriculomegaly, lissencephaly, and pachygyria—the smooth brains with reduced gyral ridges suggestive of cell migration abnormalities and first trimester problems. Although strongly suspected, the causal relation between in-utero exposure to Zika virus and microcephaly is yet to be established.[8] Infection in pregnancy might also result in infants born without microcephaly, but with more subtle neurological and developmental abnormalities. The potential for Zika virus transmission in semen and through blood transfusions is causing additional concern.

Several theories have been put forward to explain these new observations of neurological complications. Could they relate to a high background prevalence of antibodies against related flaviviruses, for example, after dengue infection, or yellow fever vaccination—an antibody-dependent enhancement process similar to that seen in secondary dengue infection? Does the microcephaly relate to toxins or nutritional deficiencies? Are these simply rarer manifestations of the disease, which have now been recognised because there are hundreds of thousands of infections? Zika virus is similar to dengue in that most patients develop a syndrome of fever and rash, and there are many unrecognised infections. For dengue, controversy over apparent neurological manifestations existed for more than 80 years, until a well designed case-control study carefully excluded other possible explanations of neurological disease, and proved a definitive link;[9] a whole range of neurological complications are now recognised.[10] Similar rigorous approaches are needed for Zika virus disease, as well as improved diagnostic techniques.

The only intervention available for Zika virus is mosquito control, which, for *Aedes* spp mosquitoes, is notoriously difficult to sustain. The full range of mosquito vectors for Zika virus is not yet clear. Growing resistance to insecticides is an important issue, and breeding site destruction and the prevention of bites might be better ways forward. Unlike Ebola virus, for which there were vaccines on the shelf awaiting clinical evaluation, for Zika virus the cupboard is bare—although investigators are working hard to fill it. Understanding the range of neurological disease in Zika virus infection is important not just for the individuals affected, but also to support policy decisions. Experience with Japanese encephalitis in Asia has shown that development of a vaccine is not enough: policy makers need to understand the burden of disease to help to guide vaccine implementation.[11] This development and implementation will be some years off. For now there is an urgent priority to understand the scale and full range of neurological disease associated with Zika virus infection.

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Corrections

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