ZIKA VIRUS: THE STORY SO FAR
ON 1 FEBRUARY 2016, the WHO declared the Zika virus, and its potential connections with the rise in congenital malformations and neurological complications, a public health emergency. Transmitted primarily through the bite of infected Aedes mosquitos, Zika has spread across 62 countries and territories. Around one in five people infected with Zika become ill, and the most common symptoms are considered mild and flu-like, lasting from a few days to a week. Yet concerns about Zika were raised in 2015, when the virus rapidly spread across the Americas alongside increased reported cases of microcephaly and Guillain-Barré syndrome.

ZIKA’S SPREAD
The Zika virus was first identified in Uganda’s Zika forest in 1947, when scientists were conducting routine checks for yellow fever in rhesus monkeys. Nearly a decade later, Zika was proven to cause human disease. It was later found in both rhesus monkeys and mosquitos across a strip of equatorial Africa – although human contraction was rare and caused only mild symptoms. The virus then spread through equatorial Asia – but, still, no outbreaks of the disease were detected.

It wasn’t until 2007 that the first significant Zika outbreak was observed in Micronesia, followed by several other outbreaks in four other groups of the Pacific islands in 2013-14; of particular concern was the outbreak in French Polynesia, where thousands of suspected infections were reported.

Soon after, Zika hit Brazil – the first country in the Americas to have confirmed cases. Exactly how the virus entered South America is not known, though it has been suggested that the virus may have been brought to Rio, Brazil, during the 2014 World Cup’s Canoeing Championships, which involved many competitors from the Pacific Islands. The number of reports in Brazil continued to grow throughout 2015, and alarm bells started to ring when the virus began to spread through Latin America at an unprecedented speed.

On 2 February 2016 – the day after WHO declared Zika and its complications a public health emergency – the first case of sexual transmission of the disease in the US was reported. Since, many travel-associated cases of Zika have been found throughout the US and are expected to increase, particularly in the summer months, which could lead to local mosquito-borne transmission of the virus.

MICROCEPHALY AND GUILLAIN-BARRÉ SYNDROME
Since 2015, concerns have been raised about Zika’s potential association with both microcephaly and Guillain-Barré syndrome, but scientific consensus on the link had not been
confirmed until recently. WHO’s Zika situation report on 7 April 2016 states: “Based on a growing body of preliminary research, there is scientific consensus that Zika virus is a cause of microcephaly and Guillain-Barré syndrome”.

Microcephaly is a rare neurological condition in which an affected infant has a shrunken head and damaged brain. The virus’ association with the development of microcephaly in the babies of affected pregnant women is a significant issue – a recent study has shown that there is roughly a 1 in 100 risk of microcephaly. Since the virus is spreading so quickly across the Americas, the number of Zika-affected microcephaly cases could be vast.

The post-viral Guillain-Barré syndrome causes the immune system to damage nerve cells. As of April 2016, an increase in the syndrome has been observed in 13 countries or territories affected by Zika, some of which have laboratory confirmation of cases in which individuals with Guillain-Barré are also infected with Zika.

RESEARCH TO TACKLE ZIKA
WHO has placed Zika in the same category of concern as Ebola, which means that research and aid is being fast tracked to help fight the infection. The UK’s investment in research on Zika has recently increased from £1 million to £4 million. An additional £2 million has been added by the UK Government, alongside a further £1 million from the Wellcome Trust. Funded projects include the development of an online database that will allow scientists from across the world to analyse visual information available and a study on Zika’s link with birth defects.

“This government’s decision to invest in science and innovation and protect science spending means we are able to react to emerging global threats like the Zika virus and allow the world class scientists we have here in the UK to conduct groundbreaking and potentially life-saving research,” stated Universities and Science Minister, Jo Johnson. “By increasing this funding, and with the support of the Wellcome Trust, more of this vital work can now get started”.

In the US, the National Institute of Allergy and Infectious Diseases (NIAID) arm of the National Institutes of Health (NIH) has classed Zika virus research as a high priority. While studies on Zika are only just underway, already the structure of the virus has been determined to be very similar to that of dengue and other flaviviruses, with the exception of a key surface protein. This finding may enable better understanding on how Zika enters human cells and help with drug and vaccine development.

ZIKA RESEARCH: STARTING FROM SCRATCH

Jimmy Whitworth, Professor of International Public Health, London School of Hygiene & Tropical Medicine

Although many governments are now classing Zika virus research as a high priority, few studies have been done on Zika in the past. Why is this the case?

Although there have been isolated outbreaks in Africa, Southeast Asia, Micronesia and French Polynesia, the Zika epidemic in Brazil caught the world by surprise. There has been very little research done on Zika as it was seen as a virus of little public health importance. Just one in five people show symptoms, which are normally mild: malaise, rash, low fever, itching and red eyes. Only very recently have we suspected Zika may cause congenital infections and microcephaly.

What are the key challenges faced with conducting this research?

One of the key challenges for researchers studying Zika is the lack of knowledge we have about the virus (although this is changing quickly). In many ways, we have started from scratch. We also need volunteers to enrol so that we can conduct crucial large cohort studies and, understandably, pregnant women in epidemic areas may be reluctant to take part. Microcephaly is
a devastating condition for parents to come to terms with, and researchers must be prepared to handle emotional situations.

We also do not yet have rapid near-patient tests that reliably diagnose Zika infections. There is a lot of cross-reactivity with other related viruses, such as dengue, that are common in Brazil, and tests are not sensitive enough to pick up acute infections for more than a few days. It is difficult to do accurate epidemiological studies without a clear and consistent case definition, and a good diagnostic test would help this enormously.

**What are the implications of the association between microcephaly and Zika?**

The link to microcephaly has not definitely been proven, but there is strong scientific consensus that the link exists. Zika itself is only a mild virus, so the focus should be on preventing microcephaly in babies. Pregnant women, or women wanting to get pregnant, should heed Public Health England’s advice, which currently includes the recommendation that pregnant women should postpone non-essential travel to areas with active Zika transmission until after pregnancy.

**While the development of a safe and effective vaccine is still years away, what action needs to be taken to try and curb the spread of Zika?**

Controlling Zika depends on the management of mosquitoes. Currently this relies on either insecticides or destroying breeding sites, but due to widespread insecticide resistance and the impracticality of eliminating standing pools of water on a city-wide scale, these methods are unlikely to work on their own. Other options therefore need to be considered.

WHO’s support for GM mosquito trials is encouraging, as controlling future Zika outbreaks will require integrated vector management strategies that complement current methods.