

From 1976 to 2018: Reflections on early investigations into the Ebola virus

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In 1976, at the microbiology lab at the Institute of Tropical Medicine in Antwerp, Belgium, one of the authors received a package from Kinshasa, Zaire (now Democratic Republic of Congo (DRC)): a blue thermos flask containing a blood sample from a Belgian nun who had fallen ill from a mysterious, unidentified disease. The disease was spreading in the Equateur region along the Zaire river and the working hypothesis for the epidemic was “yellow fever with haemorrhagic manifestations”(1). After isolating and observing the virus, it was soon determined that the mysterious illness was not yellow fever but rather what appeared to be a Marburg-like virus, recognition of which led the team to inform the World Health Organization (WHO). Shortly thereafter, the WHO instructed the lab to transfer ~~all the~~ specimens to the Microbiological Research Establishment at Porton Down, United Kingdom, which, unlike the lab in Antwerp, had a maximum containment unit for highly pathogenic viruses. While ~~deciding to retain~~ ~~retaining~~ some specimens in Antwerp (1), the team shared the materials with Porton Down, some of which were later sent to the Centers for Disease Control and Prevention in Atlanta, United States. Laboratory investigations carried out in Antwerp_(2), Porton Down_(3), and Atlanta_(4) observed and cultured filoviruses by electron microscopy, and serological testing in Atlanta identified a new virus, which was later called Ebola (5). Working in harmony with their Zairean colleagues, in particular Professor Jean-Jacques Muyembe, across their respective labs, and with affected communities, the 1976 outbreak in Yambuku was contained in just under 11 weeks. ~~In~~ ~~By~~ an ~~amazing-unexplained~~ coincidence, around the same time, there was an outbreak of Ebola virus infection (Sudan strain) in South Sudan (5).

Together, this work informed the world’s understanding of what was then an unknown, and deadly, virus. Indeed, one particularly impactful study conducted during this time was published in *Transactions of the Royal Society of Tropical Medicine and Hygiene* by E.T.W. Bowen, G.S. Platt, D.I.H Simpson, L.B. McArdell, and R.T. Raymond in 1978, called “Ebola haemorrhagic fever: experimental infection of monkeys”(6). The team at Porton Down found that when infected with the Ebola virus, rhesus and vervet monkeys presented with symptoms that closely resembled those experienced by humans, which uniformly resulted in a fatal illness. This study demonstrated for the first time that non-human primates could improve our understanding of a disease that just two years earlier had evaded identification. Importantly, it showed that rhesus monkeys would be suitable to study both the pathogenesis of the virus and new vaccines or therapies for use in humans, thereby laying the foundations for future research into the prevention and treatment of a virus that had just claimed the lives of more than 300 people around the village of Yambuku. While the scientific research methods used in this study are unlikely to have been approved by research ethics councils today(7), its findings undoubtedly helped shape our knowledge of the virus.

While we reflect on great scientific discoveries and advancements in our understanding of the Ebola virus, we must also ask why, nearly four decades later, were there no approved drugs, no vaccines, and no diagnostic tests for Ebola when the outbreak began in West Africa? 38 years after its discovery, control efforts remained largely the same in 2014 as they were in

the 1970s, and with tragic consequences. Despite warranting a vaccine much earlier, Ebola was not a particularly attractive disease for investment by either the pharmaceutical industry or the public sector, as it largely affected relatively small populations in remote areas across Africa. There were many shortcomings in the local and global response to the devastating 2014 Ebola outbreak in West Africa (8); however, a silver lining was that, for the first time, biomedical and social science research was conducted during the outbreak, including on experimental therapies and vaccines. The London School of Hygiene & Tropical Medicine has been involved in the evaluation of such experimental vaccines from Merck and Janssen, two companies that have invested heavily in these products, with the support of the European Union's Innovative Medicines Initiative, the United States' Biomedical Advanced Research and Development Authority, and the Wellcome Trust. A ring vaccination trial in Guinea showed that the rVSV-ZEBOV vaccine, which was originally developed in Canada, offered maximal impact on the spread of the Ebola virus amongst contacts of patients with the disease (9).

Encouragingly, as the current Ebola outbreak unfolds in DRC, we are seeing what appears to be a major paradigm shift amongst the global health community. Alongside DRC health officials' strong track record of controlling Ebola outbreaks, there has been a swift and rigorous response from the international community. For the first time, Merck's rVSV-ZEBOV vaccine has been deployed on the ground, although its contribution to containing this outbreak is not yet clear ~~yet~~. We are seeing first-hand how research has translated into the availability of critical tools and to a better understanding of how to meaningfully engage affected communities in response activities. Although the outbreak appears to be abating (10), we must remain vigilant in our efforts until it is controlled.

While the Ebola virus will certainly remain a challenge in the future, it is through cutting-edge research like Bowen and colleagues' study that we can ensure we are informed by the best evidence, from clinical to social sciences, to better prevent and control future outbreaks. Critically, as we learned from the epidemic in West Africa, we need to make sure that this research is translated into policy and action on the ground, with the full participation of ~~African~~ scientists and policy makers in affected regions in setting the research agenda. Over 40 years after its discovery and after devastating consequences, we are now seeing encouraging progress in response efforts to control the current outbreak in DRC.

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