Sleepwalking into the next pandemic

Governments and funders must prioritize research on emerging and re-emerging infectious diseases such as monkeypox to prevent another pandemic.

In 2019, a little over 1,000 academic articles were published on coronaviruses; this increased to 250,000 articles 3 years later. It is unsurprising that research should increase on a virus that killed millions, but coronaviruses were well known to have pandemic potential, having jumped twice from animals to humans in the twenty-first century, causing severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). There have been no known SARS-CoV cases since 2004, but MERS-CoV still causes occasional human cases, with a high mortality rate in the Eastern Mediterranean region.

What little research was carried out on coronaviruses between the time of SARS and COVID-19 unquestionably saved lives. The ChAdOx1 (Oxford–AstraZeneca) vaccine and Pfizer's antiviral agent Paxlovid were developed for MERS and SARS, respectively, and then were quickly repurposed for SARS-CoV-2. Much more coronavirus research could and should have happened in the 15-year period after SARS — and now the same mistakes have been made with monkeypox.

Since the 1970s, monkeypox virus, an orthopoxvirus related to smallpox, has sporadically jumped from animals to humans, with most recorded cases in Western or Central Africa. In 2017 an outbreak spread in the Niger Delta after a 40-year absence in Nigeria. Orthopoxvirus research dropped off the cliff after the eradication of smallpox — funding that should have re-started when monkeypox emerged in Nigeria in 2017, or before.

Now that there are more than 3,400 new human cases of monkeypox in at least 40 countries (at the time of this writing), and one death, research is finally accelerating, but many questions remain unanswered. The animal reservoir seems to be mainly rodents (not monkeys), but the relative importance of squirrels, rats and mice is unclear. Vaccines against smallpox are assumed to be effective, but this is based on a single study, and more recent data are lacking. The antiviral agent tecovirimat (approved for smallpox) is now approved for monkeypox in the European Union and United States, but its efficacy was initially shown in only a single patient. Large-scale sequencing of the virus, which may explain why it is now transmitting from person to person, has identified mutations, but their importance is as yet unknown.

The lack of research on monkeypox, despite hundreds of cases and dozens of deaths annually, has left the world woefully unprepared for this global outbreak. Every zoonotic infection should be a cause for concern, but research funding seems to flow only when high-income countries are heavily affected. It took 11,310 tragic deaths from Ebola virus in Guinea, Liberia and Sierra Leone before vaccine trials began in Guinea in 2016 — with a vaccine that is now an essential component of responses to Ebola. Dengue virus causes millions of cases and thousands of deaths each year in more than 100 countries, but the one approved vaccine is recommended only for those who have had a previous infection, which limits its usefulness. If dengue cases start to increase in the United States and Europe, which may well happen because of climate change, research will no doubt increase. This mirrors the inequity seen during COVID-19, when low- and middle-income countries were last in line for vaccines and antiviral agents.

Governments and funders are sleepwalking toward another pandemic unless they boost research and development (R&D) on emerging infections. Funding should flow directly to the sites of outbreaks, especially in low- and middle-income countries. This will not only boost research infrastructure in disease hotspots but also help to ensure that research reflects local priorities, rather than neo-colonialist attitudes, which remain all too prevalent in global health. R&D should include disease surveillance, genome sequencing, vaccine development and research on antiviral agents.

Some progress has been made — but not enough. The World Health Organization (WHO) has an R&D blueprint for emerging infectious diseases, including Ebola, Marburg, Crimean-Congo hemorrhagic fever, Lassa fever and Nipah, that includes research priorities for diagnostics, therapeutics and vaccines. The WHO has also established a new Hub for Pandemic and Epidemic Intelligence in Berlin; several governments and funders have also announced their own pandemic intelligence centers, including a joint effort between the United Kingdom and United States. Every country should have a blueprint for pandemic preparedness research.

Investment in R&D gives a return on investment of as much as a 20%, as well as helping to prepare for epidemics and pandemics. India's investment in vaccine production before COVID-19 reduced its reliance on imported vaccines. South Africa's genome-sequencing capacity warned the world of new SARS-CoV-2 variants. Most countries have invested in crucial laboratory diagnosis and sequencing capacity for SARS-CoV-2, but many labs are now being dismantled, with ensuing staff cuts. Countries should instead invest in their public health workforce, as this not only improves population health but also boosts the economy: a healthy worker is a productive worker. Disease-surveillance infrastructure should be maintained and pivoted to other diseases, in order to track viral mutations, monitor antimicrobial resistance and identify emerging infections. Countries such as Brazil that are maintaining their disease-surveillance capacity as SARS-CoV-2 cases decrease will reap the benefits of new scientific discoveries (including viruses of pandemic potential), a highly skilled workforce, investment in their biotech and pharmaceutical industries, and economic growth.

Surveillance forms part of a One Health approach, an old idea that is gaining fresh traction, and that African countries endorsed in 2021. One Health unites environmental, animal and human health so that farmers, veterinarians and grassroots community activists are trained to be alert to the signs of any new outbreak, often using apps and smartphones in the field. The WHO is well placed to support disease surveillance in low- and middle-income countries, but much of the WHO's emerging infection research relies on voluntary contributions — funders should give more.

Epidemics and pandemics can be prevented if research capacity is boosted for emerging infections between outbreaks, especially disease surveillance in low- and middle-income countries. There is no excuse for failure. ❐

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