The viral arms race

To keep ahead of an increasing number of SARS-CoV-2 variants, pathogen surveillance and testing must become a joined-up global, rather than local, endeavor.

An arms race is underway between SARS-CoV-2 and the world's population. While governments rush to vaccinate as many people as possible, the virus is rapidly evolving escape mutants. In India, Latin America and Africa, new viral variants are starting to dominate infections. Many countries, such as the United Kingdom, Denmark and the United States, have ramped up sequencing capacity, enabling public health agencies to monitor the prevalence of highly transmissible variants, update diagnostic primer designs and inform the development of future vaccine booster and multivalent shots. As nations strive to open their economies and relax travel restrictions, it is an attractive and important notion that rapid integration of sequencing and testing might rationally guide public health policy and countermeasures. In some places, it may even work. But globally, the notion is more dream than reality.

After about ten months of relative quiescence at the start of the pandemic, SARS-CoV-2 has been shifting shape. Mutations are arising largely through errors by the virus's RNA-dependent RNA polymerase. Recombination between different strains in a single co-infected person or via zoonoses (transmission between animals and humans and vice versa) are also contributing. Although most variants acquire just one or two new mutations, in rare cases—perhaps due to chronic low-level infections or immune suppression—multiple mutations may recombine in a single isolate (as in the case of B.1.1.7 or B.1.1.28 subclade P.1).

Other than D614G-bearing viruses, few SARS-CoV-2 variants were detected during the early months of 2020, probably because of a lack of selective pressure and insufficient surveillance. While the original viral lineages spread like wildfire across an immunologically naïve world, selective pressure on the virus has risen as more people acquire partial immunity (from natural infections or, more recently, from vaccination). Today, thousands of variants are circulating in hundreds of thousands of infected people across the globe.

Many of the details of SARS-CoV-2 variant evolution, phylogeny and annotation are still being worked out. At the end of February, the World Health Organization provided formal definitions for 'variant of interest' or 'variant of concern' (VOC): the former is a "virus containing phenotypic changes" and non-synonymous mutations compared with the reference isolate; the latter, a virus displaying "increased transmissibility," "detrimental change in COVID-19 epidemiology" or "increased virulence or other change in disease presentation" or resulting in decreased "effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics."

USA-WA1/2020, containing D614G, quickly became the dominant form. Since then, several VOCs have been identified, including B.1.1.298 in Denmark (linked to infection among farmed mink), B.1.1.7 in the United Kingdom, B.1.1.248 (P.1) in Brazil, B.1.351 in South Africa and B.1428/B.1429 in the United States. Denmark and Britain have played prominent roles in VOC identification, with both countries having established pathogen surveillance consortia (COG-UK and TestCenter Denmark) and national public health systems capable of facilitating clinical sample and data sharing. According to GISAID, Denmark has sequenced and shared 20% of its total COVID-19 samples; the United Kingdom, 9%.

In contrast, the United States has lagged behind. From June to December, the US Centers for Disease Control's (CDC) SPHERES network and NS3 program shared 4,000 or fewer SARS-CoV-2 genomes with GISAID every month. At the end of the year, US pathogen surveillance ranked an abysmal 43rd in the world.

Part of the problem is the fragmented US healthcare system overlaid on over 60 overworked and balkanized state and local public health agencies acting like independent fiefdoms. Another challenge is the lack of any federal mandate or funding to incentivize commercial labs to sequence COVID-19 samples. Finally, rigid US patient privacy requirements have slowed sharing of data associated with samples to a glacial pace.

Since the turn of the year, however, the CDC has turned things around. By early February, 5,000–8,000 coronavirus samples were being processed per week, and last month the United States shared ~44,000 sequences in GSAID—more than any other country. A new US president triggered a massive injection of federal funding, making $1.7 billion available to track viral mutations, create six academic "centers of excellence" for R&D and establish a national data-sharing network. All of which leaves SARS-CoV-2 surveillance on a firmer footing than at any time.

But there are still reasons for concern and vigilance.

Currently, it takes too long to get sequencing results back to state and municipal agencies; and for the United States, this means that there is still no window for meaningful public health action to control potential clusters or transmission, especially when some VOCs reduce vaccine efficacy and compromise approved antibody treatments.

Second, while regional and national surveillance efforts are improving, too little is being done to coordinate SARS-CoV-2 tracking internationally or to fill obvious gaps in surveillance in poorer countries. Spot checks in health facilities across 24 African countries revealed only 8% of health facilities can conduct PCR tests, let alone sequencing. The massive surge in India and lack of surveillance on the ground makes the need all too clear.

Finally, there is danger from public complacency and pandemic fatigue. In April, 1.36 million people passed through US airports in one day and CDC guidance on masks was relaxed. Despite rapid progress in vaccine immunizations in the United States, uptake is stalling. Worse still, millions are not turning up for their second vaccine shot, maintaining a pool of partially immune incubators for SARS-CoV-2 escape variants. As the virus recedes from TV and smartphone screens, the impetus for testing is dwindling just when the need to monitor variants is more important than ever.

Now is the time to act. And it is time to act internationally. No national pathogen surveillance network can be effective if new VOCs are constantly imported from the rest of the globe. Investment in global surveillance is critical to any hope of ending or controlling the pandemic. ❐

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