



Operational intricacies of sequencing-based surveillance in developing countries

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The recent COVID-19 pandemic highlights the concept of a sentinel event as an important implement for the prevention and analysis of the root causes of an emerging virus. As noted by Hu and colleagues in their manuscript on “*Implementing sequencing-based surveillance in developing countries: findings from a pilot rollout for hepatitis A in China*”, the efficiency of a traceback investigation for a common-source exposure is facilitated by identifying identical sequence patterns and overlapping epidemiologic characteristics. The complexities of a viral outbreak vis-à-vis early detection and management are compounded by geography and temporal trends (time/space), with sequencing-based surveillance revealing the virologic links among sporadic cases—thus advancing the ability to detect and mitigate undesirable effects by weeks to months. To this extent, sequence-based surveillance provides direct and indirect clues about the rate of viral progression, aids the understanding of transmission routes, and informs therapeutic implications downstream to the evolving nature (variants) of the virus. For example, the previously unknown betacoronavirus, now known as 2019-nCoV (a clade within the subgenus sarbecovirus, Orthocoronavirinae subfamily), was detected by unbiased sequencing of human airway epithelial cells in samples from patients with pneumonia (1). Sequencing also was instrumental in identifying the mutation of a surface spike protein that mediates SARS-CoV-2 entry into cells (2). Comparable sequencing of hepatitis A virus (Picornaviridae family) has played a pivotal role in improving preparedness and rapid response in recent

outbreaks (3).

The cross-species emergence of viruses from animal vectors to humans reflect their genetic diversity, recombination activity, as well as other factors including climate change and proximity of new construction to native species habitats (e.g., zoonotic transmission, ecological and environmental mechanisms). The constant antigenic modification of viruses and potential for human harm merit the implementation and refinement of sequencing-based surveillance program utilizing next-generation technology (4). In the post COVID-19 context, wherein influenza has largely remained dormant during the pandemic, the emergence of new strains poses a public health concern, especially among younger age groups who have not developed natural immunity to influenza during this void. Unfortunately, many underdeveloped regions of the world do not have the bioinformatics capabilities and trained personnel to readily analyze virus genomic data. The need for well-developed sequencing efforts further coincides with the increasing use of antiviral agents and the information derived about antiviral resistance or reduced susceptibility (e.g., neuraminidase and matrix gene segments) (5). Over the past decade, increased access to open-source genetic databases and advanced bioinformatic tools has in part eased the transition to sequencing-based surveillance (6).

There are many lessons to be learned about the operational intricacies of sequencing-based surveillance in developing countries, as illustrated in this pilot rollout for

hepatitis A in China. The authors are to be applauded for their informative manuscript.

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