

# The Novel Adenovirus: A Call for Advances in Health Infrastructure and Pandemic Preparedness

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Over the past several months, more than 500 cases of acute severe hepatitis of unknown origin have been reported worldwide.<sup>1</sup> Documented cases among youth 1 month to 16 years old have presented with severe gastrointestinal symptoms and acute hepatitis (non-hepatitis A-E), along with markedly elevated liver enzymes. While the exact origin remains uncertain, World Health Organization public health experts hypothesize that the emergence of a novel adenovirus may be the cause of these hepatitis outbreaks.<sup>2</sup> Meanwhile, the nation's top infectious disease expert, Dr Anthony Fauci, stated that "We are certainly right now in this country out of the pandemic phase" in an April 2022 televised interview in reference to COVID-19.<sup>3</sup> While this information may be assuring after more than 2 years of enduring the pandemic, it also serves as a potential threat to our nation's public health. This announcement may signal to health systems that now is the time to reduce precautions toward pandemics, potentially leaving our nation susceptible to future outbreaks beyond the current adenovirus.

Despite the turmoil caused by the COVID-19 pandemic, we have built significant health infrastructure to combat future biothreats. Indeed, health infrastructure expenditures grew in 2020 at the fastest rate since 2002, and spending on health care increased by 36.0%.<sup>4</sup> The research and development of vaccines have been streamlined, enabling the production of 2 vaccines against COVID-19 from Pfizer-BioNTech and Moderna at an unprecedented rate. In addition,

the Biden administration has established a senior position on global health at the National Security Council to formulate international strategies to distribute vaccines and combat the spread of COVID-19. More broadly, Congress recently passed the Build Back Better Act, which is a comprehensive programmatic package aimed at supporting pandemic preparedness by enhancing disease surveillance and contact tracing, expanding medical education, and increasing funding for medical equipment.<sup>5</sup>

However, recent public health messaging regarding the waning of the pandemic risks is diminishing this robust health infrastructure developed over the past 2 years. The effects of loosening pandemic preparedness are evident by examining recent measles outbreaks, with cases surging by nearly 80% worldwide in 2022 due to disrupted childhood vaccinations during the COVID-19 pandemic.<sup>6</sup> Moreover, the effects of failing to prepare for a possible pandemic altogether are demonstrated through monkeypox. The virus has rapidly spread to countries worldwide in recent months, and the 40 000 confirmed cases are in part attributed to Western countries having "largely ignored" warnings from African researchers for years.<sup>7</sup>

Inevitably, the end of the COVID-19 pandemic will be followed by the beginning of another one—if not from the current adenovirus, measles, or monkeypox, then potentially from other pathogens—and we must be prepared for it. The absence of continually maintained health infrastructure enables disease to spread and cause havoc. As such, we urge public health experts to utilize the emerging outbreak of acute severe hepatitis as a signal not to reduce pandemic mitigation measures but rather to use this time of relative stability to greatly stockpile and enhance them. In particular, we advocate for advancing diagnostics and therapeutics, building a robust data infrastructure, preparing domestic pandemic response workforces, and combating misinformation as key priority areas for public health agencies in the coming months and years (Table).

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**TABLE**

**Interventions and Mechanisms of Change**

Intervention	Mechanisms of Change
Advancing diagnostics, therapeutics, and vaccines	<ul style="list-style-type: none"><li>• Diagnostic production facilities must be established nationwide and be prepared to roll out versatile diagnostics so that the spread of a microbe can be monitored from the start.</li><li>• Taxpayer dollars must be allocated to continually fund research into antimicrobial drugs and vaccines to prepare for an adenovirus or alternative biothreat pandemic.</li></ul>
Data infrastructure for public health	<ul style="list-style-type: none"><li>• Health facilities must use integrated, real-time data on infections, hospitalizations, deaths, and immunizations to track the spread of a biothreat.</li><li>• Health facilities must employ registries and health information exchanges for seamless transfer of data between health systems to allow greater consistency in reporting and help locate at-risk or disproportionately affected regions.</li></ul>
Domestic pandemic-response workforces	<ul style="list-style-type: none"><li>• 911 calls must be scanned for pandemic-related emergencies, and community paramedics and EMTs trained in virus-response protocols must be dispatched to provide appropriate out-of-hospital treatment to patients.</li><li>• Paramedics and EMTs must consult with patients' primary care providers about underlying health concerns that may leave a patient at risk of severe infection, necessitating immediate transport to the emergency department.</li></ul>
Combating misinformation and consistent messaging across public health agencies	<ul style="list-style-type: none"><li>• Public health agencies across the city, state, and federal levels must consult with one another to maintain consistent messaging.</li><li>• Primary care providers must serve as disseminators of accurate information for the public.</li></ul>

Abbreviation: EMT, emergency medical technician.

### Advancing Diagnostics, Therapeutics, and Vaccines

Versatile diagnostics have proven to be crucial during the COVID-19 pandemic. With their varying levels of sensitivity, ease of use, cost, and response time, the 3 major methods for detecting SARS-CoV-2 (PCR, antigen rapid detection, and antibody tests) have enabled health experts to precisely track COVID-19 in the human population.<sup>8</sup> Although adenoviruses can also be detected using a variety of methods, our health facilities must be prepared to roll out these diagnostics at a large scale in the event of an adenovirus pandemic. Diagnostic production facilities must be established throughout the country to be prepared for any emergent biothreat so that its spread can be monitored from the start.

Currently, no approved antiviral therapies specific to adenovirus infections exist. In most cases, severe adenovirus infection is treated with broad-spectrum antivirals such as cidofovir and ganciclovir, which are often nephrotoxic and only effective at high serum concentrations.<sup>9</sup> Given the current outbreak and the threat to pediatric populations—10% of whom have required liver transplantation—research into therapeutics must be expedited. Current research focuses on drug candidates that target the adenovirus replicative cycle, but progress remains slow due to difficulty identifying viable animal models and drug screening platforms.

Although a vaccine specific for adenovirus types 4 and 7 is approved for US military personnel, there

is currently no adenovirus vaccine available to the general public. Years of previous research on related viruses and multibillion-dollar government funding that allowed firms to run multiple trials in parallel allowed the country to see vaccines against COVID-19 within 1 year.<sup>10</sup> To maintain such a rapid vaccine development process would require taxpayer dollars to continually fund vaccine research and development in preparation for an adenovirus or alternative biothreat pandemic.

### Data Infrastructure for Public Health

Since the start of the COVID-19 pandemic, US states have used different approaches to track COVID-19 cases and hospitalizations, complicating efforts to monitor the spread of the virus.<sup>11</sup> The United States must use advances in technology and modern data science to improve disease surveillance. During the COVID-19 pandemic in Louisville, Kentucky, the city's LouieSTAT program helped aggregate COVID-19 data with demographic and geographic metainformation, allowing government officials to efficiently track the virus while also revealing disparities in COVID-19 health outcomes.<sup>12</sup> While such data infrastructure can be transformative for communities, US states have used different approaches with varying efficiencies to track COVID-19, and the inconsistency has complicated disease surveillance. Integrated, real-time data on infections, hospitalizations, deaths, and immunizations will be needed

to track the spread of the adenovirus in the event of a pandemic. Local health facilities must collect data within their designated counties and employ registries and health information exchanges for seamless transfer of data between health systems. These facilities can then share health information with state- and national-level health care systems, allowing greater accuracy in reporting. Surveillance data will help locate sociodemographic regions most affected by the adenovirus, therefore informing officials of public policies to implement. At-risk or disproportionately affected regions may be supplied with increased health equipment and resources to combat the adenovirus. In addition, quarantining and lockdowns may be designated only for specific towns or cities where the spread is most severe, as opposed to national shutdown policies as in the COVID-19 pandemic.

### Domestic Pandemic-Response Workforces

Pandemic-response workforces must be prepared with the flexibility and surge capacity to manage a potential adenovirus pandemic. With hospitals reaching full capacity and health workers being overworked throughout the COVID-19 pandemic,<sup>13</sup> the necessity for a team of out-of-hospital health professionals capable of treating infected individuals is clear. Community paramedic operations must be expanded to serve pandemic mitigation purposes. 911 calls can be scanned for hepatitis-related emergencies, and paramedics and emergency medical technicians trained in adenovirus-response protocols can be dispatched to patients. These prehospital health professionals can then provide oxygen therapy and other appropriate treatments to treat individuals outside the hospital, reserving the emergency department for only the most severe cases. These professionals can also consult with patients' primary care physicians about underlying health concerns that may leave a patient at risk for severe adenovirus infection.

### Combating Misinformation and Consistent Messaging Across Public Health Agencies

Throughout the COVID-19 pandemic, the public has been bombarded with misinformation from unreliable sources. One of the most significant drivers of public attitudes about COVID-19 was President Donald Trump's social media posts, which often contained false information about the virus being a "hoax."<sup>14</sup> Ultimately, misinformation led to public distrust of advice from public health officials, including the importance of COVID-19 vaccinations. To prevent misinformation regarding the ongoing adenovirus

outbreak, we recommend public health agencies across the city, state, and federal levels consult with one another to maintain consistent messaging. In addition, there is an opportunity for primary care providers to serve as disseminators of accurate information and necessary therapeutics for emerging outbreaks, given Americans' substantial trust in their doctors.

### Conclusion

COVID-19 has promoted significant improvements to our nation's health infrastructure. With the end of this pandemic in sight, legislators may decrease health care funding and ultimately turn their attention away from building strong tactics for pandemic mitigation. This comes at a particularly dangerous time with the outbreak of the novel adenovirus. We urge the Biden administration and public health officials to continue building a robust health infrastructure by advancing diagnostics, therapeutics, and vaccines; utilizing data infrastructure for disease surveillance; developing domestic pandemic-response workforces; and maintaining consistent messaging across public health agencies.

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