

Leveraging a preexisting global infectious disease network for local decision-making during a pandemic

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Summary: Using the COVID-19 pandemic, we demonstrate the value of leveraging established international clinical collaborations during health emergencies to accelerate best practice development and inform rapid clinical decision-making at a time when information and evidence are frequently evolving or absent.

Abstract

Emerging infectious disease epidemics require a rapid response from health systems; however, evidence-based consensus guidelines are generally absent early in the course of events. Formed in 2017 by five high-level isolation units spanning three continents, the experience of the Global Infectious Disease Preparedness Network (GIDPN) early in the course of COVID-19 provides a model for accelerating best practice development and improving decision-making in health emergencies. The network served as a platform for real-time, open and transparent information-sharing during unknowns of an active outbreak by clinicians caring for patients, by researchers conducting clinical trials and transmission and infection prevention studies, and by teams advising local and national policymakers. Shared knowledge led to earlier adoption of some treatment modalities as compared to most peer institutions and to implementation of protocols prior to incorporation into national guidelines. GIDPN and similar networks are integral in enhancing preparedness for and response to future epidemics/pandemics.

Keywords: COVID-19; communicable diseases, emerging; disease outbreaks; health emergencies; clinical networking

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Background

Emerging infectious disease epidemics require health systems to respond rapidly to reduce morbidity and mortality in the ill, prevent ongoing nosocomial and community transmission, and preserve the functional ability to deliver care; however, evidence-based consensus guidelines are generally absent early in the course of events. During the first wave of COVID-19 in the spring of 2020, hospitals' approaches to clinical management and infection prevention and control (IPC) practices varied widely, but as evidence and best practices accumulated, outcomes significantly improved over time [1]. Earlier elucidation of best practices could have markedly reduced the extent and impact of COVID-19 spread in the spring wave, and future preparedness approaches should focus on mechanisms for achieving that goal. The experience of the Global Infectious Disease Preparedness Network (GIDPN) early in the course of COVID-19 provides a model for accelerating best practice development and improving decision-making in health emergencies.

The emergence of high-consequence infectious diseases (HCIDs) (e.g., viral hemorrhagic fevers, Middle East Respiratory Syndrome [MERS]) has increased in recent decades, potentially fueled by ecological and environmental factors and increased global fluidity of people and goods. A new infectious disease has emerged, on average, every year for the past 30 years [2], while others have emerged in new geographic regions. Previous HCID outbreaks have underscored the occupational risks that healthcare workers assume when treating these patients, as they have exhibited significantly higher infection rates than the general population [3-6]. As a result, special clinical units have been developed to mitigate nosocomial transmission and protect healthcare workers treating patients with these diseases. Termed "high-level isolation units (HLIU)", these facilities are equipped with extensively trained staff, biosecurity measures, robust standard operating procedures atypical of routine clinical settings, advanced engineering controls, and frameworks for rapidly conducting clinical research [7].

Globally, an increasing number of HLIUs have been established, either in response to previous regional HCID events or in anticipation of the next HCID threat. Five of these units, each representing core contributors to global health systems preparedness for HClDs and each with firsthand experience caring for patients with HClDs, partnered in 2017 to form the GIDPN. These founding members represent HLIUs at the Shanghai Public Health Clinical Center in China, University Hospital Frankfurt in Germany, National Centre for Infectious Diseases (NCID) in Singapore, National Medical Center in Seoul, South Korea, and the Nebraska Biocontainment Unit at the University of Nebraska Medical Center (UNMC) in the United States. Each of these units has extensive experience in treating patients with HClDs, some of which include Severe Acute Respiratory Syndrome (SARS), MERS, Ebola virus disease (EVD), and Lassa fever, and each plays a leading role in HCID preparedness and response in their respective countries; during the early part of the COVID-19 pandemic, all were designated treatment units for initial cases of COVID-19 in their respective countries (see Supplementary Material for a history and roles of HLIUs in their respective COVID-19 country-level response).

GIDPN was formed in 2017 to share best practices, explore development of a clinical trials network and clinical response force, and ensure rapid information- and resource-sharing during outbreaks of HClDs. The original five founding member institutions each have robust training programs, highly trained staff, advanced personal protective equipment (PPE) and PPE procedures, rapid response research platforms, emerging infectious disease clinical treatment protocols, and frequent exercises and drills to test and validate standard operating procedures. The collective experience and expertise of these units has led to significant contributions to national and international guidelines and best practices and improved public health and health systems preparedness. We detail GIDPN activities pre-COVID-19, lessons learned through rapid information-sharing during the COVID-19 pandemic, and the value of such global networking during response to an emerging infectious disease event.

GIDPN activities prior to the COVID-19 Pandemic

GIDPN was formed to establish a platform for best practice sharing and mutual learning, leveraging the diversity in experiences, infrastructure, and geographic representation of the network members. The network initiated with international training initiatives and a series of Grand Rounds, in which each HLIU presented on their experience, challenges, lessons learned, and best practices to other network members. Representatives from member units observed and evaluated large-scale exercises conducted by other units. Training exchanges offered the opportunity for network members to present on their experiences to larger audiences in other members' countries, and representatives from several units conducted joint capacity-building training programs for viral hemorrhagic fevers in West Africa. In addition, network members participated in two global HLIU workshops: one organized by the US National Emerging Special Pathogens Training and Education Center in 2018 on high-level isolation management and care, and the other organized by UNMC in January 2020, specific to transport and mortuary care for HCIDs. Informally, the expertise of the network also allowed GIDPN members that were redesigning their units or constructing new HLIUs to seek insight and recommendations into facility planning and HLIU construction. The expansion of the network in early years from formal networking events to informal engagements during training and exercises set the foundation for the transparent communications now inherent to the network.

Leveraging GIDPN during the COVID-19 Pandemic

In early 2020, when COVID-19 emerged in Wuhan, China, GIDPN members began sharing information and seeking technical advice from each other via email, as HLIUs readied to care for potential patients with the novel coronavirus. Beginning in early February, biweekly virtual meetings were scheduled to support rapid exchange of best practices, treatment modalities, concerns, and challenges that each HLIU was encountering. When science and knowledge were evolving daily, the network served as a platform for real-time open and transparent dialogue. This was conducted by clinicians caring for patients, by researchers conducting clinical trials and transmission and infection prevention studies, and by teams advising local and state/regional policymakers and decision-makers.

Shared knowledge led to earlier adoption of some treatment modalities as compared to most peer institutions and to implementation of infection prevention protocols prior to incorporation into national guidelines. Here, we detail specific lessons learned and impacts of these conversations as they related to 1) early clinical and epidemiological observations, 2) therapeutics and rapid response clinical trials, 3) early transmission and infection prevention studies and protocols, and 4) diagnostics.

Early clinical and epidemiological observations

As COVID-19 impacted some member countries earlier than others, firsthand information from those institutions caring for patients with COVID-19 was invaluable, both clinically and epidemiologically. From the epidemiological standpoint, for example, the Nebraska Biocontainment Unit team solicited existing data on infections in children and transmission phenomena while advising local and state health officials on community-wide mitigation measures to implement in early March. The Singapore NCID team was able to provide particularly valuable information on how the government and community were managing the outbreak given the relative control Singapore had achieved when compared to neighboring countries. Even earlier, as multiple GIDPN members were at the forefront of receiving large groups of individuals repatriated from COVID-affected areas (e.g., cruise ships, medical evacuations), one of the first GIDPN calls during the response centered around the logistics of quarantine, isolation, testing, and identification of positive cases in these cohorts.

Clinically, on a regularly scheduled biweekly call in early spring, the medical director of the Frankfurt HLIU discussed the success the team had with improving blood oxygenation of patients with COVID-19 by proning, including awake proning of non-intubated patients; this directly led to UNMC being an early US adopter of the process. Other clinical discussions that informed local practices included the appropriate testing strategy for diagnosis (i.e., single vs multiple tests); shared early observations of the use of convalescent plasma and its relationship to neutralizing antibody titers and outcomes; and conversations on early ICU admission and elective intubation in well-controlled environments.

Target treatments and therapeutics and rapid response clinical trials

During the early phase of the COVID-19 pandemic, many off-label or even unlicensed therapeutic agents were used prior to the availability of clinical trials, including agents such as lopinavir / ritonavir, azithromycin, and hydroxychloroquine. Information on “repurposed” medication was shared among the network members, and there was general concurrence in the group that these agents should be used in the context of randomized controlled trials (RCTs) such as the World Health Organization SOLIDARITY/RECOVERY trial. Group members also agreed that inclusion of patients into RCTs should come at a high priority. As the pandemic progressed, all of the above agents were proven ineffective, validating the group’s approach. The one pharmaceutical intervention the group did endorse based on early experience and known side effect profile in critical illness was dexamethasone, a substance that was later shown to be beneficial in more advanced disease stages of COVID-19 [8].

Transmission and infection prevention studies and protocols

UNMC and NCID were two of the first research teams to publish evidence supporting aerosol transmission of SARS-COV-2 [9,10]. During biweekly network calls, prior to study publications, the research teams presented preliminary findings to GIDPN members; these findings, in turn, informed PPE selection and isolation precautions well before national and international guidelines adopted such recommendations. For example, in early March, UNMC shared preliminary environmental sampling findings showing pronounced aerosol generation and contamination with moderate flow nasal cannula and significantly enhanced risk with other methods of non-invasive ventilation or high flow oxygen. This led to a more robust, evidence-informed conversation on benefits and drawbacks of early mechanical intubation versus non-invasive intubation and appropriate precautions for both scenarios.

Diagnostics

Global evidence to inform strategies for de-isolation of SARS-CoV-2 positive patients (i.e., time- or test-based) was lacking in the first several months of the pandemic and was a key discussion topic with GIDPN members. A conversation with the NCID team, which released a position statement on the subject in May 2020 [11], influenced UNMC's decision to move to a time-based de-isolation strategy in early June 2020, which occurred prior to US Centers for Disease Control and Prevention (CDC) recommendations. Conversations also provided advice and experience on how changes to this strategy were communicated and rolled out in other member units. Moreover, the group discussed optimal specimen types and yield according to duration of illness as well as presence or absence of pneumonia that informed diagnostic processes [12].

Discussion

The expertise and varying global experiences of GIDPN partners were leveraged during the early months of the COVID-19 pandemic to inform rapid clinical decisions at a time when information was frequently evolving and sufficient evidence on IPC processes, therapeutics, and treatment were absent. The value of such international clinical networking amid a global pandemic of a novel disease to the five GIDPN members cannot be understated. Frank conversations on early clinical and epidemiological characteristics and anecdotal evidence of the success of various therapeutics prior to availability of clinical trials informed clinical teams' decision-making within the local context (e.g., existing resources, surge situation). Member units authored some of the early COVID-19 hallmark studies related to clinical observations of patients, aerosol transmission, and epidemiological investigations, and often the design of these studies was shaped by early discussions within the network [9,10,12-26]. Sharing of preliminary research findings from these studies, as well as from more informal, quality improvement studies, allowed access to real-time data well before it became available in the scientific and medical communities.

During a pandemic where information and guidance were lacking, the clinical networking facilitated by GIDPN allowed for rapid epidemiologic and clinical decision-making in a local context. Members benefited from the rapid information exchange which, in many cases, led to local decisions to adopt treatment modalities and implement IPC protocols well before peer institutions or before incorporation of such processes in national guidelines or recommendations. While this exchange had clear value for member institutions, a global gap in practice remains in effectively and rapidly disseminating the expertise and lessons learned generated at these HLIUs to the broader network of healthcare facilities that will care for most cases during a pandemic. Although many findings discussed in GIDPN exchanges were ultimately published in the literature, coordinated development of evidence updates and improved integration with national and international health organizations could facilitate faster and more effective dissemination of best practices to a wider network of facilities. Moreover, the success of national systems of HLIUs in the US, Europe, and Asia serve as examples on which a larger international network could be built. An expanded network, comprised of GIDPN founding members, other highly experienced global HLIUs, and health facilities and systems in all regions of the world could serve as a platform to research and strengthen clinical and health systems preparedness in current and future partner countries and subregions. Such a network could develop and implement technical assistance both before and during outbreaks of HCIDs, develop standardized training for healthcare workers and health systems, provide mentoring and consultation services for expansion of isolation capacities, enhance research infrastructure at member institutions, and facilitate health emergency response research networks for real-time iterative improvement of HCID outbreak management. A wider global network of units and health systems, coupled with mechanisms for integration with national and international organizations for faster dissemination, could create a stronger line of defense against emerging HCIDs and future epidemics/pandemics across its network.

The global infrastructure of high-level isolation care has drastically changed in the last decade: the once infrequent, sporadic cases of HCIDs being treated in these specialized units has become an increasingly frequent occurrence, and many HLIUs have been established in the last

decade in anticipation of emerging infectious disease events to come. To date, as an international network of HLIUs, GIDPN has been leveraged to enhance treatment and management of patients with HCIDs through best practice and information-sharing and served as an invaluable resource during the COVID-19 pandemic. However, the COVID-19 pandemic also highlighted the role HLIUs are likely to play in pandemics of novel or reemerging special pathogens that outstrip the national and international capacity of HLIUs. The units have clear value for early stages of such pandemics, but surge capacity must be addressed. We are at an optimal point in time, as the continued vulnerabilities in global health security are once again highlighted through the COVID-19 pandemic, to plan for these types of pandemics and how best to leverage HLIU expertise, experience, and national roles to increase HCID preparedness and capacity for the future. The value of such a network was highlighted during the pandemic; GIDPN and similar networks will become increasingly integral in enhancing local, national, and global preparedness for and response to future epidemics/pandemics.

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Notes:**Author Contribution**

JJH led writing of the manuscript. JJL and JVL supervised the manuscript. TW, SV, YSL, BC, YS, and ALH contributed to the original draft and review and editing of the subsequent draft. JJL, TW, SV, YSL, BC, YS, ALH, and JVL established the GIDPN network. All authors were active in conversations and network activities pre-COVID and in the information sharing during the COVID-19 pandemic, detailed in this manuscript.

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Potential Conflicts

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