Hospital Experiences Responding to the COVID-19 Pandemic: Results of a National Pulse Survey

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***Abstract*- As the coronavirus spreads throughout the country and the supply of qualified healthcare providers becomes limited, pharmacists are at the front-line providing essential patient care services during this public health crisis. We applaud the ongoing efforts of the federal government, states, and the private sector to educate, contain, prevent, mitigate, test, treat, and respond to the devastating COVID-19 pandemic that is plaguing our nation and the world. As front-line providers and highly trusted and trained healthcare professionals, pharmacists play a critical role in patient care and public health. Pharmacists around the country are serving their communities and helping patients cope with this pandemic. However, there is much more that pharmacists can do for their patients and ease the burden on the healthcare system if additional authorities are granted and barriers to access for pharmacist patient care services are removed. Pharmacists are the most accessible healthcare providers and the first touch point of patient engagement with the healthcare system. In fact, 90% of all Americans live within five miles of a community pharmacy. In rural and underserved communities and in areas experiencing physician shortages, pharmacists may be the only healthcare provider that is immediately accessible to patients. As of May 2018, according to the Bureau of Labor Statistics, there are over 309,000 employed licensed pharmacists in the United States and its territories. Pharmacists practice in community pharmacies, hospitals, clinics, physician offices, long term care and other settings to provide patient care.**

***Index terms*- COVID-19, One Health, pandemic, SARS-Cov-2**

INTRODUCTION

The first cases of atypical pneumonia of unidentified aetiology were reported on December 30, 2019, from Wuhan, China. By January 7, 2020, a novel betacoronavirus, severe acute respiratory syndrome coronavirus (SARS-CoV-2) was identified, while the disease has been named COVID-19. COVID-19 has now been declared a pandemic, affected nearly every country, with over 2.3 million confirmed cases and >160,000 deaths. The initial clinical case series from China largely comprised of hospitalised patients with severe pneumonia. Further data suggested that approximately 80% patients have mild disease, 20% require hospital admission, and approximately 5% require intensive care admission [1]. Mortality rates are higher among people over 60 years and with coexisting conditions; hypertension, diabetes and cardiovascular disease being the most common. Here we provide an update for clinicians on the recent developments about virology, diagnostics, clinical presentation, and treatment options for COVID-19 based on current literature.

Virology

Metagenomic sequencing and targeted real-time polymerase chain reaction (qRT-PCR) assays identified a novel human CoV (SARS-CoV-2) in bronchoalveolar lavage fluid taken from the initial patient cluster in Wuhan [2]. Infectious SARS-CoV-2 has been cultured on monkey Vero, human Huh7 and primary human airway epithelial cells [3], where it is cytopathic. Furthermore, serum antibodies (IgM and IgG) from cases neutralized SARS-CoV-2 in cell culture and detected virus-infected cells by indirect immunofluorescence [3].

Phylogenetic analysis reveals that SARS-CoV-2 is closely related to SARS-CoV (~80% similar) in the Sarbecovirus sub-family (genus Betacoronavirus) [2]. While an intermediate host has yet to be determined, it shares strong genetic similarity (>95%) to known bat coronaviruses from China, suggesting a likely bat

origin. Relatively similar coronaviruses have been found in pangolins whose receptor-binding domain (RBD) of Spike (S) glycoprotein is more like to SARS-2-CoV-2 than known bat viruses [4].

SARS-CoV-2 shares most of its gene content with SARS-CoV, including the S glycoprotein, the RNA-dependent RNA polymerase (Nsp12) and two proteases papain-like protease (PLpro) and 3C-like protease (3CLpro) [3]. There is also substantial antigenic cross-reactivity between SARS-CoV-2 and SARS-CoV [3, 5]. A recent study confirmed that the angiotensin-converting enzyme 2 (ACE2), expressed in the human respiratory tract epithelium, is the entry receptor for SARS-CoV-2 similar to SARS-CoV and has been shown to cause pneumonia in lab mice only expressing human ACE2 [6, 7]. This is likely mediated by the RBD of the S glycoprotein [8]. Although there is obvious homology between SARS-CoV and SARS-CoV-2, and cross neutralization has been observed [9], significant biological differences, specifically in the S glycoprotein have been noted [5, 10, 11].

Clinical presentation

A key difference between COVID-19 and seasonal influenza-associated pneumonia is the potential severity of disease even in young adults without comorbidities [12]. In a study that compared three well-conducted Chinese case series to a reference group of patients with influenza-associated pneumonia from 73 German sentinel hospitals, the severity of pneumonia even in adults aged <60 years without chronic preconditions was significantly greater in COVID-19. For instance, 28% of COVID-19 patients treated on the ICU had no reported comorbidity. The rate of ARDS and mechanical ventilation was markedly higher among COVID-19 patients. The median duration of ventilation was 9 days for non-invasive, and 17 days for invasive ventilation [12].

Across all studies, the most common symptoms at onset of illness were fever, cough, fatigue, and myalgia. However, available data suggest that only half of patients are febrile at the time of admission [13, 14]. Gastrointestinal symptoms, including anorexia, nausea, vomiting and diarrhoea are also common,

Source	Mode of transmission	RNA by PCR (Days since onset of symptoms)	Viable virus (Days since onset of symptoms)
Nasopharynx	Droplet	Up to 37 days	Up to 7 days (in mild cases)
Sputum	Droplet/airborne during aerosolize-producing procedures	Up to 37 days	Up to 7 days (in mild cases)
Stool	No evidence of faecal-oral transmission	> 30 days	Only 1 report; uncertain
Blood	No viable virus to date	Up to 14 days	No
Urine	No viable virus to date	No	No
Conjunctiva	No viable virus to date Macaques with corneal inoculation develop infection	Yes	No

Transmission patterns

A review of modelling studies based on Chinese case numbers report a median basic reproduction number (R0) of 2.79 [48], though R0 as high as 5.7 have been reported [49].These estimates are substantially higher than the reproduction number for seasonal influenza (~1.3) [50], and indicate that control measures would need to prevent >60% transmission to stop the epidemic. Of note, R0 will vary by setting, and can be substantially reduced by countermeasures, as have been observed in China [51].

It is now clear that a significant proportion of individuals with COVID-19 have very mild or no symptoms. Asymptomatic infection at the time of laboratory testing have been reported [52, 53], though a large proportion go on to develop symptoms. For

instance, among 55 asymptomatic carriers with positive qRT-PCR for SARS-CoV-2 in pharyngeal swab samples, 14 went on to develop mild, 39 ordinary, and 2 severe COVID-19 [54]. There have been several reports of SARS-CoV-2 transmission from asymptomatic or presymptomatic persons [55, 56], which poses significant challenges to contact tracing. Nevertheless, the relative contribution of asymptomatic or pre-symptomatic transmission on the overall transmission dynamics of the pandemic remains uncertain. Thus, household studies to study secondary human transmission of SARS-CoV-2 and serosurveys to determine the incidence of asymptomatic and subclinical infections are needed.

A further consideration is super spreading events, whereby a small number of cases are responsible for a disproportionate number of secondary cases. This was a feature of both SARS- and MERS-CoV, responsible for multiple nosocomial outbreaks [57, 58]. Several super spreading events has been reported for COVID-19 [17]. Rapid identification and mitigation of these events will be crucial to controlling this pandemic.

Treatment options in clinical trials

At present, there are no approved antivirals for SARS-CoV-2. Several antivirals that have shown promise against SARS- or MERS-CoV in vitro and in vivo are currently being evaluated in clinical trials for COVID-19. Lopinavir/ritonavir (LPV/r), a protease inhibitor used as an antiretroviral, showed inconclusive findings for the treatment of SARS, but demonstrated strong in vitro and in vivo antiviral activity against MERS-CoV when combined with interferon-beta (IFNb) [59]. The first of a number of clinical trials involving LPV/r was recently published [60]. Among 199 seriously ill laboratory-confirmed COVID-19 patients, no significant difference in clinical improvement, mortality or viral clearance was observed between LPV/r (n=99) and standard care (n=100) arms. However, treatment was instituted late in infection; median time from symptom onset to treatment was 13 days, and >40% of patients had undetectable viral load before or during treatment. The results were complicated by the variable use of other treatments, including interferon, glucocorticoids and antibiotics. Of note, day 28 mortality was lower (not significantly) in those with early treatment (19% vs. 27%) and those who received LPV/r also had lower vasopressor and non-invasive ventilation use.

Another promising drug is remdesivir, a novel nucleotide analogue that interferes with nsp12 polymerase [61]. It has shown in vitro activity against a wide range of RNA viruses including SARS and MERS-CoV [62, 63], and has also demonstrated superior antiviral activity compared to LPV/r-IFNb against MERS-CoV in a mouse model [59]. Against SARS-CoV-2, it has shown promising antiviral activity in Vero E6 cells and Huh7 cells [64]. Remdesivir has been given to a small number of patients with severe COVID-19 through compassionate use, however, given the lack of randomisation and control group interpretation of the findings is difficult [65]. There are ongoing RCTs assessing its efficacy and safety in patients with COVID-19 worldwide, and a study in France evaluating its impact on viral shedding in high and moderate .

Pharmacists Test and Treat:

Pharmacists are trained to treat infectious diseases and can significantly expand access to care, if barriers are removed. In a growing number of states pharmacists currently have the authority to test for and treat infectious diseases, such as influenza and strep infections. For example, in Idaho, pharmacists are authorized to prescribe products to treat strep/flu pursuant to a rapid diagnostic test using an evidence-based protocol. Florida recently passed a law permitting pharmacists to test and treat for strep, flu

and other non-chronic ailments. Additionally, forty-nine states and the District of Columbia allow for pharmacists to practice in collaboration with advanced practice prescribers, including in several states that allow the ability to test and treat for infectious diseases, prescribe and administer vaccinations, and manage maintenance medication. However, pharmacists' authorities to test and treat are inconsistent across the states. At this time of need, we need consistency in authority across the country for pharmacists to use their training, expertise, and knowledge to test and treat patients.

Pharmacists are Immunizers: Nearly all practicing pharmacists have been trained to administer vaccines to patients of all ages. Pharmacists play a critical role in increasing influenza vaccination rates across the United States. In 2013, an additional 4.1 million adults were vaccinated because of pharmacists' efforts. These additional vaccinations are estimated to have resulted in 81,000 to 134,000 fewer adult influenza infections that year. Additionally, the odds that an adult would receive the flu shot increased by 7.8 percent in states that allowed pharmacists to be immunizers.

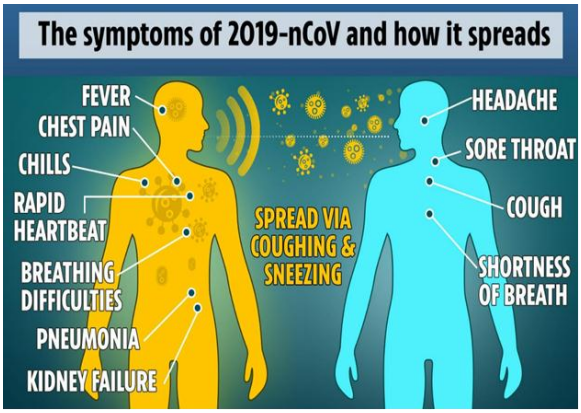
Pharmacists are Responders: As medication experts and providers, pharmacists are trained to respond quickly to patient needs - whether it is managing medication, identifying therapeutic needs and alternatives, testing, immunizing, counseling patients, compounding drugs that are in shortage, and more. Pharmacists can help respond to the COVID-19 pandemic by administering tests once they are commercially available, treating COVID-19 when treatments become available, and by testing for and treating influenza and strep throat infections. By testing and treating flu and strep in the pharmacy, the time from symptom development to treatment decreases. Importantly, caring for patients with flu or strep in the pharmacy alleviates some of the burden on hospitals and clinics so they can focus on high-risk COVID-19 patients. Pharmacists are also accessible and can respond to address patient care needs through telehealth and telepharmacy if appropriate authority is provided. President Trump has declared a national emergency under the National Emergencies Act. The Secretary of Health and Human Services ("HHS") has declared a public health emergency under Section 319 of the Public Health Service Act. The Secretary is thereby authorized to take additional actions in addition to his regular authorities. Under Section 1135 of the Social Security Act, the HHS Secretary may now temporarily waive or modify certain Medicare, Medicaid, and Children's Health Insurance Program ("CHIP") requirements to ensure that sufficient health care items and services are available to meet the needs of individuals enrolled in Social Security Act programs in the emergency area and time periods. It also allows providers who provide such services in good faith to be reimbursed and exempted from sanctions (absent any determination of fraud or abuse).

According to historians, pandemics typically have two types of endings: the medical, which occurs when the incidence and death rates plummet, and the social, when the epidemic of fear about the disease wanes.

"When people ask, 'When will this end?,' they are asking about the social ending," said Dr. Jeremy Greene, a historian of medicine at Johns Hopkins. In other words, an end can occur not because a disease has been vanquished but because people grow tired of panic mode and learn to live with a disease. Allan Brandt, a Harvard historian, said something similar was happening with COVID-19: "As we have seen in the debate about opening the economy, many questions about the so-called end are determined not by medical and public health data but by sociopolitical processes."

Endings "are very, very messy," said Dora Vargha, a historian at the University of Exeter. "Looking back, we have a weak narrative. For whom does the epidemic end, and who gets to say?" In the Path of Fear An epidemic of fear can occur even without an epidemic of illness. Dr. Susan Murray, of the Royal

College of Surgeons in Dublin, saw that firsthand in 2014 when she was a fellow at a rural hospital in Ireland.In the preceding months, more than 11,000 people in West Africa had died from Ebola, a terrifying viral disease that was highly infectious and often fatal. The epidemic seemed to be waning, and no cases had occurred in Ireland, but the public fear was palpable. "On the street and on the wards, people are anxious," Murray recalled recently in an article in The New England Journal of Medicine. "Having the wrong color skin is enough to earn you the side-eye from your fellow passengers on the bus or train. Cough once, and you will find them shuffling away from you."



The Dublin hospital workers were warned to prepare for the worst. They were terrified and worried that they lacked protective equipment. When a young man arrived in the emergency room from a country with Ebola patients, no one wanted to go near him; nurses hid, and doctors threatened to leave the hospital. Murray alone dared treat him, she wrote, but his cancer was so advanced that all she could offer was comfort care. A few days later, tests confirmed that the man did not have Ebola; he died an hour later. Three days afterward, the World Health Organization declared the Ebola epidemic over. Murray wrote, "If we are not prepared to fight fear and ignorance as actively and as thoughtfully as we fight any other virus, it is possible that fear can do terrible harm to vulnerable people, even in places that never see a single case of infection during an outbreak. And a fear epidemic can have far worse consequences when complicated by issues of race, privilege and language."

Black Death and Dark Memories

Bubonic plague has struck several times in the past 2,000 years, killing millions of people and altering the course of history. Each epidemic amplified the fear that came with the next outbreak. The disease is caused by a strain of bacteria, Yersinia pestis, that lives on fleas that live on rats. But bubonic plague, which became known as the Black Death, also can be passed from infected person to infected person through respiratory droplets, so it cannot be eradicated simply by killing rats. Historians describe three great waves of plague, said Mary Fissell, a historian at Johns Hopkins: the Plague of Justinian, in the sixth century; the medieval epidemic, in the 14th century; and a pandemic that struck in the late 19th and early 20th centuries. The medieval pandemic began in 1331 in China. The illness, along with a civil war that was raging at the time, killed half the population of China. From there, the plague moved along trade routes to Europe, North Africa and the Middle East. In the years between 1347 and 1351, it killed at least one-third of the European population. Half the population of Siena, Italy, died.

"It is impossible for the human tongue to recount the awful truth,"

Specific Recommendations:

1. Authorize Test-Treat-Immunize and other pharmacist-provided services As health systems become overburdened and reach their capacity for providing care, pharmacists can step in and relieve some of that burden by increasing access and providing faster testing and treatment for patients. Pharmacists are trained and authorized to provide these services in some states, but consistent application across all states is necessary to ensure pharmacists are fully utilized during the pandemic.

The following actions should be taken to ensure access to pharmacist patient care services:

- Allow pharmacists to order, collect specimens, conduct, and interpret necessary tests and, where appropriate, initiate treatment for infectious diseases, including but not limited to flu, strep, and COVID-19, and interpret and discuss test results with patients.
- Allow all pharmacies to be granted a CMS certificate of waiver to provide all CLIA-waived point-of-care tests.

- Ensure access to and effective use of personal protective equipment (PPE) by all involved in testing.
- Expand current state pharmacist immunization authority to include all FDA approved vaccines, including the forthcoming novel vaccine for COVID-19, for all indicated populations.
- Allow pharmacists to independently evaluate and manage medications through therapeutic interchange, chronic care dose adjustment, refill authorizations, quantity modifications (e.g., 90-day fills), and other forms of prescription adaptation.
- Allow pharmacists to administer any injectable medication.

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