Editorial: COVID-19

The COVID-19 pandemic has disrupted virtually all aspects of human activity worldwide more than any other catastrophes in the past 100 years, with the possible exception of the two world wars. COVID-19 is a viral disease that is highly contagious and often lethal, especially to elderly persons with underlying disease.

Because little is known about many aspects of the disease, Jeff Williams and I decided to devote an entire issue of the *Journal of the Louisiana State Medical Society* to COVID-19. Fortunately, Fred Lopez, M.D. of the LSU Health Sciences Center in New Orleans, an internationally recognized expert in infectious diseases, agreed to be the editor of this issue, and he has assembled other experts to contribute.

All of us, regardless of our medical specialty, need to know more about COVID-19, and this issue of the *Journal* provides a good starting point in this endeavor.

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Editor-in-Chief

Several years ago, I wrote a guest editorial entitled "Infectious Diseases in the 21st Century: No End in Sight."[1] In it I quoted Dr. Robert Petersdorf, a legend in the field of infectious diseases, who wrote in the late 1970s, when referring to graduating fellows in infectious diseases: "Even with my great personal loyalty to [the discipline of] infectious diseases, I cannot conceive of a need for 309 more infectious diseases experts unless they spend their time culturing each other."[2] Times have definitely changed. Over the past four decades or so, the advent of AIDS and hepatitis C, enhanced vaccine development, the impact of multidrug-resistant bacteria, foodborne epidemics, the emergence of infections due to pathogens such as the Zika and Ebola viruses, and our perpetual struggle with mutating influenza viruses have increasingly positioned the field of infectious diseases at the forefront of medicine and public health. And now, of course, the world is grappling with SARS-CoV-2, the virus responsible for COVID-19, causing the general population to think more about infectious diseases than it ever has before—or ever wanted to.

Because of the significance of the global pandemic, the *Journal of the Louisiana State Medical Society*, a vanguard of the medical community in our state since 1844, is providing an update on COVID-19 in this issue. Articles written by various medical professionals address the disease's clinical aspects (epidemiology, diagnostics, therapeutics, complications, and prevention); its impact on student and resident training; and the challenges associated with leading a Department of Medicine during a pandemic.

Hurricane Katrina or COVID-19? As a Louisiana native, I have often asked myself which has proven more formidable, having lived through the experience of caring for patients during the former at the iconic Charity Hospital and now caring for patients with the latter at our university teaching hospital.[3] For many involved in healthcare in this state, Hurricane Katrina has provided a referential point to affix experiences in time (i.e., "pre-Katrina" or "post-Katrina"), but with the novel coronavirus reaching its toxic tentacles into seemingly every aspect of our lives for such a protracted period, it may well become the new chronological marker in Louisiana. I do not view either disaster as an exclusive holder of this mantle but rather consider both to be examples of the resilience of our state in addressing some of its greatest recent challenges. We hope that you find this issue helpful in your understanding of COVID-19 and its collateral effects, a pandemic whose vast impact will be felt for many years to come.

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I would like to thank Michelle Holt, M.Ed., M.F.A., Managing Editor for the LSU Department of Medicine, for her assistance.

COVID-19 : Epidemiology, Clinical Presentation and Prognosis

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Abstract

Since the first case of COVID-19 was reported in Wuhan City, Hubei Province, China, in December 2019, an ensuing pandemic has challenged public health infrastructure around the world. During this time, scientists and clinicians have been striving to understand, prevent, and treat this disease, generating an enormously robust amount of data in the process. This article aims to provide clinicians with up-to-date, useful and accurate information regarding the virus's origins, transmission dynamics, clinical presentation, and prognosis that can help inform their practice in this challenging, and constantly evolving health crisis.

History and Epidemiology

Throughout human history, society has been shaped by intermittent outbreaks of infectious diseases described as "plagues" and/or "pandemics." Outbreaks of infectious diseases have changed the course of history, transforming economies and affecting the outcomes of wars, causing devastation but also leading to amazing advancements in public health and medicine.

Since the beginning of the 21st century, some of the most notable outbreaks of infectious diseases have been due to novel viruses from the family *Coronaviridae.* The 2003 outbreak of Severe Acute Respiratory Syndrome (SARS) ultimately resulted in more than 8,000 cases with an approximate 10% mortality rate. The disease, first documented in Hong Kong, spread rapidly over multiple continents, sparking worldwide fear and causing disastrous economic impacts (1). No cases have been reported since 2004. Again, in 2012, a SARS-like coronavirus illness emerged in Saudi Arabia. Deemed Middle East Respiratory Syndrome (MERS), this outbreak led to more than 1,000 cases with an even higher mortality rate estimated at almost 35% (2). In both instances, these viruses emerged in areas with dense human populations where there exist so-called "wet markets." In these markets, fresh meat, fish, and produce are sold, allowing for frequent mixing of different animal species in close contact with human patrons. SARS-CoV and MERS-CoV originated from animal reservoirs. The SARS virus was originally traced to wildlife market civets, which likely acted as an amplifying intermediate animal host, and ultimately to bats. Likewise, MERS was traced to bats, with dromedary camels acting as intermediate hosts. These viruses gained the ability to not only infect humans, but also achieve human-to-human transmission. The resulting illnesses included severe lower respiratory tract infections with extra-pulmonary manifestations due to viruses abilities to infect a broad range of cell types while simultaneously evading host immune response and triggering cytokine dysregulation (1, 2). SARS-CoV and MERS-CoV served as harbingers of the pandemic we find ourselves in today, fully realized in COVID-19 caused by SARS-CoV-2.

In December 2019, a cluster of severe pneumonia cases were described in Wuhan City, Hubei Province, China. It was noted that a number of the patients affected had either visited or worked in the same local seafood market prior to becoming ill. Shortly thereafter, a novel coronavirus, now called SARS-CoV-2, was isolated via PCR from bronchoalveolar lavage fluid collected from infected patients (3). Since isolation of the virus, much work has been done to determine its animal origins. Like SARS and MERS, this virus likely originated in bats. SARS-CoV-2 shares 96.2% sequence identity with a bat coronavirus, BatCoV RaTG13, first isolated from *Rhinolophus affinis* (intermediate horseshoe bat) in Yunnan province. Though a number of intermediate animal hosts have been proposed, including the pangolin, thus far the intermediate host or hosts have not been definitively identified. A WHO task force continues to investigate this issue (4).

SARS-CoV-2 spread rapidly thereafter, with the first case on US soil being reported on January 19, 2020, in Washington state (5). Eleven days later, on January 30th, the WHO declared a Public Health Emergency of International Concern (PHEIC), the organization's highest level of alarm. Ultimately, on March 11, 2020, the COVID-19 was declared a pandemic by the WHO (6).

The incubation period for SARS-CoV-2 is estimated to be 2-14 days, with a mean of approximately 5-6 days (7, 8), prompting the widespread recommendation of a 14-day self-quarantine for patients exposed to or diagnosed with infection. The median time from illness onset to hospital admission is estimated to be 4 days, and median time from illness onset to death in patients who ultimately succumb to infection is estimated at 13 days (7).

SARS-CoV-2 respiratory droplets are primarily transmitted via close person-to-person contact (including being within 6 feet of an infected person). Airborne transmission by smaller droplets and particles that remain suspended in air and travel further than 6 feet can sometimes occur. Fecal aerosol transmission may also be possible. Contact transmission seems to be a less frequent contributor. While the virus can persist on an inanimate surface for multiple days (9), there have been studies that showed difficulty in actually culturing live virus from these surfaces (10).

Droplet transmission via larger respiratory particles (greater than 5 μm in diameter) has been the most widely accepted mode of transmission of SARS-CoV-2 by most public health organizations (11), and is the basis of the at least 6-foot separation recommendation for social distancing. However, our understanding of transmission is evolving, including several, well-documented instances of COVID spread, where the most plausible explanation is under favorable conditions (i.e. poor ventilation, high concentration of particles, and extended exposure) airborne transmission is possible (12, 13, 14).

Symptomatic patients are contagious. Though asymptomatic transmission has been well described, including early in the pandemic aboard the Diamond Princess cruise ship (15), exactly when a patient becomes contagious in asymptomatic infection or in the pre-symptomatic phase of infection is more difficult to establish. While PCR testing provides evidence that SARS-CoV-2 is present, it does not necessarily translate to being contagious. Infectivity in viral culture is the gold standard for determining presence of live virus, and such data does not exist for the vast majority of patients. Viral load or cycle threshold in RT-PCR has been used as a surrogate marker for infectivity in culture in many studies, and it does appear that viral load is highest within the first week of symptoms (16, 17). One recently published decision analytical model by Johansson et al., assesses the proportion of transmission from pre-symptomatic individuals (18). Applying a mean incubation period of 5 days, they estimate that 59% of COVID-19 transmission is from asymptomatic patients, 35% from pre-symptomatic and 24% from never symptomatic patients.

The basic reproduction number, R_0 (“R naught”), is the average number of secondary cases generated by one infected individual in a totally susceptible population. R_0 greater than 1 means that human to human transmission can occur and persist; an R_0 less than 1 means transmission will decline and eventually be extinguished (19). A meta-analysis of 12 studies by Liu et al. determined the average estimate of the R_0 of SARS-CoV0-2 is 3.28 with a median of 2.79 (20). As a point of comparison, the R_0 of measles is widely cited to be 12-18, and the R_0 of influenza is approximately 1.3 (21). This number declines as the number of immune individuals in a population increases, through natural infection or vaccination. However, it is important to note that while first generation of COVID-19 vaccines have been shown to decrease severity of illness, their ability to generate sterilizing immunity in the upper respiratory tract continues to be evaluated (22). Thus, their effect on COVID transmission is not yet known and investigations into this issue are ongoing. It is imperative that other mitigation measures be continued (social distancing, mask wearing, hand washing, etc.) while vaccinations are being carried out.

As of February 14, 2021, there have been an estimated 108.7 million cases and 2.39 million deaths worldwide, with 27.6 million cases and over 485,000 deaths in the U.S., and over 380,000 confirmed cases and 9,292 confirmed deaths in Louisiana (23). This equates to approximately 8.3% of the population of Louisiana having been infected with COVID-19.

Clinical Presentation

One of the most challenging aspects of the pandemic has been the wide range of illness severity seen in affected patients. In particular, asymptomatic patients, those who will never develop symptoms in the course of their infection, and pre-symptomatic patients, who will eventually develop symptoms, have made containment of spread challenging. In a review of populations with broad testing, for example Iceland and Vo', Italy, approximately 40-50% of patients were asymptomatic at the time of testing positive (24). A large meta-analysis by Byambasuren et al. published in December 2020 looked at studies which followed patients for at least 14 days to assess whether they remain asymptomatic or are merely pre-symptomatic at the time of positive testing (25). By their estimate, approximately one in five patients are never symptomatic.

Numerous studies have attempted to determine clinical characteristics of asymptomatic patients; however, a significant number of asymptomatic cases have been reported in all age groups, both genders, and a variety of co-morbid conditions (26). Our understanding of why certain patients will remain asymptomatic or have longer pre-symptomatic phases of infection remains unclear.

Acutely symptomatic patients can present with a variety of symptoms, owing to the ACE2 receptor utilized by the virus to enter cells being expressed on tissues in nearly all organ systems of the body (19). The most commonly reported include fever (77.4%-98.5%), cough (59.4%-81.8%), malaise (38.1%-69%), dyspnea (3.2%-55.0%), myalgia (11.1%-34.8%), sputum production (28.2%-56.5%), anosmia (25%), and headache (6.5%-33.9%) (27). To a lesser extent sore throat (12%), arthralgia (11%), confusion (11%), dizziness (11%), and diarrhea (10%) have also been reported (27). The prevalence of certain symptoms has evolved during the pandemic. For example, gastrointestinal symptoms including not only diarrhea, but also nausea, vomiting, and elevated liver function tests seem to have become more commonly reported in later phases of the outbreak (28). When present, symptoms on average last approximately 8 days (27).

In patients with respiratory complaints, abnormalities on chest imaging are common. CT findings associated with COVID-19 are especially well described. Findings are typically bilateral, although unilateral abnormalities have been described particularly in mild cases or early in a patient's course. Ground glass opacities and consolidation are the most common finding (94.5%); less common, but still frequently described findings include air bronchograms, linear opacities, interlobular septal thickening, bronchiectasis, pleural effusion, and nodules (29). It is notable that these findings are non-specific and can be associated with a variety of disease processes, particularly other viral pneumonias. For this reason, the American College of Radiology does not recommend using CT as a first-line or diagnostic test for COVID-19 (30).

As per NIH treatment guidelines (31), moderate illness is defined as lower respiratory disease based on clinical assessment or imaging, but with SpO_2 of greater than 94% on room air. Severe illness is defined as SpO_2 <94% on room air, a respiratory rate of greater than 30 breaths per minute, PaO_2/FiO_2 of less than 300 mm Hg, or infiltrates in greater than 50% of the lung on imaging. Individuals who are aged 65 years or older or with comorbidities such as cardiovascular disease, chronic lung disease, chronic kidney disease, or diseases that affect the immune system (including diabetes) are considered at high risk for developing more severe illness (32). One study estimates that 1 in 5 people of the global population, or 1.6 billion people, have at least one of these underlying conditions and are therefore at increased risk (33). An updated list of medical conditions that increase risk or might increase risk for severe illness from COVID-19 is maintained by the CDC on its website (32). Furthermore, disparity among U.S. ethnic groups is also present with COVID-19. African American/Black and Hispanic populations are at higher risk of SARS-CoV-2 infection and COVID-19-related death.

Though further study is needed to conclusively determine a cause, current data suggests this disparity is due to increased exposure risk and/or limited access to healthcare rather than increased susceptibility (34).

Numerous existing severity scores for community acquired pneumonia have been evaluated to assess their ability to accurately risk stratify patients with COVID-19. One retrospective study by Fan et al. compared A-DROP, CURB-65, PSI, SMART-COP, NEWS2, CRB-65, and qSOFA, with the A-DROP scoring system being most accurate in predicting in-hospital death (35). Modified severity scores have also been proposed to include expanded versions of A-DROP (36), as well as entirely novel scoring systems such as the 4C Mortality Score or the COVID Inpatient Risk Calculator (CIRC). The 4C Mortality Score was developed in the UK, and includes 8 variables: age, sex, number of comorbidities, respiratory rate, peripheral oxygen saturation, level of consciousness, urea level, and C reactive protein. A score of 15 points or higher was associated with a mortality rate of 62%, and a score of less than 3 carried a mortality rate of 1%. The scoring system showed excellent discrimination and calibration, and by the authors' analysis this system out performed previously developed CAP severity scores (37). The COVID Inpatient Risk Calculator (CIRC) was developed by researchers at Johns Hopkins (38). This model uses demographics, comorbidities, symptoms, vital signs, and a range of lab values to determine the likelihood of a patient progressing to severe disease or death within 7 days of admission. For example, using CIRC, a 78-year-old Black man, with a history of MI and stroke, admitted from a nursing home with a fever, respiratory and constitutional symptoms, has an 18% chance of progressing to severe disease or death by day 4 of his hospital admission, and a 22% chance of progressing to severe illness or death by day 7 (38).

A rare complication of COVID-19 has been Multisystem Inflammatory Syndrome in both children and adults, known as MIS-C and MIS-A respectively. This syndrome was first described in the UK when a small cluster of children began returning to the hospital 2-4 weeks after initial infection with what appeared to be Kawasaki's disease or toxic shock-like syndrome (39). A broad range of symptoms were described, but most cases were associated with shock, cardiac dysfunction, gastrointestinal symptoms, and markedly elevated inflammatory markers. There were also reported cases that occurred during acute infection with COVID-19, and these patients tended to have milder associated symptoms (40). Though fewer in number, similar cases have been described in adults. Similarly, adult cases tended to include shock, cardiovascular dysfunction, gastrointestinal symptoms, dermatologic, and neurologic manifestations. Respiratory involvement was rare (41). This appears to be a post-infectious phenomenon, as the majority of both pediatric and adult patients had negative RT-PCR studies, but had positive serology for antibodies against SARS-CoV-2 (40,41). The mechanism is not fully understood, but a proposed etiology is endothelial inflammation caused by acute infection which results in immune dysregulation (42).

Other patients who have recovered from COVID-19, develop “postacute COVID-19 syndrome.” Symptoms are typically nonspecific, and most commonly include fatigue and dyspnea. Other symptoms include joint and chest pain as well as “brain fog.” As the SARS-CoV-2 outbreak is relatively new, investigations into better understanding this phenomenon are ongoing (43). One recently published study by Chaolin Huang and colleagues, followed a cohort of 1733 patients in Wuhan, China, for 6 months following discharge from the hospital for COVID-19 (44). At 6 months post-discharge, the most common symptoms reported by patients were anxiety and depression, sleep disturbances, fatigue, and muscle weakness. Patients who had more severe disease had a higher likelihood of abnormal oxygen diffusion on pulmonary function testing and persistent abnormalities on high resolution chest CT.

Mortality and Reinfection

As of February 14, 2021, the current case fatality ratio of COVID-19 in the United States is 1.8%, with 148.00 deaths per 100,000 persons (23). Though numbers of cases and deaths continue to rise, there have been numerous reports that the mortality rate has been decreasing. One study in England confirmed that patients admitted to hospital with COVID-19 in mid-April and May had a significantly lower mortality rate than patients admitted earlier in the pandemic. Their analysis included adjustments for patient demographics and comorbidities which did not seem to account for the change (45). Proposed reasons for this decline include widespread use of corticosteroids which demonstrated a mortality benefit in the RECOVERY trial (46), better healthcare provider understanding of the disease process, as well as decreased healthcare burden as mitigation measures have been introduced (45, 47). Numerous groups around the world are investigating whether this decline is real, or merely due to changes in testing and case reporting, particularly on a country-to-country basis.

Confirmed cases of reinfection have been reported. Two such instances are the case of a 33-year-old man in Hong Kong and a 25-year-old man in Nevada. In each case, genomic analysis of the virus isolated from the patient in each infection was performed, and the isolates were genetically distinct. An importance difference between the cases is that while the Hong Kong patient was mildly symptomatic in his first infection and asymptomatic in his second 142 days later, the Nevada patient experienced an increase in symptom severity during his second infection which occurred 48 days after his first infection (48,49). It is known that neutralizing antibodies are generated in response to COVID-19; however, the durability of this response is not yet known, but is likely within the range of 5-7 months (50, 51).

Emergence of SARS-CoV-2 Variants

Variant strains of SARS-Cov-2 have evolved by mutation during the course of this pandemic. Investigations of these variants will need to address questions regarding transmissibility, virulence, accuracy of diagnostic testing, efficacy of antibody-based treatments and vaccinations, and ability to reinfect individuals with prior infection. One such variant emerged in the UK in the fall of 2020, and is associated with multiple mutations including a spike protein-associated receptor binding domain mutation at position 501 where asparagine has been replaced by tyrosine, i.e., N501Y. The strain is known as B.1.1.7. and it is estimated to be approximately 50% more transmissible than the Wuhan reference strain (52). This variant may also be associated with an increased risk for severe disease (53). The UK variant does not appear to have an effect on current vaccine efficacy (54). However, both currently available vaccine-generated antibodies and COVID-19 antibodies from early natural infections may have decreased efficacy against two additional emerging variants from South Africa (known as B.1.351) and Brazil (known as P.1) due to additional mutations in the spike protein including one at position 484 where glutamic acid is replaced by lysine (i.e., E484K) (55, 56, 57, 58). By late January 2021, the UK, South African, and Brazilian variants had been detected in the United States. Even with ongoing vaccination efforts, increased vigilance and mitigation measures will be crucial to prevent surges in cases.

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Diagnostic Approach to COVID-19

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Abstract

Introduction
Accurate and timely diagnosis of SARS-CoV-2 infection is essential to control viral spread.

Methods
In this article, we review the indications for SARS-CoV-2 testing among both symptomatic and asymptomatic individuals, as well as the general characteristics, indications, and interpretation of the three major classes of COVID-19 diagnostics: nucleic acid amplification testing (NAAT), antigen testing, and antibody testing. In general, NAAT and antigen tests are utilized to make a diagnosis of acute infection. Antibody tests are serologic assays that measure the immune response to SARS-CoV-2 infection and can confirm prior recent infection. They have limited utility in confirming active infection and commercially available assays cannot confirm immunity to SARS-CoV-2.

Conclusion
NAAT assays and antigen testing are the major diagnostics utilized to confirm active infection with SARS-CoV-2, whereas, antibody testing is used to confirm prior recent infection.

Introduction

The COVID-19 global pandemic has impacted the entire world over the past year, accounting for over 100 million cases and greater than 2 million deaths worldwide. Accurate and timely diagnosis of SARS-CoV-2 infection is essential to control viral spread to limit further morbidity and mortality from this illness. In this article, we review the indications for SARS-CoV-2 testing among both symptomatic and asymptomatic individuals, as well as the general characteristics, indications, and interpretation of the three major classes of COVID-19 diagnostics: nucleic acid amplification testing (NAAT), antigen testing, and antibody testing.

Indications for SARS-CoV-2 Testing

There are no specific clinical features that can reliably distinguish COVID-19 from other respiratory viral infections (1). Providers should, therefore, have a low threshold for suspicion of COVID-19 in patients with any concerning symptoms, particularly if they have spent time in an area with community transmission or have a close contact with confirmed or suspected COVID-19 in the preceding 14 days. If possible, it is recommended that all symptomatic patients with suspected infection undergo testing for acute infection.

The Infectious Diseases Society of America (IDSA) has suggested priorities for testing when diagnostic capacity is limited. High-priority individuals include hospitalized patients (especially critically ill patients with unexplained respiratory illness) and symptomatic individuals who are health care workers or first responders, work or reside in congregate living settings, or have risk factors for severe disease (2).

Testing certain asymptomatic individuals may also be important for public health or infection control purposes. Situations where testing of asymptomatic individuals is recommended include the following instances: (2,3)

- Following close contact with an individual with COVID-19 without full PPE (this includes neonates born to mothers with active or recent COVID-19). The optimal time to test for COVID-19 following exposure remains uncertain but five to seven days post exposure is largely recommended based on the average incubation period.
- Screening residents of congregate living facilities that house individuals at risk for severe disease (e.g., long-term care facilities, correctional and detention facilities, homeless shelters).
- Screening hospitalized patients at locations where prevalence is moderate or high (e.g., ≥10 percent PCR positivity in the community).
- Prior to time-sensitive surgical procedures or aerosol-generating procedures.
- Prior to receiving immunosuppressive therapy including prior to transplantation.

Overview of Diagnostic Tests for SARS-CoV-2

There are 3 classes of tests available to diagnose active or prior COVID-19:

- Nucleic acid amplification testing (NAAT) of viral RNA, most commonly reverse-transcription polymerase chain reaction (RT-PCR) testing (detects viral nucleic acid).
- SARS-CoV-2 antigen testing (detects a specific viral antigen).
- Antibody testing (detects antibody to spike or nucleocapsid proteins).

Authorized assays for acute viral testing include those that detect SARS-CoV-2 nucleic acid or antigens. These viral specific tests detect viral nucleic acid or antigens from respiratory tract samples (including nasal, nasopharyngeal, oral, or oropharyngeal swabs or saliva samples) to diagnose active infection with SARS-CoV-2. In contrast, serologic assays detect antibodies in the blood that indicate prior infection with SARS-CoV-2. A summary of SARS-CoV-2 diagnostics is detailed below.

Table1: Summary of Diagnostic Tests for SARS-CoV-2 (4) table 1

	NAAT	**Antigen Test**	**Antibody Test**
Intended use	Detect current infection	Detect current infection	Prior infection (usually >3-4 weeks)
Analyte detected	Viral RNA	Viral Antigen	Antibodies to spike and nucleocapsid proteins
Specimen type(s)	Nasal, Nasopharyngeal, Sputum, Saliva	Nasal, Nasopharyngeal	Blood
Sensitivity	Varies by test, but generally high	Moderate	Variable
Specificity	High	High	Variable
Test complexity	Varies by test	Relatively easy to use	Relatively easy to use
Authorized use at Point-of-Care	Most are not, some are not	Most are, some are not	N/A
Turnaround time	15 mins to >2 days	Less than 1 hour	15 mins to 2 hours

Cost	Moderate (~$100/test)	Low (~$5-50/test)	Low (~$40/test)

Adapted from CDC Guidance.

NAAT Testing

Nucleic acid amplification testing (NAAT) to detect SARS-CoV-2 RNA from the upper respiratory tract is the preferred initial diagnostic test for COVID-19 when available (3). Among the available classes of diagnostic tests, NAAT has the highest sensitivity and specificity for acute COVID-19, although variability exists amongst different NAAT testing platforms. Rapid NAAT assays, defined as those assays that generate results in under an hour including the Abbott ID NOW and Cepheid GeneXpert Xpress Assays, are generally less sensitive and specific than more time-intensive standard laboratory-based NAAT methods, including RT-PCR or transcription mediated amplification (TMA) assays, which yield results within 8 to 48 hours (3). A positive NAAT PCR for SARS-CoV-2 in a symptomatic patient generally confirms the diagnosis of COVID-19 with no additional diagnostic testing required. In some cases, an inconclusive or indeterminate result indicates that only one of the two or more genes targeted by NAAT testing was identified. These results can be considered presumptive positive results, given the high specificity of NAAT assays. In a symptomatic patient where suspicion for COVID-19 is low, a single negative rapid or standard NAAT assay is sufficient to exclude the diagnosis. In a symptomatic patient where suspicion for COVID-19 is high or the prevalence is >10% in the general population, testing should be repeated between 24-48 hours later with a standard NAAT assay such as RT-PCR if the initial rapid diagnostic is negative (3).

Of note, detectable virus in asymptomatic patients following resolved infection does not usually indicate relapsed or new infection. Patients with COVID-19 can shed detectable SARS-CoV-2 RNA either continuously or intermittently in upper respiratory tract specimens for weeks after the resolution of symptoms (5). Prolonged viral RNA detection after symptom resolution does not indicate that a patient is contagious as this virus shed is unlikely to still be transmissible (6).

Antigen Testing

Antigen tests are immunoassays that detect the presence of a specific viral antigen, which implies active viral infection. They are usually rapid, inexpensive, and can be performed at the point of care, yielding greater accessibility with a faster turnaround time than most NAAT assays. Antigen tests are typically less sensitive than NAAT assays and are most accurate in confirming a diagnosis in the early stages of infection when viral replication is high. Given their rapid turnaround time, low cost, and high specificity, antigen testing is often utilized in serial screening of congregate settings or other sites of localized outbreaks. When used in clinical diagnosis in symptomatic patients, positive antigen tests can be interpreted as indicative of SARS-CoV-2 infection. Negative antigen tests could represent a false negative given their reduced sensitivity and should generally be confirmed using a more sensitive NAAT RT-PCR assay if clinical suspicion is high. When used for serial testing in congregate settings, negative antigen tests do not need to be confirmed (4). In general, antigen tests should be used in settings where prevalence is moderate and early in disease onset to yield the most accurate results.

Serologic (Antibody) Testing

Serologic tests detect antibodies to either the SARS-CoV-2 spike protein or nucleocapsid in the blood. They identify patients who have been previously infected with SARS-CoV-2 as well as patients with active infection with prolonged symptoms that extend for enough time to generate a humoral immune response (i.e., typically about three weeks). False positive serologic testing was described early in the pandemic due to cross-reactivity with other human coronaviruses when using low specificity assays in low prevalence areas (7). Therefore, to be of value, FDA-approved anti-SARS-CoV-2 antibody tests are required to have high sensitivity and specificity (i.e., ≥99.5%) and should be used in areas of moderate to high prevalence.

Because serologic tests are less likely to be reactive in the first several days to weeks of infection while the host humoral response is generated, they have very limited utility in the diagnosis of acute infection (8). As such, the IDSA discourages their use for confirmation of infection in the first two weeks following symptom onset (7). Checking serologic testing with IgG or total antibody (rather than IgM, IgA or IgG/IgM assays) three to four weeks after the onset of symptoms optimizes the accuracy of testing for evidence of recent infection (7).

Commercially approved antibody assays detect both neutralizing antibodies that confer active immunity to repeat SARS-CoV-2 infection and binding antibodies that lack this protective ability. Therefore, current commercially available serologic assays cannot determine whether antibodies detected are protective against future SARS-CoV-2 infection. Confirmed and suspected cases of reinfection with the virus in seropositive patients, although rare, have been reported, confirming that these assays should not be used to demonstrate immunity (4). The CDC recommends that results of antibody testing not be used to determine housing arrangements in congregate settings such as dormitories or prisons, to make decisions about returning to work, or to alter work and personal protective equipment requirements for health care workers and first responders (4). Additionally, the effectiveness and durability of anti-SARS-CoV-2 antibody responses have not yet been defined. As such, serologic testing cannot be used to determine immune status since they are unable to define whether detectable antibody is able to effectively neutralize virus to prevent infection or how long such a protective response might exist (7).

Of note, currently available messenger RNA platform COVID-19 vaccines (produced by Pfizer and Moderna) generate a neutralizing antibody response to the spike protein. As such, these vaccinations will likely yield positive results for serologic assays that detect antibodies to the spike protein but not those that detect antibodies to the viral nucleocapsid. General responses in vaccinated patients to commercially available serologic assays are currently being studied and additional guidance is likely forthcoming in the near future.

Conclusions

In conclusion, given the profound impact of SARS-CoV-2 infection worldwide and its ongoing high prevalence in our local community, healthcare providers should have a low threshold for diagnostic testing to confirm COVID-19 in patients with any concerning symptoms. NAAT assays and antigen testing are the major diagnostics utilized to confirm active infection with SARS-CoV-2. Negative test results with rapid NAAT assays and lower sensitivity antigen diagnostics should be confirmed with a high sensitivity RT-PCR NAAT assay when suspicion for infection remains high. Antibody testing is used to confirm prior recent infection but cannot confirm immunity to SARS-CoV-2. Future areas of study will likely include development of increasingly accurate rapid diagnostics and commercial serologic assays that can detect neutralizing antibodies that confer durable immunity to SARS-CoV-2.

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Prevention and Treatment of SARS-CoV-2: An Update

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MEC reports the following disclosures: grants to institution (Janssen), Scientific Advisory Board (Roche)

Abstract word count: 166
Manuscript word count: 3777

Abstract

Introduction: As the SARS-CoV-2 virus continues to spread globally, effective prevention and treatment strategies are critical to controlling the virus and halting its destructive impact worldwide.

Material Content: This article highlights evidence behind prevention modalities including non-pharmaceutical and pharmaceutical interventions and, in the context of vaccines, discusses prevention of both asymptomatic infection and progressive disease. Recent developments are discussed, including the safety and efficacy of multiple vaccines. Various treatment modalities are also discussed under the framework of COVID-19 staged progression from early viral response to hyperinflammation.

Discussion: Rigorous studies have demonstrated efficacy of various prevention and treatment strategies and led to dissemination and uptake. A number of vaccines have remarkable efficacy in preventing symptomatic disease, with early data demonstrating protection against viral replication as well. Repurposed and novel treatments have been found to have real impact on hospitalization and mortality rates. Science has prepared us to face the challenge of COVID-19, and current and future interventions are promising to halt the pandemic and its global impact.

Introduction:

The outbreak of severe acute respiratory syndrome coronavirus-2 (SAR-CoV-2), the virus that causes COVID-19, began in Wuhan, China in December 2019 and by March 2020 had been declared a global pandemic by the World Health Organization.[1] As of February 2021 there have been more than 100 million diagnosed cases worldwide.[2] In Louisiana, more than 400,000 have been diagnosed and almost 10,000 have died.[3] As the virus continues to spread globally, effective prevention and treatment strategies are critically needed to control the virus and halt its destructive impact worldwide.

Prevention:

Multiple methods have been studied to prevent both person-to-person transmission and disease progression. When considering these methods, it is important to understand the difference between prevention of infection (i.e., when the virus invades the host and begins replicating), and disease (i.e., when cellular damage ensues and symptoms appear in the host). Most studies have focused on prevention of disease and/or progression to severe illness, since evaluation of this outcome does not require frequent SARS-CoV-2 viral testing. Here we highlight evidence behind prevention modalities including non-pharmaceutical and pharmaceutical interventions and, in the context of vaccines, discuss prevention of both infection and disease.

Non-pharmaceutical Interventions:

Masking is an important component of infection prevention that has been shown to have efficacy in preventing SARS-CoV-2 transmission.[4–7] Both commercially available and surgical masks offer a degree of protection,[8] although N95 or similar respirators are likely to have the most benefit.[9] There is concern regarding emergence of new, more transmissible variants of the virus, with prominent examples being B.1.1.7 from the United Kingdom and B.1.351 from South Africa.[10,11] In response to these variants CDC is now recommending more widespread use of two masks, i.e. wearing a cloth mask over a disposable mask to reduce tranmissibility.[12] A recent study conducted by the CDC showed that the cumulative exposure of the receiver was reduced 96.4% when both the source of exposure and the person being exposed were wearing a cloth mask over a disposable surgical procedure mask.[13] Although controversial, mask mandates have been associated with a decline in hospitalization rates, presumably through a decline in total number of cases.[14] Similar to masking, use of protective eyewear has also been associated with reduced transmission.[9]

Physical distancing, which was implemented early in the pandemic, has been shown to be effective at preventing and delaying spread of the virus and continues to be encouraged.[15] Per guidance from Centers for Disease Control and Prevention (CDC), people should maintain at least 6 feet of distance inside and outside when interacting with others.[12] Large droplets remain the primary source of transmission of this infection and these tend not to travel beyond 6 feet.[16] A recent meta-analysis found that transmission of coronaviruses was lower with physical distancing at lengths of one meter or more, and that protection was increased as distance was lengthened.[9]

Ventilation is an additional mitigation strategy advocated for by the CDC based on the idea that ventilation that can help reduce the concentration of virus particles in the air.[17] Improvements to increase ventilation include such recommendations as opening windows and doors (when safe and weather-permitting), evaluating ventilation systems to ensure they are operating properly, reviewing the positioning of supply and exhaust air diffusers and/or dampers, and improving central air filtration, among others.[17]

Fomite transmission remains a theoretical concern, as SARS-CoV-2 has been shown to remain viable on plastic and stainless steel for up to 72 hours.[18] However, spread from touching surfaces has not been frequently observed and is thus not thought to be a common way that the virus spreads.[19] The CDC continues to recommend frequent hand washing or using a hand sanitizer with at least 60% alcohol and disinfection of frequently used surfaces.[19]

Vaccines:

Several vaccines have been developed globally and gained emergency authorization. The two that are currently part of the vaccination campaign in the United States are the Pfizer-BioNTech BNT162b2 and the Moderna mRNA-1273 vaccines.[20,21] Both are lipid-nanoparticle packaged mRNA vaccines that encode a prefusion stabilized SARS-CoV-2 full-length spike protein.

The Pfizer-BioNTech BNT162b2 vaccine was evaluated in a randomized placebo-controlled trial with 43,448 participants (21,720 vaccine recipients and 21,728 placebo recipients).[20] All participants were 16 years of age or older assigned in a 1:1 ratio to receive two doses, 21 days apart, of either vaccine or placebo. Eight cases of Covid-19 at least 7 days after the second dose were observed among vaccine recipients and 162 were observed among placebo recipients, corresponding to 95% vaccine efficacy.[20] The safety profile of the vaccine was favorable and adverse events mostly consisted of mild to moderate reactions at site of injection that resolved within 1-2 days. Four related serious adverse events were reported in vaccine recipients, and no deaths were considered related to the vaccine.

The Moderna mRNA-1273 vaccine was evaluated in a randomized, observer-blinded, placebo-controlled trial conducted in 99 centers across the United States. The study assigned individuals at high risk for SARS-CoV-2 infection or its complications to receive two intramuscular injections of mRNA-1273 or placebo, with doses separated by 28 days. The primary end point was prevention of Covid-19 illness (onset at least 14 days following the second dose) in participants who had not previously been infected with SARS-CoV-2. The study enrolled 30,420 participants, 15,210 participants in each arm. Symptomatic Covid-19 was confirmed in 196 participants, 185 in the placebo group and 11 participants in the vaccine group, yielding an efficacy of 94.1%. Safety profile was favorable with headache, fatigue and mild to moderate reaction at the injection site most commonly reported.[21]

Other notable vaccine initiatives that have undergone phase 3 trials but do not yet hold an emergency use authorization (EUA) include the Astra-Zeneca, Johnson & Johnson (Janssen) and Novovax vaccines.[22]

The University of Oxford/AstraZeneca AZD1222 (ChAdOx1 nCoV-19) vaccine has been shown to be efficacious and safe.[23] The vaccine is a two-dose regimen of chimpanzee adenovirus-vectored vaccine that expresses the full spike protein. Results from four ongoing blinded, randomized, controlled trials were pooled for an interim analysis; two of four ongoing trials reported on efficacy and all four reported on safety. Participants greater than or equal to 18 years were randomly assigned 1:1 to the vaccine or control with meningococcal group A, C, W, and Y conjugate vaccine or saline. Two vaccine doses containing 5×10^{10} viral particles (standard dose; SD/SD cohort) were administered; a subset in the UK trial inadvertently received a half dose as their first dose (low dose) and a standard dose as their second dose (LD/SD cohort).[24] The primary efficacy analysis included 11,636 participants and as primary endpoint evaluated for symptomatic COVID-19 in seronegative participants with a nucleic acid amplification test (NAAT)-positive swab more than 14 days after the second dose. Vaccine efficacy was 70.4% overall, but surprisingly was lower in the SD/SD arm (62.1%) versus the LD/SD arm (90.0%). While zero COVID-19-related hospital admissions occurred in vaccine recipients, ten occurred in the control groups, two of which were severe. Regarding safety, no serious adverse events or deaths associated with treatment in vaccine recipients.

The Janssen vaccine, Ad26.COV2.S, is a recombinant vector vaccine that uses a human adenovirus to express the SARS-CoV-2 spike protein. This vaccine requires only a single injection and can be stored in a refrigerator for months. Initial safety profile was established with data from published phase 1 and 2 trials,[25] and the vaccine is currently being evaluated as part of the ENSEMBLE trial.[26] ENSEMBLE is a phase 3, randomized, double-blinded trial in which participants receive either the single dose vaccine or placebo. The study included 44,325 participants recruited from study sites including Argentina, Brazil, Chile, Colombia, Mexico, Peru, South Africa, and the United States and was able to evaluate efficacy in locations with emerging variants. Although data from this study have not yet been published, NIH reported on a preliminary analysis of 468 participants who developed symptomatic Covid-19.[27] Reportedly the vaccine has 66% efficacy at preventing development of moderate to severe Covid-19 at 28 days post vaccination, with a level of 72% protection in the United States. Notably, efficacy of 85% at preventing severe/critical Covid-19 was observed across all regions, and there were no deaths in the vaccine arm relative to five COVID-19 deaths in the placebo arm. Complete safety data are forthcoming.

The Novavax vaccine (NVX-CoV2373) is a recombinant SARS-CoV2 spike protein nanoparticle vaccine with Matrix-M1 adjuvant. It has been studied as a two-dose vaccine series administered 21 days apart. Phase 1-2 trial data have been published establishing the safety of the vaccine and showing a robust immune response, inducing a high titer of antibodies in excess of that seen in the convalescent serum of symptomatic Covid-19 patients.[28] Although Phase 3 data have not yet been published, the manufacturer has released results of a preliminary analysis of UK phase 3 trial.[29] The trial enrolled more than 15,000 participants, ages 18-84. The primary endpoint was symptomatic COVID-19 (polymerase chain reaction [PCR]-confirmed) occurring at least 7 days following second vaccine dose. Initial, recently reported results were based on the first 62 Covid-19 cases in trial participants, with 56 being in the placebo group and 6 in the vaccine group. Based on these numbers, an efficacy of 89.3% was reported. Notably the trial was conducted in a region with wide circulation of the UK virus variant, which was detected in 50% of participants with PCR confirmed symptomatic Covid-19. Post-hoc analysis suggested 95.6% efficacy against the original Covid-19 strain and 85.6% against the new variant. Although no specific data on adverse events in the phase 3 trial have been released, it was reported that adverse events requiring medical attention occurred at low levels and were evenly distributed between the intervention and placebo group.

Vaccines to Prevent Asymptomatic Infection

Early promising data provide biological plausibility that vaccines will prevent not only disease and progression to severe COVID-19, but also asymptomatic infection and therefore stand to limit asymptomatic transmission. Earlier nonhuman primate (NHP) models have examined the airways of macaques following vaccination with both the Novavax and Janssen vaccines.[30,31] These studies demonstrated low or no detectable RNA in respiratory tracts of macaques following vaccination.

The University of Oxford/AstraZeneca study evaluated for asymptomatic infection in addition to the aforementioned outcomes. Although the total number of cases was small (n=69), there was a signal for efficacy in preventing asymptomatic transmission (58.9% efficacy in LD/SD group and 3.8% in SD/SD group). A more recent analysis of "real-world" data on the Pfizer vaccine roll-out in Israel has demonstrated an encouraging finding, that is, that viral loads are significantly reduced in those who have been vaccinated.[32] The study, which has not yet been published as peer-reviewed, was able to examine post-vaccination infections via laboratory data. The authors compared the mean viral load for infections that occurred on days 12-28 following the first vaccine dose to viral loads of uninfected controls and found a four-fold reduction in the samples from vaccinated individuals. This finding offers provides hope that asymptomatic transmission will also be reduced with vaccination, which is critical to achieving herd immunity.

Treatment

The push to find effective treatments for COVID-19 has been a race against time, as more sickness, death, and economic devastation occur with each passing day. Initial attempts at repurposing already existing pharmacologic agents in order to treat COVID-19 were unfortunately not met with great success. Lopinavir-ritonavir,[33–35] azithromycin,[36,37] hydroxychloroquine[35–38] were studied due to reported in vitro activity; however, in subsequent trials these agents were not shown to have significant benefit in symptomatic improvement or mortality. However, there are exceptions, for example remdesivir and dexamethasone (see below). Fortunately, our treatment arsenal now includes more than a few different therapeutic options, and our management of COVID-19 has improved since early 2020, as evidenced by declining mortality over time. This section will focus on pharmaceutical interventions to treat COVID-19 symptoms and improve outcomes, and includes a discussion of SARS-CoV-2 pathophysiology influencing the current treatment paradigm.

Pathophysiology and Treatment Paradigm

The staged progression of COVID-19 illness was described early in the pandemic, and our current treatment paradigm is still based on this understanding of SARS-CoV-2 pathophysiology.[39] In essence, there are two phases of disease: 1) a "viral response" phase, engendered by the virus itself, which is in some cases followed by 2) a "host inflammatory response" phase, as evidenced by elevated levels of inflammatory markers including IL-6, d-dimer, ferritin, and C-reactive protein (see Figure 1).[39] The viral response phase corresponds to milder clinical symptoms such as dry cough, fever, and myalgias, while the hyperinflammatory response is characterized by shortness of breath, hypoxia, shock and/or acute respiratory distress syndrome. Results of clinical trials have mostly supported this framework for considering disease progression, i.e. anti-viral therapies have shown efficacy when administered early in disease course, while they are not effective later, while the opposite is true for immunomodulatory agents.

Monoclonal and Polyclonal Antibody Treatment

In the context of COVID-19, monoclonal antibodies (mABs) bind to SARS-CoV-2 spike protein and block viral entry into human cells, a process called neutralization. They function as anti-viral therapy and have been shown to prevent progression to severe disease when administered early in the course of COVID-19 infection.

LY-CoV555, or bamlanivimab, has demonstrated efficacy in treating outpatients but not in those who are hospitalized. In an interim analysis of an ongoing phase 2 trial (BLAZE-1), 452 outpatients with recently diagnosed mild or moderate COVID-19 (within 3 days of first positive test) were randomized to receive a single IV infusion of one of three doses of LY-CoV555 or placebo. By day 29, viral loads were reduced in addition to reductions in hospitalization or emergency department visits in the mAB group relative to the placebo group.[40] Furthermore, in a post-hoc analysis of patients at high risk (BMI ≥35 or ≥65 years old) for disease progression, 4 of 95 patients (4%) in the mAB arm were hospitalized or visited the emergency department, compared to 7 of 48 (15%) of those in the placebo arm.[41] Bamlanivimab currently holds an EUA for treatment of mild to moderate COVID-19 in adults and children 12 years of age and older who have positive PCR-testing for SARS-CoV-2, weigh at least 40 kg), and who are at high risk for progressing to severe COVID-19 and/or hospitalization. Consistent with our treatment paradigm for early (viral response phase) versus late (host inflammatory response phase) disease, bamlanivimab is not recommended for hospitalized patients or those who require supplemental oxygen. This is due to the results of a study of the mAB coadministered with remdesivir which did not demonstrate efficacy among hospitalized with COVID-19.[42] The trial had to be stopped early due to demonstrated futility of the treatment.

REGN-COV2, a neutralizing monoclonal antibody cocktail consisting of casirivimab and imdevimab, was evaluated in a study in non-hospitalized patients with COVID-19.[43] The two mABs are noncompeting, neutralizing human IgG1 antibodies that target the receptor-binding domain of the SARS-CoV-2 spike protein. The study was a multicenter, randomized, double-blind, and placebo-controlled trial in which participants were assigned 1:1:1 to receive placebo or REGN-CoV-2 at two different doses. Six of 93 patients (6%) in the placebo group and 6 of 182 patients (3%) in the combined REGN-COV2 group had a medically attended visit, a relative difference of approximately 49%. The neutralizing titers achieved with REGN-COV2 were more than 1000 times the titers achievable with convalescent-phase plasma, and REGN-COV2 had a significant and rapid effect on viral load reduction. Casivirimab and imdevimab combination has gained EUA approval and is available for patient at least 12 years of age and over 140 pounds with mild to moderate SARS-CoV-2.

Convalescent plasma (passive infusion of polyclonal antibodies isolated from those with prior SARS-CoV-2 infection) has been frequently administered to patients since the early days of the pandemic. Data regarding its efficacy has been mixed but support early administration during the viral response phase. PlasmAr was a randomized (2:1), double-blind, placebo-controlled, multicenter trial comparing convalescent plasma versus placebo in patients hospitalized with COVID-19.[44] In total, 228 patients were assigned to receive convalescent plasma and 105 were assigned to placebo. Median duration of symptoms prior to enrollment was 8 days. No significant differences were observed in clinical status or overall mortality at 30 days between patients treated with convalescent plasma and those who received placebo. Another randomized, double-blind, placebo-controlled trial was conducted to examine effects of high titer convalescent plasma when administered early, within 72 hours after onset of symptoms. In the study, which involved 160 pateints (80 in each arm), severe respiratory disease developed in 16% of those who received convalescent plasma 31% of those who received placebo (relative risk, 0.52).[45] Convalescent plasma currently maintains FDA EUA for treatment of SARS-CoV-2.[46]

Remdesivir

Originally developed to treat hepatitis C and respiratory syncytial virus, and then later repurposed and studied to treat Ebola virus and Middle East respiratory syndrome (MERS-CoV),[47] remdesivir has been studied in several studies for SARS-CoV-2. The drug inhibits viral RNA-dependent, RNA polymerase and was found to have in vitro inhibitory activity against SARS-CoV-2.[48] Remdesivir was subsequently evaluated in the Adaptive Covid-19 Treatment Trial (ACTT-1), which was a randomized, double-blind, placebo-controlled trial to evaluate remdesivir for treatment of Covid19.[49] All participants were hospitalized, and stratification occurred based on disease severity. Those who received remdesivir had a median recovery time of 10 days, as compared with 15 days among those who received placebo. No statistically significant difference in mortality was noted. Subsequently, remdesivir has gained FDA approval for the purpose of treating SARS-CoV-2.[50] Another trial that evaluated its efficacy has been the WHO Solidarity Trial, which was a large, open-label, randomized trial to evaluate the effect of remdesivir, hydroxychloroquine, lopinavir, and interferon beta-1a in patients hospitalized with COVID-19. The authors concluded that the agents studied—including remdesivir—had little or no effect on hospitalized patients with Covid-19 based on outcomes in overall mortality, initiation of ventilation, and duration of hospital stay.[35] This has caused the WHO to issue a conditional recommendation against the use of remdesivir due to lack of evidence of efficacy.[51] Remdesivir does however remain part of NIH recommendations for SARS-CoV-2 management in the appropriate clinical context.[52]

Immunomodulatory Agents:

Consistent with the host inflammatory response discussed above, the phenomenon of “cytokine storm” is suspected to play a large role in pathogenesis of SARS-CoV-2,[53] and therapeutic agents targeting cytokine pathways have also been studied.

Anti-IL-6 receptor monoclonal antibodies (e.g., tocilizumab, sarilumab) have been investigated in hopes of using them to modulate the immune response in COVID-19. Early studies did not demonstrate significant efficacy, although more recent studies may show some benefit. The COVACTA trial was a double-blind, randomized trial to evaluate tocilizumab plus standard therapy versus placebo plus standard therapy in 452 patients with severe Covid-19 pneumonia.[54] Results have not yet been published with peer review, but reportedly no difference in mortality was seen at 28 days; however, median time to hospital discharge and duration of ICU stay were 8 and 5.8 days shorter, respectively, in patients randomized to tocilizumab. The EMPACTA trial evaluated tocilizumab plus standard therapy versus placebo plus standard therapy in 389 patients.[55] Patients had COVID-19 pneumonia and were not intubated. Results showed that tocilizumab reduced the rate of mechanical ventilation or death (12.0% versus 19.3%). More recently, the RECOVERY platform trial assessed tocilizumab plus standard care versus standard care alone in patients hospitalized with COVID-19 with various degrees of hypoxia. Per preliminary data, patients assigned to tocilizumab (n=2022) were more likely to be discharged from the hospital alive within 28 days (54% vs. 47%).[56] Among patients in the tocilizumab group there were 596 (29%) deaths compared to 694 (33%) in the standard care group. Although these recent studies hint at the potential for IL-6 inhibitors, and particularly tocilizumab, to reduce duration of ICU stay and hospitalization, there is a more modest trend reduction in mortality. The RECOVERY platform trial results are encouraging in light of the large sample size, but it is not yet clear how these findings will impact current guidelines.

Another attempt at using immune modulation for treatment of SARS-CoV-2 was with Baricitinib in combination with remdesivir. Baricitinib is an orally administered, selective inhibitor of Janus kinase (JAK)-1 and 2. Interestingly, baricitinib was identified as a SARS-CoV-2 therapeutic candidate based on artificial intelligence algorithms. Baricitinib inhibits the intracellular signaling pathway of cytokines known to be elevated in severe Covid-19, including IL-2, IL-6, IL-10, interferon-γ, and granulocyte–macrophage colony-stimulating factor, it reduces SARS-CoV-2 cellular entry and infectivity, and it also improves lymphocyte counts in patients with COVID-19. ACTT-2 trial was a randomized, double-blind, placebo-controlled trial designed to evaluate remdesivir and baricitinib versus remdesivir and placebo.[57] Patients who required supplemental oxygen and received combination treatment with baricitinib plus remdesivir recovered a median of one day faster than patients who received remdesivir and placebo. Patients receiving noninvasive ventilation or high-flow oxygen had a median time to recovery of 10 days in the baricitinib arm versus 18 days in the control arm. The study was not sufficiently powered to assess for a difference in mortality. Baricitinib plus remdesivir was shown to be superior to remdesivir alone in reducing recovery time and has received an EUA for use in SARS-CoV-2.[58]

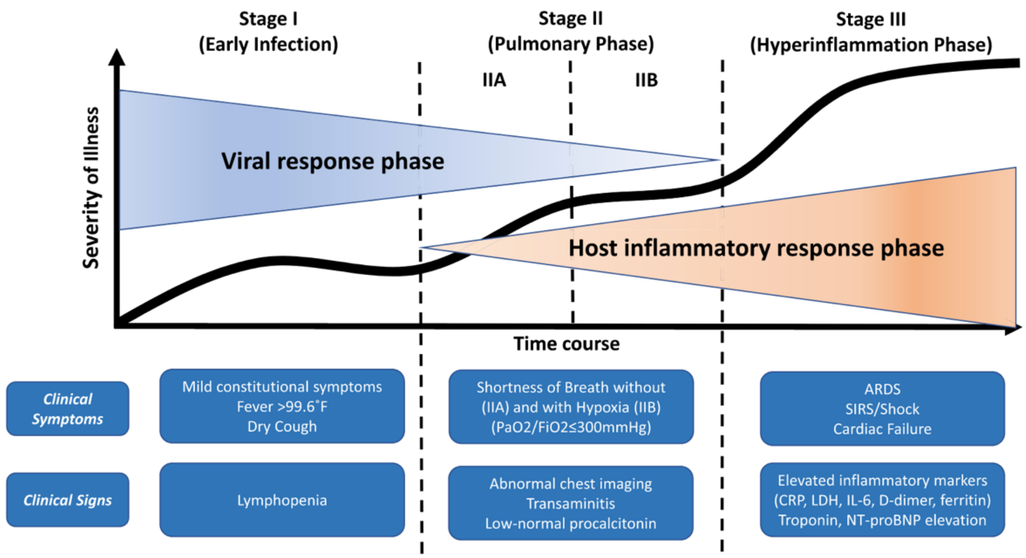
Steroids

The RECOVERY platform trial was a randomized, controlled, open-label platform trial which sought to evaluate the efficacy of hydroxychloroquine, lopinavir-ritonair, azithromycin, and dexamethasone. The dexamethasone arm of the trial was significant for demonstrating a mortality benefit in patient requiring noninvasive oxygen support and invasive mechanical ventilation.[59] Patients on dexamethasone and mechanical ventilation were observed to have a mortality rate of 29.3% versus 41.4% when compared to the standard care group. Among those receiving oxygen without invasive mechanical ventilation a more modest benefit in mortality was observed with 23.3% with dexamethasone plus standard care versus 26.2% with standard care alone. Among patient not requiring supplemental oxygen or respiratory support, no statistically significant difference was noted with dexamethasone.

Conclusion:

The COVID-19 pandemic has presented a devastating global health crisis that has taken almost 2.5 million lives worldwide. However, scientists, physicians, and public health organizations have risen to the challenge. Rigorous studies have demonstrated efficacy of various prevention and treatment strategies and led to dissemination and uptake. A number of vaccines have been developed and demonstrate remarkable efficacy in preventing disease. Furthermore, there is hope that they protect against viral replication and thus lead to establishment of herd immunity. Also inspiring hope is treatment for COVID-19 which has evolved over time. An early understanding of the escalating progression of disease—from viral response to host inflammatory response— facilitated evaluation of therapeutic modalities. While initial studies of repurposed drugs were largely unsuccessful, later studies of repurposed and novel agents have demonstrated real impact on hospitalization and mortality rates. Science has prepared us to face the challenge of COVID-19 and current and future interventions are promising to halt the pandemic and its global impact.

Figure 1.



Reprinted from J Heart Lung Transplant, 39(5): 405-407, Siddiqi H and Mehra M, COVID-19 illness in native and immunosuppressed states: A clinical–therapeutic staging proposal, p 405-407, May 2020, with permission from Elsevier.

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COVID-19 AND CARDIOVASCULAR DISEASE

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Abstract:

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has overwhelmed healthcare systems, strangled economies and led to over 2.3 million deaths globally. Up to half of infected people are asymptomatic. If symptoms appear, they range from mild respiratory and gastrointestinal symptoms to cardiovascular and pulmonary complications that may prove fatal. Underlying cardiovascular diseases are associated with significantly worse patient outcomes and increased mortality. Accordingly, it is imperative that people with cardiovascular disease avoid SARS-COV-2 exposure and seek prompt medical attention if they develop symptoms. In this review, we will highlight the cardiovascular and thrombotic manifestations of COVID-19 infection.

Background:

With at times several thousand newly diagnosed cases on average daily and total deaths approaching 9,000 in Louisiana (as of January 2021), the COVID-19 pandemic is far from being over[1]. The fear of COVID-19 owing to its high infectivity has markedly influenced our lifestyle, not only changing the way we interact and function but also how we eat and breathe. The main symptoms of COVID-19 include fever, cough, dyspnea, sore throat, fatigue, anosmia, dysgeusia, headache and gastrointestinal problems[2].

Pathogenesis:

SARS-CoV-2 is a single-strand RNA coronavirus. It enters human cells via endocytosis by binding the angiotensin converting enzyme 2 receptor (ACE2). ACE2 is expressed in lung alveolar cells, cardiac myocytes and vascular endothelium, amongst others (figure below)[3]. Like a few other members of the coronavirus family, it is believed to have moved from bats to an intermediate host (possibly the Malayan pangolin) and then to humans[4]. Depending on the surfaces where it resides, the virus can survive up to 3 days[5]. It can be transmitted by symptomatic and asymptomatic carriers via respiratory droplets and aerosols. It has a median incubation period of about 5 days[6]. SARS-CoV-2 can disrupt the innate immune response inciting an out-of-proportion systemic inflammatory response with consequent tissue injury and multiorgan failure in severe cases. In particular, the cellular immune response activates the macrophages and lymphocytes and stimulates their proliferation causing a release of proinflammatory cytokines and chemokines[7]. Cytokine storm, which may contribute to multiorgan dysfunction, results from uncontrolled T cell activation along with dysregulated release of IL-1, IL-6, interferons and TNF-α[7]. Immunometabolism alterations with immune system activation are postulated to result in endothelial disruption, plaque instability and thrombosis leading to atherosclerosis and acute coronary events[8]. There have been reports of activated T cells, macrophages and SARS-COV-2 invading the myocardium directly causing fulminant myocarditis and arrhythmias[9,10]. Thrombocytopenia and elevated D-dimer levels are commonly associated with a complicated course of the disease[11]. SARS-CoV-2 impairs the balance between coagulation system and fibrinolysis via dysregulated inflammatory cascade and endothelial damage. Viral invasion of the endothelial cells has also been reported [12,13]. Formation of neutrophil extracellular traps (NET) in COVID-19 patients contribute to occlusion of pulmonary microvessels and organ damage[14]. In a recent study, NET was detected in coronary thrombus samples of all COVID-19 patients who presented with STEMI[15]. Increased release of von Willebrand and tissue factor along with other cytokines promote coagulation and disseminated intravascular coagulation (DIC)[16]. Liver dysfunction and elevated antiphospholipid antibodies are also hypothesized to play a role in thrombotic complications of COVID-19[17].

The cardiovascular system and COVID 19

Cardiovascular manifestations of COVID-19 include acute myocardial injury, acute coronary syndromes, myocarditis, congestive heart failure, cardiogenic shock, cardiac arrhythmias, as well as arterial and venous thromboembolism (VTE).

Myocardial injury

Acute myocardial injury is defined as a rise and/or fall of high sensitivity cardiac troponin (hs-cTn) values above the 99th percentile of upper reference limit[18]. It is more prevalent in COVID-19 patients with more severe illness and underlying cardiovascular disease (CVD). Numerous studies have highlighted the correlation between elevated hs-cTn levels and disease severity [19,20,21,22]. A single center, retrospective case series of 187 patients with COVID-19 reported that patients with CVD were more susceptible to myocardial injury compared to patients without CVD (54.5% vs 13.2%)[19]. Similarly, in-hospital mortality for COVID-19 patients without CVD and normal cTn was 7.2% but 37.5% in patients who had CVD but normal cTn. In comparison, COVID-19 patients who had CVD and elevated cTn the mortality was 69.4%. Progressive increases in cTn portend worse outcomes. cTn levels were unchanged in survivors whereas they continued to rise in non-survivors till the time of death. The median time of death from symptom onset in this study was 18.5 days[23]. It is of paramount importance to accurately identify and differentiate myocardial injury from various types non-ST elevation myocardial infarction (NSTEMI) as their management differs significantly. Acute myocardial injury is managed by treating the underlying disease process.

Acute coronary syndrome (ACS)

The risk of atherosclerotic plaque disruption and acute coronary syndrome is increased in severe systemic inflammation[24]. ACS has been reported in patients with influenza and SARS infections[24,25,26]. The incidence of ACS in COVID-19 is unknown. In a case series involving 18 patients with COVID-19 and ST segment elevation, 9 patients underwent coronary angiography, 6 had obstructive coronary artery disease and 5 underwent percutaneous coronary intervention. Patients with non-obstructive disease had worse prognosis with a 72% in-hospital mortality[27]. Another case series from Italy involving 28 patients with COVID-19 and ST segment elevation myocardial infarction, assessment by coronary angiography showed that 17 patients had evidence of a culprit lesion that required revascularization[28]. Of note, ST segment elevation myocardial infarction was the first clinical manifestation of COVID-19 in 24 of these 28 patients who had not yet received a positive test result for COVID-19 at the time of coronary angiography. These observations suggest that patients with COVID-19 can present without the hallmark symptoms of this infection. Importantly, a global decline in patients with myocardial infarction seeking medical care has been noted, perhaps owing to the fear of seeking medical care and risking exposure to the virus causing COVID-19. A global survey by the European Society of Cardiology reported a greater than 50% decline in the incidence of myocardial infarction during the peak of COVID-19[29]. Concomitantly, patients with cardiovascular illness and COVID-19 experienced higher mortality, perhaps related to late presentations in the course of their acute coronary syndromes[30].

Recommendations about the management of acute myocardial infarction during the COVID-19 pandemic are unchanged from those prior to the pandemic, with primary PCI still the standard of care for patients presenting with STEMI within 90 minutes of first medical contact[31]. Patients with NSTEMI and COVID-19 should be treated with optimal medical therapy, and urgent coronary angiography with possible percutaneous coronary intervention (PCI) offered to patients who have high risk presentation based on the presence of elevated cardiac biomarkers, sustained ventricular tachycardia, hemodynamic instability, recurrent ischemic chest pain despite ongoing medical management, new pulmonary edema or mitral regurgitation murmur, recent PCI (less than 6 months) or previous coronary artery bypass grafting (CABG) or new onset systolic heart failure (EF<40%)[31].

Heart failure and cardiogenic shock

Nearly a quarter of people hospitalized for COVID-19 have acute heart failure with a mortality rate as high as 49%.[32,33] Elevated B-type natriuretic peptide (BNP) and pro-BNP levels are also commonly seen (50% of the hospitalized patients) and portend a worse prognosis[34]. A prospective study involving 100 hospitalized COVID-19 patients reported 39 patients with right ventricular (RV) dysfunction, 16 patients with left ventricular (LV) diastolic dysfunction and 10 patients with LV systolic dysfunction (2 patients had prior diagnosis of LV systolic dysfunction)[35]. In hospitalized patients, RV dysfunction/failure is precipitated by increased pulmonary vascular resistance or pulmonary pressure. This increase can result from pneumonia, pulmonary embolism, hypoxic pulmonary vasoconstriction, hypercarbia, decrease in lung volume, or use of positive end expiratory pressure and pressors in intubated patients[33]. Right ventricular longitudinal strain (RVLS) using echocardiography is a powerful predictor of morbidity and mortality has been found to be more accurate than RV fractional area change and tricuspid annular plane systolic excursion in predicting worse outcomes[36]. Acute decompensation in preexisting heart failure patients with COVID-19 is believed to result from exacerbation of the pre-existing comorbid conditions in the setting of an inflammatory surge[37].

COVID-19 patients with heart failure (HF) should be managed as per current HF guidelines including use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers[38]. Optimal fluid and diuretic usage to restore and maintain euvolemia is of primary importance. Management of cardiogenic shock in these patients requires a multidisciplinary approach. The use of mechanical circulatory support (MCS) should be carefully weighed as the outcomes have not been very promising. In a case series of 52 COVID-19 patients, only 16.7% of the patients who were treated with ECMO survived[39].

Myocarditis

The prevalence of myocarditis among COVID-19 patients is unclear[40]. In a case series of 150 COVID-19 patients, 7% of the deaths were attributed to myocarditis[41]. Studies have reported fulminant myocarditis with findings of myocardial inflammatory mononuclear infiltrate during autopsy[9,10]. SARS-CoV-2 particles have been identified in cardiac tissue suggesting direct infection[12,13]. Glucocorticoid therapy and other antiviral agents have been administered to treat myocarditis as more effective treatment strategies are sought.

Arrhythmias and cardiac arrest

Both tachyarrythmias and bradyarrhythmias have been reported in COVID-19 patients. Arrhythmias resulting from inflammatory stress, hypoxia, metabolic derangements and ischemia are more prevalent in critically ill patients. Arrhythmias were reported in 44.4% of ICU patients compared to 6.9% in non-ICU patients, however, the type and duration of arrhythmias were not reported in this study[42]. Another study of 700 COVID-19 patients concluded that arrhythmias and cardiac arrest (with an incidence of 7.7%) are consequences of systemic infection and inflammation generally correlating with disease severity[43]. New onset atrial fibrillation was noted in 25 patients, 10 patients had non-sustained ventricular tachycardia and 9 developed clinically significant bradyarrhythmias. All cardiac arrests (in 9 patients) and most of the arrhythmias occurred in critically ill patients. Only 1 case of torsade de pointes was reported despite many patients being managed with medicines that prolong the QT interval. Other studies have also reported a low incidence (less than 1%) of torsades de pointes in COVID-19 patients[44,45]. As in the general population, QT interval prolonging agents should be avoided in high risk COVID-19 patients who have a baseline QTc of ≥500 ms or with known congenital long QT syndrome and should be discontinued if QTc exceeds to 500 ms during monitoring[45].

Cardiometabolic Syndrome:

The COVID-19 pandemic has highlighted the importance of improving cardiometabolic health. There is a need to devise an all-encompassing prevention program for patients to reduce chronic disease risks and create a healthy culture[46]. Cardiometabolic-based chronic disease results from the interplay between primary and metabolic drivers[47]. Primary drivers include genetic, environmental and behavioral aspects whereas abnormal adiposity, dyslipidemia, dysglycemia and hypertension constitute the secondary drivers[47]. Concerted efforts should be made to decrease the severity of metabolic drivers for primary prevention. Lifestyle changes, diligent use of insulin and antihypertensives in admitted patients and continuation of statins should be emphasized[46].

Thromboembolic disease and DIC

COVID-19 predisposes patients to arterial and venous thrombosis due to platelet activation, excessive inflammation, endothelial dysfunction and stasis. Elevated D-dimer levels are a common finding and warrant further investigations for acute venous thromboembolism (VTE) in the presence of other clinical manifestations[11]. In patients with out of proportion hypoxemia, hemodynamic instability and/or unexplained right ventricular dysfunction, VTE should always be considered. Thrombotic complications were reported in 31% of critically ill patients with COVID-19; 25% patients had segmental and subsegmental pulmonary embolism, 3% had ischemic strokes (arterial thrombotic events), 2% had catheter related upper extremity thrombosis and 1% had proximal deep venous thrombosis of leg[48]. Elevated D-dimer levels (>1 g/L) in patients with COVID-19 are strongly associated with in-hospital death with a mortality of 42% and odds ratio of 18.4 (p< 0.005) as reported in one of the retrospective studies[49]. Analysis of 183 patients with COVID-19 also found that non-survivors had significantly higher D-dimer levels and fibrin degradation products along with longer prothrombin time at the time of admission. 71.4% patients who died fulfilled the diagnostic criteria of DIC in accordance with International Society on Thrombosis and Haemostasis whereas only 0.6% of the survivors had DIC[50]. These hemostatic changes in COVID-19 reflect coagulopathy that predisposes to thrombotic events.

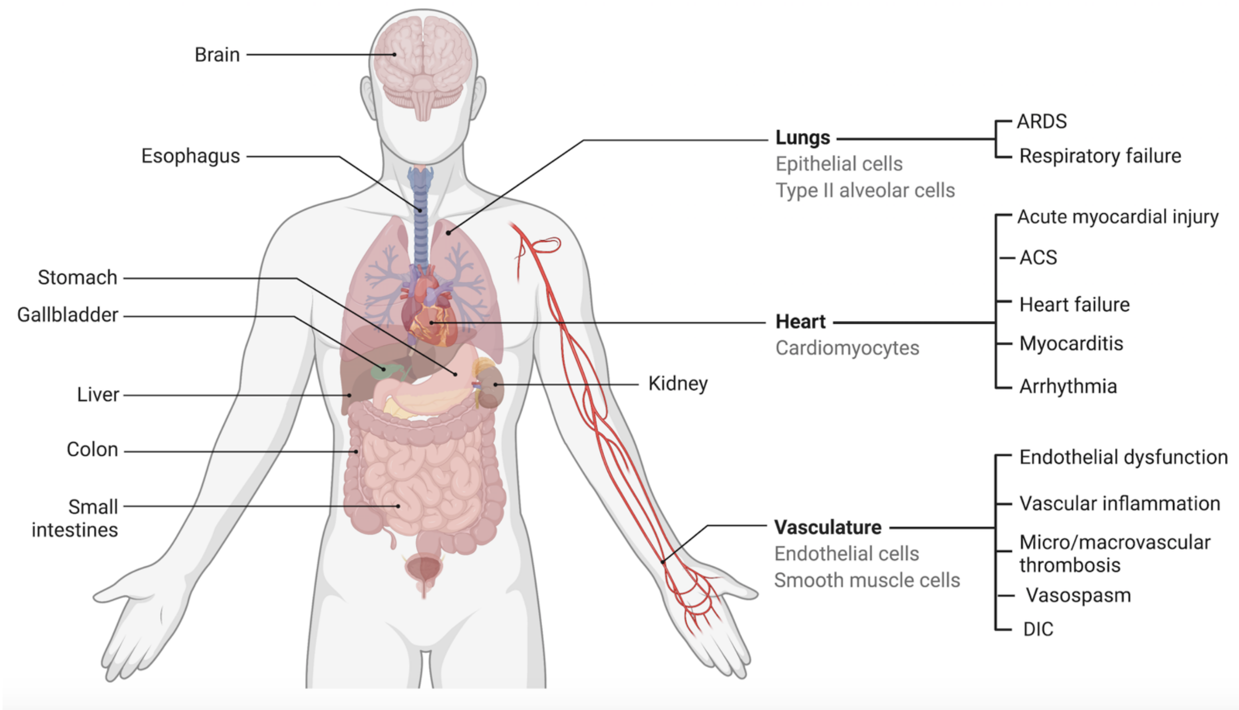
The choice of anticoagulant agent for the treatment of VTE depends on the patient's comorbidities and admission status. In hospitalized patients, parenteral anticoagulation with unfractionated heparin (UFH) or low molecular weight heparin (LMWH) is recommended as these agents are short acting[51]. UFH has fewer known drug-drug interactions with investigational COVID-19 therapies and can be reversed with protamine. The limitation of UFH is that it takes time to achieve therapeutic aPTT and increases the exposure of healthcare workers in order to monitor blood levels. Consequently, LMWH is preferred.

The guideline panels of American Society of Hematology, American College of Chest Physicians and World Health Organization recommend treating all hospitalized and critically ill patients with COVID-19 with prophylactic dose anticoagulation[52,53,54]. A meta-analysis which compared thrombotic and bleeding outcomes in patients with COVID-19 treated with prophylactic dose anticoagulation versus intermediate or therapeutic doses concluded that the odds of VTE and mortality were not different between these groups[55]. As per the recent National Institutes of Health (NIH) COVID-19 treatment guidelines, VTE prophylaxis is not recommended for patients with COVID-19 who are discharged from hospital[56]. Non-hospitalized patients with COVID-19 should not be initiated on anticoagulants and antiplatelet therapy for the prevention of VTE or arterial thrombosis unless they have other indications for the therapy[56]. For pregnant patients hospitalized with COVID-19, American College of Obstetricians and Gynecologists and Maternal Fetal Medicine recommends prophylactic dose anticoagulation unless contraindicated[57,58].

Conclusion:

In patients with COVID-19, cardiovascular complications are not uncommon and portend a worse prognosis, especially in patients with preexisting cardiovascular disease. Cardiovascular treatment strategies in COVID-19 patients continue to evolve. Considerations for the preventive and therapeutic use of antithrombotic agents to mitigate the thrombotic and hemorrhagic events in these high-risk patients should always be the priority. There should be a focus on prevention, acute management, and long-term outcomes of coronavirus disease–related cardiometabolic syndrome. Healthcare workers must educate patients especially those with cardiovascular diseases to seek prompt medical care if they become ill.

Figure: Expression of ACE2 in various tissues. The disease manifestations of COVID-19 in lungs, heart and vasculature is shown on the right. (Created with BioRender.com)



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The Effects of the COVID-19 Pandemic on the Undergraduate Medical Education Experience at Louisiana State University School of Medicine in New Orleans

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The Effects of the COVID-19 Pandemic on the Undergraduate Medical Education Experience at Louisiana State University School of Medicine in New Orleans

Abstract: The COVID-19 pandemic affected students at Louisiana State University School of Medicine in New Orleans (LSU SOM NO) as it did at many other medical schools around the world. School administrators, faculty, and students had to adjust their teaching, learning, and assessment strategies in a matter of days to weeks to complete training requirements and ensure continuing education. Four classes of students and the incoming matriculating class of August 2020 faced an array of unique and universal challenges. Guidance from the American Association of Medical Colleges (AAMC) and the Liaison Committee on Medical Education (LCME) shaped the approach taken by course directors, clerkship directors, and faculty within the Offices of Undergraduate Medical Education and Student Affairs to ensure compliance with national recommendations and accreditation standards. Here we describe our efforts and the challenges that lie ahead.

Introduction

In early March of 2020, cases of patients with COVID-19 surged in the New Orleans metropolitan area. The COVID-19 stay at home order for Louisiana was issued on March 22nd.[1] This necessitated a comprehensive shift in educational strategies for students in their pre-clerkship and clerkship phases. Faculty leaders in the Offices of Undergraduate Medical Education and Student Affairs utilized guidance from our hospital partners and national organizations, such as the AAMC and LCME, to craft a plan for continuing education while keeping our students safe and compliant with city and state regulations. Hospital partners and national organizations recommended that medical students cease clinical work in the immediate weeks following the stay at home order, primarily because of the shortage of Personal Protective Equipment (PPE). This article outlines the changes initiated by class in addition to the overall changes to the medical school experience. All classes encountered different challenges, including curriculum variations in the pre-clerkship phase, postponement or cancellation of important rituals and ceremonies, and alterations in the residency interview and match selection process.

The Class of 2020

Faced with graduation only weeks after the onset of the COVID-19 outbreak in the United States, like many schools around the country, the possibility of an early graduation for senior year medical students was considered. Leaders at LSU SOM NO decided against pursuing the option given concerns about licensure, supervision, and safety for students who were in a limbo status, being unable to officially start residency training until July 1. Following guidance issued by the AAMC, stating that any student participation in the care of patients with COVID-19 should be voluntary [2], we quickly developed a new senior year elective so that students who were interested in contributing to local medical volunteer activities could participate and receive credit. Due to PPE shortages, these activities were limited to research, community testing with supervision, following up with patients with COVID-19 who had been discharged from the hospital or sent home from the emergency department, and serving at our city convention center, which was converted to a treatment site. Most student participation involved analyzing patient charts and data from our hospitals' intensive care units, contributing valuable skills to the creation of some of the New Orleans early evidence-based ICU protocols for care of these patients.[3]

The United States Medical Licensure Examination Step 2 Clinical Skills Examinations (USMLE Step 2 CS) has historically been required for graduation from our school. In response to the pandemic, the National Board of Medical Examiners (NBME) suspended, and subsequently discontinued, Step 2 CS testing.[4,5] During the initial suspension, several of our students were scheduled for but had not yet taken the examination. The school moved forward with its defined process through the Academic Standards Committee to waive the requirement of Step 2 CS for those graduating students. The state licensure boards took similar action with respect to licensing requirements.

Changes for the class 2020 were not limited to clinical and testing responsibilities, however. Two important ceremonies were cancelled: Match Day, the ritual at which students discover their residency locations, and graduation. Instead of celebrating their years of hard work surrounded by classmates and family, students opened an email from the National Resident Matching Program (NRMP) in solitude. This represented a great disappointment for students, families, and faculty who deserve commendation for quickly adapting to a new harsh reality. The traditional graduation ceremony was originally scheduled for May 14, 2020. Per LSU SOM NO tradition, the day before graduation is precommencement. Members of our Student Affairs office, in conjunction with our Information Technology staff, quickly created a virtual precommencement event, which was conducted via Zoom and streamed on YouTube for family and friends. As per our tradition, student awards were given, and students were symbolically hooded by student-selected faculty or family members with terminal doctoral degrees. The class president and other class officers worked tirelessly to make the event meaningful for their peers, including delivering ceremonial goody bags to the students' residences without in-person contact. We have promised the Class of 2020 the best reunion ever, once in-person gathering is possible again.

<u>The Class of 2021</u>

When the stay at home order was issued in New Orleans, the third-year students were removed from conventional, in-person clinical rotations. Our clerkship and site directors worked closely and swiftly with members from the Offices of Undergraduate Medical Education and Student Affairs to transition clerkship didactic activities to virtual sessions and allow students to participate in telemedicine visits. Approximately 8 weeks after transitioning to all-virtual participation, our hospital partners allowed students to return to in-person clinical duties, seeing patients on a limited basis. The lengths of clerkships were adjusted, and we met with students and clerkship faculty frequently to ensure that core clinical conditions and clerkship requirements were met in accordance with accreditation standards. This was achieved for nearly all of our third-year students by the end of the year, with few exceptions completing requirements in the beginning of their senior year.

The disruption came at a critical point in the third-year timeline: at the end of the third year students prepare for away rotations, take USMLE Step 2 examinations, and begin work on residency applications. The AAMC issued guidance, that quickly became normative across the country, recommending that all away senior rotations be cancelled, with the sole exception of students applying to residencies in disciplines not available at their home schools .[6] In such cases, schools were instructed to partner with another school, as close as possible in the same geographic region, to allow only one rotation per student in the given discipline. Accordingly, LSU SOM NO partnered with LSU Shreveport to offer rotations for students in three disciplines. Additionally, residency programs were advised that all interviews were to be conducted virtually. National specialty organizations offered guidance to program directors in their disciplines to make the process more transparent and uniform across the country.[7] This directive required a quick pivot for programs to develop virtual materials and to design ways to connect virtually with prospective applicants. These necessary and proactive measures provoked anxiety in both students and program directors, but the relevant parties adapted, and the virtual interview process took place with similar timing to previous interview seasons. The loss of in-person interviews warranted creative solutions, such as making informational videos about residency programs and New Orleans and creating quiet 'interview rooms' on campus for our students to interview with reliable internet access. The medical education community looks on in interest to see the impact this will have on match outcomes and on the residency application process going forward. It has certainly saved applicants and programs a great deal of money.

The cancellation of USMLE Step 2 CS for seniors was referenced above, but the administration of USMLE Step 2 CK (Clinical Knowledge) examinations, which are taken after the junior year, was also severely disrupted. Prometric test centers, which administer these examinations, closed nation-wide and were only allowed to re-open on a case by case basis pending the viral activity and restrictions within their geographic regions. This generated widespread cancellations and rescheduling of Step 2 CK, leading to significant anxiety for students in this class. Despite the disruption, and at the time of this publication, student scores on this examination have not deviated from prior years.

Similarly to the class of 2020, traditional Match Day activities for this class have been cancelled. Match Day will be a brief virtual ceremony prior to the distribution of match results. Students who oversee planning of this event are utilizing various social media platforms to increase the opportunities for students to interact with their classmates. Final decisions regarding graduation and precommencement are still pending.

The Class of 2022

Within 3 days of the New Orleans stay at home order, we transitioned all classes for the sophomore students to a virtual format, using Zoom as the platform. Our Information Technology department played a vital role in helping us modify our strategies, including working out licensure issues, training faculty, and providing space and support for classes. New formats for Team-Based Learning (TBL) sessions, which are a core piece of our interactive learning curriculum, were also shifted to a virtual platform, wherein students formed their own Zoom small groups and then joined a 'large group Zoom' for clinical application exercises, similar to how in-person TBL sessions in our TBL classroom were conducted previously.

The same USMLE examination cancellations described above also occurred for the class of 2022 with respect to the Step 1 examination, which is taken at the end of the second year. Typically, students are given several weeks to dedicate study time and take this examination prior to starting their third-year clerkships. The cancellations produced a delay in taking the examination for many of our students, changing their preparation and compounding more anxiety on the common nervousness surrounding the examination. While most students were eventually able to reschedule their examinations before their clerkships, some traveling far distances to do so, approximately one quarter of the class had to take the examination at some point during their clerkships. It is difficult to fully attend to clerkship responsibilities and prepare for Step 1, so there have been more students than usual taking time out of clinical duties to take the examination. In some cases, this means a delayed start to their senior year. We are evaluating the full impact on scores, although, as with Step 2 CK, the average for students taking it so far has been similar to prior years.

With respect to starting clerkships, the class of 2022 started their clerkships on time, and except for brief interruptions to take the Step 1 examination and quarantine restrictions, students have not been removed from clinical activities due to increasing COVID 19 cases in our communities.

<u>The Class of 2023</u>

As with the class of 2022, within 3 days of the stay at home order in New Orleans, we quickly transitioned to a virtual format, including all lectures and TBL sessions. Thus, this class of students did not have a significant disruption to their educational and curricular continuity. Indeed, they are expected to take the Step 1 examination before starting their clerkships and will start their clerkships on time in July of 2021.

This continuity notwithstanding, there are two notable exceptions that were disruptive for this class. The first is a valued clinical experience, the Longitudinal Selective (LS), which allows our second-year students to spend time in clinical or research experiences. This did not occur for this class due to concerns about student safety and hospital concerns about numbers of learners in clinical environments. The second is the opportunity for some students to participate in clinical preceptorships in our Area Health Education Center (AHEC) programs around Louisiana, which normally occurs in the summer between first and second years. This was not available that summer.

Another opportunity for students between their first and second years is research. We were able to offer virtual basic science and clinical research projects, and participation in these was higher than in previous years. This expands the potential for students to engage in research activities in the future.

The Class of 2024

The group of students who started medical school in August of 2020, in addition to having a virtual first year of school, had orientation virtually, significantly limiting their ability to meet their classmates in person and gather as a class. We were very concerned about welcoming them to LSU SOM NO and helping them build connections with our faculty, our administrative staff, senior students, and their peers. Leaders from the class of 2023, who are responsible for planning orientation activities, did a spectacular job of devising a virtual orientation that extended throughout the summer. Class of 2023 leaders planned virtual social events, activity fairs, and meet and greets. They created a dedicated orientation web page, developed a comprehensive orientation handbook, and assigned big buddies to the first year students. Traditionally, a "big buddy" is a second year student who would meet their assigned student in-person during orientation and offer advice on how to successfully transition to medical school. The Associate Dean for Student Affairs and the Assistant Dean for Undergraduate Medical Education met virtually with every incoming student in small groups over the course of two weeks in July. When school started, students came on campus in preassigned small groups to pick up computers and student identification badges. While not ideal, the orientation experience has elements that worked even better than in person and we will be looking to continue some of those in the year ahead.

There have been several educational experiences that were delivered differently than in prior years. The most significant for freshmen students was the removal of in-person dissection labs in the Gross and Developmental Anatomy course. Course faculty provided prosected cadavers prior to examinations for students to review and delivered laboratory experiences virtually using a software program. Sessions were highly interactive, requiring students to teach and provide formative examination questions for their peers. Elements of this approach were deemed very successful and are being considered for inclusion in future years. Physical examination sessions were limited and required students to come prepared to demonstrate skills in groups of two. This approach entailed much faculty volunteer time for observation, and anecdotal comments indicate that students learned the physical examination skills more completely than in years past. The Office of Undergraduate Medical Education is exploring options for delivering these sessions in the future.

Student Assessment

Over the course of their education, our students take approximately 45 examinations, and this number held true despite the pandemic. We did not decrease our expectations of the students with respect to meeting educational and accreditation standards, although we did have to address certain challenges. One primary challenge was testing our students virtually, which we did in the first few months of the pandemic, using several mechanisms and many faculty members and administrators. Currently, most of our student testing is provided on campus, in rooms equipped to maintain social distancing, and we require students to wear masks, complying with city guidelines and institutional recommendations. We have had to remain flexible so that students who are ill or quarantined can still be tested remotely and proctored virtually.

Overall Student Well Being and Emotional Health

In addition to the COVID 19 pandemic, the year 2020 presented numerous stressful situations to our students and other Louisianans, including increased awareness and unveiling of systemic racism, a highly partisan presidential election, and several hurricanes. Additionally, the pandemic has taken an unequal toll on marginalized communities, and many of our students have had family members who were sickened with or lost their lives to the virus. Such stressors alone, but added to the responsibilities of medical school, have been very hard for students, particularly those in the first-year class who have been challenged with the task to learn and function optimally in the isolated virtual environment without the traditional methods to form new social support. The Associate Dean for Student Affairs and Assistant Dean for Undergraduate Medical Education increased the frequency of virtual “check-ins” for students in all classes, and the Campus Assistance Program (CAP) has been increasingly utilized, along with the school’s part time learning specialist. A surge in the use of these supportive outlets is perhaps a positive aspect from this past year, as students, faculty, and administrators have started to acknowledge when they require assistance and to normalize seeking help as good professional behavior.

Co-curricular and Volunteer Activities

LSU SOM NO students participate in thousands of volunteer activities annually, providing valuable service to the community. When COVID arrived in our area, many of the service locations, including community clinics, schools, shelters, and soup kitchens closed temporarily. The annual service project for the first-year class, Camp Tiger, which has taken place for over 30 years, was cancelled. Camp Tiger provides a week of free activities for 130 children with special needs from the surrounding community. Each camper is paired with two or more medical students who provide fun, while maintaining safety, for the camper. Students raise funds to support the camp, and the last in-person event held prior to the COVID 19 shutdown was the annual Camp Tiger auction. A virtual event is planned for the spring this year to provide a semblance of the joyous experience the children have come to anticipate. More information on Camp Tiger can be found on their website, listed here. https://www.lsuhsc.edu/orgs/camptiger/camp-tiger.

Students were eager to serve our community, especially in a time of such community need. Working with the Student Government Association Vice President for Community Service, we created a project intake form that enabled groups to propose projects and recruit student volunteers. The projects were reviewed for supervision and safety, and once approved, project leaders began harnessing student volunteers. Students quickly organized around activities such as collecting PPE, providing babysitting services for residents, shopping for and delivering meals to elderly persons, calling home-bound adults to provide support, and signing up for the NOLA Ready Volunteer Corps. This allowed the school to track student activities.

Lessons Learned

As described above, students at all levels experienced negative feelings and challenges during the past year. One of the most substantial among these is student isolation, ranging from studying alone to being unable to participate in team-building activities, such as interest groups and community service projects. The effects of the lack of peer-to-peer interactions were often subtle, but significant. For example, for residency interviews, students were unable to garner the wisdom from those in previous classes to plan their progress and their approach to their education. Likewise, faculty members, who value in person interaction with their students, often felt dissatisfied with conducting virtual lectures and other sessions.

However, numerous conversations among faculty and students indicate that despite the difficulties we have faced over the past year, there are positive aspects that should be acknowledged. Faculty and students alike were forced to become more flexible, handle uncertainty, and adapt quickly to new and evolving situations. Faculty recognized the value of having face-to-face conversations with students after class to further explain difficult concepts. Clinical faculty were able to take part in more didactic sessions because they could do so remotely from their clinics or offices. Faculty could also respond to questions from students by name because of the Zoom arrangement, so it could be argued that they got to know the students better than they would have in the classroom. Students saved money and time in the interview process. They learned the technological aspects of medicine, such as telemedicine, but given their time away from the clinical environment, they grew to appreciate more the value of the doctor-patient relationship. Physical isolation with the flexibility of technology also gave students an opportunity to strengthen pre-existing social relationships, whether it was catching up with family or friends, which they may not have previously had time to do while having to attend in-person curriculum duties. Finally, we learned that virtual experiences have a valuable place in medical education, and our ever-evolving curriculum will likely continue to include them in some fashion.

Conclusion

As we watch the evolution of the COVID-19 pandemic, we are providing vaccinations to our students and faculty. Throughout the process, we have held students to the same standards as we did previously, including accreditation standards, their medical knowledge, and their professional attitudes. Our Aesculapian Society, a student-run organization that fosters continual academic quality and improvement and serves as a liaison between students and faculty, is as active as ever. We continue to work with our hospital partners to ensure that our students are learning in a safe environment. We will maintain our flexibility as the pandemic evolves and anticipate that our community will continue to work together to ensure excellent medical education is received as our students prepare to become the future physicians for the state of Louisiana.

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An Internal Medicine Residency Response to the COVID-19 Pandemic in Louisiana

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ABSTRACT:

The novel human coronavirus disease, COVID-19, was first identified in Wuhan China in December 2019 and quickly spread to the entire planet. While New Orleans enjoyed Mardi Gras in February of 2020, we were unaware that the ongoing mix of tourism and gathering of large crowds would fuel the spread of the COVID-19 pandemic to our city and state. New Orleans saw its initial and largest COVID peak to date in early April 2020. At the peak, all the hospitals in the greater New Orleans area quickly became inundated with patients affected by COVID-19. The goal of this article is to share our experience, our designed responses to the multitude of issues facing our internal medicine residency program, and the lessons we learned during the COVID-19 pandemic.

INTRODUCTION

The novel human coronavirus disease, COVID-19, that was first identified in Wuhan China in December 2019, represents the fifth documented pandemic since the 1918 flu pandemic.[1] The initial rapid ascent of COVID-19 in New Orleans and Louisiana was likely the result of a combination of increased global tourism in our city and the gathering of large crowds for the Mardi Gras celebration that occurred in February 2020. With the subsequent availability of testing, the first reported case of COVID-19 in Louisiana occurred on March 9, 2020 at the Veterans Administration Medical Center in New Orleans. By the following day, there were two more cases at separate New Orleans area hospitals. The World Health Organization declared coronavirus a pandemic on March 11, 2020. Reported coronavirus cases rapidly increased and the first Louisiana death was reported on March 14, 2020. During the following ten days, schools closed, hospitals limited visitors, bars and restaurants shut down, and drive through testing sites opened. Confirmed cases increased to over one thousand, and a “stay at home” order was issued for Louisiana. By the end of March, there were over four thousand COVID-19 cases in Louisiana and a few states set up interstate checkpoints to prevent travelers from New Orleans from entering. On April 1, 2020, Louisiana had the highest per capita deaths from COVID-19 in the U.S. A pre-publication report by researchers at Scripps Research Institute, Tulane University, and LSU Health Shreveport proposes that the coronavirus most likely arrived in New Orleans about two weeks before Mardi Gras[2]. These researchers suspect that one case source exploded into 50,000 confirmed cases over those first few months after evaluating genome sequencing and cell phone tracking data.[2,3] As of this writing, there have been over four hundred thousand cases of COVID-19 with over nine thousand deaths in Louisiana. The largest peak in the New Orleans area occurred in April 2020 with other smaller peaks in July 2020 and January 2021 (Figure 1). Here we share the responses that the internal medicine residency program at Louisiana State University Health Sciences Center (LSUHSC) in New Orleans made to the pandemic with regards to resident/intern-delivered patient care, communication, resident/intern education, resident/intern wellness, residency recruitment, and the COVID-19 vaccination efforts that have ensued since March 2020.

PATIENT CARE AND RESIDENCY STRUCTURE AT OUR TEACHING HOSPITALS PRE-PANDMIC AND DURING THE PANDEMIC

PRE-COVID-19 PANDEMIC STRUCTURE

Residents and interns from the Internal Medicine Residency program at LSUHSC in New Orleans rotate at three hospitals for inpatient ward rotations (University Medical Center, Touro Infirmary, and Ochsner-Kenner Medical Center) in the greater New Orleans area that includes Orleans and Jefferson Parishes.

University Medical Center (UMC) is unique in that it is an academic training hospital, where both LSUHSC and Tulane Health Sciences Center have independent internal medicine rotations. Pre-pandemic, LSUHSC internal medicine had four ward teams each with one resident and two interns and a cap of twenty patients' maximum on each team that took call every four days. A separate night float resident and intern managed admissions from the Emergency Department and general floor call. There was no cap on new patient admits because there was no other hospitalist service available. The medical intensive care unit (MICU) was a closed unit with resident teams from LSUHSC internal medicine programs, Tulane internal medicine programs and the LSUHSC emergency medicine program. We also had residents and interns on ambulatory rotations, consult rotations, quality improvement/patient safety rotations, and interns on emergency medicine rotations.

Pre-pandemic at Touro Infirmary (Touro), LSUHSC internal medicine had four medicine ward teams with one resident and one intern each that took call every four days and one night float intern on Monday through Friday. We only had enough residency cap positions to maintain the ward services. We did not have any residents on consult or elective rotations at that site due to cap limitations.

Pre-Pandemic at Ochsner-Kenner Medical Center (OKMC), LSUHSC internal medicine had four medicine ward teams with one resident and one intern each took call every four days. There were two night float interns who rotated every three days. We also had five other house officers on consult rotations.

INITIAL COVID-19 PEAK RESPONSE AND MODELS

Pandemic response at UMC

Following the first reported case of COVID-19 in New Orleans on March 9, 2020, a rapid increase in cases occurred at all three of our hospital sites. The initial rise COVID-19 at UMC occurred during the third week of March, 2020. At first we responded by cohorting all the patients with COVID-19 on one Medicine ward team. Two days later, we had two medicine teams that were devoted to COVID-19 patients and by the fourth week of March we quickly realized we would need more medicine teams devoted to COVID-19 patients. At this point, to meet the demands of the rapidly increasing number of patients with COVID-19, we shifted from a reactionary model to a proactive model that would allow us to care for a maximum capacity of patients, cohort patients, cohort at-risk house officers and faculty (those who were pregnant or had underlying health issues, etc.), and reduce the need for continual schedule changes. We created two more medicine ward teams, giving us six ward teams (Teams 1 to 6). Team 1 was staffed by faculty and residents who were either pregnant or had underlying reasons that put them at greater risk of adverse outcomes from COVID-19, and we designated this the non-COVID team. Team 1 admitted all patients who tested negative for COVID, clinically did not appear to have COVID, and had clear alternate diagnoses. Teams 2 thru 6 admitted all the COVID patients on a rotating call system. We went from an every fourth night call to an every sixth night call. The call team took admits from the Emergency Department (ED) and transfers from the MICU. Patients with COVID-19 took longer to improve; therefore, one unforeseen benefit of the every sixth night call schedule was that the medicine teams were able to achieve more patient dispositions prior to their next call. These early days were characterized by fear of transmission, feelings of helplessness over patients who were decompensating, and lack of available testing. Resident and intern wellness benefited from the decrease in call-day frequency. UMC brought in a private locums hospitalist group towards the end of April, which helped reduce the burden on our academic ward teams.

The MICU took direct admits from the ED and floor transfer for patients who required more care than could be provided on the medicine wards. Patients who were stepped up to the MICU, would usually go back to the same medicine team when stabilized. The cap for the residents and interns on the medicine teams remained at twenty. However, at times more than twenty patients were admitted to the medicine teams and these patients were seen by the faculty attending physician without the residents to abide by ACGME regulations. Similar to previously published reports on reorganizing a medicine residency program in response to COVID-19 and on internal medicine resident work absence during the COVID-19 pandemic[4,5], coverage for our extra medicine ward teams was accomplished by pulling residents and interns off most consult services, ambulatory rotations, and quality improvement rotations. We added more house officers to the pulmonary consult service and the infectious disease consult service. We maintained a resident on the cardiology service. Interns that were previously assigned to the ED remained on that service. The medical and surgical ICUs quickly filled and a third MICU unit, supervised by faculty from critical care, was created with the use of residents and interns from programs such as oral maxillofacial surgery, emergency medicine, medicine/pediatrics, general surgery and vascular surgery.

Pandemic response at Touro

At Touro, we maintained the same pre-pandemic structure that had been in place since we only had enough graduate medical education residency cap positions to maintain the ward services and we did not have any residents on extras services at that site. The hospital administration decided that all COVID patients would be admitted to either our resident ward teams or to two other private hospitalist groups.

Pandemic response at OKMC

At OKMC, we maintained the four inpatient medicine ward teams with one resident and one intern each that took call every four days and two night float interns rotating every three days. We added one extra intern, who was pulled off the consult services, as a “float” intern who would assist the ward teams with the highest number of the most complicated patients as requested by the hospitalist faculty at that site. This was a simple solution to offload teams on a day to day basis without having to constantly adjust house officer schedules. We shifted the remaining house officers on the consult services to either pulmonary/critical care or infectious diseases teams.

Pandemic response in our continuity clinic

Prior to the COVID-19 pandemic, all internal medicine residents and interns had a half-day per week continuity clinic. At the onset of the pandemic, the medicine clinic closed to patient visits and effectively ended our continuity clinics by April 2020. During this time, we assigned three to four house officers on ambulatory rotations to the medicine clinic to manage telemedicine patient visits and prescription refills. Challenges to telemedicine and virtual patient encounters included the technical aspects such as computer system requirements for both the patients and medical trainees. A published case study on building telemedicine capacity for trainees during the COVID-19 pandemic demonstrated that a successful program required development of technical proficiency, virtual information gathering (inclusive of history, collateral information, and physical exam), and interpersonal communication skills.[6] Our house officers were able to overcome these challenges and continue to provide care to their clinic patients during this time.

Pandemic Response after the initial COVID-19 peak decreased

We maintained this new organization for patient care at all sites through May and transitioned back to our pre-COVID structure in June 2020 as the number of patients hospitalized with COVID-19 decreased significantly and continuity clinic activity returned. UMC maintained the locums private hospitalist service and supported LSUHSC to develop a direct care hospitalist service that was not reliant on residents or interns. A comparison of the internal medicine residency program's patient care services pre-COVID-19 and through the pandemic is included in Table 1. Although we have had two additional peaks in COVID-19 activity, neither was severe enough to require changes to our patient care coverage.

COMMUNICATION

A key to successful management of patients and physician well-being during a pandemic or other disaster is communication. Communication is essential to maintain community and a sense of normalcy.[7] Wayne State University School of Medicine developed a 'Virtual Conversation Series" to connect students with physicians on the COVID-19 frontlines.[8] Learners positively rated this method of communication and this study demonstrated that information on patient experiences, resource shortages, and mental health challenges could be disseminated through the use of this ZOOM-based platform.[8]

Several methods and levels of communication were used to update leadership, faculty, residents and interns on the COVID-19 pandemic trends, testing, treatments, rotation changes, didactic education opportunities, wellness initiatives, and vaccinations. Each of our hospital partners established COVID-command centers and held weekly meetings to provide hospital workers, medicine faculty and house officers updates on topics such as COVID-19 hospital census, personal protective equipment supplies, medication availability, wellness, and, more recently, vaccinations. At each site we would send a representative to this meeting who would report back to the internal medicine faculty and house officers. The electronic health record system, EPIC, was amended with a COVID-19 information tab. This site contained information on treatment regimens and updated testing and quarantine guidelines.

Our hospitalists also recognized the importance of maintaining updated communication at the beginning of the pandemic. The hospitalist faculty and house officers would meet daily to discuss patient care issues, access to personal protective equipment (PPE), COVID-19 testing and treatment regimens. This was an excellent opportunity for faculty to receive house officer feedback and provide support. Many early changes resulted from these meetings and were frequently based on resident suggestions. At UMC, our hospitalists would also meet with the Tulane University hospitalists to gain additional perspective on many of the issues that we faced.

The internal medicine program director started a daily "COVID CENTRAL" email that included the day's COVID-19 census at each of our hospital sites, COVID-19 epidemiologic data from New Orleans, Louisiana and the United States, updates on PPE, updates on COVID-19 testing, updates on COVID-19 clinical treatment trials and medications, updates on wellness initiatives and support programs, updates on educational and scholarly activities, vaccinations, and "shout-outs" to house officers and faculty members for their specific accomplishments and heroic efforts. These emails were shared with all LSUHSC medicine department clinical faculty and house officers as well as leadership in the Department of Medicine, School of Medicine and at UMC. This effort increased transparency of the situation and helped build a sense of community during a time where separation of clinical sites could produce feelings of isolation.

The residency department maintained communication across all our clinical sites through emails, weekly Chief Resident Committee meetings, and monthly Resident Education Committee meetings. The program director had weekly telephone meetings with the Chairman of the Department of Medicine. The program director attended monthly meetings of the Graduate Medical Education Committee (GMEC) where COVID-19 issues related to residency program function and education were discussed. We continue to use the Zoom format to maintain communication across all our hospital sites and for our regularly scheduled residency program meetings and educational didactic conferences.

RESIDENT AND INTERN HEALTH AND WELLNESS

At the beginning of the COVID-19 pandemic, PPE consisted of a surgical mask or N95 respirator mask, eye protection, disposable gloves, and disposable gowns. We reviewed PPE donning and doffing with all house officers as recommended by the Centers for Disease Control at that time. N95 respirator masks were only required for use during procedures that would increase the risk of aerosols. However, a few weeks into the pandemic, N95 masks were used for all COVID-19 patient encounters. To further reduce PPE use, only one person on the medicine team would go into the patient's room. Some faculty saw all the admitted COVID-19 patients and simply filled in the subjective and physical exam portions of a house officer derived progress note. During the month of April some PPE became scarce and gowns and masks were re-used. Creation of COVID-19 units in the hospital was greatly beneficial for conservation of PPE; gowns could simply be wiped down and gloves exchanged between patient rooms in these units. The OKMC site offered the medicine ward teams an ability to perform virtual patient rounds, thus reducing exposure and decreasing the use of PPE. One house officer and one hospitalist faculty member formed a relationship with the LSU Engineering Department and developed 3-D printed face shields and gowns. We also received PPE donations from other sources that were distributed throughout our hospitals for use. Fortunately, none of our hospitals ran out of PPE.

COVID-19 testing of patients and hospital workers changed as rapid automated methodologies became available. Initially, only patients with symptoms of COVID-19 were tested. However, a few patients who did not have symptoms and were admitted for other medical reasons also tested positive for COVID-19 as testing became more available. Furthermore, some patients who had been transferred from outside medical sites were not tested for COVID-19 and when tested at our hospital, were positive despite lack of symptoms. For these reasons, house officers were instructed to wear proper PPE and to treat all patients as though they had COVID-19 until a negative test was available.

The use of surgical masks on all patients and hospital workers was instituted close to the end of March 2020. At that time, checkpoints at hospital entrances were established and the temperature of all hospital workers inclusive of physicians and all patients was checked and clean face masks were offered to those who needed them. This practice has been maintained to this date. The City of New Orleans mandated social distancing and the use of face masks early in the pandemic.

Despite our precautions, about seven internal medicine house officers tested positive for COVID-19 during the initial peak and another seven tested positive or had close contact with someone with COVID-19 during the third holiday peak of COVID-19 in November and December 2020. Thus about 20% of our internal medicine house officers tested positive for COVID-19. The Associate Dean for Academic Affairs at LSUHSC was informed of all resident-COVID-19 related issues. Despite an inability to accurately determine where these house officers were infected, we believe several were likely infected outside of the hospital despite social distancing and the use of surgical masks. Of note, a previously published study on the impact of COVID-19 on New York City resident physicians demonstrated no correlation between programs that reported suboptimal PPE and the number of COVID-19-positive residents.[9] We followed the guidance of the CDC for quarantine and return to work that was in effect at each of these times. The program director remained in phone contact with COVID-19-infected house officers while they were under quarantine. The Internal Medicine Chief Residents undertook the task of altering rotations with little notice, to fill gaps in patient care coverage. House officers very professionally adapted to these changes in their schedules. A few faculty also contracted COVID-19. Fortunately, no house officers or faculty had any significant lasting negative outcomes, and all were able to return to their rotations at the end of their respective isolation or quarantine periods.

During this pandemic, internal medicine residents and interns have been affected by the pressures of medical care of patients with COVID-19 and changing rotation schedules as well as social distancing, isolation, and stigma.[10] Previous published reports suggest that residents can be psycho-educated about the possible range of psychological responses associated with the COVID-19 pandemic.[10,11] Risk factors for burnout during the COVID-19 pandemic include worry about reduced learning opportunities, post-training job opportunities, loss of social interaction, and fear of own health and well-being.[12] Self-care such as adequate sleep, maintaining social connections, and work-life balance should be emphasized.[11] We also ensured a long term commitment to the well-being of our residents and interns through communication and feedback.

There were several outreaches to boost and maintain the morale and wellness of front line workers in our hospitals inclusive of the internal medicine programs house officers. During the initial peak of the COVID-19 pandemic, several local restaurants brought food to the hospital that was distributed to the front line workers by a "BWELL" coordinator. The hospitals ran campaigns that included signage inside and outside the hospital declaring that front line workers were heroes in their fight against COVID-19. UMC created a "Wellness Room" in their conference center that had low ambient light for relaxation and meditation. They also placed several thank you notes that had been written by school children who were supporting the efforts of the front line health workers. Another wellness initiative created by the leadership at UMC was "Coffee Talks", a forum for house officers to discuss their clinical learning experience during the pandemic. The LSUHSC Psychiatry department offered a "Virtual Psychological First Aid Group". Other wellness initiatives included a twenty-four hour emotional support line staffed by professionally trained mental health experts and a LSUHSC Campus Assistance Program. These efforts highlight the positive impact of synergy provided by both the academic health sciences center and the hospital administration in regards to resident well-being.

RESIDENT EDUCATION

Prior to the COVID-19 pandemic, residents and interns participated in daily morning reports or noon reports at each hospital site, weekly medicine grand rounds, weekly resident education conferences, a monthly journal club, and monthly guideline lectures. The Section of Hospital Medicine had bi-monthly hospitalist lectures and the Section of Comprehensive Medicine had monthly primary care lectures. There were previously very limited virtual lectures, virtual educational experiences and no virtual scholarly activities. By the third week of March 2020, all didactics were cancelled due to concerns about social distancing. We did continue to meet at each hospital site to review COVID-19-related issues that affected patient care and physician well-being.

Our discontinuation of structured scheduled medical education sessions was similar to that seen with many other residency programs during this pandemic.[13] As the initial peak of COVID-19 resolved, we re-instituted structured lectures but used Zoom as a virtual delivery platform. We also re-started our morning reports and noon reports at our hospital sites. Touro and OKMC moved their morning reports to larger rooms to allow for social distancing. The noon report at UMC continues to be presented by Zoom for those who do not wish to attend in person. Although Zoom offers a safe alternative to in-person lecture attendance, there is evidence that learners find in-class lectures provide more effective engagement with presenters and peers.[12] A majority of learners in this study noted decreased attention with online conferences. Learners reported performing other activities simultaneously during the conferences.[14] Enabling webcams to provide visual feedback may lead to improved attention during the lecture. A comparison of the internal medicine program's resident education pre-COVID-19 and through the pandemic is included on Table 2.

Another area of resident education that has changed for the moment is the scholarly activity associated with scientific and professional society meeting attendance and presentation. Our departmental research day was changed to a virtual meeting. Our residents and interns will be participating in several other regional and national meetings that have converted to a virtual format.

RESIDENCY RECRUITMENT

Residency programs across the country conducted virtual interviews during the 2021 match process. Furthermore, medical students were unable to do "away" clinical rotations with different programs. Our approach to introduce medical students from outside LSUHSC to our residency program was to host three virtual "Meet and Greet" sessions on Zoom during the months of September and October. We invited 150 students from local and regional medical schools to participate. During the sessions, the program director and chief residents provided an overview of the residency program. Participants were then separated into small breakout groups with current residents for a candid review of the program and to have all their questions answered. We held our formal virtual Zoom interviews during the months of November, December and January, during which time we interviewed close to 300 applicants. Applicants interviewed with three separate faculty, just as all applicants have done in the past; groups of residents then met with the applicants at the end of their interview day to answer any remaining questions and give a final review of our program.

COVID-19 VACCINATIONS

COVID-19 vaccination was offered to house officers and attending faculty at each of our hospital partner sites. The internal medicine residency program coordinator organized a vaccine appointment schedule with our hospital partners. Vaccinations were begun on December 15, 2020. Although vaccination was not mandatory, all internal medicine house officers have completed the vaccination series. LSUHSC also developed a vaccination plan for faculty and students. The next phase of vaccinations will need to include new house officers in July 2021 who may not have been vaccinated as medical students.

CONCLUSION

The Internal Medicine Residency program at LSUHSC in New Orleans has successfully navigated through the enduring COVID-19 pandemic due to the dedication, perseverance and professionalism exhibited by the leadership at LSUHSC, the leadership of our hospital partners, our clinical faculty, and our house officers. Patient care was maintained by profoundly changing the rotation schedules and creating extra inpatient treatment teams. Communication was increased to ensure improved patient outcomes, to ensure faculty and house officer well-being, and to maintain the academic mission of our training program. We foresee that we will continue to utilize virtual platforms in combination with in-person interactions for future conferences and residency recruitment. We have now returned to normal residency function, aware that we can be adaptive if needed in the future. We look forward to the end of the COVID-19 pandemic.

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FIGURE 1: COVID-19 Cases in New Orleans March 2020 to February 2021
(Centers for Disease Control data: https://covid.cdc.gov/covid-data-tracker/#county-view)

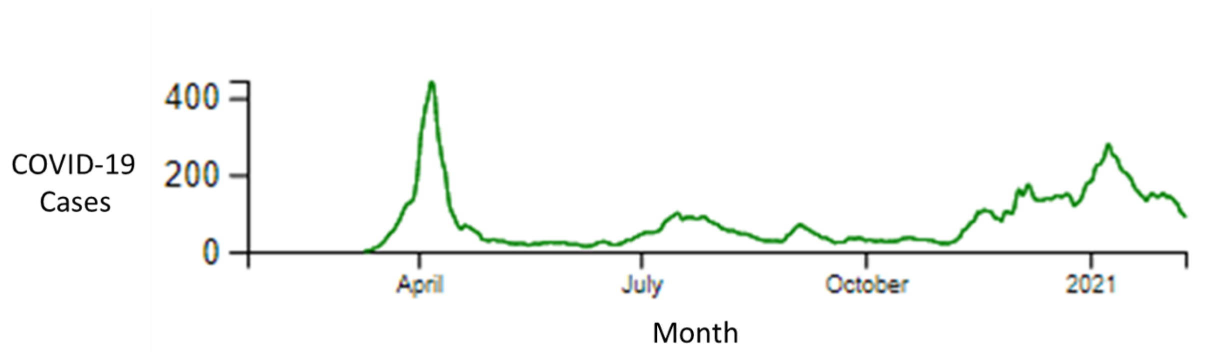

TABLE 1: Program Patient Care: Comparison of Pre-COVID, COVID-19 First Peak, and COVID-19 Post First Peak

	PRE-COVID-19	COVID-19 First Peak: March-May 2020	COVID-19 Post First Peak: June 2020- February 2021
Patient Care Services	University Medical Center • 4 ward teams • Call every 4 days • 20 patient cap/team • MICU step down team • 1 MICU team • Subspecialty consult rotations • Ambulatory rotations • Quality improvement/patient safety rotations • Emergency room rotations • Continuity clinic patient visits for all residents and interns	University Medical Center • 6 ward teams • Call every 6 days • 20 patient cap/team • Initiation of private hospitalist service • Cohort COVID-19 patients on specific units • 2 MICU teams • Opened extra MICU • Subspecialty consult rotations limited to pulmonary, infectious disease, and cardiology • Emergency room rotations • Continuity clinic limited to telemedicine and prescription refills with only 4 ambulatory residents	University Medical Center • 4 ward teams • Call every 4 days • 14 patient cap/team • Private hospitalist service • Cohort COVID-19 patients on specific units • MICU step down team • 1 to 2 MICU teams • Subspecialty consult rotations • Ambulatory rotations • Quality improvement/patient safety rotations • Emergency room rotations • Continuity clinic patient visits for all residents and interns
	Touro Infirmary • 4 ward teams • 14 patient cap/team	Touro Infirmary • 4 ward teams • 14 patient cap/team • Cohort COVID-19 patients on specific units	Touro Infirmary • 4 ward teams • 14 patient cap/team • Cohort COVID-19 patients on specific units
	Ochsner-Kenner Medical Center • 4 ward teams	Ochsner-Kenner Medical Center • 4 ward teams	Ochsner-Kenner Medical Center • 4 ward teams

	• 14 patient cap/team • Subspecialty consult rotations	• 14 patient cap/team • Extra float intern on Wards team • Cohort COVID-19 patients on specific units • Subspecialty consult rotations limited to pulmonary and infectious Disease	• 14 patient cap/team • Cohort COVID-19 patients on specific units • Subspecialty consult rotations

TABLE 2: Resident Education: Comparison of Pre-COVID, COVID-19 First Peak, and COVID-19 Post First Peak

	PRE-COVID-19	COVID-19 First Peak: March-May 2020	COVID-19 Post First Peak: June 2020- February 2021
Resident and Intern Education	• In-person daily morning reports at Touro Infirmary and Ochsner Kenner Medical Center • In-person daily noon report at University Medical Center • In-person and recorded weekly Medicine Grand Rounds • In-person and recorded weekly resident/intern education conferences • In-person monthly journal club • In-person and on-line monthly guidelines lectures • In-person Bi-monthly Section of Hospital Medicine Conferences • In-person monthly Primary Care lectures	• Virtual/on-line and in-person daily and then weekly meetings with faculty, residents and interns in the hospital to review COVID-19 updates and discuss patient issues, health and wellness issues	• In-person daily morning reports at Touro Infirmary and Ochsner Kenner Medical Center • Virtual/on-line and in-person daily noon report at University Medical Center • Virtual/on-line weekly Medicine Grand Rounds • Virtual/on-line resident/intern education conferences • Virtual/on-line monthly Journal club • Virtual/on-line monthly Guidelines lectures • In-Person ultrasound course for residents • Virtual/on-line monthly intern basics lectures

Leadership in the Time of Covid

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ABSTRACT

Like medical departments throughout the United States and the world, the Louisiana State University (LSU) Department of Medicine has experienced a year of profound challenges as it contended with the myriad ramifications of COVID-19. At the same time, these challenges have presented opportunities for growth, and there have been many lessons learned that have helped us to handle this crisis and would be useful in coping with *any* crisis.

"In the shock and devastation … residents began … to take stock, to evaluate shortcomings and areas in which lack of preparedness was evident in a city that had perhaps grown too complacent about the potential for disaster. It is only wise to make such assessments and then attempt to learn from them."

The above sentences are not about the COVID-19 crisis but are, rather, excerpted from an article I coauthored several years ago about the challenges faced and the lessons learned from shepherding the Department of Medicine in the LSU School of Medicine through the cataclysmic damage and suffering wrought on the city of New Orleans by Hurricane Katrina in August 2005.[1] Given that the focus of the present article is also on the challenges and lessons that resulted from a disaster—the pandemic, of course—I felt compelled to look back at what I had previously written and noted that many of the same points could still be accurately made. Not merely in New Orleans this time, but in the whole country and nearly the whole of the world, there had been insufficient preparation for disaster, resulting in shock and devastation. The only thing to do in such situations is to look squarely at such mistakes and learn from them. Katrina and COVID-19 have been the two great tragedies that have indelibly marked my 32 years of service as chair of the LSU Department of Medicine. While the difficulties they caused were different, they were definitely both responsible for the two most trying times in my professional career. At the same time, both illustrate the truism that strength arises from struggle, crisis from opportunity; and ultimately there was considerable overlap in many of the lessons learned.

Pandemics, like hurricanes, start small. The storm that would become Katrina—initially too insignificant to be worthy of a name—was born on August 19, 2005, ten days before it would slam with all its fury into the city of New Orleans. In the warm, late-summer waters north of Puerto Rico, it quietly took shape, formed out of the rather unholy, though seemingly innocuous, union of the remains of Tropical Depression Ten and a tropical wave. The origins of what would come to be known as COVID-19—initially too insignificant to be worthy of a name—are less clear, though the World Health Organization researchers currently looking into that very issue in Wuhan have recently affirmed that it appears to have been zoonotic in nature. Like a storm in its infancy, the early stages of an unusual disease attract the attention of those highly specialized professionals trained to study such anomalies, but the threat only garners widespread notice once it is large enough to be of pervasive danger. Although the novel coronavirus began infecting humans in the waning days of 2019, it was not until January 2020 that reports thereof started to trickle out to the world, and very few people really seemed to pay it much attention at first. No one was stockpiling PPE or formulating disaster plans. Here in New Orleans, we were our characteristically exuberant selves, holding our decadent Mardi Gras festivities without a second thought of the invisible pathogen spreading its deadly way through the crowds of revelers. Exactly one month later, New Orleans (Orleans Parish) had "the highest per-capita death rate for the coronavirus among all American counties to date."[2]

In March 2020, like every March, I was scheduled to attend on our hospitalist service at University Medical Center of New Orleans (UMCNO) with the two incoming Medicine chief residents. I was happy: treating patients and teaching students and residents are two of my favorite activities. Little did I know that COVID-19, which had seemed so far away and disconnected from our reality here in New Orleans, was about to slam into our city the way that Katrina had 15 years prior. UMCNO admitted its first recognized case of COVID on March 9, and when I learned about that upon reporting for service the following day, I made arrangements for another physician to cover for me and left. That day, March 10, 2020, was my last day on the medical service at UMCNO; because my age put me in the high-risk group for experiencing severe complications or death if I were to contract the disease, it was no longer safe for me to have exposure to patients—or to almost anyone, with the exception of my wife. It was fortunate that I left the hospital when I did because later that evening, my service admitted its first COVID-19 patient. I transitioned to working from home as of March 11, 2020, and on March 16, pursuant to the closure of schools statewide ordered by Governor John Bel Edwards, the LSU Health Sciences Center (LSUHSC) began allowing those employees who could work from home to do so. One week later, Louisiana was the fourth state to receive a federal major-disaster declaration, and Governor Edwards enacted a statewide stay-at-home order, although LSUHSC was recognized as essential and never officially closed its doors. During this time, just like in the aftermath of Katrina, we had to scramble to adapt in order to function in this new reality; however, unlike Katrina, the problem of COVID was not localized to New Orleans, and there was no one outside of the city who could come and help us, or even send supplies, because they were all dealing with the exact same crisis. Like everyone in every city, town, country, and continent on earth, we had to figure out how to handle this on our own. Moreover, unlike Katrina, which hit New Orleans and then was gone, leaving us to try to rebuild our city from amidst the wreckage, the pandemic is a catastrophe that has not gone quickly away, leaving a vast trail of ruin and a finite number of deaths as its lingering echo. No, the pandemic has held the U.S. for a year in its ever-tightening, ever-deadly grip, with spiraling death tolls that seem to know no limits and an unremitting social isolation, among other tragic consequences. The challenges that COVID-19, then, has presented to the LSU Department of Medicine are the same challenges mirrored in medical centers throughout the United States and all over the globe, a knowledge that is peculiarly comforting and of no solace whatsoever all at the same time.

CHALLENGES

Financial Difficulties

Like the vast majority of both individuals and businesses throughout the world, the LSU Department of Medicine experienced a substantial impact to its economic well-being due to COVID-19. Paradoxically in this time of tremendous medical need, our physicians' ability to treat patients actually diminished due to the fact that the UMCNO Medicine clinic was all closed for some time. Furthermore, fear of contracting COVID-19 kept many patients away from the hospital and our clinics, even when the latter *were* open. In addition to a decreasing patient population, the department lost several high-producing faculty during this time: one died, two retired, and three left the department. At the same time, the LSU School of Medicine instituted a hiring freeze, so we were unable to either replace our lost faculty (and staff) or hire faculty/staff to fill new positions and needs. Although our department is now, thankfully, on a financial footing that is comparable to pre-COVID levels, the fiscal difficulties of the past year certainly added to our complications.

A Dearth of Morale

Like most people throughout the whole of the country and much of the world, the members of the LSU Department of Medicine experienced a plummeting morale beginning in mid-March 2020. Initially, this was impelled largely by fear. At that time, people were unsure exactly how the virus was spread, and the risk of serious illness and possibly death seemed to be lurking everywhere. This fear was only exacerbated by the concurrent social isolation it necessitated, quickly transmogrifying the world into a much more frightening place than most of us had ever known it to be. In those early days, there was a belief that this isolation would last two weeks …

then one month … then two…. But as time spooled relentlessly out to encompass a no-end-in-sight future, the sharp fear settled into a dull numbness, and morale remained largely nonexistent. Practical matters soon became paramount. While LSUHSC was fortunate enough not to have to lay anyone off, throughout society so many of those who had jobs (including many of our own spouses and other loved ones) were terrified that they would lose them; those who lost their jobs had no idea how they would be able to find another one and, failing that, how they would be able to afford basic necessities like housing and food. People worried about their children and the many known and unknown ways the gaps in their education would come to affect their futures. People worried about their own health and that of their loved ones. And, still isolated, they worried alone. Others—far too many others—died alone. Depression and anxiety were ubiquitous and inevitable.

Problems Specific to Physicians and Other Healthcare Workers

While everyone has been subject to a loss of morale during this pandemic and so very many people and businesses have suffered in their economic outlook, there are a number of problems that are either specific to or heightened for physicians and other healthcare workers during a public-health crisis. The aforementioned depression and anxiety were certainly exacerbated; health professionals have been fearful of the same threats to their own physical well-being and that of their families and other loved ones as anyone else, but unlike most people, they are not able to have any remove whatsoever between themselves and the disease, any illusion of safety. There is no social distancing for those on the front lines in the war against a pandemic. And as has been widely reported, many physicians, nurses, and others had to do this work without the benefit of adequate PPE, so their worries were more than valid. In addition to the physical concerns was the emotional toll that SARS-CoV-2 exacted on health professionals. Witnessing so much suffering and death—much of it evitable—and being unable to forestall it would be hard for anyone to take, especially when combined with gruelingly long hours, lack of sufficient sleep, and constantly being on one's feet and on high alert, conditions endured by many. Although I could not be with them personally as they worked in the hospital (which was difficult and frustrating in its own way), I heard the exhaustion in the voices of our faculty members when I spoke to them on the phone and saw the fatigue etched on their faces when I saw them on Zoom. I vividly remember speaking late one evening on the phone to a faculty member who suddenly broke down in tears when I asked how she was doing because a COVID-19 patient of hers—a relatively young man who had recently indicated signs of improvement in his condition—had unexpectedly crashed and died that day. A seasoned professional, she was embarrassed by her tears, but personally, I saw in them only the evidence of her humanity. I never heard any of our faculty complain, and all comported themselves with the utmost professionalism—sometimes even heroism—in spite of the burnout (or higher than usual propensity thereto) that they may have been feeling.

Of course, depending on the specialty or subspecialty of a given healthcare professional, he or she may have had more direct responsibility for COVID-19 patients and thus more acute experiences of depression, anxiety, and burnout. In the large, 14-section LSU Department of Medicine, there are four sections that were severely impacted: the Sections of Emergency Medicine, Hospital Medicine, Infectious Diseases, and Pulmonary/Critical Care Medicine. The chief of our Section of Pulmonary/Critical Care Medicine, Carol Mason, M.D., described her section's experience during this time thusly:

> As the first surge developed, the numbers of [COVID-19] patients began to climb significantly, and we found that most of the hospitalized patients

> were elderly and that they did not recover quickly. As the waves of pandemic surges continued, we at least learned about a few treatments that had some benefits, but, those treatments were not enough. We still experienced far too many patients who did very poorly with COVID-19. In high numbers, the elderly patients succumbed to COVID-19 despite all of the teams' efforts. Provider exhaustion was common, and many a tear was shed in the ICUs, by both family members and the ICU staff. Unfortunately, those who died were rapidly replaced with another COVID-19 patient waiting in the ER, seemingly in an endless loop. The morgues were overwhelmed in several hospitals and funeral homes. And, even now, the COVID-19 surges are not over, with no apparent end on the horizon. Our teams (fellows and residents) were *outstanding* in their efforts in this fight for the patients, though so many of the patients did not respond but worsened.

I feel certain that this firsthand account speaks to the experiences of so many of the most essential healthcare workers.

Communication Issues

Like people across the globe, the faculty and staff in the LSU Department of Medicine quickly came to learn during the pandemic that *zoom* is more than just a verb meaning "to move rapidly." Face-to-face meetings have been replaced with Zoom conferences, and events such as Medicine Grand Rounds, Medicine Research Day, awards ceremonies, and graduation had to be held on that platform. While this technology has been indispensable in allowing much of the business of our department to continue while maximizing safety, it is also fraught with its own challenges, such as so-called "Zoom fatigue," which has been widely reported, as well as issues such as transmission delays (which make communication difficult even when they are minor) and a decrease in the ability to perceive nonverbal communication cues. And of course, sometimes the technology itself has simply failed to work. This has been a problem for our faculty and learners as well, as our preclinical courses also had to transition to Zoom for a time.

While the youngest (i.e., preschool and elementary school) learners are certainly the most affected by this disruption to their customary education, even adult students are not immune from the difficulties of learning from behind a screen rather than in person. The importance of authentic human interaction cannot, it seems, be overstated.

Lessons Learned

Fifteen years ago, in the first article I authored about the impact of Hurricane Katrina on the LSU Department of Medicine, I wrote, "I am … aware that in every hardship, there is an opportunity for growth,"[3] and I enumerated a list of ten lessons that I believed to be the most important takeaways from the crisis. As noted above, I feel that the same lessons apply to the challenges posed by COVID-19.

1. **Difficult problems must be handled as quickly and directly as possible while still maintaining sensitivity.** The COVID-19 pandemic, without a doubt, is one of the most difficult problems I have had to navigate in my 32-year tenure as chair of the LSU Department of Medicine. A department chair is usually adept at putting out one or more fires at any given time, but at times COVID-19 has seemed to be a never-ending conflagration. So many issues needed to be handled immediately. The most pressing of those was, of course, finding ways for our physicians to treat patients both with and without SARS-CoV-2 safely. We were required in short order to establish another medical team as well as another MICU team to care for the ever-increasing number of COVID-19 patients. Not only that, but we had to find physicians to staff the services. It was exceedingly gratifying to see how many physicians volunteered to staff the extra teams; they truly epitomize the very best qualities of our profession.

2. **It is essential to have a plan and be willing and able to modify it quickly and sometimes frequently.** In order to fulfill both the educational and medical components of our mission, so many of our plans and customary means of operating have had to be modified. We needed to come up with ways for our students and residents to continue their education and satisfy all program requirements while still maintaining the highest standards of safety. This was especially difficult with our third- and fourth-year students, who needed to be exposed to a wide variety of patients without any of them being COVID-19 patients. Our senior students had the additional complication of not being able to do any away rotations. As for our patients, we quickly developed an initial plan for diagnosing and treating COVID-19 cases, but that plan had to be changed frequently as newer diagnostic tests and treatment regimens were developed.

3. **Tragedy can bring out the best in people.** Knowing the professionalism that the Department of Medicine's faculty and staff exemplifies every day, it was not surprising to me to see the plethora of ways that they showed leadership, took ownership, and went beyond their usual obligations to do the very best for their patients, trainees, and/or colleagues. I am inordinately proud of every one of them.

4. **Believe in the abilities of others, and when you give them a task, endow them with responsibility, authority, and accountability—then get out of their way.** As the leader of our department, I am mindful of not micromanaging others. In the case of the physicians who were tasked with the responsibility of caring for COVID-19 patients, I got out of the way and let them do their job, which they did with skill, caring, and compassion. In the case of the staff members who, due to the hiring freeze, had to assume the burden of additional job responsibilities while still functioning in their own positions, I trusted them to learn the skills they needed and ask

questions when necessary. In all cases, I tried to express my gratitude for all the extra obligations our department members were undertaking.

5. **The importance of effective, reliable communication in the face of a disaster like COVID-19 cannot be overstated.** Unlike the immediate aftermath of Hurricane Katrina, there was never a time when we were without working phones or an instance when we did not know where people were or how to locate them. On the contrary, we were able to avail ourselves not only of our phones but also of new technologies, such as Zoom, in order to communicate. Despite the problems discussed earlier that Zoom can cause, it was paramount in enabling us to continue our work with efficiency (for the most part) and safety. In addition, in many of his presentations, Dr. Anthony Fauci has emphasized the cruciality of not only communication but of *factual* communication during this pandemic. This was especially necessary because of the newness of the virus and the fact that we were (and still are!) constantly adding to our understanding of it and trying to combat the misunderstandings and downright falsehoods that propagate so easily via the internet and social media. Like most, if not all, of our faculty, I made sure to keep abreast of the most current knowledge about the virus via educational webinars, articles, and Zoom conferences. The Department of Medicine continued to hold monthly meetings of either section chiefs or all faculty to disseminate pertinent departmental information, as well as weekly Medicine Grand Rounds to keep our faculty, fellows, residents, and students on top of the most updated medical knowledge. It is notable that attendance at Grand Rounds significantly increased over the past year, which is an unexpected benefit and almost certainly a result of the convenience of being able to attend from any location, rather than having to be physically present.

6. **In any catastrophe, it is imperative to be available, accessible, accountable, and affable.** The past year has presented me with innumerable problems to handle and rapid decisions to be made. I made a point of keeping our faculty informed of changes via email and during Zoom meetings. I communicated frequently with my section chiefs and other faculty and staff members and made sure that they all knew that I was available to talk with them at any time.

7. **An effective leader listens.** The COVID-19 crisis saddled many faculty members, residents, students, and administrative staff with large and, at times, insurmountable problems, and many of them wanted me to listen to what they had to say. They needed to be reassured that someone heard them and cared about their concerns. I have always tried to listen and remember that no situation is all about me.

8. **A good leader recognizes the importance of morale and should do everything possible to prevent its erosion.** As discussed above, the loss of morale has been one of the most significant challenges to everyone over the past year. I have tried to model a tone of positivity for the department while emphasizing the importance of teamwork. I made an effort to start meetings with words of encouragement, stressing how much I care about the members of the Department of Medicine and their inspiring dedication.

9. **Be willing to adapt to the situation.** Adaptability has become the order of the day as we have struggled to cope with our "new normal." The experience of our faculty in the Section of Emergency Medicine perfectly illustrates this, as detailed by the chief of the section, Keith Van Meter, M.D.:

> The Section of Emergency Medicine has been on the frontline of the COVID crisis in New Orleans since February 2020. Our faculty physicians, residents, fellows, and administrative staff have risen to the challenge. We have remained flexible during these constantly changing

> times and have learned new ways to continue our missions, [from] the delivery of patient care [to] the delivery of academic lectures. Last year, we worked closely with the hospital to find ways to deal with an anticipated crush of patients. We secured and manned tents on our ramp so patients could be screened before entering the hospital. Our faculty physicians manned telemedicine visits so we could screen patients in a safer manner. Our faculty physicians worked with the DHH to set up and staff a hospital at the Convention Center for COVID patients. We worked with the hospital to determine the most efficient use of the PPE that was on hand. We sampled all the testing methods and figured out what worked best for our department. As we learned that this medical crisis would present itself differently than we had anticipated, we adapted. The tents came down, but the telemedicine link remained. We continue to keep abreast of upcoming updates and are prepared for another surge of cases at any time.
>
> Academically, we have adapted also. Our conferences, faculty meetings, peer-review meetings, CCC meetings, and journal clubs have been held on Zoom. Usual social events have been done virtually or not at all. Even residency graduation in June was held virtually so everyone could still attend. We have several COVID-related projects coming from the Emergency Department at UMC, and our faculty and residents are at the forefront of identifying and pursuing opportunities for research.

Although this highlights the tremendous flexibility demonstrated by the Emergency Medicine faculty and staff, it is representative of the experiences of all of our sections, particularly the four most directly affected by the pandemic. All of the faculty and staff therein are to be commended for the adaptability they displayed during this time of uncertainty and rapid change.

10. **Remain optimistic and accentuate the positives.** The incredible stress of life in a pandemic has led almost inevitably to the temptation to dwell on the many negatives it engenders. However, as the aphorism (often attributed to basketball coach John Wooden but in fact of indeterminate origin) goes: “Things turn out best for those who make the best of the way things turn out.” We have much for which to be grateful. Though our responsibilities are many, we may be grateful that we still have jobs. Though we may be tired, we may be grateful that we still have our health. And though the war against this epic disease has seemed, at times, to be a

fight we cannot win, we may all be grateful that we now have new diagnostic methods and new therapies being developed at a phenomenal rate, not to mention the incredibly effective Pfizer and Moderna vaccines currently in use and the many other vaccines at various stages of being developed, studied, and approved. I am exceedingly encouraged when I consider how far we have all come in the past year, and as I look to the future, I am truly filled with optimism and hope.

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Note: This article would not have been possible without the superb and extensive assistance of the editor of the LSU Department of Medicine, Michelle Holt, M.Ed., M.F.A.