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COMBATING COVID-19

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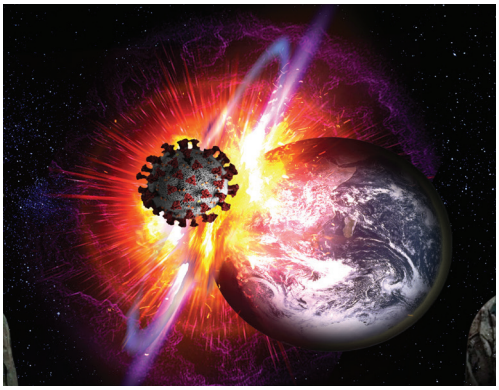

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This special topic issue focuses on COVID-19 and pandemic-related content. While the medical community is still actively working this mission, *The Medical Journal* offers a venue to share timely, pertinent research, experiences, and lessons learned with the military medical community. Undoubtedly, the COVID-19 battlefield will look different between now, as I write this, and when this issue becomes available.

Circumstances seem ever-changing in combatting this virus. The medical community will have learned more about transmission trends, perhaps new treatments or therapeutics, and new vaccines are expected to begin soon. Certainly, the medical community has a long road ahead in discovering, studying, and treating the after effects of COVID-19. With this evolution in mind, information contained herein may very well change between now and publication.

It is inevitable that new discoveries will unfold once populations begin new treatments and vaccines. *The Medical Journal* anticipates revisiting this topic again in the future once trends unfold and studies reveal more conclusive results. Future related topics will include not only the medical aspects of mitigating the virus, but also lessons learned in strategic planning, organization, and acquisition and logistics, among other areas of interest. It is with deep and sincere appreciation *The Medical Journal* is able to share in this journey.

Training During Social Distancing: The Effects of Remote Virtual Psychiatric Readiness Curriculum on Military Behavioral Health Providers

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Abstract

There is inconsistency in the training of military medical providers on the regulations and procedures outlining US Army-specific psychiatric readiness related competencies. These competencies are necessary to ensure the appropriate categorization of a soldier's psychiatric readiness. There exists a need for a formal, comprehensive training curriculum accessible to all providers that is time- and cost-effective. Due to the COVID-19 pandemic, there is are additional barriers of social distancing, remote virtual healthcare delivery, and geographic dispersion of healthcare personnel. To address these concerns, we developed a curriculum to target these competencies and deliver them virtually. The curriculum was developed and executed based on Kern's six-step approach to curriculum development, and the objective was to train military behavioral health providers on temporary duty limitations, administrative separations, and medical board referrals based on current US Army policies and procedures. The training was implemented virtually and conducted over the course of 3-hour training sessions to two separate groups. Evaluation of training objectives was conducted via a survey of paired before and after questions, analyzing the change in perceived confidence among learners. Among the 58 respondents, training resulted in statistically significant improvement in confidence in recognizing when a US Army soldier needs a temporary profile, writing a temporary e-profile, deciding when it is critical to contact a US Army soldier's commander, executing administrative separation, deciding when a US Army soldier is at medical retention determination point (MRDP), and in referring a US Army soldier to medical board. Results show the feasibility of virtual training to enhance medical readiness-related competencies of healthcare providers at the enterprise-level to help improve medical readiness. Limitations included immediate and subjective aspects of our results. It is unclear whether our training or similar training sessions resulted in changes in behaviors such as increased profiling or medical board referrals.

Background

Military medical services are vital in ensuring the medical readiness of a military unit. Military readiness requires that soldiers are physically and psychiatrically fit for worldwide deployment. To this end, military medical providers must possess readiness related competencies. These include temporary duty limitations to enable a service member to recover, and when such recovery is not possible, subsequently administratively or medically separate them from military service. The US Army has specific regulations and procedures that outline these steps.[1–7] Outside the policies, there are also information systems that end-user medical providers must know to issue a profile properly.[3] In the US Army, a profile is the official electronic document that specifies an individual soldier's duty limitations and its specific duration.[3] Commanders rely on these tools to make important decisions and determine how many of their soldiers can deploy. Psychiatric medical readiness competencies are especially challenging given the nature of the specialty where diseases are replaced by disorders.[8] This results in ambiguity, both in diagnosis and judging a patient's recovery. Therefore, applying readiness policies and regulations to psychiatric conditions pose a greater challenge.

Understanding and proper execution of psychiatric

fitness policies and procedures is critical because of its impact on recent US military operations. Mental disorders were the fourth leading cause of medical evacuations between 2001 and 2010, resulting in the evacuation of 6,910 service members.[9] It was the leading cause of medical evacuation from Operation Iraqi Freedom (OIF)[9] among females. Besides immediate operatonal implications for this, a study showed that psychiatric redeployments were associated with increased attrition rate.[10] The rates of attrition were four times higher for psychiatric conditions (53%) versus other conditions (14%).[10] Careers ended for more than half of the service members who were evacuated for psychiatric reasons. [10]

Despite the importance for medical providers to have a mastery of readiness competencies, data suggests there are gaps. One study showed that only half of US soldiers needing duty limitation were placed on behavioral health profiles.[11] In addition to this, just a quarter of soldiers received minor behavioral health profiles related to stimulant or anti-depressant prescriptions.[12] The same author reported that some of the reasons for a lack of behavioral health profiling were insufficient provider training and inadequate provider experience with the profiling regulations and procedures.[12]

While procedures are outlined clearly in numerous policies and regulations, there is no comprehensive and formal curricula to help a new behavioral health provider become proficient in the military behavioral health readiness competencies. Such training is often delivered ad-hoc and informally by senior behavioral health providers to their peers. The efficacy of such training is unknown and is not always possible, especially in smaller, remote military treatment facilities if peer expertise does not exist. Based on the studies by Curley et. al.,[11–13] the inadequate profiling and readiness behaviors by behavioral health providers, an urgent need for the creation of a formal curricula exits. The COVID-19 pandemic has added complexity to this pre-existing challenge. There are added barriers of social distancing, remote virtual healthcare delivery, and a geographic dispersion of healthcare personnel.

We attempted to fill this gap by creating a formal 3-hour curriculum that targeted temporary duty limitations, administrative separations, and medical board referrals for psychiatric conditions. The content was based on US Army policies and procedures. We then delivered the training virtually with learners participating from several remote locations during the COVID-19 pandemic. Here we describe our curriculum, including providing the training virtually, and we demonstrate the effectiveness of virtual training during the COVID-19 pandemic using objective data from the immediate self-reported impact of the training on the learners.

Methods

The curriculum development took place based on Kern's six-step approach to curriculum development.[14] As part of prior readiness policy development by the authors (R.A. and O.T.), general and learner needs assessments were done. Learner needs were identified based on informal assessments with active duty psychiatrists, psychologists, and social workers. Additionally, needs inputs were received from civilian behavioral health providers and military psychiatry residents. This resulted in the goals and agenda for the training.

The training goals and objectives were informed by the learner's assessments and literature reviews.[11–13] Data from the literature suggested a lack of training and competence in behavioral readiness procedure to be a significant barrier for military behavioral health providers.[11–13] The resulting goals that informed the curriculum included the following: 1. US Army medical fitness standards and referral to the medical board; 2. US Army administrative separations; and 3. Communicating duty limitations to commanders.

The educational strategies included case-based learning and scenarios. There was a significant emphasis on task training to help change the practice behaviors of the learners. There were no prerequisite requirements for a learner to enroll in the training. The training began with information targeting the attitudinal competencies of the learners. Specifically, it focused on highlighting the strategic mission of the Army behavioral health providers achieving medical readiness. The knowledge elements of the training included specific policies on behavioral health in the US Army. Since the educational strategy included task-specific training, most of the time was spent providing specific skills. The learners were provided with decision algorithms, which included deciding if a soldier needs a referral for a medical board or administrative separation. Templates for official forms were also provided to help the learners easily execute these tasks in their practice. Clinical cases were used to stimulate discussion on targeted goals and objectives. As part of the skills-based teaching, step-by-step instructions were provided on using the Army's Behavioral Health Administrative Review (BHAR) website, and the completion of the Army's e-profile.

The training was implemented virtually due to the COVID-19 pandemic while the social distancing rules were in place. The majority of learners were teleworking and were in remote locations. The training was

conducted using presentation slides over two separate sessions. The first training session was conducted over three hours in March of 2020, using the Defense Collaboration System (DCS)[15] as the virtual teaching delivery tool. This session was attended by trainees from two different military treatment facilities that included psychiatrists, social workers, psychiatric nurse practitioners, and psychologists. The second, three-hour training session was conducted in April 2020 by military psychiatry and psychology residents. This session implemented off-the-shelf distance learning tools[16] during scheduled academics while the trainees were socially distanced in their homes. The first session was hosted using the DCS tool available to the Department of Defense (DoD) personnel.[15] The author (R.A.) received self-directed online training on the tool. The tool allowed users on and off the DoD network to join the training session. The tool also allowed for presenting teaching slides to the learners. The learners were able to ask questions via the chat option or voice. The training was facilitated by the author O.T. For the second session, the off-the-shelf tool[16] was selected based on the learners' familiarity and ease of use, including the ability to attend the training on personal mobile devices. Similar to DCS, the learners were able to engage in discussion using chat or voice options. The second session was facilitated by the author R.A.

The evaluation targeted assessing the objectives of the training. A survey was created based on expert recommendations.[17] It was electronically delivered to the learners using electronic survey system.[18] Learners were provided a web link and a quick response (QR) code at the end of the training and were requested to complete the survey. The majority of the measurements in the survey were paired questions designed as "Before this training…" and "After this training…" to enable an analysis of change in perceived confidence among the learners. All questions were based on a Likert scale of 1-to-5, with a 5 suggesting greatest confidence or knowledge. A free-text area was provided for additional evaluation and feedback. The results of the survey were analyzed using software.[19] A paired-T test was used to compare the change in the paired (pre- and post-training) questions.

Results

A total of 45 learners attended the first session, and 48 learners attended the second session. There was 38% (N=17), and 85% (N=41) survey completion rate, respectively, with a total of 58 surveys. The majority of the learners were on active duty (81%), and psychiatry residents (67%).

There were significant improvements in learner's perceptions related to clinical readiness behaviors such as writing profiles, communication with commanders, referral to the medical board, and administrative separations. Confidence levels in recognizing when a US Army soldier needs a temporary profile improved from a before training confidence score of (2.78 ± 1.155) to an after training score of (3.83 ± 0.976), $t(57) = -9.962$, $P < 0.001$, $d = 1.31$. Confidence levels in writing a temporary e-profile for an active duty US Army soldier improved from a before training confidence score of (2.74 ± 1.292) to an after training score of (3.74 ± 0.947), $t(57) = -8.668$, $P < 0.001$, $d = 1.14$. Confidence levels in deciding when it is critical to contact an active duty US Army soldier's commander improved from a before training confidence score of (3.17 ± 1.201) to an after

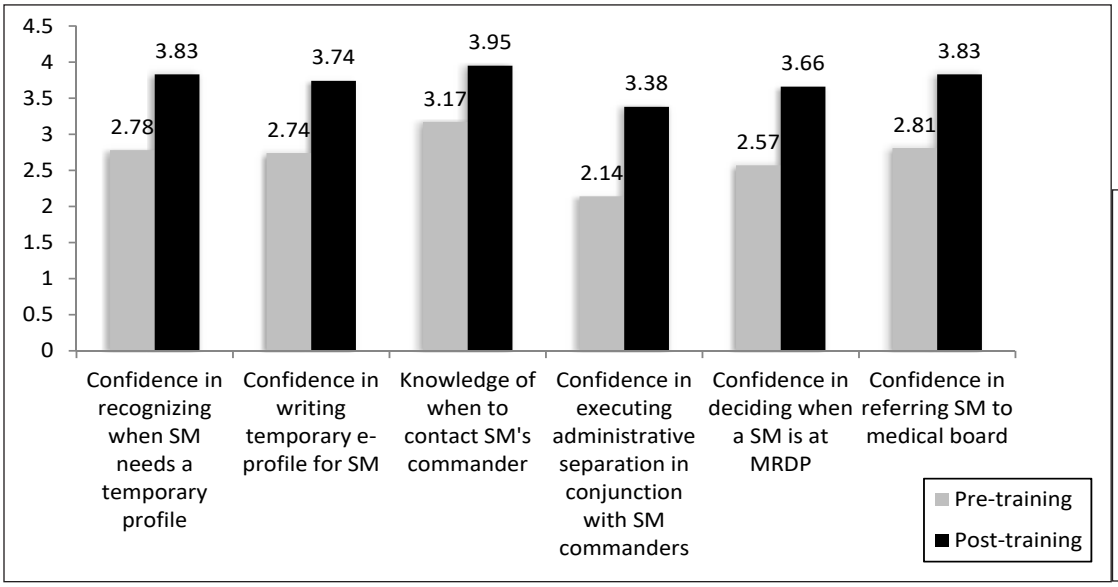

Figure 1. Effects of behavioral health readiness virtual training on US Army behavioral health providers. Perceived confidence among the learners improved significantly ($p<0.05$) among all the areas evaluated. SM:Service Member; MRDP: Medical Retention Determination Point.

training score of (3.95 ± 0.926), t(57) = -6.876, P < 0.001, d = 0.90. Confidence in executing administrative separation in conjunction with a US Army soldier's commanders improved from a before training confidence score of (2.14 ± 1.017) to an after training score of (3.38 ± 0.855), t(57) = -13.342, P < 0.001, d = 1.75. Confidence level in deciding when a US Army soldier is at medical retention determination point (MRDP) improved from a before training confidence score of (2.57 ± 1.156) to an after training score of (3.66 ± 1.206), t(57) = -9.805, P < 0.001, d = 1.29. Confidence level in referring a US Army soldier to a medical board improved from a before training confidence score of (2.81 ± 1.206) to an after training score of (3.83 ± 0.976), t(57) = -8.192, P < 0.001, d = 1.08. These differences are illustrated in Figure 1.

Discussion

As suggested in the literature,[11–13] there is a need for uniform, effective, and less intrusive training to help improve the competencies of behavioral health providers who serve the active-duty military population. Ideally, such training is done live so that new providers within the military health system can interact with instructors and peers. We show the feasibility of a brief, live virtual training with immediate positive effects. There are limitations to our results, i.e., it is unclear whether the perceptions have resulted in changed behaviors. Future curricula should follow the long-term behaviors of providers by observing pre- and post-training profiling, as well as medical board submissions for objective outcomes. Despite these limitations and its virtual nature, our curriculum presents a possible solution to an enterprise-level challenge. Regular, enterprise-level training events mimicking ours could be delivered virtually and can assist not only larger academic military treatment facility providers, but also close the gap for providers in remote locations. Improved fidelity in such administrative actions will enable commanders to have a greater understanding of their medical readiness.

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Pooling Nasopharyngeal Swab Specimens to Increase Testing Capacity for SARS-CoV-2

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Abstract

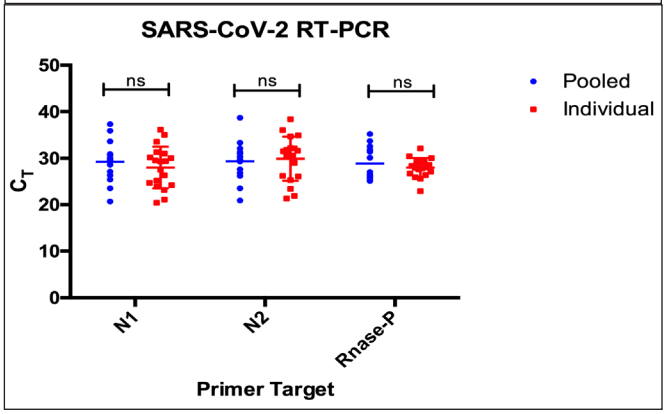
The recent emergence of SARS-CoV-2 has led to a global pandemic of unprecedented proportions. Current diagnosis of COVID-19 relies on the detection of SARS-CoV-2 RNA by reverse transcription polymerase chain reaction (RT-PCR) in upper and lower respiratory specimens. While sensitive and specific, these RT-PCR assays require considerable supplies and reagents, which are often limited during global pandemics and surge testing. Here, we show that a nasopharyngeal swab pooling strategy can detect a single positive sample in pools of up to 10 samples without sacrificing RT-PCR sensitivity and specificity. We also report that this pooling strategy can be applied to rapid, moderate complexity assays, such as the BioFire COVID-19 test. Implementing a pooling strategy can significantly increase laboratory testing capacity while simultaneously reducing turnaround times for rapid identification and isolation of positive COVID-19 cases in high risk populations.

Introduction

In December 2019, an outbreak of pneumonia with unknown origin began in Wuhan city, the capital of Hubei province in China.[1] The following month, Chinese researchers had isolated a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), from patients with viral pneumonia.[2] Pneumonia associated with SARS-CoV-2 was later designated as coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO) in February 2020.[3] It was determined that after a zoonotic transmission event in Wuhan, Hubei, China,[4] widespread person-to-person transmission quickly occurred that led to the infection and death of over 80,000 and 3,000 people in China, respectively. To date, according to the WHO, there have been 4,258,666 reported cases of COVID-19, including 294,190 deaths worldwide.[5]

Since the initial outbreak in China, COVID-19 has been declared a global pandemic affecting at least 216 other countries, territories or areas. To monitor and diagnose COVID-19, the US Food and Drug Administration (FDA) approved an emergency use authorization (EUA) for the Centers for Disease Control and Prevention (CDC) 2019-nCoV Real-Time RT-PCR Diagnostic Panel on February 4, 2020.[6] This protocol allows for the rapid detection of SARS-CoV-2 RNA from clinical specimens such as, nasopharyngeal and oropharyngeal swabs, sputum, bronchoalveolar lavage, and tracheal aspirates. As evidenced by the ongoing SARS-CoV-2 pandemic, increased demand for testing can overwhelm diagnostic laboratories and lead to drastic shortages in supplies and reagents. A strategy to overcome high testing demand is to pool specimens before ribonucleic acid (RNA) extraction, test pools, and then retest individual specimens from positive pools. Similar strategies have shown to increase testing capacity for the detection of common infectious diseases such as influenza, human immunodeficiency virus (HIV), Hepatitis, and *Chlamydia trachomatis*.[7–11]

Figure 1. Comparison of mean C_T value between positive pooled and individually tested samples. Data are represented as the mean ± standard error the mean.



In this study, we examined the feasibility of pooling nasopharyngeal swab specimens submitted for COVID-19 testing using the CDC 2019-nCoV RT-PCR diagnostic panel without compromising clinical sensitivity. Our data shows that pooling respiratory samples during times of increased volume and low disease prevalence can save time and reagents without significant modifications to laboratory infrastructure or workflow.

Methods

This study was determined to meet the exempt criteria listed in 32CFR219.104(d) from the Landstuhl Regional Medical Center Exempt Determination Official. During an outbreak cluster of SARS-CoV-2 in Stuttgart, Germany, 494 nasopharyngeal (NP) swabs were collected and placed into 1.0 ml of normal saline. Specimens were submitted to the Virology Laboratory at Landstuhl Regional Medical Center for routine SARS-CoV-2 testing using the CDC 2019-nCoV RT-PCR assay. Post clinical testing, specimens were de-identified and randomly assigned into pools of 10 to create 50 distinct pools (the 50th pool contained 4 specimens diluted in 0.6 ml of transport media). Pools were created by combining 100 ul of each specimen to create 1.0 ml pools. Viral transport media was added to each pool at a 1:1 ratio for nucleic acid extraction performed on the Roche MagNA Pure 24 platform using the MagNA Pure 24 Total NA Isolation kit (Roche). Elution volume was set to 50 ul to concentrate viral RNA. Each round of extraction contained a human specimen control to monitor for PCR inhibition and specimen quality. Detection of SARS-CoV-2 was performed using the CDC RT-PCR COVID-19 assay, which contains primers and Taqman probes for two specific regions of the SARS-CoV-2 nucleocapsid (N) gene and the human Rnase-P (RP) gene, which is used as an internal positive control for human nucleic acid. PCR was performed according to the CDC protocol using the TaqPath 1-Step RT-qPCR Master Mix, CG kit (Life Technologies) on the Applied Biosystems (ABI) 7500 Fast real-time PCR system. PCR results were interpreted as recommended in the CDC RT-PCR COVID-19 instructions for use. A pool was considered positive if the C_T was less than 40. Detection of SARS-CoV-2 in pooled samples using the BioFire COVID-19 Test was performed according to the manufacturer's instructions for use on the BioFire FilmArray 2.0 and FilmArray Torch systems. All statistical analyses were conducted using Graphpad Prism 6.0.

Table 1. RT-PCR C_T values of pooled specimens positive for SARS-CoV-2.

Positive Pool	Ct Values		
	N1	N2	Rnase-P
2	28.6	29.7	31.8
8	25.4	26.2	25.7
11	35.9	38.7	33.7
12	29.7	31	32.5
13	30.7	32.1	31.4
15*	29.5	30.3	30.1
18	27.1	27.6	25.2
19	20.7	20.9	25.1
20*	26.3	26.8	25.2
22	29.5	30.3	30.1
25	30	29.3	25.8
41*†	37.3	Und.	26.5
43*	23.5	23.5	27
47	30.9	31.3	26.2
50	33.6	33.3	26.2

* Pool containing 2 positive specimens

† Inconclusive RT-PCR result

Und.: Undetected

Results

The prevalence for individual clinical samples was 4% (19/494) for SARS-CoV-2 RNA. Among the pooled samples, 30% (15/50) were positive for SARS-CoV-2 RNA, while the remaining 70% (35/50) did not have detectable levels of SARS-CoV-2 RNA (Table 1). We observed one inconclusive RT-PCR result in our pooled analysis as defined by amplification of only a single SARS-CoV-2 target. In this case, the N2 target for pool 41 failed to amplify while N1 was detected with a relatively high C_T (37.3). There were no invalid reactions in our analysis, as defined by reactions where Rnase-P failed to amplify. Out of the 15 positive pools, 4 pools contained 2 positive specimens, while the remaining 11 pools contained only 1 positive specimen (Table 2).

The mean C_T value and standard deviation for N1 and N2 of the pools were 29.2 (4.4) and 29.4 (4.3), respectively. Similarly, the mean C_T values of individual positive specimens were 28.0 (4.5) and 29.9 (4.8) for N1 and N2, respectively. Despite dilution, there was no significant difference in mean C_T value between the pooled and individually tested specimens (Figure 1).

To determine if a pooling approach is feasible with rapid, moderate complexity tests, we tested the 15 SARS-CoV-2 positive pools and 15 of the SARS-CoV-2 negative pools using the recently released BioFire COVID-19 Test. The BioFire COVID-19 test is a nested multiplexed RT-PCR test that automates all aspects of nucleic acid testing including sample preparation, extraction, and PCR, and which can detect SARS-CoV-2

within a single nasopharyngeal swab specimen in under 60 minutes. As expected, SARS-CoV-2 RNA was detected in all 15 positive pools (Sensitivity 100%, 95% CI 78.2%-100.0%) whereas SARS-CoV-2 RNA was not detected in all 15 negative pools using the BioFire COVID-19 Test (Specificity 100%, 95% CI 78.2%-100.0%) (Table 3).

Table 2. RT-PCR C_T values of individual specimens positive for SARS-CoV-2.

Pool	Sample	Ct Values		
		N1	N2	Rnase-P
2	2696	25.2	26.2	27.6
8	2610	24.7	26.1	28.6
11	2535	31	34.7	25.9
12	2697	23.9	34.9	30.4
13	2624	21.1	21.9	28.3
15	2595	29.3	30.6	29.5
15	2620	26.3	31.6	29.1
18	2586	29.4	32.1	26.7
19	2803	20.4	21.3	27.9
20	2665	30	31.5	28.6
20	2785	27.5	29	25.6
25	2662	29.5	30.6	27.8
41	3010	33.5	32.2	28
41	2975	36.1	36	27.1
43	3186	35	38.4	29.3
43	3202	24.2	25.3	32.1
47	3164	30.2	31.8	30
50	3104	31.3	30.5	22.9
22	2497	23.2	23.4	26.4

Discussion

We found that a single NP swab specimen containing SARS-CoV-2 RNA can be consistently detected in a pool of 10 samples. Our data shows an estimated false negative rate of approximately 7% (1 out of 15); although, this pool was inconclusive (the N2 primer failed to amplify) and was treated as a positive pool. Unlike other pooling strategies that pool purified RNA extracts, [12,13] our method utilized pooling clinical specimens prior to RNA extraction, which removes the extraction bottleneck and allows running an endogenous internal control to monitor extraction quality.

A linear increase in threshold cycle is expected as specimens are pooled; however, we did not observe a significant change in C_T values for either primer pair in our pooled samples. Given that PCR efficiency of each primer pair can differ, any inconclusive result for a pool should be treated as positive and individually tested. Case in point, the only inconclusive result in our study was found in pool 41, where the N2 target failed to amplify. This pool contained 2 positive specimens and one inconclusive specimen. This suggests there may have been PCR inhibitors present in the individual sample that carried over to the pooled specimen resulting in an inconclusive result. Both positive specimens in pool 41 had relatively high C_T values. In our lab, specimens with high C_T values are commonly observed in convalescent patients 14-30 days after symptomatic infection, and do risk escaping detection when combined in larger pools due to loss of sensitivity. It should also be noted that a negative pool result would not differentiate between a true negative and an inconclusive or invalid result due to improper sample collection or storage. Given the clinical performance of this and other published pooling protocols,[7,12,13] it is possible that larger pools could be used with further RT-PCR optimization to allow lower detection limits for low-concentration RNA.

Disease prevalence should also be taken into consideration when implementing a pooling strategy. Recently, Noriega and Samore used a Bayesian modeling approach to show testing throughput more than doubles when prevalence rates are ≤8%, and this occurs with optimal pool sizes between 4 and 12 samples. Conversely, as prevalence increases, they show improvements in testing throughput diminishes significantly.[14] During this surveillance period, SARS-CoV-2 prevalence was determined to be approximately 4% (19/494), which is ideal for pool sizes of 10. In this study, we found that 30% (15/50) pools were positive for SARS-CoV-2. This equates to 200 individual extractions and RT-PCR reactions (50 pools and 150 individuals), representing a 60% savings in extractions and RT-PCR reactions, which is significant during times of surge testing and in limited-resource situations.

Recently, numerous rapid molecular diagnostic platforms have received an Emergency Use Authorization from the FDA. These include low to moderate complexity assays from BioFire, Cepheid, and Abbott that can detect SARS-CoV-2 in approximately 1 hour.[15,16] Using the recently released BioFire COVID-19 Test, we found that this platform could reliably detect a single positive sample in pools of up to 10 specimens, with equal rates of detection as the CDC COVID-19 RT-PCR assay. This is not surprising given the published limits of detection for the CDC COVID-19 RT-PCR and BioFire COVID-19 test are in the range of 102 RNA copies/ml. These results support the use of rapid molecular diagnostic platforms for routine disease surveillance of critical working groups such as healthcare providers and military units, where large-scale quarantines can have grave consequences.

Table 3. CDC 2019-nCoV RT-PCR and BioFire COVID-19 Comparator Analysis. Sensitivity 100% (95% CI 78.2%-100.0%), Specificity 100% (95% CI 78.2%-100.0%), Accuracy 100% (95% CI 88.4%-100.0%).

		BioFire COVID-19 Test	
		Positive	Negative
CDC 2019-nCoV RT-PCR	Positive	15	0
	Negative	0	15

In summary, we show that a pooled-sample strategy can augment a laboratory's testing capability and relieve extreme pressure from limited resource situations without sacrificing RT-PCR sensitivity and specificity. Importantly, a pooling strategy can reduce turnaround times for prompt identification and isolation of infected individuals to effectively curb the transmission of COVID-19 and other infectious disease outbreaks.

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Treatment of Patients Hospitalized with COVID-19 in a US Military Role 3 Facility in Afghanistan: A Case Series

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Abstract

Background: COVID-19, caused by SARS CoV-2, is an acute respiratory viral illness. We present the experience of treating patients hospitalized with COVID-19 in a Role 3 hospital in an active warzone.

Methods: This is a retrospective care series of patients treated for COVID-19 at Craig Joint Theater Hospital, Bagram, Afghanistan from May to August 2020. Data extracted included demographics, admission and disposition information, past medical history, comorbidities, Transportation Command (TRANSCOM) severity classification (i.e. Category A, Category B), and treatments received.

Results: This series included 15 Category A and 55 Category B patients. Most patients were non-US contractors with one chronic condition. Most patients received medical treatments in accordance with Department of Defense Practice Management Guidelines. For Category A patients, mechanical ventilation use declined from a mean average of 10.67 days to 2.83 days following the introduction of high-flow nasal cannula. Average hospital length of stay was 6 days (range 2-23). One death occurred in a patient greater than 60 years old with three known prior medical conditions. Most patients were discharged to a non-medical isolation facility. Aeromedically evacuated patients were mostly US military and US contractors.

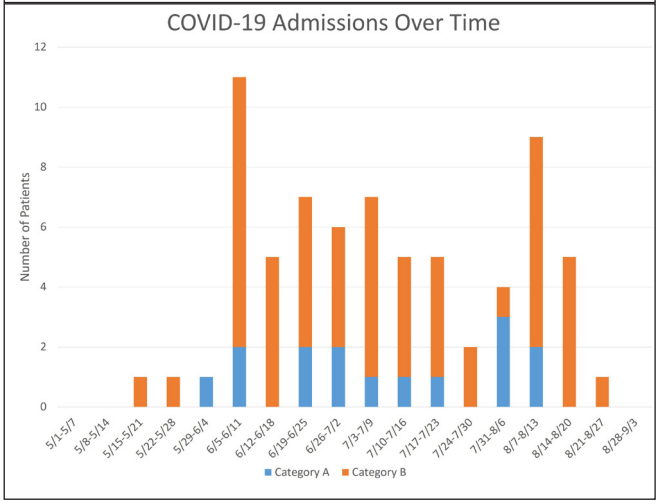
Conclusion: We faced several challenges including retrofitting a Role 3 facility designed for trauma care for management of a highly contagious respiratory viral illness. Logistics constraints impacted timely delivery of medical therapies and equipment and decreased efficiency of aeromedical evacuation. Despite these challenges and the simultaneous trauma mission, most patients received medical care in accordance with treatment guidelines with a low mortality rate.

Introduction

Coronavirus disease 2019 (COVID-19) is a novel pandemic acute respiratory illness caused by the SARS CoV-2 virus. According to the World Health Organization, as of 6 September 2020, there have been more than 26 million confirmed cases of COVID-19 worldwide, including more than 870,000 deaths.[1] Afghanistan reported its index case in Herat province on 24 February 2020.[1] As of 6 September 2020, Afghanistan's Ministry of Public Health has reported more than 38,000 confirmed cases with more than 1,400 deaths related to COVID-19, though this is likely under-reported due to limited public health resources and testing capabilities in Afghanistan.[2]

Craig Joint Theater Hospital (CJTH) in Bagram Airfield (BAF) is a Role 3 United States (US) military treatment facility (MTF) in Afghanistan. As a Role 3 hospital, CJTH provides the highest level of critical care and surgical capabilities within the theater of operations, serving NATO Resolute Support (RS) military forces, US and non-US contractors, Afghan forces, and select local nationals. CJTH has an Intensive Care Unit (ICU) and an Intermediate Care Ward (ICW); however, it lacks the complete spectrum of medical capabilities

Figure 1. Number of Admissions for COVID-19 at CJTH from May 2020 – Aug 2020.



that can be found in Role 4 hospitals akin to hospitals based in the continental US.[3] The establishment of an Army Field Hospital (COVID-19 Tent) adjacent to the established hospital added additional staffed beds for a worse-case scenario influx of patients with COVID-19 that would otherwise exceed medical capacity in the Combined Joint Operations Area – Afghanistan (CJOA-A). Here we provide an overview of the medical care delivered for patients hospitalized with COVID-19 in an austere MTF during a global pandemic. The challenges faced encompass the following areas: caring for medically complex patients over a prolonged period of time in an austere environment; the impact of delivery delays of medical equipment and treatments on medical care; the challenge of providing adequate facilities for anticipated surges of patients; and evacuation of critically ill and COVID-positive patients during a time when border closures affected patient movement. The experience of CJTH in the summer of 2020, will be evaluated and summarized as to the challenges faced, lessons learned, and success of the combined experience during a pandemic.

Methods

Data from the electronic medical record and provider sign-out documents were retrospectively reviewed to identify patients who received care for COVID-19 disease at CJTH between 1 May and 30 August 2020. Records reviewed included history and physical, discharge summary, lab results, daily progress notes, and nursing notes. Patients included those admitted to the ICU, ICW, and the COVID-19 Tent. Data was abstracted from patient records up to the discharge date. A laboratory-confirmed case was defined as a positive result for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) on a PCR assay (i.e., Gene Xpert, Biofire, ABI 7500). A clinically confirmed case of COVID-19 was defined as diagnostic if a patient had five or more COVID clinical signs or symptoms, including at least 1 of the typical symptoms (i.e., fever, cough, shortness of breath). A confirmed clinical case was also defined if a patient had three typical signs or symptoms and radiological evidence compatible with COVID-19 or met epidemiologic criteria (close contact with a person with clinically compatible symptoms or confirmed case of COVID-19, or travel to or residence in a place with ongoing community transmission).

Data from the electronic medical record that was obtained included demographic data; admission, discharge, and disposition information; past medical history; comorbidities and complications during admission; respiratory management; medical treatments for COVID-19 including emergency use authorized medications and those enrolled as part of the Landstuhl Regional Medical Center (LRMC) Treatment Protocol for Remdesivir and Convalescent Plasma; and COVID-19 and respiratory viral PCR results if available. Patients were categorized as Category A, B, or C according to definitions established by the US Transportation Command (TRANSCOM).[4] Category A patients are those who were intubated or who had oxygen saturation <85% on room air and <92% on 5 liters per minute (L/m) oxygen. Category B patients are those with oxygen saturation < 90% on room air or >92% on 4L/m oxygen. Category C patients are those with oxygen saturations >92% on room air. Analysis for this case series included all Category A and B patients. We excluded patients who did not have a clinical- or lab-confirmed diagnosis and those with COVID-19 without symptoms or with mild symptoms (Category C) who were admitted for non-COVID-19 related care.

Descriptive statistics were used to summarize the data. Frequencies and percentages were obtained for categorical variables. Means with ranges and standard deviations (SD) were noted for continuous variables. Approval for this case series was obtained from the US Central Command (USCENTCOM) Office of Command Surgeon (CCSG).

Results

In total, 84 charts were reviewed. Fourteen were excluded as they did not have a clinical- or lab-confirmed diagnosis of COVID-19. Seventy patients were included in our analysis with 15 Category A (Cat A) and 55 Category B (Cat B) (Table 1). Figures 1 and 2 respectively show the number of admissions and the overall census for COVID-19 from May 2020 to August 2020 at CJTH. Seven patients had a switch in disease

severity from Cat B on admission to Cat A during their hospitalization. Most patients (n=38/70, 54.3%) came from a base other than BAF. Average age was 46.76 years (Range 25.96-74.68; SD 10.05). Patients were mostly male (n=66/70, 94%) and included 12 different nationalities (Table 1). The minority of patients admitted were active duty US (n=8/70, 11%) or coalition military (n=3/70, 4%). Consistent with the higher relative number of contractors in theater, contractors were the largest group admitted for COVID-19 (n=48/70, 68%), 65% of which were non-US nationals (Table 1).

In total, 60% (n=42/70) of the patients admitted to CJTH had a prior medical condition or chronic medical condition and 16% (n=11/70) had >3 prior or chronic medical conditions (Table 1). Beyond COVID-19, 76% (n=53/70) of all admitted patients had some additional comorbidity documented at the time of diagnosis. These included community acquired pneumonia (CAP), pulmonary embolism, new diagnosis of hypertension, new diagnosis of diabetes, and "Other" (e.g., electrolyte abnormalities, elevated liver enzymes, anemia, thrombocytopenia, gastroesophageal reflux disease, acute kidney injury, proteinuria, hyperlipidemia, etc.). CAP was diagnosed in 43% (n=30/70) of patients admitted to CJTH for COVID-19. Complications were rare and included hospital acquired pneumonia (HAP) or ventilator associated pneumonia (VAP) (n=4/70, 5.7%) and central line-associated bloodstream infection (CLABSI) (n=1/70, 1.4%) (Table 2).

On average, patients were admitted to CJTH 5.77 days after onset of symptoms (range 0-16). Initially, most patients were admitted to the ICW (n=42/70, 60%) or COVID-19 Tent (n=18/70, 26%) (Table 3). Practice patterns reflected the DoD COVID-19 Practice Management Guide[4] with 96% (n=67/70) receiving chemoprophylaxis for venothromboembolic (VTE) events and an additional three patients received full-dose anticoagulation for VTE diagnosed at or near admission. All thirty patients diagnosed with CAP were prescribed appropriate antibiotics. Several patients were also treated as part of a treatment protocol or through emergency use authorization (EUA) with convalescent plasma or remdesivir, as supply allowed. Specifically, 9% of COVID-19 patients admitted to CJTH (n=6/70) were administered convalescent plasma as part of a treatment protocol and 17% (n=12/70) were administered remdesivir (6 EUA, 6 treatment protocol). Steroids were administered to 53% (n=37/70), the majority of which was given after the National Institutes of Health (NIH) released treatment guidelines on 25 June 2020 recommending

Table 1. Demographics.

	All (N=70)	Category A (N=15)	Category B (N=55)
Age (yr), mean [range, SD]	46.76 [25.96-74.68, 10.05]	49.68 [31.9-74.68, 12.18]	45.97 [25.96-64.22, 9.37]
Male [%]	66 [94%]	14 [93%]	52 [95%]
Categories of Patient, n [%]			
Local National	3 [4.3%]	2 [13%]	1 [2%]
Afghan National Army/ Police	1 [1.4%]	1 [7%]	0 [0%]
Contractor (OCN*)	31 [44%]	8 [53%]	23 [42%]
Contractor (US)	17 [24%]	1 [7%]	16 [29%]
DoD Civilian/OGA	7 [10%]	0 [0%]	7 [13%]
Active Duty (US)	8 [11%]	2 [13%]	6 [11%]
Active Duty (Coalition)	3 [4.3%]	1 [7%]	2 [4%]
Nationality			
Afghan	4 [6%]	3 [20%]	1 [2%]
Azerbaijani	1 [1%]	0 [0%]	1 [2%]
Bosnian	2 [3%]	1 [7%]	1 [2%]
Bulgarian	2 [3%]	1 [7%]	1 [2%]
Fijian	1 [1%]	0 [0%]	1 [2%]
Georgian	1 [1%]	0 [0%]	1 [2%]
Indian	9 [13%]	3 [20%]	6 [11%]
Macedonian	2 [3%]	0 [0%]	2 [4%]
Nepalese	4 [6%]	1 [7%]	3 [5%]
Portuguese	1 [1%]	0 [0%]	1 [2%]
Ugandan	11 [16%]	3 [20%]	8 [15%]
US	32 [46%]	3 [20%]	29 [53%]
Past Medical History			
Hypertension	10 [14%]	1 [7%]	9 [16%]
Diabetes Mellitus	5 [7%]	2 [13%]	3 [5%]
Obesity	10 [14%]	3 [20%]	7 [13%]
Active Smoker	8 [11%]	3 [20%]	5 [9%]
Chronic Lung Disease	6 [9%]	4 [27%]	2 [4%]
Other	30 [43%]	6 [40%]	24 [44%]
Prior or Chronic Conditions			
Any	42 [60%]	9 [60%]	33 [60%]
1	21 [30%]	3 [20%]	18 [33%]
2	10 [14%]	2 [13%]	8 [15%]
3+	11 [16%]	4 [27%]	7 [13%]

*Other Country National (OCN)

Figure 2. COVID-19 Inpatient Census at CJTH from May 2020 – Aug 2020.

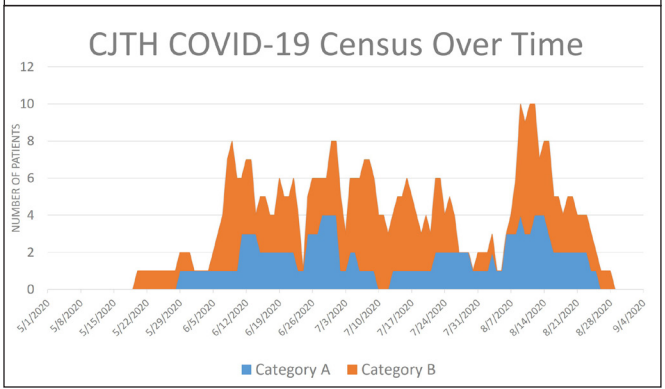


Table 2. Comorbidities, Complications, Management.

	All (N=70)	Category A (N=15)	Category B (N=55)
Patients diagnosed with any comorbidity, n [%]	53 [76%]	15 [100%]	38 [69%]
Diagnosed Comorbidities, n [%]			
Pneumonia (Community Acquired)	30 [43%]	15 [100%]	15 [27%]
Pulmonary Embolism	3 [4%]	2 [13%]	1 [2%]
New Hypertension	5 [7%]	2 [13%]	3 [5%]
New Diabetes Mellitus, Type 2	3 [4%]	1 [7%]	2 [4%]
Other	43 [61%]	11 [73%]	32 [58%]
Complications			
HAP/VAP*	4 [5.7%]	3 [20%]	1 [2%]
CLABSI§	1 [1.4%]	1 [7%]	0 [0%]
CAUTI¶	0 [0%]	0 [0%]	0 [0%]
Management/Therapies, n [%]			
Anticoagulant Therapy			
VTE Chemoprophylaxis dose	67 [96%]	13 [87%]	53 [96%]
Full dose/treatment dose	3 [4%]	2 [13%]	1 [2%]
Antibiotics	30 [43%]	15 [100%]	15 [27%]
Steroids	37 [53%]	11 [73%]	26 [47%]
After 25 June 2020%	*36 [77%]*	*11 [92%]*	*26 [58%]*
Convalescent Plasma	6 [9%]	6 [40%]	0 [0%]
EUA	*0/6 [0%]*	*0/6 [0%]*	*0/0 [0%]*
Trial	*6/6 [100%]*	*6/6 [100%]*	*0/0 [0%]*
Remdesivir	12 [17%]	8 [53%]	4 [7%]
EUA	*6/12 [50%]*	*4/8 [50%]*	*0/4 [0%]*
Trial	*6/12 [50%]*	*4/8 [50%]*	*4/4 [100%]*
Respiratory Therapies			
# requiring mechanical ventilation	12	11	1
Ventilation Days, mean [range]	5.58 [1-15]	6 [1-15]	1
# flight ONLY	5	*4*	*1*
# for hypoxemic respiratory failure	7	7	0
Ventilation Days, mean [range]		8.86 [4-15]	
Patients requiring paralysis	5	5	
Paralyzed Days, mean [range]		3.4 [2-6]	
Patients requiring Hi Flow NC (HFNC)	10	10	
HFNC Days, avg [range]		5.2 [2-9]	
HFNC w/o intubation		4/10 [40%]	
HFNC Days, avg [range]		5.7 [3-9]	
Pre-Intubation		4/10 [40%]	
HFNC Days, avg [range]		4.25 [2-6]	
Post-Intubation		2/10 [20%]	
HFNC Days, avg [range]		6 [4-8]	

*HAP/VAP = Hospital Associated Pneumonia/Ventilator Associated Pneumonia. § CLABSI = Central Line Associated Bloodstream Infection. ¶ CAUTI = Catheter Associated Urinary Tract Infection. % On 6/25/2020, the National Institutes of Health COVID-19 Treatment Guidelines Panel released recommendations for dexamethasone in patients with COVID-19.

dexamethasone in hospitalized patients with COVID-19 who are mechanically ventilated or who require supplemental oxygen (Table 2).[5]

Twelve patients in total underwent mechanical ventilation with average time on ventilator of 5.58 days (range 1-15 days) (Table 2). Of the 12 patients who required mechanical ventilation, 5 (41.67%) were intubated for safety and resource concerns related to aeromedical evacuation on the day of discharge and were counted as only 1 day of mechanical ventilation. The total duration of mechanical ventilation for those patients after discharge from CJTH is unknown. Among the 7 patients mechanically ventilated for management of hypoxemic respiratory failure, 5 (71.4%) required paralytics with average duration of paralysis of 3.4 days (range 2-6 days). Among all 12 mechanically ventilated patients, 6 (50%) also required use of hi-flow nasal cannula (HFNC) either prior to (n=4/6) or following (n=2/6) mechanical ventilation. An additional 4 patients were placed on HFNC without the need for mechanical ventilation. Among these 4 individuals, HFNC was used for 5.75 days on average (range 3-9 days) (Table 2) (Figure 3). The average number of ventilator days among Cat A patients prior to the receipt of HFNC in theater on 17 June 2020 was 10.67 days compared to 2.83 days after its arrival.

Overall length of stay for patients admitted to CJTH for COVID-19 averaged 6.01 days (range 2-23). Those requiring ICU care spent an average of 7.7 days (range 0.5-22) in the ICU. Among the sub-group of patients evacuated from CJTH, average length of stay trended toward being somewhat increased at 6.82 days (range 2-23). Upon discharge, 53% (n=37/70) of patients went to BAF isolation non-medical facilities and 47% (n=33/70) were evacuated from CJTH. Most evacuated patients (n=14/37, 42%) moved to Landstuhl Regional Medical Center Role 4, with other evacuation locations including local Afghan Hospitals, isolation facilities at other bases in Afghanistan, hospitals, or hospitals in other countries (i.e., Germany, Bosnia, United Arab Emirates, India, Bulgaria, Turkey, non-Afghan run facilities in Afghanistan). Most evacuations were out of country and involved fixed wing military air or civilian air ambulance, while within-theater evacuations

Figure 3. Schematic of Supplemental Oxygen and Duration for Category A Patients at CJTH from May-Aug 2020.

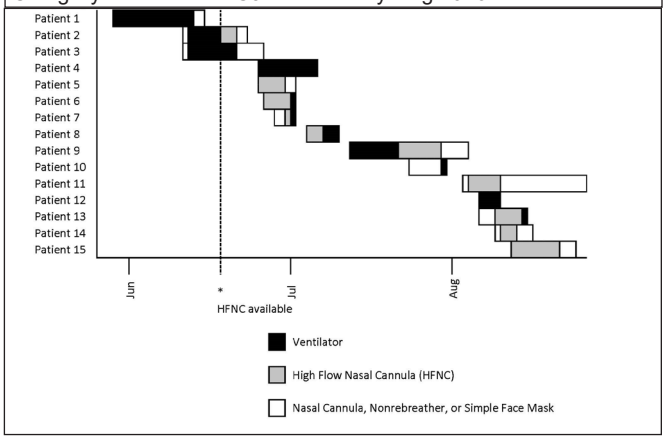


Table 3. Length of Stay and Disposition.

	All (N=70)	Category A (N=15)	Category B (N=55)
Days (symptoms to diagnosis), mean [range]	3.42 [0-14]	3.21 [0-13]	3.47 [0-14]
Days (symptoms to admission), mean [range]	5.77 [0-16]	6.43 [1-16]	5.6 [0-14]
	6.014 [2-23]	10.87 [4-23]	4.69 [2-13]
Admission Disposition, n [%]			
Field Hospital	18 [26%]	2 [13%]	16 [29%]
Intermediate Care Ward (ICW)	42 [60%]	6 [40%]	35 [64%]
Intensive Care Unit (ICU)	10 [14%]	7 [47%]	2 [4%]
ICU at any point in Hospitalization	15 [21%]	11 [73%]	4 [7%]
Days in ICU, mean [range]	7.7 [0.5-22]	9.73 [6-22]	2.125 [0.5-4]
Discharge Disposition			
Base Isolation/Outpatient	37 [53%]	4 [27%]	32 [58%]
Deceased	1 [1%]	1 [7%]	0 [0%]
Evacuation from MTF *(see below for destinations)*	33 [47%]	10 [67%]	23 [42%]
LRMC (role 4)	14 [42%]	2 [20%]	12 [52%]
Local Afghan Hospital	3 [9%]	3 [30%]	0 [0%]
Base Isolation/Outpatient	1 [3%]	0 [0%]	1 [4%]
CONUS Hospital	7 [21%]	1 [10%]	6 [26%]
Other Country Hospital	8 [24%]	4 [40%]	4 [17%]
Germany	1		1
Bosnia	1		1
Dubai	1	1	
India	1	1	
Kabul (non-Afghan hospital)	1		1
Bulgaria	2	1	
Turkey	1	1	
US embassy	1		1
Type of Evacuation			
Civilian Air Ambulance	9	4	6
Ground (Local)	2	2	1
Military Air (STRATEVAC)	16	3	14
Other	1		1
Rotary w/wo ground (Local)	1		1
Length of Stay (LOS), mean [range]			
Overall Hospital LOS	6.01 [2-23]	10.87 [4-23]	4.69 [2-13]
LOS for evacuated patients	6.82 [2-23]	11.3 [4-23]	4.87 [2-13]

were executed primarily with ground ambulance and/or rotary aircraft (Table 3).

Discussion

In this case series, most of the patients were contractors rather than active duty members. The mean age was 46 years, younger compared to the mean age ranging from 55-63 years seen in other studies among patients hospitalized for COVID-19.[6–9] The majority of our patients had chronic medical conditions, consistent with other studies that have shown that those with chronic medical illness are more likely to be hospitalized;[6,9,10] however most of our patients had only one chronic condition. Furthermore, Department of Defense Instruction indicates that both active duty members and contractors who are deployed meet certain medical fitness standards. For contractors, this includes a medical assessment within 12 months of deployment and requires that any chronic medical conditions are stable. Medical conditions that usually preclude medical clearance include heart failure, recent myocardial infarction, and uncontrolled hypertension, diabetes, or asthma.[11] Our patients' overall younger age and requirement to meet medical fitness standards may have prevented more severe disease progression in our patient population. The one death that occurred in this series was a patient greater than 60 years old who had three known prior medical conditions, consistent with other reports that older patients and those with more chronic medical conditions have higher risk of severe disease.[6,9,10,12]

Data from this series also suggests that the majority of our patients were Category B patients who were initially admitted to the ICW or the COVID-19 Tent. As a deployed MTF whose primary mission is to care for traumatically injured patients, CJTH has primarily open bays geared for handling traumas rather than single-occupancy or negative pressure rooms to contain infectious respiratory diseases. The COVID-19 Tent was envisioned to accommodate a potential patient surge. However, it also served as a place to cohort inpatients with COVID-19, minimizing exposure to other patients and hospital personnel. In our case, the COVID-19 Tent opened 7 July 2020 coinciding with a time when there was a steady number of patients with COVID-19 at CJTH. After 7 July 2020, 62% of category B patients were initially admitted to the COVID-19 Tent. Overall, only 29% of the Category B patients were initially admitted to the COVID-19 Tent.

We experienced several reasons for hesitancy in initially admitting patients to the COVID-19 Tent, to include patients exceeding the weight capacity of the beds; concern that patients could not safely ambulate to the separate restroom facility approximately 25 meters over uneven ground; being prescribed refrigerated medications (refrigeration not available) or those requiring two-staff verification; the logistics of restocking medications and supplies in the COVID-19 Tent to match the ebb and flow of patient admissions; the burden for staff in the COVID-19 Tent

to continuously wear full personal protective equipment (PPE) (i.e. N95 mask, gown, gloves, faceshield) for their entire shift (6-8 hours); and finally, the COVID-19 Tent could continuously support a patient requiring only 1 to 4 liters of supplemental oxygen via nasal cannula. A patient with a tenuous disease course requiring greater than 4 liters of oxygen per minute would require transfer to the ICW or ICU to support increased oxygen demands. In our case series, we noted seven such patients who had a change in their disease status from Category B to A. In summary, the COVID-19 Tent was beneficial for a certain subpopulation of stable patients with COVID-19 and enabled cohorting patients with a similar disease, however, improvements in several areas are needed to maximize its utilization as a dependable source for providing medical care for any future similar contingency scenarios.

Many of the patients received medical treatments that were in line with clinical practice guidelines. Almost all patients received either pharmacologic venous thromboembolism (VTE) prophylaxis based on guideline recommendations for the hypercoagulable state associated with COVID-19[4,13,14] or received full-dose anticoagulation for VTE diagnosed at or near admission. We note an increase in the administration of dexamethasone among our patients after the NIH gave recommendations for its use on 25 June 2020, based on RECOVERY trial data.[5] Furthermore, 6 patients were enrolled in convalescent plasma clinical trials, 6 patients in remdesivir clinical trials, and an additional 6 patients received remdesivir through emergency use authorization (EUA). Anecdotally we experienced instances of delivery delays for convalescent plasma and remdesivir. However the austere environment did not prevent participation in cutting edge treatment protocols or delivery of guideline-based medical care.

The delivery of high flow nasal cannula (HFNC) to CJTH was also delayed. It arrived to CJTH on 17 June 2020. As shown in Figure 3, we noted a trend toward fewer ventilator days among Category A patients after the introduction of HFNC. Specifically, patients requiring mechanical ventilation spent a mean of 10.67 ventilator days before the arrival of HFNC compared to 2.83 ventilator days after its arrival. We question if our first few Category A patients may have avoided intubation if we had HFNC as these patients quickly escalated need from nasal cannula, nonrebreather, and finally to intubation and mechanical ventilation. Some studies suggest that HFNC may decrease the need for intubation and mechanical ventilation in patients with COVID-19.[15,16] In this case series, a total of ten patients (14%) utilized HFNC at some point during their hospitalization compared to a wide range of 11% to 63% in other studies.[8,9,12] It was used in two patients after extubation to mitigate risk for reintubation. Four patients were able to avoid intubation altogether. An additional four patients were intubated despite first utilizing HFNC. Interestingly however, three of these four patients in the latter group were intubated only for aeromedical evacuation purposes and not for decompensating hypoxic respiratory failure. It is possible that the benefit of HFNC to avert the need for mechanical ventilation was negated by the need for intubation for flight purposes. The limitation of this, however, is that we did not follow these patients after discharge and the total duration of mechanical ventilation need after discharge from CJTH is unknown. Furthermore, the Theater Patient Movement Requirements Center (TPMRC) allowed patients with higher oxygen needs on nasal cannula to be aeromedically evacuated without the need for intubation, which may have contributed to a lower number of ventilator days among our patients over time.

The disposition and hospital length of stay for our patients were affected by local policy indicating that all symptomatic patients hospitalized with COVID-19 be prepared for evacuation out of theater.[17] This policy changed shortly after compilation of our data, to only include only those with high risk and/or moderate to severe symptoms instead of all patients. The overall average hospital length of stay was 6 days, and it was similarly 6.8 days specifically among those who were evacuated. However, this encompassed a wide range spanning 2 to 23 days. This variability and prolonged time to evacuation was thought to be impacted by heterogeneous policies in response to the global pandemic to include closed borders by different nations and challenges obtaining diplomatic and air clearances, difficulty in finding accepting facilities, and resistance to evacuation among contractor companies due to the relative clinical stability of patients. For example, some of our critically ill Category A patients stayed with us for weeks and were ultimately discharged to Isolation without the need for supplemental oxygen, still awaiting their host country clearance for evacuation. Others were able to be aeromedically evacuated within 5 days.

A closer look at our admission and disposition data for our patients show that more than half of our patients came from other than Bagram Airfield, showing that we were able to transport patients within the theater of Afghanistan without much difficulty. Most of our patients were also non-US contractors, while

most of the aeromedical evacuations were for US nationals, both military and contractors. This suggests that it was easier for us to coordinate with US military and US contracting companies for aeromedical evacuations, with less efficiency being seen when coordination was required for the movement of other nationalities.

A limitation of this case series is that it looked at the patient population of only one MTF, and the situations and policies encountered may not be generalizable to experiences at other MTFs in the deployed setting. Furthermore, the captured data ended at the time of hospital discharge, and the data that was gathered is not fully reflective of patients' full disease course or progression.

In this paper, we highlight challenges encountered while caring for patients with COVID-19 in the deployed environment during a global pandemic. Delivery delays for medical equipment and medicines impacted our approach to respiratory management and the promptness of enrolling patients in treatment protocols. Despite these challenges, the patients treated at our facility were still able to receive care in accordance with treatment guidelines, and we were able to achieve a low COVID-19 mortality rate. The COVID-19 Tent was beneficial for a certain population of patients with stable disease, allowed cohorting of patients, supported continued care for patients as they found themselves with prolonged hospital stays, helped minimize risk of exposure to other patients and personnel in the hospital building, and supported PPE conservation. During the period of study, there were no known secondary infections among the CJTH medical staff. Improvements are needed to enhance utilization and streamline care of patients in this facility. Finally, local policy directed evacuation of symptomatic hospitalized patients with COVID-19 out of theater, but this was met with the drawback of having to intubate patients for flight purposes. Host countries closing their borders during a global pandemic, thus prolonging patients' hospital stay in theater, was at times also an insurmountable challenge. We believe that these findings will contribute to a better understanding of the unique challenges experienced in the deployed environment and will contribute to process improvements in care.

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Installation Management Command's COVID-19 Pandemic Efforts Rely on Multiple Collaborative Partnerships

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Introduction

The Installation Management Command (IMCOM) delivers quality base support from the strategic support area, enabling readiness for a globally responsive Army. IMCOM has more than 75 installations, covering more than 13 million acres, in 17 time zones, 12 countries and 58 services. In early March 2020, the COVID-19 pandemic required IMCOM to shift focus in ensuring health protection measures were implemented early and quickly, which relied on medical expertise. The IMCOM Surgeon and the Deputy Surgeon serve as the command's key advisors for all matters related to health care and medical readiness. During the COVID-19 pandemic, the IMCOM Surgeon and the Deputy Surgeon were critical in the consolidation of various information from multiple organizations. They promoted the integration of force health protection principles during COVID-19 operations. All of the military members at IMCOM headquarters (HQ) were considered mission essential while other personnel were identified on a phasing structure in the early stages of the pandemic, which meant civilian personnel were instructed to telework.

IMCOM Crisis Action Team

The IMCOM Surgeon and the Deputy Surgeon were part of the IMCOM Crisis Action Team (CAT) and were identified as mission critical. The role of the IMCOM Surgeon and Deputy Surgeon is advising senior leadership regarding information received from higher headquarters and articulating it to support the IMCOM garrisons. The surgeon team provided situational awareness on COVID-19 cases that were occurring at the global, national, state, local community and base/post levels. The surgeon team utilized different platforms to gather pertinent data. At the global level, Centers for Disease Control (CDC), Federal Emergency Management Agency (FEMA), and Defense Health Agency (DHA) Surveillance Data were utilized to identify global cases and trends. At the national and state levels, the Johns Hopkins University website was utilized to identify new cases, deaths, hospitalizations and positivity rates.[1] At local and joint base/post levels, since IMCOM HQ is in Joint Base San Antonio-Fort Sam Houston, Texas, the JBSA Crisis Action Team provided local trends and Brooke Army Medical Center (BAMC) bed and equipment capabilities and capacities. The City of San Antonio (COSA) and the KSAT local news station's COVID websites also provided civilian hospital bed and equipment capabilities and capacities.[2,3] This information was prepared and provided via the IMCOM CAT at least twice a day to ensure the IMCOM Commanding General and his command team had timely information to act on when needed and required. The information was often provided to the IMCOM garrisons, and garrison leaders were advised to utilize their local resources as well.

The IMCOM Garrisons

IMCOM's garrison commanders and their command teams serve as the tip of the spear for IMCOM. It is through their leadership in support of installation senior commander's priorities that 75 Army installations have safely sustained critical services to their populations throughout the COVID-19 pandemic. During the pandemic, the support and guidance provided by the Military Health System (MHS) has been an invaluable resource to garrison commanders and to IMCOM HQ. Working in close collaboration with military medical treatment facility (MTF) commanders and Army Public Health Center (APHC) representatives, IMCOM garrison commanders were provided pandemic response expertise and protection strategies to effectively mitigate risks to beneficiaries across the globe as part of the Garrison Pandemic Response Plan.

MEDCOM Support

The Medical Command (MEDCOM) teams in

coordination with installation Public Health Emergency Officers (PHEO) provided detailed guidance on testing requirements, isolation and quarantine recommendations, as well as tracking and tracing suspected close contact individuals. The partnership of garrison and medical teams helped ensure adequate housing and barracks facilities were identified and available for all isolated and quarantined individuals.

Telecommunication

Telecommunication has emerged as a critical resource as a result of the pandemic. Just as IMCOM garrison commanders have embraced telecommunication through virtual town halls and the Digital Garrison application, so has the MHS expanded its telecommunication capabilities through virtual provider appointments and virtual medical readiness screening.

DoD and HQDA Support in IMCOM Preparation of Pandemic Playbooks

The pandemic response guidance from both DoD (DHA) and HQDA (Office of The Surgeon General (OTSG)/MEDCOM) provided a solid framework from which garrison commanders and their MHS partners established local pandemic response playbooks. These playbooks were critical in capturing best practices and lessons learned to create a common operating picture which could be shared across installations.

OTSG & MEDCOM Direct Support

During the COVID-19 pandemic, the direct support provided by OTSG and MEDCOM was instrumental in ensuring Army installations had the requisite information and resources they required. One example is the biweekly touchpoint established between IMCOM deputy commanding general (DCG) and OTSG DCG Operations. The touchpoints provided IMCOM with opportunities to address critical issues immediately at the general officer (GO) level. The daily information updates provided by OTSG Chief G-33 Operations were an invaluable resource in coordinating IMCOM efforts with FEMA, USNORTHCOM, DHA, and HQDA priorities. The daily updates provided by APHC provided tremendous insight into emerging COVID-19 testing capabilities, treatments, vaccine development, and risk mitigation measures.

Operation Warp Speed Messaging and Way Ahead

The 8 September 2020 DHA Operation Warp Speed letter to stakeholders was a valuable update in the enterprise COVID-19 vaccine development and distribution plan. IMCOM is also tracking that 5 DoD Medical Facilities have been selected for participation in Phase 3 vaccine trials (Walter Reed, Fort Belvoir Community Hospital, Naval Medical Center San Diego, BAMC and Wilford Hall).

The IMCOM HQ, in coordination with Army Materiel Command, is eager to support MHS, Defense Logistics Agency, and Operation Warp Speed accelerated vaccine distribution efforts to ensure installation populations are afforded this vital protection as soon as it is available.

Conclusion

The COVID-19 pandemic required IMCOM to respond in a timely manner in support of all the garrisons worldwide. The collaborative partnerships with multiple entities enabled timely information gathering and sharing to protect the health of the force. This continued collaboration is essential in enabling global readiness for the Army, especially in delivering a safe and efficacious COVID-19 vaccine in the future.

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The 1993 Hantavirus Pulmonary Syndrome Outbreak and Lessons for Today

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Abstract

While grappling with the implications of the current COVID-19 pandemic, we have perhaps overlooked recent history dealing with previous outbreaks. In the spring of 1993, America was presented with an outbreak of Hantavirus Pulmonary Syndrome caused by the Sin Nombre virus. This article recounts the investigation into this disease and discusses the spectrum of issues that medical communities must face as it deals with a mysterious outbreak.

Keywords: hantavirus pulmonary syndrome, outbreak, Navajo, ARDS, cross-cultural medicine

Introduction

Before this current coronavirus pandemic, Americans had a pretty clear stereotype of viruses. In general, we knew we could catch a "flu-bug" with its accompanying fever and nausea, or we could get acquired immunodeficiency syndrome (AIDS), which we eventually learned is a disease that is not just reserved for the homosexual population. Besides that, strange viruses were just diseases for other countries—especially the developing world. This developed, as some researchers have noted, into a strong association between immigrants and disease in American society, and a propensity to blame outsiders for any infectious outbreaks.[1]

The early 1990s was a time when the United States demonstrated its technological might in the unprecedented war with Iraq. It was also a period when biotech companies emerged in an explosion on the market demonstrating a new unique handle of recombinant DNA technology. However, in the spring of 1993, America was presented with an outbreak of Hantavirus Pulmonary Syndrome, and suddenly we had to reevaluate our stereotypes. This disease, caused by the Sin Nombre virus, demonstrates the spectrum of issues that the medical community must face as it deals with a mysterious outbreak.

Outbreak

On 29 April 1993, Florena Woody, 21, began feeling muscle aches in her neck and back. She had her boyfriend, Merrill Behe, 19, massage them for her but it did not seem to help. The couple, both part of the Navajo tribe, lived with Florena's family in Littlewater, New Mexico, with their baby Maurice. Florena came down with and a cough. A few days later her symptoms worsened, and she was taken to Crownpoint Hospital (a rural clinic operated by the Indian Health Service with about ten doctors) on May 8, and saw Dr. Christine Golnick. Florena continued to deteriorate. The next morning, she was seen by Dr. Tom Hennessey (Dr. Golnick's husband) and Dr. Doug Waite. They ordered an X-ray after Florena continued to have trouble breathing. They noticed that her lung film was colored white (called a whiteout), indicating they were filling with fluid. The doctors decided to medevac her to New Mexico Medical Center in Albuquerque, NM, where there was well-equipped intensive care unit. Florena's condition worsened, however, and she went into cardiac arrest and died before the helicopter arrived (Doug Waite, MD, personal communication, April 2001).[2]

Merrill Behe became sick two days later on 11 May. He went to the hospital, but doctors sent him home with acetaminophen, erythromycin (antibiotic) and amantadine (anti-viral medication) to help with his flu-like symptoms. On 14 May 1993, the day of Florena's funeral, Merrill's condition had worsened. His father-in-law decided to have his cousin Karoline take him to the Gallup Indian Medical Center. It was farther away than Crownpoint Hospital, but they thought the doctors there may be better than the ones that failed Florena. Merrill started having trouble breathing on the trip. They pulled over at a B.J.'s Convenience Store in Thoreau, NM, where Merrill collapsed. Paramedics were unable to revive him as they drove him to Gallup Medical Center.[2]

The attending physician at Gallup, Dr. Bruce Tempest, declared Merrill dead. He first called Dr. Waite to discuss the case and its implications. By Monday, 17 May, he began calling the Department of Health, the Office of the Medical Examiner, and the Indian Health Services (IHS) epidemiologist, Dr. Jim Cheek. The

investigation into this mysterious killer had begun.

Investigation

Merrill and Florena, the two index cases, were classified as dying of acute respiratory distress syndrome (ARDS) of unknown etiology. It is interesting how these first cases were put together. Thousands of people die every year from ARDS, and these two were pronounced dead at hospitals more than 70 miles apart. This area is a rural environment and very spread out. However, a single medical provider, the Indian Health Service, services this whole area. After Florena died at Crownpoint, one of her doctors, Dr. Waite, called his friend Dr. Tempest in Gallup as he routinely does with strange cases. Dr. Tempest immediately suggested pneumonic plague since it is endemic to the area and causes ARDS. Dr. Waite, a bit embarrassed that he did not think of plague, then had samples sent off to be tested and had everyone in the clinic put on tetracycline for prophylaxis in case it was plague, which is highly infectious (Doug Waite, MD, personal communication, April 2001).

On Friday, 14 May 1993, Dr. Tempest called back Dr. Waite saying he had a similar case (Merrill Behe) with a bilateral whiteout and an elevated white blood cell count. Dr. Waite then remembered a case down in Ft. Defiance (where the Navajo Nation is located) he had heard about three weeks earlier, and Dr. Tempest recalled a case he had treated a month earlier. By the end of the day, the two doctors had retrospectively gathered about four to five cases: all young, healthy individuals suffering from ARDS with no etiology. The Hantavirus outbreak uniquely demonstrates how, based on the communication network between the IHS doctors, a subtle outbreak can be identified. If it were not for this network, these cases of ARDS, relatively spread out, would have gone unnoticed (Doug Waite, MD, personal communication, April 2001).

Disease investigations often have to operate in a cross-cultural context. As virologists travel in foreign lands, they learn customs and taboos in order not to offend individuals they are trying to obtain information from, as well as to see how certain behaviors may have contributed to the disease. In this case, the investigators had to operate in the context of Navajo Indians. Richard Malone, the State Medical Examiner, looked into Merrill Behe's death soon after he arrived at Gallup and naturally came to the conclusion that an autopsy was warranted. However, this is a difficult subject for Navajos. It is taboo for Navajos to touch dead people as it may arouse the *chindi*, the evil spirit or ghost left behind at death.[3] Even speaking of the recently dead was forbidden since it could arouse this *chindi*.[3,4] As Dr. Malone interviewed Behe's family at the hospital, he also learned of Florena's death and that they were in town for the funeral at 2:30 p.m. The time of this event is important here. Merrill Behe died at 11:53 a.m. Dr. Malone finished talking with the Behe's at 1:30, one hour before the start of the funeral. Fortunately, Malone was able to get both families to agree to autopsies before the funeral services started.[2] In the following month, Navajo President Peterson Zah was pleading with his people to cooperate with investigators. In order to facilitate the investigations, several dozen local medicine men were asked to participate in the search for the cause of illness.[5]

The IHS epidemiologist, Dr. Cheek, went to Merrill Behe's trailer home. He had suspected a chemical poison that is associated with ARDS, such as phosgene or phosphine—chemicals used to poison prairie dogs in order to control plague. Dr. Cheek's team found no evidence for chemical contaminants at Behe's home. However, they did find it overrun with rats and mice, so they took several samples of food and rodent feces to be sent to the lab. Incidentally, they did not take proper precautions this time, only later realizing the chance they took not wearing personal protective equipment.[4] As phone calls were made in the area, Dr. Cheek was initially aware of five possible cases through Drs. Tempest and Waite (Doug Waite, MD, personal communication, April 2001). This number rose to 10 a few days later, 20 May 1993. By 26 May, there were 19 cases with 12 dead, ranging in ages from 19-58. All of these cases were around the Four Corners Indian reservation area, and most of them were Navajo.[6] What particularly scared investigators, at this point, was that most of the victims were young and healthy individuals. Normally, it is the immunocompromised, the very young, and the elderly that are stricken with the flu and other diseases causing ARDS. This new disease did not seem to discriminate.[4,7]

Dr. Cheek then notified Dr. Bruce Breiman, a former colleague at the Center for Disease Control and Prevention (CDC). Several other informal calls were made. The following day, 27 May, the CDC was officially called to take part in the investigation. This formal invitation is important. In dealing with public health, local health departments are first to remedy the situation. The CDC is normally invited, maintaining professional courtesy, even though this case originated on an Indian reservation, which is technically federal jurisdiction. The next day, Ruth Berkelman, the deputy director of the National Center of Infectious Diseases (NCID), which is a subdivision of the CDC, called for a meeting. C.J. Peters, head of the Special Pathogens branch at CDC, described the meeting: "Individually…

we are a mix of medical detective, scientist, healer, and just plain human being, so it's not unexpected that there's a kind of schizophrenia operating at the these meetings."[4] He describes in general how the team must carefully and scientifically go through the process of diagnosing the mystery killer, even though they are feeling hurried that more people are getting sick and dying each day.[4]

The NCID team was not used to dealing with the type of problem that lay before them. First of all, normally, outbreaks occur in remote areas overseas, not in this country. This caused a bit of anxiety for many of the scientists. The last true deadly respiratory outbreak in America was the Legionnaires' disease outbreak of 1976 in Philadelphia. It took several months for scientists to identify that disease. At the rate this seemed to be spreading and killing people, they could end up with a major epidemic. Based upon the medical reports and autopsies they had faxed to them, they had the following information. The patients were mostly rural Native Americans who died from lack of oxygen from their lungs filling up with fluid. This was seen as the "whiteout" described on x-rays, as opposed to dark, normal lungs. Though there were a variety of experts in virology and bacteriology, the etiology of this disease baffled them all. C.J. Peters remarked, "It's a sobering feeling when you've got all these experts gathered around a table…and essentially they all shrug, throw up their hands, and say, 'not mine.'"[4]

The CDC team needed to react quickly, but resources were limited. They certainly have an unlimited budget when it comes to a national crisis; however, manpower was the limiting factor as there were several other hotspots in the world at that time. At this point, many were assuming this to be a bacterium, since the patients had significant leukocytosis (elevated white blood cell (WBC) count) with a predominance of neutrophils. This picture is seldom seen in viral infections. They ended up sending Dr. Rob Breiman, part of the bacterial division, Jay Butler, and several others, one of whom isolated the Legionella bacterium, to make up the field team in Albuquerque. By 31 May 1993, they began sending samples back.[4]

The Special Pathogens Division had several challenges when they received the samples. As with any potentially harmful unknown substance, they had to decide at what level of protection to work with the samples. There are four levels of protection known as "Biosafety Levels" one through four. Level 4 yields the most protection; however, it entails wearing special protective garments and there are only a limited number of people trained in operating in that environment. Additionally, once samples are brought in level 4, they cannot be taken out for further tests in different labs. Dr. Peters' team decided to begin work at level 3. They also had difficulty with the samples themselves. They often arrived in Styrofoam coolers and were poorly labeled. They began conducting several tests simultaneously, including antibody cross-reactivity tests with other known pathogens, as well as enzyme-linked immunosorbent assay (ELISA) tests. The first hit they got was on 3 June 1993, when they noticed some cross-reactivity with the hantaviruses. This was confirmed the next day with an ELISA. Pierre Rollin was in charge of processing these unknown samples. He immediately faxed a copy of the ELISA results to Dr. Tom Ksiazek who was working up at United States Army Medical Research Institute of Infectious Diseases (USAMRIID) located at Ft. Detrick. Alarmed by the results, Dr. Ksiazek hurried back down to the CDC in Atlanta. These results were not definitive, however, as they needed to do genetic testing. Dr. Stuart Nichols was the genetic sequencing expert at the CDC. He explains how he conducted the reverse transcriptase-polymerase chain reaction (RT-PCR):

> Based on the serologic evidence of the presence of antibodies in the patient sera that were cross-reactive with known hantaviruses, we designed several sets of nested primers using the sequences available at the time in GenBank. The set designed based on Puumala and Prospect Hill [hantavirus strains] viruses worked. Once we had a specific sequence for Sin Nombre we modified the primers to give a better match with Sin Nombre and hence better sensitivity to the RT-PCR assay (Stuart Nichols, PhD, email communication, April 2001).

They found that it not only was a hantavirus, but it was new, not matching any other known strains. Another scientist, Dr. Sharif Zaki, made monoclonal antibodies to the hantavirus and was able to use these antibodies to identify a vast amount of hantavirus antigens in the lung tissues.[4]

The hantavirus strains that were used by Dr. Nichols were originally isolated in 1978 by a team of doctors from Korea, NIH, and the CDC. The virus causes Korean Hemorrhagic Fever, and the Chinese had seen signs of this as early as 960 A.D.[4] It was a notable virus in the Korean War when 2500 American soldiers became ill, with 121 deaths between 1951-1954.[4] These hantaviruses caused a similar leukocytosis as seen with this current virus, but were all associated with a hemorrhagic disease of the kidney. Additionally, Korean Hemorrhagic Fever only has a 5-10% mortality rate, whereas this new disease was initially killing 60-70% of its victims. Because of these reasons, the hantavirus

diagnosis was initially met with skepticism until the data had been reviewed by several different experts.[4] On 11 June 1993, the CDC released the Morbidity and Mortality Weekly Report stating that this mystery illness "is associated with a previously unrecognized hantavirus."[8] The mystery was solved.

The disease was found to be transmitted by rodents. It was also found that there was no evidence for person-to-person transmission. Incidence of the disease leveled off after the initial outbreak. In 1993, 27 died of the 48 confirmed cases. The CDC continued that year to publish guidelines in preventing the disease. The public became more aware of the importance to avoid rodents and rodent-infested areas.[6] As physicians now are better at recognizing the disease, the mortality rate has dropped. As of January 2017, there have been 728 cases with a mortality rate of 36%.[9] Within the few years following the outbreak, strains of the viruses emerged elsewhere, especially in South America.[10]

Epidemiology

Soon after the recognition of the disease on 11 June 1993, a team composed of CDC officials, Navajo, and local health officials donned protective suits and went out to all of the sites where the sickness had been reported. There they collected rodent samples to be sent back to the lab. These samples tested positive for the virus. The most prevalent were in the deer mouse, *Peromyscus maniculatus*, where 30% of the mice tested positive.[4,10]

One certainly asks, however, why this virus suddenly appeared in May of 1993. Here, the hantavirus teaches a unique lesson in epidemiology. El Niño rains, created by the warmer waters off the Pacific Coast, accounted for a large increase in the warm, wet weather of the Southwest. This, in turn, caused a bloom in vegetation, specifically in the piñon nut pine trees. The piñon nut is a primary source of food for deer mice. Female deer mice typically have about four to five offspring each pregnancy, and breed about three times a year. The purpose of producing this many deer mice pups is to ensure that some will survive the difficult arid surroundings of the area. However, from 1992-1993, there was an abundance of food available causing a rodent bloom. Several sources, including the journal *Science* and the general media at that time, state that there was a tenfold increase in the mouse population.[4] However, this seems to be an oversimplification of the evidence. The sources were quoting reports by Dr. Robert Parmenter, who is a mammologist at the Sevilleta Long Term Ecological Research Site near Albuquerque, New Mexico. He has later clarified this issue stating:

> Some sites showed small increases, but many showed very large increases. Compared to the low population sizes in 1989-1990, the 1993 densities were between 2 and 30 times higher. Compared to 1992, the differences were smaller in some areas. So while the blanket assessment of a ten-fold increase was overly broad and didn't reflect the spatial and temporal heterogeneity, the general connotation that the mouse numbers were up a lot was probably just fine (Robert Parmenter, PhD, email communication, April 2001).

The epidemiologists at the time had the real data. It was only the popular press that seemed to cling to this tenfold value. The rain-vegetation-rodent causation factors have continued to be observed as the peak season for HPS comes after the rains in the spring (Robert Parmenter, PhD, email communication, April 2001).

One can assume, then, there have been isolated cases of HPS in the past. Soon after the Morbidity and Mortality Weekly Report (MMWR) outlined the disease, the editor, Rick Goodman, was reminded of a case he dealt with as a first year resident in 1978. He was particularly troubled by the unknown death, and had kept in contact with the widow. He was able to obtain tissue samples still on file from the hospital, and have them sent to and tested at the CDC. The tests came back positive for HPS.[4] The earliest case of HPS has been confirmed in the death of a 38 year old man from Utah in 1959.[10]

The virus was finally cultured by both the CDC and USAMRIID independently in November of 1993.[11] Even today, the exact pathophysiology of the virus has not been completely worked out. Based upon current research, HPS primarily results from interruption vascular permeability in the lungs. The virus interacts with pulmonary endothelial cells through β3-integrins on the cell wall. This results in loss of capillary integrity and a dramatic increase in the pulmonary vascular permeability so that plasma leaks into the lungs. This pulmonary edema, therefore, is what manifests as the whiteout observed on the chest plain films of infected patients.[12-14]

Implications

The science of and the investigation into this disease is only part of the hantavirus story. There are a variety of implications in looking at the interactions of the media, society, and traditional Navajo culture. The first news of the hantavirus outbreak came on 27 May 1993, when the *Albuquerque Journal* ran a story entitled "Mystery Flu Kills 6 in Tribal Area." The news and rumors spread quickly nationwide. And, much like the

AIDS epidemic in the 1980s being called a "gay flu" or COVID-19 called the "Chinese virus," this disease became known as the "Navajo Flu." On 1 June 1993, 27 Navajo third-graders from Chinle, Arizona, were going to visit their pen pals at a private school in Los Angeles, but officials canceled it fearing the spread of the disease.[15] Even other Native Americans, particularly the Ute tribe, were quick to point out they did not have this "Navajo Disease" when one of their members was incorrectly diagnosed with HPS.[6] In general, the media made it difficult for the epidemiologists to conduct their investigation. The press continued to try to interview bereaved Navajos about their lost loved ones despite knowledge of their taboos. They would ask about their sexual habits and try to find any information from their confidential medical records. Some were even run off reservations at gunpoint because of their persistence. Epidemiologists, then, had a very difficult job working amidst these circumstances.[4]

Though some of the traditional Navajo beliefs made it difficult for the epidemiologists, their medical traditions are in line with the prevention of the disease. It is forbidden for Navajo to have contact with mice because they are "bearers of illness from ancient times," and if they even touch clothing, those "garments must be burned."[16] The CDC states that the best way to combat HPS is by prevention. Specifically, the CDC admonishes people to avoid all contact with rodents in these areas. The Navajo's oral tradition also claims that there have been similar outbreaks in 1918 [perhaps related to the Spanish Flu] and 1933-1934. Some elders even predicted the 1993 outbreak based upon the similar weather patterns, crops, and number of mice. Certainly one can say that the taboos of avoiding contact with mice is based upon bubonic plague which is transmitted from rodents in the same way as HPS; however, their oral medical tradition predates the onset of bubonic plague in the area.[10]

The Navajo certainly felt the prejudices of the time as they kept hearing about the "Navajo flu." There was an immediate distrust of the press and many were run off reservation as they tried to conduct interviews. By mid-June, signs in Littlewater read "No Media Allowed. No Newspaper, TV, Radio, Etc. This Means You."[17] Some New Mexico State University students conducted a "March of Justice" in Window Rock, Arizona, to protest the widespread discrimination. One student, Regina Clauschee-Shebala was quoted as saying, "In restaurants, people don't want to touch our plates when we are through eating…people read about rodent droppings and think we are dirty."[17] This was echoed by Navajo Nation President Peterson Zah who spoke to officials in Washington, D.C. about the media bias and how "Navajos have been made to feel like plague-bearers and lepers whose touch is to be feared by the healthy."[18]

The Navajo sentiment at the time made it difficult for C.J. Peters to name this strain of the hantavirus. He was initially going to name it the Four Corners virus; however, Navajo officials were totally opposed to this. He then submitted the name Muerto Canyon virus. Muerto Canyon, or Canyon of Death, is nearby to the outbreak. This angered Navajos who wanted the site to be a memorial for an Indian massacre. National Park Service officials were also opposed to it since they did not want the tourist industry affected. Dr. Peters and others ultimately named the virus Sin Nombre, Spanish for the "No Name" virus.[4]

The hantavirus outbreak also caused old anti-government feelings to manifest themselves in the Navajo. These feelings could be first traced back to the 18th Century, when small pox was spread among Native Americans, to later in the 20th Century as over 400 Navajos died from radiation-related diseases working in uranium mines. Even during the time of the outbreak, there was ongoing litigation to receive compensation from the uranium-associated deaths."[19] US Department of Health and Human Services Secretary, Donna Shalala, officially urged that the investigators respect all Navajo beliefs in order to be sensitive to these issues.[6]

The outbreak has also been fuel for anti-government conspiracy theorists. There have been rumors of the government spreading plague in the area through prairie dogs. Additionally, this desert area is a prime area for weapons testing, so there was some speculation that HPS could be due to the US biological warfare program, a theory even touted by *Scientific American*.[20] Many of these theories, along with the speculation of the government causing the AIDS epidemic, floated around on the internet during that time. These theories and questions slowly subsided as additional research emerged and the disease incidence waned. However, this certainly demonstrates America's propensity to latch on to conspiracy, whether due to a general governmental distrust or desire for sensationalism. The COVID-19 pandemic is no exception, with theories focused on scapegoating foreigners (the virus manufactured by a Chinese lab), political rivals (Bill Gates), infrastructure (5G internet service towers), and maligned causes (vaccination).[21]

Conclusion

The 1993 Hantavirus Pulmonary Syndrome outbreak in the Four Corners area has many lessons to offer 21st Century America. The Sin Nombre virus is first

a lesson in the amazing teamwork of a variety of individuals working together to combat a mysterious disease. From the first IHS physicians, Dr. Waite and Dr. Tempest discussing the case on the phone, to the coordination of the IHS, CDC, USARMRIID, and the New Mexico health officials, and local Navajo leaders and medicine men, it took the combined effort of many to control this outbreak.

When a strange virus surfaces, many will react by placing blame, finding scapegoats, and sensationalizing, which is likely an indicator of a variety of latent prejudices that seem only to manifest when facing a threat we cannot control.[22] This behavior serves to distract and slow the important work of investigators and health officials as they both try to identify and contain infectious diseases, which was noted in a recent study by the Annenberg Public Policy Center on coronavirus conspiracy theories.[23] Viruses are incredibly resilient and adaptive entities that know no borders. Perhaps comfortable lifestyles serve to distract us from the fact that there are chaotic forces out there in the world that we cannot control. Distractions can lead to complacency, so that when a true contagious virus appeared, the lessons from the Sin Nombre virus were forgotten or ignored.

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Treating COVID-19 Acute Severe Hypoxemic Respiratory Failure: First Case Report Utilizing Dexamethasone, Remdesivir, and Convalescent Plasma in Operation Inherent Resolve

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Abstract

Coronavirus 2019 (COVID-19) has spread across the globe with a concerningly high infectivity resulting in the World Health Organization deeming it a pandemic. It has resulted in thousands of deaths and placed enormous strain on communities, healthcare systems and healthcare workers as they battle shortages of ventilators, supplies, and difficulties in protecting patients and hospital staff alike. Challenges in managing the disease have led to new treatment and management strategies as healthcare teams struggle to adapt. We present the first case of COVID-19 managed in the austere deployed environment of Operation Inherent Resolve in which the patient was treated with dexamethasone, remdesivir, COVID-19 convalescent plasma, positive pressure ventilation, and proning. We discuss some of the inherent and unique challenges of caring for a patient in this resource constrained environment with a brief review of the literature on the treatment and management.

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2019 (SARS-CoV-2 2019) debuted in Wuhan, China, and has since spread across the globe resulting in thousands of deaths.[1] The World Health Organization dubbed it Coronavirus Disease 2019 (COVID-2019) and declared it a pandemic due to its infectivity and contagion rate. COVID-19 deaths are primarily due to pulmonary complications such as acute respiratory distress syndrome (ARDS) which leads to multiorgan failure in high risk individuals, particularly in the elderly and those with comorbidities.[1] As the disease has spread, governments and medical systems across the world have been forced to adapt to the growing numbers of patients seriously affected by the virus resulting in government lockdowns and intensive care units reeling to expand their capabilities. Cities, including New York City, faced critical shortages of ventilators necessary to care for these patients. In other parts of the United States, military medical units were deployed to assist cities most seriously affected.

New strategies to deal with the increasing number of patients requiring respiratory support such as using a single ventilator to support two intubated patients emerged.[2] Initial efforts to avoid non-invasive ventilation, in favor of intubation, due to fears it would spread viral particles were walked back.[3] Hospitals have had to tackle issues dealing with protecting their healthcare workers including providing supplies of personal protective equipment (PPE) and development of safe protocols while healthcare workers have dealt with the psychological impact of caring for patients during this pandemic.[4,5]

Meanwhile, there have been extensive efforts to find medications and therapies that improve outcomes. Hydroxychloroquine and chloroquine were considered a promising option at first,[6] but ultimately failed to consistently demonstrate benefit and may in fact cause harm.[7,8] Remdesivir has emerged as a potentially viable treatment option and is a nucleoside analog prodrug that inhibits viral RNA-dependent RNA polymerase leading to inhibition of viral replication.[9] It has been shown to significantly reduce time-to-recovery compared to placebo (10 vs 15 days, $p<0.001$) and increased survival compared to placebo (mortality at 15 days 6.7% vs 11.9%).[10] Importantly it also decreased the need for the

use of resources such as oxygen. Another study, however, failed to demonstrate mortality benefit in critically ill COVID-19 patients.[11] The International Task Force on the management of COVID-19 found that 86% of their members suggested the use of remdesivir in patients with COVID-19 requiring supplemental oxygen, and 77% suggested the use of remdesivir in patients requiring mechanical ventilation.[12]

Dexamethasone has also shown promise and is hypothesized to dampen the hyperactive immune response believed to be contributing to the cytokine storm, ARDS, and multiorgan failure in COVID-19 patients.[13] The CoDEX trial found significant reduction in the mean ventilator-free days in moderate-to-severe COVID-19 patients in the dexamethasone group compared to the standard care group (6.6 days vs 4.0 days, p=0.04).[14] The RECOVERY trial found significantly lower 28-day mortality in the dexamethasone group compared to the standard of care group (22.9% vs 25.7%, p<0.001).[15] The International Task Force also found that 84% of the members suggested use of dexamethasone in patients requiring supplemental oxygen, and 96% suggested use in patients requiring mechanical ventilation.[12]

COVID-19 convalescent plasma (CCP) has also been investigated for its abilities to offer passive immunity. CCP includes polyclonal antibodies directed against the SARS-CoV-2 virus. In a meta-analysis by Sarkar et al. CCP was found to reduce mortality, increase viral clearance, and improve the COVID-19 clinical condition.[16] An open-label multicenter cohort study across 2807 acute care centers in the United States with over 35,322 severe or life-threatening COVID-19 patients found that CCP had significant reduction in 7 day mortality rates when given within 3 days of diagnosis compared to 4 days or greater after diagnosis (8.7% vs 11.9%, p<0.001), suggesting that earlier initiation may provide more benefit.[17] In another underpowered study, a statistically significant mortality benefit was not achieved, but trends toward mortality benefit were seen with CCP.[18] The PLACID Trial involving 464 patients failed to show a benefit in either mortality or progression to severe disease.[19] A cochrane review of 20 studies concluded there is uncertainty in regards to the safety and efficacy of CCP.[20] The International Task Force makes no recommendations regarding CCP. The authors are not aware of any studies focusing on treatment of COVID-19 patients with a strict combination of dexamethasone, remdesivir, and CCP.

The military has faced particularly unique challenges as they have been forced to deal with a worldwide pandemic while in deployed environments. Issues faced include limited medical supplies and oxygen, limited capacity, competing missions, the potential impact of COVID-19 on the primary mission, unforgiving temperatures, threat of indirect and direct fire, issues with resupply, limitations in personnel, travel restrictions, challenges with quarantine, difficult decisions regarding patient transfer to higher levels of care, and return to duty. Finding treatment options that improve outcomes and reduce the logistic burdens of COVID-19 is paramount. The authors summarize their experiences and share the nuances of treating moderate-to-severe COVID-19 patients in an austere deployed setting as well as discuss the first known case of treatment with combination dexamethasone, remdesivir, and CCP for acute hypoxemic respiratory failure secondary to COVID-19 in Operation Inherent Resolve.

Case Presentation

A 22-year old male enlisted service member presented to an US Army Role II facility with a two-day history of nausea, vomiting, anorexia, cough, body aches, and a headache. His unit was notably experiencing a COVID-19 outbreak. The patient's exam was remarkable for a temperature of 103.3 °F, a heart rate of 120 beats per minute, and the patient was in no respiratory distress. He was diagnosed with COVID-19 by polymerase chain reaction (PCR) and placed in isolation. He continued to exhibit fevers over the following five days and began experiencing respiratory decline on day two of isolation. Given resource constraints involving portable ventilators, limited supply of oxygen, and absence of an adequate dedicated nursing staff, the decision was made to evacuate the patient to a higher level of care.

The patient arrived at the US Army Role III facility on hospital day seven and was isolated in the COVID-19 intensive care unit (CICU) tent. Upon arrival he complained of dyspnea with exertion, had a temperature of 101.0 °F, and an oxygen saturation of 85% on room air. Physical exam was remarkable for a bedside ultrasound showing diffuse B-line profile and dense consolidation of the lower left lobe with dynamic air bronchograms. Full laboratory workup showed neutrophilic leukocytosis with lymphopenia, elevated c-reactive protein, a positive d-dimer, and an acute hypercapnia on a bedside venous blood gas. Upon arrival, the patient was started on non-invasive ventilation using pressure support mode to simulate continuous positive airway pressure (CPAP) via portable ventilator along with aggressive self-proning. On that same day, he was also started on dexamethasone 6 mg intravenous (IV) daily, convalescent plasma (one unit per day for two days), and remedesivir 200mg IV upon arrival and 100mg IV daily for the next four days.

The patient had significant improvement in acute severe hypoxemic respiratory failure over the proceeding days and avoided endotracheal intubation. The patient was taken off non-invasive ventilation on hospital day eight. He was discharged on hospital day 10 and returned to his military unit after completing his remaining time in isolation with appropriate precautions until fully cleared by a cardiorespiratory standpoint for full duty.

Discussion

Finding treatment options that can hasten or improve recovery from COVID-19 for patients in the deployed environment offers intangible value as the unique challenges of treating COVID-19 are not simply limited to treatment of patients in deployable rapid assembly shelter (DRASH) tents while taking indirect fire. The climate in Iraq is unforgiving with daily temperatures in the summer averaging into the 110s °F. Isolation tents with fully functional air-conditioned units will still average 90 °F leading to increased physical strain on medical staff in full PPE. Additionally, indirect fire occurring on a consistent basis required patients to wear kevlar blankets and medical staff to add 30 pounds of body armor. Lack of adequate quarantine facilities led to repurposing one field tent to serve as the main CICU (Figure 1).

Asymptomatic and minimally symptomatic COVID-19 patients also required isolation housing units with separate latrines and showers. This taxed an already overburdened staff who were required to provide all life support materials (e.g. food), maintain accountability, and provide twice daily vital sign checks. Medical resupply quickly became the vital link in treating patients as deployed hospitals are designed to treat traumatic wartime injuries and expeditiously evacuate patients out of theater for definitive treatment. Field hospitals were not designed to maintain and treat medically critical patients for extended periods of time. The inability to evacuate out of theater due to COVID-19 related travel restrictions quickly made the ability to regenerate oxygen the foremost resupply requirement. This was followed by the need to rapidly resupply depleted sedation medications and investigative treatments such as remdesivir and CCP, which demonstrated promise in reducing oxygen requirements, hastening recovery and improving outcomes.[9,10,16,17,21] These investigative treatment therapies were unavailable at lower echelons of care for critical patients which led to increased intra-theater medical evacuations to the Role III hospital. After transporting COVID-19 patients, however, US Army Air Medical Evacuation Black Hawk DUSTOFF units had mandatory stand down periods of 16 hours to clean aircraft and equipment before being mission ready. Additionally, there were instances of non-available medical staff due to becoming COVID-19 positive themselves.

The unpredictability of the supply chain to provide a steady stream of medications and medical class VIII is a constant factor affecting all aspects of clinical decision making. The limitation of a continuous oxygen supply and generation has a direct impact on management of ARDS. Oxygen generation through the portable oxygen generation system (POGS) (Figure 2) and expeditionary deployable oxygen concentration system (EDOCS) is significantly affected by the environment to include severe temperatures that often exceed 120 °F in countries like Iraq.

Figure 1. US Army Role III COVID-19 intensive care unit (CICU).

There is no capability for high flow nasal cannula and the only option for positive air pressure is through the portable ventilator, which has no preset non-invasive mode. The authors have had success using a full face mask and the ventilator's pressure support mode with a set positive end expiratory pressure (PEEP) without additional pressure support to simulate Continuous Positive Airway Pressure (CPAP) setting which has provided adequate mean airway pressure. This has led to alveolar recruitment and enhanced airway clearance which ultimately prevented many endotracheal intubations. The authors' practice in mechanical ventilation in the austere environment focuses on conservation of oxygen. This is achieved by obtaining the lowest level of supplemental oxygen as well as

low tidal volume ventilation targeting tidal volumes of 6 ml/kg predicted body weight (PBW) with aggressive self and manual proning following the ARMA trials and PROSEVA trial.[22,23] A high PEEP strategy is used to increase mean airway pressure by utilizing bedside drive pressure to regulate the degree of alveolar recruitability with goal to achieve lowest FiO2 requirements to preserve oxygen.

Prolonged field care without the ability for renal replacement therapy (RRT) or on-site extracorporeal membrane oxygenation (ECMO) has led to conservative fluid management strategies often using albumin and loop diuretics to achieve a negative fluid balance.[24] Additionally initial pH-guided fluid resuscitation with a bicarbonate drip is often employed to facilitate management of hyperkalemia which can be seen with COVID-19 related microthrombi induced acute kidney injury.[25] Initial full anticoagulation with enoxaparin 1mg/kg subcutaneous twice a day is started if d-dimer is greater than 1000 ng/ml to prevent worsening microthrombi induced kidney dysfunction.[26,27] This anticoagulant is chosen due to the limited laboratory capability to routinely monitor heparin therauputic levels with aPTT.

This limited laboratory capability also precludes performance of culture and sensitives as a part of the infectious workup. Some Department of Defense (DoD) Role II and III facilities do have a system that allows for point of care PCR testing of COVID-19 and other respiratory infectious pathogens, but resupply of test cartridges continues to be a limiting factor. The inability to perform antibiotic drug peaks and troughs limits the spectrum of antimicrobials that can be safely administered and monitored which, in combination of limited laboratory capabilities mentioned earlier, has modified the author's approach to early community acquired pneumonia (CAP) antibiotic coverage in hospitalized COVID-19 patients. The authors escalate to linezolid with beta-lactam antibiotics for worsening of ARDS if it is thought to be secondary to bacterial pneumonia based on beside ultrasound showing dynamic air bronchograms and/or respiratory panel that has clinical worsened while on empiric CAP antibiotic coverage.

Dexamethasone, remdesivir, and CCP have been used to treat hypoxemic COVID-19 patients requiring supplemental oxygen. An investigational treatment protocol was used in the OIR area of operations to administer both CCP and remdesivir under the investigational new drug application. To the authors' knowledge, this is the first use of a combination of dexamethasone, remdesivir, and CCP for COVID-19 in OIR, and first published report of using this combination in isolation. The patient presented made a hasty recovery after initiation of this combination of medications. There is yet ongoing research regarding the efficacy of remdesivir and CCP with promising but conflicting mortality benefit.[10,11,20] Studies have also demonstrated quicker resolution in symptoms and reduction in use of medical resources such as oxygen with use of these medications.[10,14,21] This reduction in resource utilization alone is enormously beneficial in the deployed environment even in the absence of a mortality benefit.

Figure 2. US Army Role III portable oxygen generation system (POGS).

The Army's main wartime mission will always be to win the ground war. The medical mission to support the warfighters is therefore trauma focused and designed to stabilize and transfer to higher echelons of care. At the height of the COVID-19 pandemic, several units assigned to the Army's Defense Support to Civil Authorities (DSCA) mission were activated to serve as Urban Medical Augmentation Task Forces (UMAT) to help relieve the medical burden on civilian hospital centers. The authors' unit was augmented with a request for forces (RFF) from the rear detachment which included critical care nurses, licensed practical nurses, respiratory technicians, and other specifically requested medical support personnel. Unfortunately this unit did not arrive with their own class VIII, ventilators, life support items, or tents.

With the unforeseen and still unpredictable events of the COVID-19 pandemic there is a need to look at creating an expeditionary forward chemical, biological (to include infectious diseases), radiological, nuclear, and

explosive (CBRNE) augmentee team. Similar to the quick reactionary force of the 82nd Airborne Division, this augmentee team can have predetermined medical equipment and supplies set aside ready to be deployed within hours' notice based on the ground commander's request for support. This quick reactionary force can be specialized in CBRNE and have the ability to deploy quickly to service members that require CBRNE medical care. The make-up of this unit can include an infectious disease expert such as a physician or public health nurse; the ability to have a negative pressure (airborne isolation) tent and MEDEVAC; and a preventative medicine team who can assist in reporting, isolation, quarantine, and contact tracing.

Conclusion

The majority of data on COVID-19 comes from established civilian medical centers. We present the first patient treated in the theatre of Operation Inherent Resolve (OIR) with dexamethasone, remdesivir, and CCP, which offers promise in improving outcomes and limiting use of resources such as oxygen. We also discuss the management of COVID-19 in the austere deployed environment which imposes several unique challenges to include limited medical supplies, limited space and personnel, issues with resupply and transport of patients, harsh climates, enemy fire, and competing missions. Continued research and shared lessons learned across all armed service components will be required in order to provide evidence based recommendations to standardize personnel, equipment, supply chains, and treatments to best reduce the disease burden on current and future deployed hospital units.

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Emergency Department Adaptations to COVID-19

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Abstract

Background: The COVID-19 pandemic creates unique challenges for healthcare systems. While mass casualty protocols and plans exist for trauma-induced large-scale resource utilization events, contagious infectious disease mass casualty events do not have such rigorous procedures established. COVID-19 forces Emergency Departments (EDs) to simultaneously treat seriously ill patients and evaluate large influxes of 'worried well'—while maintaining both staff and patient safety.

Methods: The objectives of this project are to create an avenue to evaluate large surges of patients while minimizing hospital-acquired infections. After identifying areas for improvement and anticipating potential failures, we devised eight healthcare delivery innovations to address those areas and meet our objectives: (1) Parallel ED Lanes (2) Universal Respiratory Precautions (3) Respiratory Drive Through (RDT) (4) Medical Company (5) Provider Triage (6) ED Quarterback Patient Liaison (EDQB) (7) Virtual Registration (8) Virtual Ward.

Results: To date, no staff members have contracted COVID-19 within the ED footprint. Our RDT has seen 16,994 patients and the medical company 1,109. Provider triage has redirected 465 patients, while our EDQB has interacted with 532 and redirected 93 patients for same-day appointments with their Primary Care Manager (PCM).

Conclusion: The system of care establish at our Military Treatment Facility (MTF) has been effective in maximizing staff and patient safety, while providing a new patient-centered healthcare delivery apparatus.

Introduction

The COVID-19 pandemic creates challenges for healthcare systems. EDs are forced to treat seriously ill patients and evaluate large influxes of 'worried well' - all the while maintaining staff safety. In this article, we outline eight techniques employed by the Carl R. Darnall Army Medical Center's (CRDAMC) ED to address the challenges associated with COVID-19. CRDAMC is a tertiary Army Medical Center serving over 100,000 beneficiaries; the ED averages more than 70,000 visits annually.

Methods

Given the novelty of COVID-19, guidelines do not exist to direct EDs on appropriate responses. We developed an eight-pronged response plan using the 2018 influenza season as a model for anticipated patient volumes and to identify areas for improvement to be implemented prior to a large surge of COVID-19 cases at our MTF. These plans were implemented with two large goals: (1) to enhance patient and staff safety, and (2) to create innovative approaches to maintain patient-centered access to care despite new barriers erected by the unknown of COVID-19.

1. Parallel ED Lanes. Leaders began by redesigning the CRDAMC ED floorplan and workflow to establish two parallel ED lanes. Patients presenting with possible COVID-19 symptoms are directed to the Respiratory ED. Those with non-respiratory conditions are routed to the Medical/Trauma ED. The two lanes have separate registration desks, waiting rooms, triage processes, minor care areas, and fully-equipped treatment rooms. To maintain the integrity of the lanes, CRDAMC engineers reconfigured airflow within the Respiratory ED to increase negative pressure rooms from two to seven, creating a negative-pressure pod. In this way, CRDAMC limits potential patient-to-patient COVID-19 transmission. Segregating patients based on medical complaints

is frequently done in pediatric clinics. Even so, it is not frequently observed in EDs in the United States.

2. Universal Respiratory Precautions. To mitigate the risk of staff exposure to COVID-19, the ED implemented universal respiratory precautions. The personal protective equipment (PPE) requirements of the Respiratory ED include droplet and contact precautions. Staff don N95 masks, gowns, gloves, and face shields or protective eye equipment during patient interactions. Precautions are less strict in the Medical/Trauma ED. In this lane, staff treat patients as though they are asymptomatic COVID-19 carriers. Consequently, both patients and staff wear facemasks and staff wear eye protection. Staff utilize a single surgical facemask or N95 mask per shift, determined by their assigned work location, as recommended by the Centers for Disease Control.[1] These directives help maintain the supply of PPE and reduce confusion regarding the level of PPE required for patient interactions. Furthermore, the phrase "Universal Respiratory Precautions" provides an easily understandable terminology to the healthcare team. It also depoliticizes and destigmatizes the facemask-for-all approach.

3. Respiratory Drive Through (RDT). CRDAMC's beneficiaries are principally young, healthy, and medically literate. Consequently, we anticipated a large demand for COVID-19 assessment by mildly ill or asymptomatic (but concerned) beneficiaries. The four-lane RDT, established in the ED's parking garage, enables high-volume evaluation of patients within the safety of their vehicles. Examination includes a full set of vitals and a limited physical assessment akin to the pediatric assessment triangle, performed by a licensed, independently credentialed provider. Most patients require no additional care. If indicated, CRDAMC personnel collect lab specimens and provide guidance on further evaluation, quarantine, isolation, and/or return to duty. All patients are offered follow-up principally via telehealth with their PCM.

4. Medical Company. A borrowed area support medical company (ASMC) and its facilities round-out the ED's COVID-19 team. An ASMC is an Army-unique capability that provides a 40-bed medical treatment facility to brigade combat teams. ASMC's are equipped with a tent-based treatment facility capable of resuscitation and patient holding. Additional capabilities include radiography, electrocardiography, pharmacy, and laboratory. In CRDAMC's COVID-19 system of care, the medical company is co-located with the RDT, in the ED parking garage. It acts as an intermediate care facility between the RDT and the ED. RDT providers direct concerning patients to the medical company for further resuscitation and care.

5. Provider Triage. Neither the RDT nor the medical company are manned or equipped for continuous operations. Also, patients sometimes bypass both resources to access the ED directly. In both scenarios, an ED triage nurse evaluates patients with respiratory complaints and ensures their isolation from ED workflow. The triage nurses are empowered to call forward one of the providers on duty to rapidly evaluate these patients. After performing a medical screening exam (MSE), depending on the patient's symptom severity, the provider either recommends treatment in the Respiratory ED or, if open, redirects appropriate patients to the medical company or RDT. This process decreases potential COVID-19 patients that are stable and minimally symptomatic from entering the main ED, reducing patient-to-patient and patient-to-staff transmission.

6. ED Quarterback (EDQB) Patient Liaison. CRDAMC beneficiaries are enrolled in a robust insurance program with access to primary care. Even so, some patients do not know their PCM or how to access them. As a result, patients may present to the ED for concerns that are better handled by a PCM, and this problem has increased significance during a pandemic. In the tradition of continuous process improvement, CRDAMC established the EDQB. The EDQB, a registered nurse, meets with low-acuity patients to attain three goals. First, the EDQB listens to patients, seeking to understand how patients become lost in the system, why existing primary care access doesn't meet their needs, and what other barriers to care exist. Second, the EDQB educates patients on different avenues to access their PCM and other healthcare resources. Finally, if amenable to patients, the EDQB transfers them, via a warm hand-off, to same-day appointments within their primary care homes (which are equipped for COVID-19 testing and treatment), the Woman's Healthcare walk-in Clinic, and/or embedded behavioral health clinics. This practice saves patients from long ED waits, safeguards them from hospital-acquired infection, and refocuses assets to a higher level of care.

7. Virtual Registration. Partnered with the Defense Health Agency Innovation Group (DIG), CRDAMC has embarked on an initiative to allow patients to register for their ED visit prior to physical presentation. CRDAMC will achieve this objective through an on-line portal, accessible via smartphone, and strategically placed kiosks. Such workflow minimizes contact between COVID-19 patients and ED administrators. Further, it allows the EDQB to intervene prior to ED arrival – directing patients to the RDT, the medical company, or to their PCM as needed. By offloading the ED, the virtual registration process will decrease ED overall length of stay,

door-to-provider times, and door-to-disposition metrics.

8. Virtual Ward. Finally, CRDAMC is partnered with the US Army Medical Material Development Activity (USAMMDA) to create a virtual COVID-19 ward. In the immediate future, the CRDAMC ED will use USAMMDA's MEDHUB technology to discharge to home a subset of COVID-19 ED patients (and others) that require monitoring but not immediate intervention. CRDAMC will monitor such patients remotely with cardiac and pulmonary telemetry and will teleconference with them daily or as needed. This initiative alleviates PPE supply issues, maintains coordinated care of patients, ensures a manageable hospital census, and is patient-centered, allowing patients to recover at home.

Results

To date, our facility has tested almost 20,000 patients for COVID-19. Our patient and staff safety innovations—parallel ED lanes and universal respiratory precautions—have been hugely successful with zero reported ED healthcare worker cases of COVID-19, as tracked by our Army Public Health Nurse team.

Our patient centered access to care and care delivery innovations have been equally effective. The RDT has been successful on many fronts. First, because healthcare workers don a single set of PPE for each shift—with gloves and face shields sanitized between patients—the RDT decreases the amount of PPE expended. Second, the process arguably decreases the viral load entering the ED and other primary care clinics on post. Finally, the RDT efficiently provides a service to large numbers of CRDAMC beneficiaries. From 25 March through 26 July, the RDT has evaluated 16,994 patients with only 1% either requesting a more detailed evaluation or being referred to the ED by RDT providers. On its busiest day to date, the RDT evaluated over 800 patients—a number that could not have been managed within the walls of the ED.

In addition, the medical company treatment tent has evaluated 1,109 total patients. Our provider first initiative has redirected 465 patients to the RDT after completing an MSE in the ED triage. In a 6-week period from May 18 through 26 June 2020, our EDQB has engaged with 532 patients presenting to the ED. Of those, 93 (17.5%) have been redirect to same day appointments with their own PCM. Our virtual registration and virtual ward innitiatives remain in the implementation phase.

Comment

As an observational study, results must be interpreted as associations only. Nonetheless, the effects of these initiatives have been felt throughout the hospital system, molding an organizational approach to COVID-19 in which the sum of the individual components has created a successful large-scale operation. The challenges that COVID-19 continues to present to healthcare systems can be met with pioneering new approaches to the delivery of healthcare. Even with increasing individual COVID-19 cases, our system has neither witnessed a COVID-19 death nor an ED healthcare worker infection; nor have our systems been overwhelmed by a mass resource utilization. As we move forward to confront future COVID-19 waves, these eight processes and the modern ecosystem they create will become permanent facility fixtures.

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Science and Technology Solutions for Scalable SARS-CoV-2 Testing to Inform Return to Full Capacity Strategy in United States Air Force Workforce Personnel

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Abstract

SARS-CoV-2 has highlighted the requirement for a drastic change in pandemic response. While cases continue to rise, there is an urgent need to deploy sensitive and rapid testing in order to identify potential outbreaks before there is an opportunity for further community spread. Currently, reverse transcription quantitative polymerase chain reaction (RT-qPCR) is considered the gold standard for diagnosing an active infection, using a nasopharyngeal swab; however, it can take days after symptoms develop to properly identify and trace the infection. While many civilian jobs can be performed remotely, the Department of Defense (DOD) is by nature a very fluid organization which requires in-person interaction and a physical presence to maintain effectiveness. In this commentary, we examine several current and emergent technologies and their ability to identify both active and previous SARS-CoV-2 infection, possibly in those without symptoms. Further, we will explore an ongoing study at the Air Force Research Laboratory, utilizing Reverse Transcription Loop-mediated isothermal amplification (RT-LAMP), next-generation sequencing, and the presence of SARS-CoV-2 antibodies through Lateral Flow Immunoassays. The ability to identify SARS-CoV-2 through volatile organic compound biomarker identification will also be explored. By exploring and validating multiple testing strategies, and contributing to Operation Warp Speed, the DOD is postured to respond to SARS-CoV-2, and future pandemics.

Introduction

Beginning in late 2019 an emerging infectious disease spread globally altering the DOD's ability to work at full capacity for the foreseeable future. The spread of SARS-CoV-2, the virus that causes the COVID-19 disease (hereafter referred to as SARS-CoV-2), has resulted in a pandemic that affects not only how people associate and work in close proximity to each other but also how the military maintains readiness and continues to support their missions.[1] The SARS-CoV-2 pandemic has had a measurable impact on routine operations of airmen affecting their readiness and the critical research efforts supporting their mission. To mitigate or control mission impact, widespread testing to assure the safety of all personnel, particularly those operating in close quarters, is essential to effectively support the overall mission of the United States Air Force (USAF) during this unprecedented pandemic. Immediate, scalable testing solutions are needed to maintain force readiness, not only for the current pandemic, but also to prepare for future mission-impacting healthcare crises.

The most immediate response to an increased demand signal for testing was the implementation of so called gold standard methods. Currently, the gold standard assay and collection method for active SARS-CoV-2 infection is reverse transcription quantitative polymerase chain reaction (RT-qPCR), requiring the collection and processing of nasal pharyngeal (NP) swabs to obtain viral RNA. NP sampling is invasive, requires special personal protective equipment (PPE), trained expertise, specialized machinery and at least a day of processing to obtain results.[2–4] With the ever-increasing backlog of samples that need to be processed nationwide, results can take days to weeks, dependent upon reagent availability and lab testing capacity. Furthermore, the increase in testing has created shortages of consumables and reagents required to conduct both RNA extraction and RT-qPCR, creating an increased lag in obtaining

results in a timely fashion.[5] Considering infected individuals can be contagious prior to the onset of symptoms,[6,7] it is paramount to obtain results quickly so an infected person can self-quarantine and proper contact tracing can occur, limiting the spread of SARS-CoV-2.

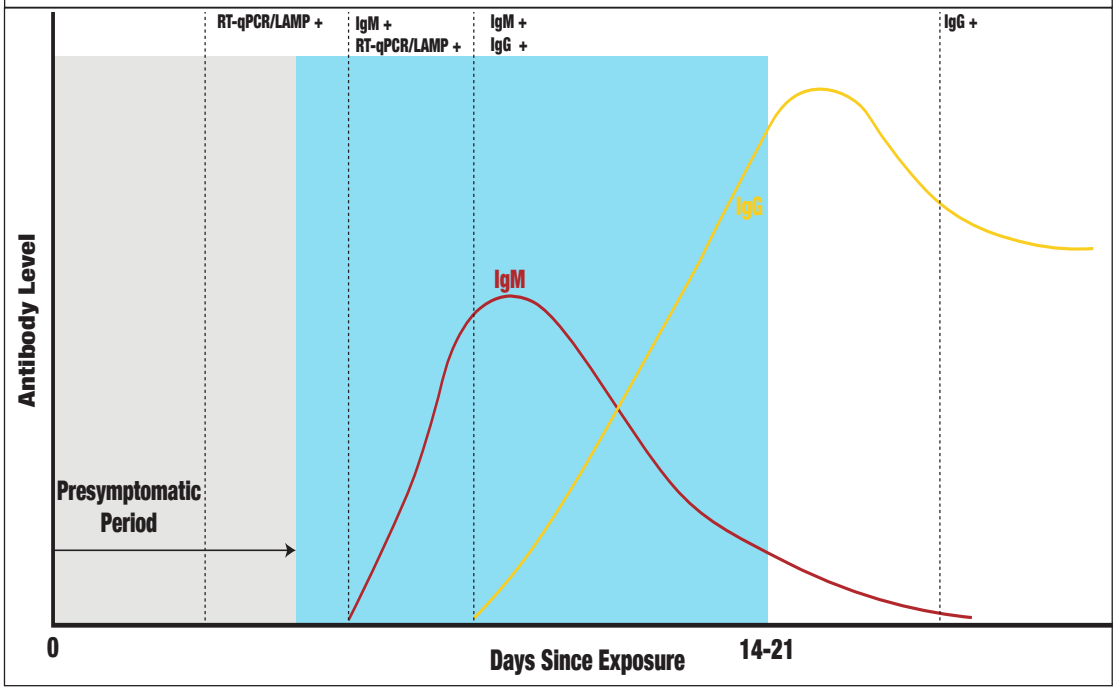
While NP swab-based RT-qPCR is the established standard, the pandemic has forced the evolution of both diagnostic and population scale testing methods. NP swab shortages limit the ability of mass testing to occur on a global scale and can be uncomfortable for the recipient. Another emergent testing matrix is saliva. Saliva is easily collected, and provides similar results to NP swabs despite potential differences in sensitivity.[8,9] Saliva sensitivity (the ability to correctly identify those with SARS-CoV-2) is potentially lower than NP swabs with significantly lower mean cycle threshold values,[9] but other evidence suggests it is more sensitive;[10] overall saliva testing is comparable to NP swabs without requiring trained technicians with substantial PPE to conduct the sampling. Saliva sampling is still largely beholden to limitations in reagents required for RNA extraction although recent protocols also show the ability to perform RT-qPCR directly on saliva treated with heat and proteinase-K using the so-called "SalivaDirect" method.[11] Such direct testing could also reduce the risk of false positive or negative results due to mishandling by limiting the number of steps in which a technician must interact with a potentially infectious sample.

Additional molecular testing methods also exist that perform with sufficient sensitivity thereby alleviating some of the supply chain issues associated with the more traditional RT-qPCR method; one such method is RT-LAMP.[12,13] RT-LAMP requires very little in the way of laboratory equipment, and has the potential to be run in austere environments. The test sample is simply added to the reaction mixture, incubated at 65 C, and with the appropriate indicator dyes, a colorimetric result is read after 20-35 minutes.[14] The method has been used previously to identify and type influenza strains, and has the potential to be effective in tracking SARS-CoV-2 outbreaks with limited equipment and within a short period of time.[15]

Beyond molecular methods for the detection of active infection, chemical detection (or biomarker analysis) may be desirable as a rapid, deployable method to identify and assess potentially infectious individuals. Breath-based sensing is one such chemical detection method and is currently commercialized and adopted as a standard-of-care for diagnosis in the clinical setting.[16] One example is the use of hand-held devices to monitor Nitric Oxide (NO) levels in asthmatic patients as a Food & Drug Administration (FDA)-approved diagnostic tool. In a 2001 study by Özkan, asthmatic patients demonstrated elevated NO levels in their exhaled breath, suggesting a correlation between NO level and airway inflammation.[17] These data drove optimization and implementation of NO sensors into a laboratory-grade NO monitoring device, which was later improved to a smaller hand-held footprint. Another example is the urea breath test (UBT) that detects the presence of Helicobacter pylori.[18–20] The bacteria utilizes the enzyme urease to neutralize the stomach acid by hydrolyzing urea into CO2 and ammonia.[18,19] From this, a breath test was designed to detect the bacteria by quantitating its metabolic byproducts. Gastric patients ingest urea that is labeled with the carbon isotope C-13 and breath samples are collected in a bag. Isotope ratio mass spectrometry (IRMS) and gas chromatography-mass spectrometry (GC-MS) are used to measure the relative level of the CO2 via the C-13 isotope.[18–20] Patients with the bacterial infection would have relatively high levels of the CO2 containing the C-13 isotope compared to healthy controls.[18] While breath biomarkers for medical conditions have demonstrated transition into validated sensing platforms, breath-based identification of active SARS-CoV-2 is a less-mature, emergent application of growing interest within the DOD.

While the above methods detect active SARS-CoV-2 infection, it is highly desirable to know the prevalence of those previously infected, or exposed to infection but otherwise asymptomatic, in returning the workforce to full capacity. One method to identify individuals within a population whom have been exposed to SARS-CoV-2 previously is through seroprevalence surveys. The analysis of serum can identify individuals with specific antibodies to the virus. Antibody testing indicates exposure to a disease, but results cannot differentiate current from past infections. Levels of IgM and IgG antibodies, which are not present in the first few days of infection, remain detectably elevated for weeks after exposure. Figure 1 details the progression of COVID-19 illustrating that during the initial and mid presymptomatic period molecular methods such as RT-qPCR and RT-LAMP can detect active SARS-CoV-2. As infection progresses IgM and IgG levels rise, and molecular methods also continue to be useful in detection. As infection subsides IgG levels lower, and IgG peaks. At this point serologic methods are effective while molecular methods can no longer detect infection, as the active disease has been eliminated. The knowledge gained on the level of exposure can be used to formulate responses to current and future pandemics. One such survey was carried out within the US in Los Angeles County earlier in the pandemic, and estimated an infection prevalence of 4.34 %.[21] The study was limited in size, with only 35 individuals

Figure 1. Hypothetical progression of COVID-19 and when certain antibodies are detectable.

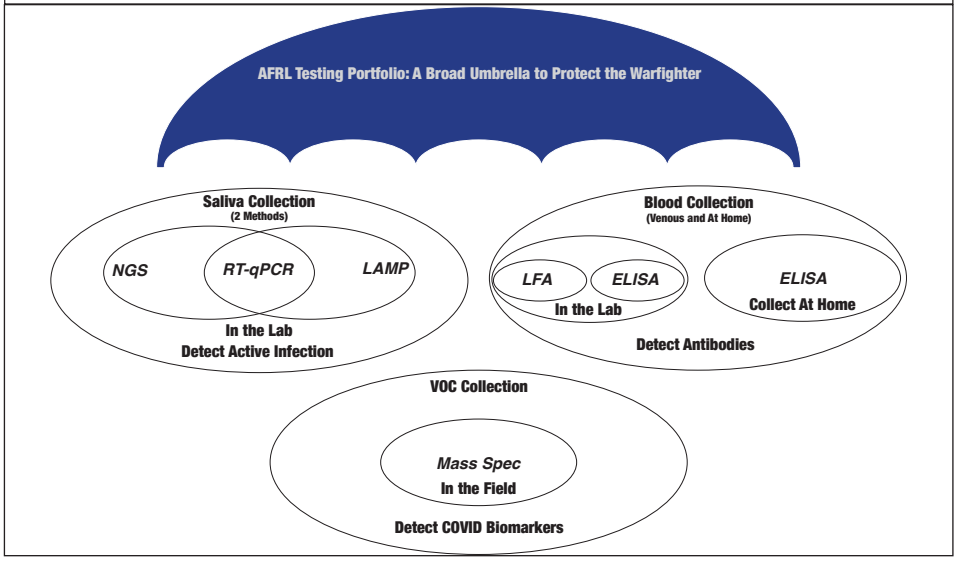


testing positive. A larger, more comprehensive study was carried out in Spain (n = 61,075) and estimated infection prevalence at 5.0 %.[22] The National Institutes of Health is currently enrolling participants in a large (n = 15,000, NCT04334954) seroprevalence study to better understand population scale infection dynamics in the US similar to the Spanish study. In either case, the studies provide critical information allowing for population-scale estimates of prior exposure, which are critical for decision makers in determining when a workforce should begin to return. The serological assays employed in these surveys are often run within a laboratory, with large (mL scale) volume blood collections used for the current gold standard in serology, enzyme-linked immunosorbent assays (ELISA). ELISA sensitivity in Emergency Use Authorization (EUA) assays varies between 92.5 and 100 %, and specificity (the ability to correctly identify those that were not infected with SARS-CoV-2) between 96.4 and 100 % .[23] One advantage of serology testing is the ability to identify asymptomatic exposure to SARS-CoV2 since detection of antibodies provides a report both clinically confirmed and asymptomatic members within a population through detection of anti-SARS-CoV2 antibodies (indicating an active immune response) despite lack of known exposure or confirmed clinical illness. Simpler still are lateral flow assays (LFAs), with pregnancy test-style read out/easy to interpret results that uses blood, serum or plasma with results reported in as little as 15 minutes, which can be mass produced cheaply, and used at home. These tests are much less sensitive, correlating to the incubation time of SARS-CoV-2 within human subjects. A recent study showed diagnostic sensitivity of 50 % in samples tested during the early onset of SARS-CoV-2 infection, but the sensitivity increased to 100 % 21 days after infection.[24]

For the military and associated workforce to return to full capacity safely at Wright Patterson Air Force Base (WPAFB) or any other air force installation, testing results must be obtained quickly and accurately to ensure a healthy workforce. Current clinical testing standards which rely on RT-qPCR are insufficient for the number of tests and speed required to achieve the transition to active monitoring.[25] Furthermore, the susceptibility of the region and local workforce is important to consider to understand the impact if a SARS-CoV-2 outbreak occurs. WPAFB aims to return to full capacity through the use of a multi-phased approach which will bring on mission essential personnel before slowly bringing on other workers to complete work on base if it can be done safely (i.e. following state and local guidelines on social distancing and mask usage). In the midst of returning to work, the pandemic continues, and there is a need to determine the extent of healthy personnel who have had previous SARS-CoV-2 infections, those who are still susceptible, and those who may have a current infection.

In light of these challenges to return to full capacity, maintain mission readiness, and protect the health of the force, WPAFB has implemented a multifaceted strategy to evaluate serological testing approaches to inform whether large scale usage is appropriate to indicate the susceptibility of the returning workforce of contracting SARS-CoV-2 infection. Methods to detect

Figure 2. An overview of sample methods employed by Air Force Research Laboratory (AFRL) in the response to the current COVID-19 pandemic.



the presence of SARS-CoV-2 in the workforce will need to transition from a "test only when symptoms are present" model to an "actively monitor the force" approach, in which serology testing will be essential. Concurrently, WPAFB is also evaluating developing approaches to test for active SARS-CoV-2 infection quickly without affecting the supply chain. Novel active infection detection methods, such as exhaled breath analytics of volatile organic compounds (VOC), may evolve as useful alternatives that are less dependent upon the existing testing supply chain. Figure 2 provides an overview of the saliva, blood and VOC studies. The purpose of this study is to evaluate evidence-based solutions for advanced, widespread, rapidly available testing in a large workforce population to inform return to full capacity decisions in the face of the SARS-CoV-2 pandemic. These methods complement essential diagnostic testing performed by clinical and public health laboratories and fulfill a World Health Organization (WHO) identified need for rapid diagnostics for infectious diseases.[26] Below we describe the methods in detail under investigation or active use at WPAFB as a model for potential use across the DoD.

Methodology & the AFRL Testing Approach

Prior to the widespread deployment of any survey or testing method, a test-cohort should be used to validate the new methodology. The following represents both a review of the methodology currently under validation at WPAFB, and serves as an example of what a validation study may look like for other service labs. While this can delay roll-out during a pandemic, ensuring that new methods are valid, sensitive, and precise is critical in retaining the trust of the workforce; 711 HPW investigators are enrolling and consenting participants by phone to validate and test both molecular and serological testing methods (Air Force Research Laboratory protocol number 20200119H). This consists of an Investigator going through each section of the Informed Consent Document (ICD) and reading that section. Individuals are then given ample time to ask questions in private. After phone consent is provided, an Investigator providing the interview records the informed consent in an electronic data workflow platform. A copy of the consent is emailed to the participant. Immediately upon enrollment, participants receive a unique identifier code, such that all participant samples and data is de-identified at the time of sample collection and for the remainder of the study. This unique identifier code is associated with all of the samples collected, processed, and analyzed for the participant throughout the study.

At the time of writing, for the molecular and serological study, WPAFB researchers have recruited a total of 333 healthy participants with no known prior SARS-CoV-2 infection from the military, civilian, and contractor workforce population at WPAFB. Participants are offered the chance to either take part in a serosurvey to detect prior infection via the presence of antibodies, a molecular survey to identify active infection and test new SARS-CoV-2 infection assays, or both. No medical intervention is being tested to prevent or treat SARS-CoV-2 infection in this study. Participants report to the sample collection site to provide saliva for the molecular survey and/or whole blood (venous blood draw) samples for the serosurvey, while a subset of participants provide blood samples using an at-home collection kit, detailed below. Upon arrival at the sample collection site, participants provide their unique identifier to the sample collection site personnel and a barcode is generated to aide in sample tracking. The protocol was approved by the Human Research Protection Program at the Air Force Research Laboratory and the 711th Human Performance Wing, protocol number 20200119H, and written informed consent was attained from all participants before any tests were administered.

Molecular Methods for the Detection of Active SARS-CoV-2 Infection

Saliva Collection

While NP swabs are considered the current gold standard in sample collection, the decision was made to focus solely on the use of saliva in molecular testing development as it represents the most likely method of easy, widespread sample collection for the workforce. The saliva collection devices employed in this study utilize preservatives in sample collection tubes that immediately inactivate and preserve viral RNA upon contact, reducing the need for PPE and ensuring low risk to research personnel. If the participant has enrolled in the molecular portion of the study, following verbal instruction from site personnel (in addition to available sample collection instruction sheet and video) on how to perform saliva sample collection the individual self-collects saliva in two sample preservation tubes, one for internal use and testing and another for use by an industry partner. Saliva sampling can be sensitive to changes in the oral environment thus participants abstained from drinking, eating, chewing gum, and tobacco use for 30 minutes prior to saliva sampling. While the saliva sampling method was produced for use at home or with limited supervision, for the purposes of this validation study the decision was made to limit collection to in-person only under the supervision of trained investigators to ensure sampling compliance.

Saliva Sample Ingestion & RNA Extraction

No widescale testing effort can be performed by hand, simply due to the sheer number of samples required. The validation team at WPAFB expanded its throughput and is achieving greater experimental accuracy by acquiring multiple automation liquid handling machines. Each instrument serves a purpose in fully automating the validation effort. For example, one reformats saliva samples into a 96 well layout and retains sample information through the use of a barcode reader. Another automates viral RNA extraction from saliva samples using a common paramagnetic bead kit. Others prepare the numerous multi-well plates needed for RNA extraction, RT-qPCR, ELISA, and RT lamp protocols under investigation. Two additional instruments then accurately transfer extracted samples from several 96 well plates and reformat them into higher-throughput 384 well RT-qPCR or RT-LAMP reaction plates.

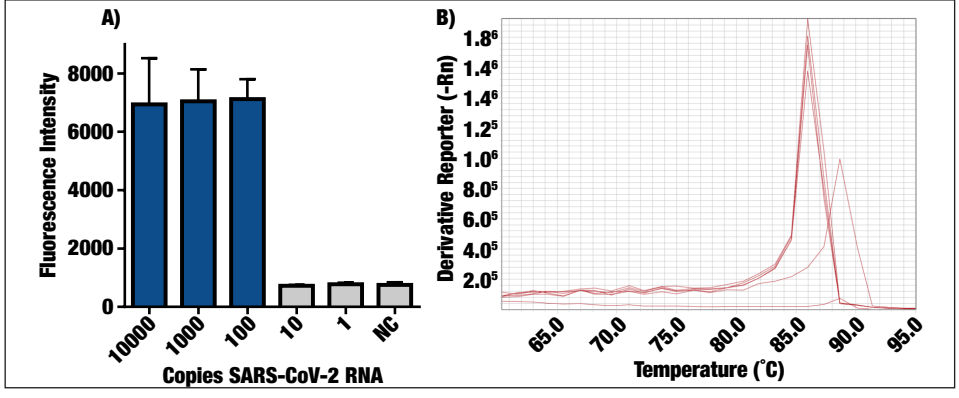
RT-QPCR

As discussed above, RT-qPCR is the current gold standard for the identification of active SARS-CoV-2 infection. In line with clinical lab use, we are employing the TaqPath RT-PCR COVID-19 Kit following the manufacturer's protocol and directions in the EUA of this product. In brief, the kit detects three SARS-CoV-2 genes (ORF1ab, N gene, S gene) in a multiplexed RT-PCR reaction. As a positive control, synthetic standards are used to eliminate the need to maintain an active viral culture of SARS-CoV-2. These standards also can be mass produced and disseminated to the numerous labs currently testing for SARS-CoV-2. The reactions are run in 384 well format to increase sample processivity. Results are then analyzed, in which positive or negative calls are made if two or more SARS-CoV-2 gene targets are detected. Of importance for any research lab validating testing methods is the protocol for reporting positive results. Should a positive result be found, in accordance with the approved internal review board (IRB) protocol, subjects will be alerted by the IRB assigned medical monitor and referred to their healthcare provider for additional guidance.

RT-LAMP

RT-LAMP is performed using WarmStart Colorimetric LAMP 2X Master Mix and GeneN-B primers4 with the additions of dUTPs/UDG to reduce carryover contamination between runs and SYTO-9 double-stranded DNA binding dye to detect product amplification by fluorescence. While the assay itself is colorimetric, a Synergy Neo2 plate reader is used to detect SYTO-9 fluorescence and provide a double confirmation of positive amplification (i.e., both a positive fluorescence and

Figure 3. An example of RT-LAMP assay sensitivity against control samples of synthetic SARS-CoV-19 RNA demonstrating (A) positive reaction and (B) specificity.



color change indicate that an amplified product was created). With the addition of SYTO-9, a positive reaction is documented when fluorescence values reach twice the intensity of negative control samples. The assay is able to distinguish as little as 100 copies of SARS-CoV-19 (Figure 3A). As a final check, and to ensure the LAMP reaction was specific to the expected SARS-CoV-19 target, the reaction products are subjected to melt curve analysis (Figure 3B), enabling identification of nonspecific amplification (Figure 3B, right most curve) and proper amplification of target (Figure 3B, left curves).

Next-Generation Sequencing

While RT-qPCR has been the method of choice for COVID testing to date,[27] it does not have sufficient capacity for the requirements of force level screening. Using next generation sequencing (NGS), private industry is developing a proprietary NGS based approach through its testing service, intended to enable testing at mass scale when fully deployed, which aims to have a high throughput testing capability that is fast, accurate, and provides reliable test results for COVID-19. Given the pressing need to ensure the nation maintains force readiness, the 711 HPW has partnered with private industry in this pilot study to evaluate NGS scalable testing capability compared to gold-standard RT-qPCR. The verification and validation will be evaluated within a subset of study participants with a testing frequency of up to 2 times per week.

Serosurvey Methods for Detecting Previous Exposure to SARS-CoV-19

Blood Collection

At the same time as saliva collection, the AFRL study is collecting blood samples from participants to detect the presence of SARS-CoV-2 antibodies using multiple methods including laboratory-based test methods (ELISA) while also comparing the performance of Point of Care (POC) LFA serology kits against the acquired laboratory-based data. Enrolled participants are referred to the sampling site for a blood draw and/or instructed on how to participate in home sampling. Up to two tubes of blood (up to 16 mL total) are obtained from a venipuncture draw administered by a certified phlebotomist. To test the POC antibody test kits, participants are asked to provide blood up to once every two weeks over an 8-week period.

In order to demonstrate the large-scale capability for detecting SARS-CoV-2 antibodies, an option for in-home, self-sampling is being performed using a private industry developed kit, identical to what is currently being used for the National Institutes of Health (NIH) seroprevalence study (NCT04334954). Kits are bar-coded by the manufacturer on the outside of the kit and on the sample return package. This kit contains a microsampling device, gauze, a finger-prick lancet and all necessary shipping materials, as well as detailed instructions for participants to collect their own 80-microliter sample of blood that is then mailed back to AFRL investigators for testing.

Gold Standard Immunoassay Testing

Enzyme-Linked Immunosorbent Assay (ELISA) is a laboratory gold standard assay for detecting antibodies and is used to manually test for the presence of SARS-CoV-2 IgG, IgM, and IgA antibodies from venous blood draws acquired from survey participants. ELISA is performed using an EUA modified two-step method developed as recently described.[28] The first phase of indirect-ELISA is performed using the Sadtler et al. methodology[28,29] using heat inactivated human serum against the Receptor Binding Domain (RBD) of the SARS-CoV2 virus (The RBD reagent is produced under HHSN272201400008C: Vector pCAGGS containing the SARS-Related Coronavirus 2, Wuhan-Hu-1 Spike Glycoprotein Gene RBD with C-Terminal Hexa-Histidine Tag, NR-52309). A presumptive positive is estimated as an Optical Density (OD) higher than 3 times the Standard Deviation plus the mean OD of four negative serum samples for each ELISA plate ((3(StanDev)) + Mean OD). Any presumptive samples are then run using a second indirect-ELISA employing a modified method as performed by Stalbauer et al.[28] using a soluble spike glycoprotein (Spike) (The soluble spike reagent glycoprotein was produced under HHSN272201400008C: Vector pCAGGS containing the SARS-Related Coronavirus 2, Wuhan-Hu-1 Spike Glycoprotein Gene (soluble, stabilized), NR-52394). The Stalbauer Spike protocol was modified as follows: Spike protein was coated on the ELISA plate at 1 ug/ml concentration with 100 ul per ELISA well and the detection antibodies (goat anti-human-IgA, IgG, or IgM) were used at a concentration of 1:10,000. Any presumptive samples that have at least two OD values greater than the cut off OD within the same serial dilution series are considered positive. The cut-off OD was calculated via the same methodology as with the RBD ELISA ((3(StanDev)) + Mean OD) except the negative pooled serum samples are serially diluted and then the Standard Deviation and mean is evaluated for the cut-off OD value. While useful, in large-scale testing, higher throughput methods are required. Our capabilities included testing for IgG SARS-CoV-2 antibodies in approximately 30 minutes and with minimal set-up. At peak capacity we can test 400 samples in a

day, making it a strong candidate for routine IgG testing. Testing outlined below were compared against the ELISA as a gold standard reference.

Lateral Flow Assay

Several POC testing kits utilizing lateral flow immunoassays (LFIA, or shortened to LFA) have recently become available to simultaneously test for IgM and IgG SARS-CoV-2 antibodies. Several suppliers produce POC SARS-CoV-2 testing kits that are either partially or fully manufactured in the US and are currently being considered for evaluation by the Air Force COVID-19 Task Force Serology Test Acquisition Program (under the National Operation Warp Speed umbrella). While both can use either serum or whole blood, whole blood is being used to evaluate the performance characteristics of both tests. One kit has two different wells: a sample well and a buffer well. The test is conducted by placing 10 uL of whole blood into the sample well, then two drops of the included buffer solution are placed into the buffer well. Another kit features a single well for both the sample and the buffer. The results of the tests are read after 15 minutes, making these tests much faster than the majority of other currently available methods. Since LFAs show the presence of antibodies indicating a past SARS-CoV-2 infection, these may serve as a test for an active immune response.[21,30] Tests that are positive will be photographed, and re-run on both LFA kits to confirm the result. LFA performance of these kits will be evaluated against laboratory reference test methods.

Identification of SARS-CoV-2 by VOC Detection

The detection of VOCs associated with SARS-CoV-2 infection is currently being carried out within a population separate from the molecular and seroprevalence study described above. The VOC study focuses on individuals with active SARS-CoV-2 infection, and all subjects will be tested using established CDC protocols prior to sampling. Patients demonstrating respiratory symptoms that have been designated as COVID-19 positive (i.e. presumptive positive) are also being sampled. Finally, in order to validate that the methods tested can differentiate COVID-19 infection from other respiratory diseases/illnesses, a population of patients experiencing respiratory symptoms that are COVID-19 negative will also be sampled. Subject breath is collected in 2L polypropylene bags, using previously established exhalation protocols.[20,31] Unlike the above molecular and serological sample collection methods, potential exists for background air contamination and so a background sample of room air will be taken within the room where each breath sample is acquired, approximately 2-3 meters from the subject. While mass spectrometry instrumentation (GC-MS, LC-MS, etc.) is commonly associated with analytical facilities, mobile instrumentation exists, and both a field portable GC-MS and a residual gas analyzer mass spectrometer (RGA/MS) is used in concert with other commercial off the shelf instrumentation (which detects O2, CO2, CO, NO, temperature, and humidity) to identify biomarkers of interest related to SARS-CoV-2.

Discussion

The assays being evaluated in this paper offer promise in providing rapidly deployable tests to improve pandemic response capacity. While these studies are not yet complete, the application of these new and existing technologies offer significant potential to not only the DoD, but also for the broader civilian population worldwide. We are addressing shortcomings in the detection of active and previous infections, as well as asymptomatic patients which can provide invaluable insight to guide scientific and operational decisions during and after an active pandemic.

Establishing a minimum viable product for SARS-CoV-2 testing solutions

Three factors will likely dictate the utility of any newly developed SARS-CoV-2 test: accuracy, availability, and turn-around time. The characteristics of these three factors will differentiate based on the purpose of the test, which can be broadly categorized into diagnostics, screening, and surveillance.[32] Diagnostic testing, intended for symptomatic individuals and those with known direct exposure, should be highly accurate with a sufficient turnaround time to support clinical decision-making, including treatment, effective isolation, and contact tracing.[33,34] Screening is intended to reduce the spread of infection through routing testing of symptomatic individuals or suspect exposure.[35] Screening requires greater frequency of testing to control the spread disease transmission, prioritizing a faster turnaround time over accuracy of results.[32] Surveillance tests are used to estimate prevalence in groups of individuals, but are not used for clinical decision-making purposes involving patient treatment.

A minimum viable product (MVP), or a testing solution with sufficient characteristics to satisfy the customer needs during on-going product development, is dependent upon the test purpose. Therefore, the minimum sensitivity and specificity for a diagnostic test should be >95% and >99% respectively, and provide results within days. In contrast, a screening test should be >70% sensitive and >90% specific, and be capable of providing a

result within hours. A test developed for surveillance will have similar sensitivity and specificity characteristics compared to a screening test, although the turnaround time is of much lesser importance. Rockefeller Foundation recommended that at least 30 million tests per week are required to bring SARS-CoV-2 under control,[36] compared to 5 million tests that have been reported weekly since the publication of this article.[37] To meet this goal, test developers must consider the MVP specific to the intended diagnostic, screening, or surveillance purpose of the test to bring the best solutions to the public in a timely manner.

Test Monitoring active SARS-CoV-2 infection in returning workforce at WPAFB

Like any large workplace, prior to WPAFB personnel returning to work there is a need to determine the percent of active SARS-CoV-2 infections that otherwise healthy workers may have. Without an accurate picture of infection military, civilians, and contractors working closely together may unwittingly place one another at an increased risk of infection and impact mission availability. To determine this percentage and develop testing strategies to potentially test a large number of military, civilian, and contractors returning to work, we have enrolled participants in a multifaceted study to assay for the presence of SARS-CoV-2 in saliva samples subjected to RT-qPCR and RT-LAMP analyses plus an emerging DNA sequencing approach to concurrently detect any active infections in a high throughput manner. A seroprevalence study is being run alongside the molecular survey to evaluate performance characteristics of POC LFAs to provide guidance on how to effectively utilize rapid antibody testing while also providing a first glimpse into the seroprevalence of individuals at WPAFB potentially exposed to SARS-CoV-2. Finally, a separate study is exploring emergent detection methods through the use of exhaled breath sampling to detect VOC biomarkers associated with SARS-CoV-2. This three-pronged approach will thoroughly evaluate and identify the best methods and practices to inform recommendations and further dissemination across the DoD.

NP swab sample collection was established early on as the standard for sample collection in clinical settings; However, supply shortages including obtaining swabs rapidly became a bottleneck in testing. More recently, alternative sample matrices such as saliva have come to the forefront, appearing to be superior to NP swabbing, both in the ease of collection and in the detection of active infection.[10] Saliva collection is both non-invasive and amenable to repeated collections over time due to the ease of collection. Furthermore, these samples can be self-collected by the patient removing the need for direct collection by a healthcare worker, thereby decreasing potential exposure of healthcare workers, conserving PPE, and reducing the need for specialized laboratory consumables and associated reagents. Additionally, saliva collection has recently been described to be as accurate as NP samples obtained with swabs even without RNA extraction.[11] Prior to implementation in an organization as large as the USAF, and before any public health decisions can be made, testing and validation as a part of a research study is required. Thus, by comparing emerging molecular technologies and sampling matrices to the NP-based gold-standard RT-qPCR based tests, we will be able to validate whether these approaches are able to determine the percentage of healthy personnel who return to work with active infection (potentially asymptomatic). This will enable organizations to impact transmission rates through early identification and quarantining.

Although RT-qPCR is the current method of choice for SARS-CoV-2 detection, it requires specialized equipment and trained personnel.[38] Furthermore, the reagent supply is limited due to the enormous demand from increased international testing, and it does not have sufficient capacity for the requirements of force level screening. In concert with RT-qPCR testing we are also validating alternate methods to test large amounts of personnel without interfering with the current supply chain. One such method is in collaboration with an industry partner to validate and verify their NGS platform to detect active SARS-CoV-2 from saliva within a subset of the WPAFB workforce. This capability repurposes installed DNA sequencing capacity across the sequencing industry, not only with this industry partner but also with other major sequencing leaders. In the near term, one industry partner is repurposing its biological factories to enable testing at mass scale (once fully operational) in support of DoD operational readiness.

A second method being evaluated, to preserve critical reagents, is RT-LAMP. This isothermal assay is fast, does not require overly specialized equipment and is portable to austere environments[4,39,40] capable of supporting variable DoD mission requirements. Further, RT-LAMP has the potential to meet World Health Organization (WHO) guidelines for low-cost, widely deployable point of care assays of 20 US dollars or less and results in less than 40 minutes.[41] However, RT-LAMP has traditionally been hampered by decreased sensitivity compared to RT-qPCR and increased potential of false-positives.[42,43] Furthermore, detection of amplification is typically achieved by indirect means such as color-change based on pH change,4 which could be non-informative if too much buffered sample is used or if the sample is acidic·

We aim to enhance the current RT-LAMP work flow by decreasing false positives while increasing sensitivity and compare results to the gold-standard RT-qPCR assay.

As an example of this optimization, we initially utilized RT-LAMP conditions using New England Biolabs WarmStart Colorimetric LAMP 2X Master Mix and various published LAMP primer sets4 testing a dilution series of Twist Synthetic SARS-CoV-2 RNA Control. Initially we found that the primer set GeneN-B performed well without the frequent presence of false positives. Further optimizations include the additions of double-stranded DNA fluorescent dye SYTO-9 to directly detect amplification and guanidine hydrochloride to increase sensitivity.[4,44]

Ultimately, we simplified the work flow by performing the reactions in a 65ºC incubator for 30 min and then reading the fluorescent signal in a plate reader. This workflow can detect 100 copies of SARS-CoV-2 RNA per reaction (Fig 2A). This set-up is potentially portable[39,40] with a standard incubator or hot block and the use of a portable fluorescence detection, making it ideal for harsh operational environments.45,46 Furthermore, we are able to detect specific versus false positives after the reaction by performing a melt curve analysis which indicated a differing melting temperature for the false positives compared to the specific positives (Fig. 2B). We envision further optimizations would allow the input of saliva directly into the reaction and detection of specific amplified products without the use of sophisticated equipment.

Ultimately, a fast test that could be used repeatedly and would non-invasively detect SARS-CoV-2 infection at the point of care without disrupting the supply chain would be needed to test the entire work force and military to ensure a healthy returning population. Exhaled breath has been used as a biological matrix in several prior studies to identify biomarkers of exposure and various disease states.[47] However, it is not known whether real-time instruments can be used for detection of biomarkers (in this case, VOCs) emanated from individuals who are either actively presenting with SARS-CoV-2 infection, or are asymptomatic as a passive screening approach.

The limited data available on COVID-19 suggests that the biochemical mechanism imparted by SARS-CoV-2 infection is different from other common respiratory conditions such as asthma, influenza, and rhinovirus, but indicates that both exhaled CO2 and NO are potential biomarkers of COVID-19 infection.[48-51] We will therefore measure CO2 and NO levels in exhaled breath to determine if they are indeed biomarkers indicative of COVID-19 infection. In addition, we will also be evaluating known exhaled breath markers of various disease states.[52] These data are invaluable in generating new, predictive models based on chemical biomarkers, and will be used to develop a machine learning based algorithm that will increase the predictive accuracy of breath-based disease tracking. Ultimately, we hope to transition a field portable system that employs mass spectrometry-based breath biomarker assessment together with real-time artificial intelligence analysis to rapidly, and accurately identify SARS-CoV-2 in military populations.

Determining Susceptibility of Returning Work Force

In order to gain a better understanding of exposure levels and potential immunity in the general population and the returning workforce during the pandemic, the analysis of serum can identify individuals with specific antibodies to the SARS-CoV-2 virus, indicating past viral infection.[53,54] Levels of IgM and IgG antibodies, which are not present in the first few days of infection, remain detectable for weeks after infection.[55,56] Researchers have not yet confirmed whether the presence of SARS-CoV-2 antibodies in a person's blood means they are fully protected from SARS-CoV-2 infection. Based on what is known about similar viruses, this protection is likely; however, more research is needed. In fact, that is one research question this study may help answer. All people in the US should adhere to public health guidelines as outlined by the CDC and local authorities. A person's behavior should not change based on antibody test results from this or other studies. The knowledge gained on the level of exposure from these studies can be used to formulate responses to current and future pandemics and the information acquired used to help OWS and the Air Force COVID-19 Task Force in their planning.

Beyond the knowledge gained from laboratory seroprevalence testing which will undoubtedly inform return to work and deployment decisions, antibody testing at home is potentially one of the most impactful methods that can be deployed subsequent to this study addressing assay limitations and providing operational guidance. LFAs are cheap, able to be mass produced, and easy to interpret by untrained individuals. As with the RT-LAMP tests noted above, LFAs meet WHO target product profiles for a low cost, widely deployable point of care (or at home) test.[41] While potentially less sensitive and precise than gold standard methods the sheer number of such tests that could be disseminated and used in the workplace cannot be denied.

Challenges, Future Strategies for Pandemic Tracking & Solutions

The methods employed at WPAFB while extensive, are not exhaustive of all that is available at the time of writing. Efforts to expand the ability to identify SARS-CoV-2 in non-standard environments are underway worldwide. One promising approach for non-invasively tracking populations is the testing of wastewater.[57,58] Viral titers in untreated wastewater lead detectable infection rates by four to ten days potentially allowing for the implementation of workforce reductions, quarantine of specific buildings or neighborhoods, or lockdowns without requiring the intensive sampling of dozens or hundreds of individuals.[59] In one European study, wastewater monitoring was able to detect as low as 2 viral "shedders" in 10,000 suggesting the method is ready for use at schools and workplaces to easily and rapidly detect emergent infections before they become rampant.[60] Newly published methodologies have also shown the advantage of normalizing SARS-CoV-2 RT-qPCR data to the abundance of a ubiquitous virus, Pepper mild mottle virus (PMMoV) that is often used as a water quality indicator.[61] The approach allows for variations in flow due to increases in usage of the wastewater system, or additional liquid due to rainfall events to be accounted for, increasing the ability of wastewater to resolve trends in infection spikes or declines in infectivity in a population.[57] NGS can also be used with wastewater samples to identify the diversity and prevalence of different SARS-CoV-2 clades within a population.[62] The approach is rapidly evolving, and even highly sensitive protein-based assays to detect SARS-CoV-2 structural proteins have been developed, with results that mirror infection dynamics in the local population.[63] Overall, wastewater sampling stands to complement public health efforts by directing precious testing resources to cities, installations, or even buildings, in which wastewater is showing an elevated or spike infection rate.

Another approach to surveil a population for SARS-CoV-2 is through the pooling of samples and performing RT-qPCR tests. In this approach if a pool is negative then all individuals represented in that pool are considered negative; however, if a pool is positive all samples in that pool have to be re-tested individually.[64-66] This method preserves reagents and resources, but is best used when SARS-CoV-2 positivity rate is expected to be low.

Testing kits are currently being manufactured that hope to provide rapid solutions to SARS-CoV-2 testing. Antigen tests are cheap, fast, POC assays. They are less sensitive that RT-qPCR tests, but if used repeatedly as a screening measure may be effective. At the time of writing, four manufacturers have EUAs to manufacture rapid antigen tests. Another promising technological advance is the use of CRISPR to detect SARS-CoV-2.[67,68] Assays based on CRISPR utilize a LAMP-like reaction initially but gain a level of specificity by using a Cas enzyme to detect the specific SARS-CoV-2 amplified product.

Impact

During the pandemic, proper testing methods, data collection, and dissemination of results within a clinical setting is vital at every stage for proper decision making. Enabling a return to work is no different. While almost every DoD facility has some form of minimal manning in effect there is no current way to establish when an installation can return to full capacity, or how to best ensure a confident, fully functional workforce. The methods reviewed here and those currently underway represent a small part of the DoD's contributions to Operation Warp Speed's SARS-CoV-2 response. These studies strive to validate scalable, alternative testing approaches for both active infection and antibody presence. While many testing methods exist, including those being researched at WPAFB and discussed here, the most critical point is that each organization must make a choice, and implement testing methods that allow for a safe, healthy return to work. Verification and validation studies provide vital insight to the public regarding the efficacy and ease of use of existing and emergent testing methods that will inform commanders across the DoD of the multitude of approaches that they can employ to ensure mission performance in a cost effective, rapidly deployable manner.

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Diagnostic Testing for COVID-19: Systematic Review of Meta-Analyses and Evidence-Based Algorithms

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Abstract

Background: Coronavirus Disease-19 (COVID-19), a disease caused by infection with the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), is a global pandemic. Diagnosis is critical and diagnostic techniques include reverse transcriptase polymerase chain reaction (RT-PCR), serologic antibody testing, and chest computed tomography (CT). Despite rigorous meta-analyses looking into these techniques, there is no summary and additionally no algorithm to help guide diagnostic testing. Our objective is to perform a systematic review of the literature and to provide evidence-based algorithms for diagnosing or ruling out COVID-19.

Methods: Data were gathered using PubMed and Ovid research databases using a predefined medical subject heading (MeSH) based search, and sources that were included in the study had their references reviewed to screen for more sources for this study. Sources were collected up to 23 August 2020. Two researchers searched through the databases for articles and data/articles meeting inclusion criteria were extracted.

Results: 395 articles were identified, and 10 studies were included. Meta-analyses of diagnostic tests were included in our systematic review. An overview was then provided for each diagnostic test. Sensitivities and specificities for RT-PCR, serologic antibody tests and chest CT were collected, and the data was stratified by categorical variables. Two evidence-based algorithms were developed for symptomatic and asymptomatic patients in the hospitalized and ambulatory settings.

Conclusions: This article provides a summary of the up-to-date efficacy of the most utilized diagnostic tests currently available for COVID-19. Additionally, this article provides evidence-based COVID-19 diagnostic algorithms for symptomatic and asymptomatic patients in the hospitalized and ambulatory settings.

Keywords: COVID-19, Meta-Analysis, RT-PCR, Chest CT, Antibody

Introduction

BACKGROUND: On March 11th, 2020 Coronavirus Disease-19 (COVID-19), a disease caused by infection with the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was declared a pandemic by the World Health Organization. Knowing that Military Treatment Facilities (MTFs) would be a battleground in the coming fight against COVID-19, the senior leadership at the Uniformed Services University of the Health Sciences (USU) decided to graduate roughly 170 physicians and 60 nurses almost two months early in order to join the fight. These servicemembers were sent to MTFs across the nation to provide support where needed. The newly minted graduates of the USU School of Medicine (SOM) assisted with front entrance and clinical screening, conducted contact tracing, took initiative in organizational planning, worked on serological screening, and aided with the care of ill patients under the supervision of board-certified physicians. Because the graduate nurses all served as registered nurses (RNs) before attending the USU Graduate School of Nursing (GSN), they were able to go directly to their next duty station and provide much-needed help on the wards. For their efforts in the fight against COVID-19, the members of the USU class of 2020 were nominated for the Humanitarian Service Medal.[1]

While the early graduates of the USU SOM and GSN were supporting the fight against COVID-19 in MTFs across the country, health care professionals around the globe were working to develop diagnostic techniques

to identify infected individuals and determine the best course of action for their care. Such diagnostic techniques included reverse transcriptase polymerase chain reaction (RT-PCR), serologic antibody testing, and chest computed tomography (CT). There are many intricacies regarding the performance of these diagnostic techniques that are unique to COVID-19. Consequently, researchers have conducted rigorous meta-analyses looking into these techniques in the months since the declaration of the pandemic. Hospitals have likely reviewed these meta-analyses to guide their local algorithms for diagnosing or ruling out COVID-19. However, evidence-based algorithms for diagnosing or ruling out COVID-19 have yet to be published to our knowledge at the time of this publication.

RT-PCR samples can include sputum, throat swab, nasopharyngeal swab, nasopharyngeal aspirate, blood, urine, feces, saliva, and rectal swabs. The test is reliant on having a minimum amount of viral target products or being used within the appropriate time frame in the viral replication cycle.

Once infected with the SARS-CoV-2 virus, different antibodies develop over time. IgM antibodies develop first after exposure to SARS-CoV-2 antigens, peaking between days 5 and 12 and then dropping slowly. IgG antibodies appear later, reaching peak concentrations after day 20, roughly, and are more specific to the antigen.[6] Various methods for antibody detection exist, in the form of enzyme-linked immunosorbent assay (ELISA), chemiluminescence enzyme immunoassay (CLIA), fluorescence immunoassay (FIA), lateral flow immunoassay (LFIA), gold immunochromatography assay (GICA), lateral flow assay (LFA), and colloidal gold-based immunochromatographic assay (CGIA). Additionally, different antibodies can be detected using these methods, including IgG, IgM, IgA, and combinations of the three. Furthermore, two different antigens exist, the nucleocapsid protein (N) and the spike protein (S), that additionally differentiate testing capabilities. Finally, the source from which the antibodies and antigens are extracted from the patient also differ between whole blood, serum, or plasma. The studies included in this systematic review used RT-PCR, or a combination of RT-PCR and clinical findings, as the standard against which the sensitivities and specificities for each antibody combination were measured.

There are several chest CT findings that are commonly found in COVID-19 including ground glass opacities (GGOs) with or without consolidation, adjacent pleural thickening, interlobular septal thickening, air bronchograms, "crazy paving pattern," bronchiectasis, pleural effusion, pericardial effusion, and lymphadenopathy. Although these findings are relatively common in COVID-19, they are also found in many other disease processes. All studies included within this systematic review used RT-PCR as the reference standard for determining presence of the disease.

OBJECTIVE: Our systematic review focused on meta-analyses evaluating diagnostic testing for COVID-19, to include RT-PCR, serologic antibody testing, and chest CT. The sensitivity and specificity of these various methods were evaluated, and ranges for these values were obtained. From our comprehensive overview of meta-analyses, we were able to develop evidence-based algorithms to aid physicians in diagnosing or ruling out patients with COVID-19 depending on the presence of symptoms, duration of symptoms, and results of previous testing, in the hospitalized and ambulatory settings.

Methods

PROTOCOL AND REGISTRATION: This study was conducted according to Preferred Reporting Items for a Systematic Review and Meta-analysis (PRISMA).

ELIGIBILITY CRITERIA: Titles and abstracts of articles were reviewed for eligibility. Articles deemed relevant were reviewed and those that did not meet inclusion criteria were excluded from the study. Data from those articles that met inclusion criteria were collected.

INFORMATION SOURCES: Sources were gathered using PubMed and Ovid MEDLINE research databases, and sources that were included in the study had their references reviewed to screen for more sources for this study. Sources were collected up to 23 August 2020.

SEARCH: Our MeSH terms included (Covid OR Covid-19 OR Coronavirus OR nCoV OR SARS-CoV-2) AND ("systematic review" OR "meta-analysis") AND (IgG OR IgM OR Antibody); (Covid OR Covid-19 OR Coronavirus OR nCoV OR SARS-CoV-2) AND ("systematic review" OR "meta-analysis") AND (CT); (Covid OR Covid-19 OR Coronavirus OR nCoV OR SARS-CoV-2) AND ("systematic review" OR "meta-analysis") AND (PCR OR RT-PCR); (Covid OR Covid-19 OR Coronavirus OR nCoV OR SARS-CoV-2) AND ("systematic review" OR "meta-analysis") AND ("diagnostic test" OR test OR diagnosis).

STUDY SELECTION

Study Inclusion Criteria:

- Pertains to the SARS-CoV-2 coronavirus strain;
- Design is a meta-analysis, or a systematic review with meta-analysis;

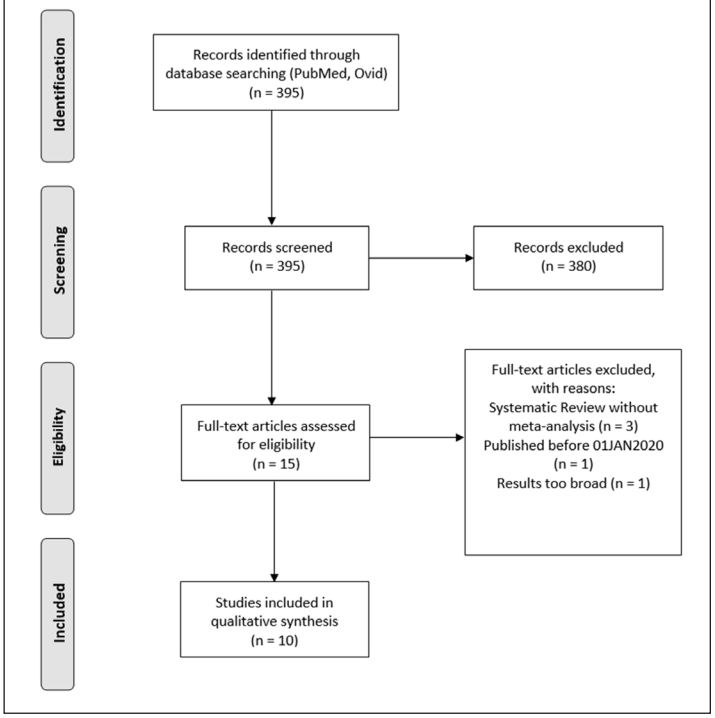
- Analyzed RT-PCR and/or antibody tests and/or Chest CT;
- Outcome parameters such as sensitivity, specificity, PPV, or NPV;
- Published after 01JAN2020.

Exclusion criteria:

- Does not pertain to the SARS-CoV-2 strain of coronavirus;
- Design is not meta-analysis, or systematic review with meta-analysis;
- Results are too broad or generalized;
- Results are given in ranges, rather than discrete points with Confidence Intervals;
- Published before 01JAN2020;
- Study had inadequate power.

DATA ITEMS AND COLLECTION PROCESS: The data collected for this overview included overall study summary data for sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of RT-PCR, chest CT and serological antibody testing when reported. These data were independently extracted from each source study.

Figure 1. Preferred reporting items for a systematic review and meta-analysis (PRISMA) flow diagram.



RESULTS

STUDY SELECTION: A total of 395 articles were identified after duplicate removal, from the following databases: PubMed and Ovid MEDLINE. Of these, 380 were excluded during the screening phase (reading titles and abstracts). 15 articles were fully appraised. Finally, 10 studies were included in the systematic review after applying inclusion and exclusion criteria to the complete article. Two reviewers independently screened the studies, while a third, senior review author resolved any disagreements (Figure 1).

STUDY CHARACTERISTICS: Two studies looked at RT-PCR, six studies looked at antibody testing, and five studies looked at chest CT. There were two studies that addressed multiple test methods (Table 1).

Table 1. Study characteristics.

Author	Number of patients	COVID-19 positive patients	Healthy/COVID-19 negative patients	Diagnostic Tests
Böger et al [3]	2,297	NR	NR	RT-PCR, Antibody, CT
Kim et al [2]	7720	NR	NR	RT-PCR, CT
Bastos et al [8]	140-3750*	NR	NR	Antibody
Caini et al [4]	2,007	748	1259	Antibody
Deeks et al [6]	15,976**	8526**	7450**	Antibody
Kontou et al [7]	7,848	3522	4326	Antibody
Zhang et al [5]	3767	2282	1485	Antibody
Adams et al [10]	1431	NR	NR	CT
Lv et al [9]	5,673	NR	NR	CT
Xu et al [11]	3186	2689	497	CT

RT-PCR = Reverse Transcriptase Polymerase Chain Reaction; CT = Chest Computed Tomography; NR = Not Reported; * = range provided by authors based on the different variables analyzed; ** = samples, not patients.

RESULTS OF INDIVIDUAL STUDIES:

RT-PCR

Kim et al. compared chest CT to RT-PCR. The pooled sensitivity of RT-PCR from upper respiratory specimens (nasopharyngeal swab, throat swab, or sputum) was 89% (95% CI 81-94%). At a disease prevalence of 1% the positive predictive value (PPV) and negative predictive value (NPV) are estimated to be 47.3% and 99.9% respectively; at 10% prevalence PPV and NPV are estimated to be 90.8% and 98.8% respectively; at 39% prevalence PPV and NPV are estimated to be 98.3% and 93.4% respectively. [2]

Böger et al. conducted a meta-analysis that evaluated various diagnostic RT-PCR tests for accuracy based on sample type. These sensitivities are listed as followed in descending order: sputum 97.2% (95% CI 90.3-99.7%), nasopharyngeal aspirate/swab 73.3% (95%

CI 68.1-78.0%), saliva 62.3% (95% CI 54.5-69.6%), rectal swab/stool 24.1% (95% CI 16.7-33.0%), plasma 7.3% (95% CI 4.1-11.7%), and urine 0.0% (95% CI 0.0-3.7%). [3]

The sensitivity of RT-PCR for detecting COVID-19 ranges from 0.0% (95% CI 0.0-3.7%) to 97.2% (95% CI 90.3-99.7%) depending on the sample source. The sensitivity of RT-PCR from upper respiratory specimens (nasopharyngeal swab, throat swab, or sputum) ranges from 73.3% (95% CI 68.1-78.0%) to 97.2% (95% CI 90.3-99.7%). The PPV for RT-PCR ranged from 47.3-98.3%. The NPV ranged from 93.4-99.9% with a disease prevalence ranging from 1.5% to 30.7% and depending on the sample source (Table 2).[2,3]

ANTIBODIES

Antibody (IgG, IgM, IgA, combinations)

Caini et al. reported that the pooled sensitivity and specificity of IgM was 82% (95% CI 75-88%), and 98% (95% CI 92-100%) respectively. The pooled sensitivity and specificity of IgG was 85% (95% CI 73-93%), and 99% (95% CI 98-100%) respectively. Finally, the pooled sensitivity and specificity of total antibodies was 85% (95% CI 74-94%), and 99% (95% CI 98-100%) respectively. [4]

Zhang et al. reported that the pooled sensitivity and specificity of anti-SARS-CoV-2 IgG was 85% (95% CI 79-90%) and 99% (95% CI 98-100%). The pooled sensitivity and specificity of IgM was 74% (95% CI 65-81%) and 99% (95% CI 97-100%). Finally, the pooled sensitivity and specificity of IgG/IgM was 86% (95% CI 79-92%) and 99% (95% CI 97-100%). [5]

Deeks et al. reported pooled specificity values and sensitivity values stratified by analytical method. Sensitivity of IgG ranged from 76.0% (95% CI 61.0-86.5%) using LFA to 94.6% (95% CI 90.7-97.0%) using CLIA. The sensitivity of IgM ranged from 51.4% (95% CI 26.5-75.6%) using LFA to 84.5% (95% CI 70.7-92.5%) using ELISA. The sensitivity of IgG/IgM ranged from 88.6% (95% CI 82.0-93.0%) using LFA to 97.5% (95% CI 94.0-99.0%) using CLIA. The pooled specificities are as follows: IgG; 99.1% (95% CI 98.3-99.6%). IgM; 98.7% (95% CI 97.4-99.3%). IgA; 98.5% (95% CI 97.2-99.2%). IgG/IgM; 98.7% (95% CI 97.2-99.4%). IgA/IgG; 99.8% (95% CI 98.9-100%). IgA/IgM; 99.8% (95% CI 99.2-100%). Total antibodies; 99.2% (95% CI 98.3-99.6%). [6]

Kontou et al. reported sensitivity and specificity values stratified by analytical method and antigen. Analytical methods used were ELISA, CLIA, LFIA and FIA, and antigens used were the N, S and NS antigen. This study reported that the sensitivity of IgG ranged from 53.7% (95% CI 12.3-95.1%) to 94.4% (95% CI 90.6-98.3%), and specificity ranged from 91.4% (95% CI 85.3-95.1%) to 99.4% (95% CI 98.8-99.9%). CLIA NS-based IgG was the most sensitive and ELISA N-based IgG was the most specific. The sensitivity of IgM ranged from 52.8% (95% CI 32.9-72.6%) to 86.0% (95% CI 50.0-100.0%), and specificity ranged from 91.4% (95% CI 85.2-95.1%) to 99.5% (95% CI 98.9-100.0%). FIA NS-based IgM was the most sensitive, and ELISA N-based IgM was the most specific. The sensitivity of IgG/IgM ranged from 77.7% (95% CI 59.2-96.2%) to 93.5% (95% CI 90.0-97.1%), and specificity ranged from 95.0% (95% CI 92.3-97.7%) to 99.4% (95% CI 98.4-99.8%). ELISA S-based IgG/IgM was the most sensitive, and LFIA S-based IgG/IgM was the most specific. [7]

Böger et al. stratified the results based on sample source (blood, serum, or blood/serum/plasma). This study found that the sensitivity of IgG ranged from 66.1% (95% CI 62.3-69.8%) to 73.9% (95% CI 69.6-77.9%), and specificity ranged from 69.4% (95% CI 66.6–72.1%) to 98.8% (95% CI 95.8-99.9%). The sensitivity of IgM ranged from 74.3% (95% CI 70.1%-78.2%) to 78.8% (95% CI 75.4-81.9%), and specificity ranged from 93.1% (95% CI 88.2-96.4%) to 93.3% (95% CI 88.6–96.5%). Finally, the sensitivity of IgG/IgM ranged from 82% (95% CI 78-85%) to 86.3 (95% CI 83.3-88.8%), and specificity ranged from 90.7% (95% CI 84.8-94.8%) to 91.6% (95% CI 86.0–95.4%). [3]

The Caini, Zhang and Deeks studies reported values for pooled sensitivity and/or specificity of antibody combinations alone, without further subdividing their results based on other factors like antigen, method, time, or sample source). Based on these three studies, the sensitivity and specificity of IgM ranges from 74% (95% CI 65-81%) to 82% (95% CI 75-88%) and 98% (95% CI 92-100%) to 99% (95% CI 97-100%), respectively. The sensitivity and specificity of IgG ranges from 85% (95% CI

Table 2. RT-PCR data.

Source	Sensitivity (95% CI)
Sputum	97.2% (90.3-99.7%). I^2= 48.3%
Nasopharyngeal aspirate, nasopharyngeal and throat swab	73.3% (68.1-78.0%). I^2 = 87.5%
Saliva	62.3% (54.5-69.6%). I^2 = 92.2%
Stool, feces, rectal swabs	24.1% (16.7-33.0%). I^2= 82.6%
Blood	7.3% (4.1-11.7%). I^2 = 85.9%
Urine	0.0% (0.0-3.7%). I^2 = 0.0%

73-93%) to 85% (95% CI 79-90%) and 99% (95% CI 98-100%) to 99.1% (95% CI 98.3-99.6%). The sensitivity of IgG/IgM is 86% (95% CI 79-92%), and the specificity ranges from 98.7% (95% CI 97.2-99.4%) to 99% (95% CI 97-100%). Finally, the sensitivity of total antibodies was 85% (95% CI 74–94%), and the specificity ranges from 99% (95% CI 98-100%) to 99.2% (95% CI 98.3-99.6%). The pooled sensitivity of IgA, IgA/IgG and IgA/IgM were not measured; however, their specificities are 98.5% (95% CI 97.2-99.2%), 99.8% (95% CI 98.9-100%) and 99.8% (95% CI 99.2-100%), respectively (Table 3).[4-6]

Antigen (N, S, combinations)

The Kontou study found that S-based ELISAs perform better compared to N-based ELISAs, in general. IgG ELISA with S antigen had a sensitivity of 81.4% (95% CI 68.8-94.0%) and a specificity of 96.1% (95% CI 91.0-100.0%). IgM ELISA with S antigen had a sensitivity of 81.7% (95% CI 70.4-93.1%) and a specificity of 99.1% (95% CI 97.6-100.0%). Combined IgG/IgM ELISA with S antigen had a sensitivity of 93.5% (95% CI 90.0-97.1%) and a specificity of 98.7% (95% CI 97.3-100.0%). [7]

NS-based IgG LFIA performed better compared to other antigen combinations, in general, with a sensitivity of 65.0% (95% CI 40.4-89.5%) and a specificity of 98.8% (95% CI 97.3-100.0%). S-based IgM and combined IgG/IgM LFIA performed better than other antigen combinations, in general, with sensitivities of 66.3% (95% CI 23.6-100.0%) and 82.8% (95% CI 77.0-88.6%) and specificities of 91.4% (95% CI 85.2-95.1%) and 99.4% (95% CI 98.4-99.8%), respectively. [7]

NS-based CLIAs perform better compared to other antigen combination CLIAs, in general. IgG CLIA with NS antigen had a sensitivity of 94.4% (95% CI 90.6-98.3%) and a specificity of 97.1% (95% CI 93.1-100.0%). IgM CLIA with NS antigen had a sensitivity of 81.0% (95% CI 72.2-89.7%) and a specificity of 98.4% (95% CI 97.0-99.9%). Combined IgG/IgM CLIA with NS antigen has a sensitivity of 90.7% (95% CI 75.3-100.0%) and a specificity of 98.1% (95% CI 94.4-100.0%). [7]

NS-based FIAs perform better compared to other antigen combinations, in general. IgG FIA with NS antigen had a sensitivity of 85.9% (95% CI 33.9-100.0%) and specificity of 95.0% (95% CI 92.3-97.7%). IgM FIA with NS antigen had a sensitivity of 86.0% (95% CI 50.0-100.0%) and a specificity of 95.0% (95% CI 92.3-97.7%). [7]

For ELISA, S-based testing significantly outperformed N-based testing for all antibody combinations in terms of sensitivity and had comparable specificities. For LFIA, NS-based testing was superior when using the IgG antibody, whereas S-based testing was superior for IgM and IgG/IgM antibodies. For CLIA and FIA, NS-based testing generally outperformed other antigens for all antibody combinations in sensitivity and specificity(Table 4).

Time (weeks)

Deeks et al. found that results for IgG, IgM, IgA, combined IgG/IgM, combined IgA/IgG, and total antibodies all showed low sensitivity during the first week since symptom onset. The highest was 30.1% (95% CI 21.4-40.7%) for combined IgG/IgM. Sensitivities for all antibodies rose in the second week, with a high of 84.0% (95% CI 64.1-93.9%) for total antibodies. IgG, IgM, and total antibody sensitivities all reached their highest values in the third week, with 88.2% (95% CI 83.5-91.8%), 75.4% (95% CI 64.3-83.8%), and 98.1% (95% CI 90.1-99.6%) respectively. IgG/IgM and IgA/IgG sensitivities both peaked in the fourth week, with 96.0% (95% CI 90.6-98.3%) and 100% (95% CI 2.5-100%), respectively. Finally, IgA sensitivity peaked in the fifth week, at 100%. Specificities exceeded 98% for all antibody combinations, with confidence intervals no more than 2 percentage points wide.[6]

Similarly, Bastos et al. found that when stratified by analytic method (ELISA, LFIA and CLIA), IgM had the lowest sensitivity in the first week for all methods with a high of 50.3% (95% CI 10.9-81.2%) for CLIA, and the highest sensitivity in the third week and beyond for all methods with a high of 90.6% (95% CI 51.8-99.4%) for CLIA. IgG had nearly identical findings, with the lowest sensitivity in the first week for all methods with a high of 53.2% (95% CI 28.7-67.6%) for CLIA, and the highest sensitivity in the third week and beyond for all methods with a high of 98.9% (95% CI 86.9-100%) for CLIA. [8]

Both studies found that antibody testing before the third week since the onset of symptoms had sensitivities less than 85.4%. After the start of the third

Table 3. Pooled antibody test data.

	Sensitivity Range (95% CI)		Specificity Range (95% CI)	
IgG	85% (73-93%)	85% (79-90%)	99% (98-100%)	99.1% (98.3-99.6%)
IgM	74% (65-81%)	82% (75-88%)	98% (92-100%)	99% (97-100%)
IgA	-	-	98.5% (97.2-99.2%)	-
Total	85% (74-94%)	-	99% (98-100%)	99.2% (98.3-99.6%)
IgG/IgM	86% (79-92%)	-	98.7% (97.2-99.4%)	99% (97-100%)
IgA/IgG	-	-	99.8% (98.9-100%)	-
IgA/IgM	-	-	99.8% (99.2-100%)	-

(-) = Pooled data not available

Table 4. Antibody test antigen data.

		Sensitivity Range (95% CI)		Specificity Range (95% CI)	
ELISA	N	72.2% (44.9-99.6%)	80.8% (76.4-85.3%)	96.7% (91.5-98.7%)	99.5% (98.9-100.0%)
	S	81.4% (68.8-94.0%)	93.5% (90.0-97.1%)	96.1% (91.0-100.0%)	99.1% (97.6-100.0%)
LFIA	S	53.7% (12.3-95.1%)	82.8% (77.0-88.6%)	91.4% (85.2-95.1%)	99.4% (98.4-99.8%)
	NS	52.8% (32.9-72.6%)	77.7% (59.2-96.2%)	98.6% (97.4-99.8%)	98.8% (97.3-100.0%)
	S/NS	55.5% (35.2-75.8%)	79.3% (64.3-94.2%)	96.4% (92.2-100.0%)	98.9 (97.8-99.9%)
	S/N/NS	80.0% (66.3-93.5%)	-	98.4% (96.9-99.9%)	-
CLIA	NS	81.0% (72.2-89.7%)	94.4% (90.6-98.3%)	97.1% (93.1-100.0%)	98.4% (97.0-99.9%)
	N/NS	79.9% (73.7-86.0%)	93.5% (89.6-97.5%)	95.4% (87.5-100.0%)	97.4% (95.3-99.4%)
FIA	NS	85.9% (33.9-100.0%)	86.0% (50.0-100.0%)	95.0% (92.3-97.7%)	-
	S/NS	78.6% (53.1-100.0%)	89.0% (59.1-100.0%)	95.0% (92.3-97.7%)	-

(-) = Pooled data not available

week and on, the sensitivity of IgM ranged from 69.9% (95% CI 58.4-79.9%) using LFIA to 90.6% (95% CI 51.8-99.4%) using CLIA. The sensitivity of IgG after the third week was 82.1% (95% CI 76.4-89.0%) using ELISA to 98.9% (95% CI 86.9-100%) using CLIA. Therefore, the superior method for testing either IgM or IgG antibodies from the start of the third week and on is CLIA. IgA showed the highest sensitivity in week three (98.7%), the second highest in week four (98.7%), and the highest again in week five and beyond (100%), suggesting that IgA is the superior antibody for detecting COVID-19 in the long term. However, the results for IgA are based on fewer than 100 samples/participants, whereas the results for IgG, IgM and IgG/IgM have more than 10 times that for some weeks (Table 5).[6,8]

Method (ELISA, LFIA, CLIA, FIA, GICA, LFA, CGIA)

Bastos et al. found that the pooled sensitivity of ELISA for IgG or IgM was 84.3% (95% CI 75.6-90.0%), and the pooled specificity was 97.6% (95% CI 93.2-99.4%). The pooled sensitivity of LFIA for IgG or IgM was 66.0% (95% CI 49.3-79.3%), and the pooled specificity was 96.6% (95% CI 94.3-98.2%). The pooled sensitivity of CLIA for IgG or IgM was 97.8% (95% CI 46.2-100%), and the pooled specificity could not be estimated because of non-convergence.[8]

Deeks et al. found that the sensitivity of ELISA ranged from 84.5% (95% CI 70.7-92.5%) to 90.7% (95% CI 83.3-95.0%), and specificity ranged from 98.8% (95% CI 96.5-99.6%) to 99.4% (95% CI 97.4-99.9%). Combined IgG/IgM was the most sensitive and specific. The sensitivity of CLIA ranged from 80.9% (95% CI 63.8-91.0%) to 97.5% (95% CI 94.0-99.0%), and specificity ranged from 94.1% (95% CI 82.7-98.2%) to 99.0% (95% CI 91.6-99.9%). Combined IgG/IgM was the most sensitive and IgG was the most specific. The sensitivity of LFA ranged from 51.4% (95% CI 26.5-75.6%) to 88.6% (95% CI 82.0-93.0%), and specificity ranged from 98.2% (95% CI 96.3-99.1%) to 99.6% (95% CI 97.3-99.9%). Combined IgG/IgM was the most sensitive and IgM was the most specific. The sensitivity of CGIA reneged from 69.5% (95% CI 44.3-86.7%) to 90.7% (95% CI 82.7-95.2%), and specificity ranged from 96.0% (95% CI 90.1-98.5%) to 99.5% (95% CI 96.5-99.9%). Combined IgG/IgM was the most sensitive and IgG was the most specific.[6]

Kontou et al. found that the sensitivity of ELISA ranged from 72.2% (95% CI 44.9%-99.6%) to 93.5% (95%CI 90.0-97.1%), and specificity ranged from 96.1% (95% CI 91.0-100.0%) to 99.5% (95% CI 98.9-100.0%). ELISA using combined IgG/IgM antibody and the S antigen had the highest sensitivity and ELISA using the IgM antibody and the N antigen had the highest specificity. The sensitivity of LFIA ranged from 52.8% (95% CI 32.9-72.6%) to 82.8% (95% CI 77.0-88.6%), and specificity ranged from 91.4% (95%CI 85.2-95.1%) to 99.4% (95%

Table 5. Antibody test time data.

	Week 1 Sensitivity Range (95% CI)		Week 2 Sensitivity Range (95% CI)		Week 3+ Sensitivity Range (95% CI)	
IgM	23.2% (14.9-34.2%)	50.3% (10.9-81.2%)	51.8% (30.3-69.6%)	74.3% (16.1-99.4%)	53.9% (38.4-68.6%)	90.6% (51.8-99.4%)
IgG	13.4% (4.7-29.6%)	53.2% (28.7-67.6%)	50.1% (24.8-77.0%)	85.4% (48.1-98.1%)	79.7% (71.4-86.9%)	98.9% (86.9-100%)
IgA	28.4% (0.9-94.3%)	-	78.1% (9.5-99.2%)	-	98.7% (39.0-100%)	100% (85.2-100%)
Total	24.5% (9.5-50.0%)	-	84.0% (64.1-93.9%)	-	69.5% (34.8-90.7%)	98.1% (90.1-99.6%)
IgG/IgM	30.1% (21.4-40.7%)	-	72.2% (63.5-79.5%)	-	77.7% (66.0-86.2%)	96.0% (90.6-98.3%)
IgA/IgG	0% (0.0-26.5%)	-	50.0% (18.7-81.3%)	-	87.5% (47.3-99.6%)	100% (2.5-100%)
IgA/IgM	-	-	-	-	-	-

(-) = Pooled data not available

CI 98.4-99.8%). In general, combined IgG/IgM LFIA tests performed significantly better in both sensitivity and specificity than either IgG or IgM LFIA tests alone. LFIA using combined IgG/IgM antibody and the S antigen had the highest sensitivity and specificity. The sensitivity of CLIA ranged from 79.9% (95% CI 73.7-86.0%) to 0.944 (95% CI 90.6-98.3%), and specificity ranged from 95.4% (95% CI 87.5-100.0%) to 98.4% (95% CI 97.0-99.9%). CLIA using IgG antibody and the NS antigens had the highest sensitivity and CLIA using IgM antibody and the NS antigens had the highest specificity. The sensitivity of FIA ranged from 78.6% (95% CI 53.1-100.0%) to 89.0% (95% CI 59.1-100.0%), and specificity across all FIA tests was 95.0% (95% CI 92.3-97.7%). FIA using IgG antibody and the S/NS antigens had the highest sensitivity.[7]

Table 6. Antibody test method sensitivities.

	ELISA Range (95% CI)		CGIA Range (95% CI)		CLIA Range (95% CI)		LFA Range (95% CI)		LFIA Range (95% CI)		FIA Range (95% CI)		GICA Range (95% CI)	
IgM	71% (40-91%)	84.5% (70.7-92.5%)	69.5% (44.3-86.7%)	-	74% (60-85%)	90.6% (51.8-99.4%)	51.4% (26.5-75.6%)	-	52.8% (32.9-72.6%)	69.9% (58.4-79.9%)	78.6% (53.1-100.0%)	86.0% (50.0-100.0%)	74% (60-85%)	-
IgG	69% (48-85%)	85.8% (78.0-91.1%)	87.3% (77.0-93.4%)	-	90% (84-95%)	98.9% (86.9-100%)	76.0% (61.0-86.5%)	-	53.7% (12.3-95.1%)	79.7% (71.4-86.9%)	85.9% (33.9-100.0%)	89.0% (59.1-100.0%)	83% (73-90%)	-
IgM/IgG	69% (50-85%)	93.5% (90.0-97.1%)	90.7% (82.7-95.2%)	-	90.2% (81.1-99.3%)	97.5% (94.0-99.0%)	88.6% (82.0-93.0%)	-	77.7% (59.2-96.2%)	82.8% (77.0-88.6%)	-	-	84% (78-90%)	-
Pooled	84.3% (75.6-90.9%)		-	-	97.8% (46.2-100%)		-	-	66.0% (49.3-79.3%)		-	-	-	-

(-) = Pooled data not available

Zhang et al. found that the sensitivity of ELISA ranged from 69% (95% CI 48-85%) to 71% (95% CI 40-91%), and specificity ranged from 99% (95% CI 96-100%) to 100% (95% CI 100-100%). ELISA using IgM had the highest sensitivity and specificity. The sensitivity of CLIA ranged from 74% (95% CI 60-85%) to 96% (95% CI 91-98%), and specificity ranged from 99% (95% CI 97-100%) to 100% (95% CI 100-100%). CLIA using combined IgG/IgM had the highest sensitivity and specificity. The sensitivity of GICA ranged from 74% (95% CI 60-85%) to 84% (95% CI 78-90%), and specificity ranged from 95% (95% CI 93-98%) to 99% (95% CI 96-100%). GICA using combined IgG/IgM was the most sensitive, while using IgG was the most specific.[5]

CLIA is the most sensitive test method for IgM, IgG, IgM/IgG, and pooled sensitivity. CLIA and ELISA have the highest specificity for IgM, IgG, IgM/IgG, and pooled specificity (Tables 6 & 7).

Sample source (Blood, Serum, Plasma)

Böger et al. found that the combined IgM/IgG test using blood as the sample had the highest sensitivity of 86.3% (95% CI 83.3-88.8%) and specificity of 90.7% (95% CI 90.7-94.8%). The IgM-only test using blood, serum and plasma had the second highest sensitivity of 77.0% (95% CI 74.5-79.5%) and the highest specificity of 93.3% (95% CI 88.6-96.5%), whereas the test using just blood had the highest sensitivity of 78.8% (95% CI 75.4-81.9%) and the second highest specificity of 93.1% (95% CI 88.2-96.4%). The IgG-only test using serum as the sample had the highest sensitivity of 73.9% (95% CI 69.6-77.9%), but did not report specificity, whereas the test using blood had the lowest sensitivity of 66.1% (95% CI 62.3-69.8%) but had the highest specificity of 98.8% (95% CI 95.8-99.9%) (Table 8).[3]

Table 7. Antibody test method specificities.

	ELISA Range (95% CI)		CGIA Range (95% CI)		CLIA Range (95% CI)		LFA Range (95% CI)		LFIA Range (95% CI)		FIA Range (95% CI)		GICA Range (95% CI)	
IgM	99.1% (97.2-99.7%)	1.00% (100-100%)	97.3% (90.0-99.3%)	-	96.7% (92.7-100.0%)	99% (97-100%)	99.6% (97.3-99.9%)	-	91.4% (85.2-95.1%)	98.6% (97.4-99.8%)	95.0% (92.3-97.7%)	-	97% (93-99%)	-
IgG	96.1% (91.0-100.0%)	99.4% (98.8-99.9%)	99.5% (96.5-99.9%)	-	97.1% (93.1-100.0%)	99% (97-100%)	99.0% (95.3-99.8%)	-	91.4% (85.3-95.1%)	98.8% (97.3-100.0%)	95.0% (92.3-97.7%)	-	99% (96-100%)	-
IgM/IgG	96.7% (91.5-98.7%)	100% (100-100%)	96.0% (90.1-98.5%)	-	94.1% (82.7-98.2%)	100% (100-100%)	98.2% (96.3-99.1%)	-	98.4% (96.9-99.9%)	99.4% (98.4-99.8%)	-	-	95% (93-98%)	-
Pooled	99.7% (99.0-100%)		-	-	-	-	-	-	96.6% (94.3-98.2%)		-	-	-	-

(-) = Pooled data not available

CHEST

Kim et al. determined that the overall sensitivity of chest CT was 94% (95% CI 91-96%) and an overall specificity of 37% (95% CI 26-50%).[2] Lv et al. determined that the sensitivity of chest CT for diagnosing COVID-19 was 99% (95% CI 97-100%), when case reports were excluded, the sensitivity decreased to 96% (95% CI 93-99%). They also found a limited sensitivity in patients under 18 years old of 66% (95% CI 15-100%).9 Adams et al. reported an overall sensitivity of 94.6% (95% CI 91.9-96.4%) and an overall specificity of 46% (95% CI 31.9-60.7%).[10] Finally, Xu et al. reported a pooled sensitivity of 92% (95% CI 86-96%).11 Based on these studies, the sensitivity for chest CT ranges from 92% (95% CI 86-96%) to 99% (95% CI 97-100%) and specificity ranges from 37% (95% CI 26-50%) to 46% (95% CI 31.9-60.7%) (Table 9.)

Table 8. Antibody test sample source data.

	Sensitivity Range (95% CI)		Specificity Range (95% CI)	
Blood, serum, plasma	69.4% (66.6-72.1%)	84.5% (82.2-86.6%)	69.4% (66.6-72.1%)	93.3% (88.6-96.0%)
Blood	66.1% (62.3-69.8%)	86.3% (83.3-88.8%)	90.7% (84.8-94.8%)	98.8% (95.8-99.9%)
Serum	73.9% (69.6-77.9%)	82% (78-85%)	-	-

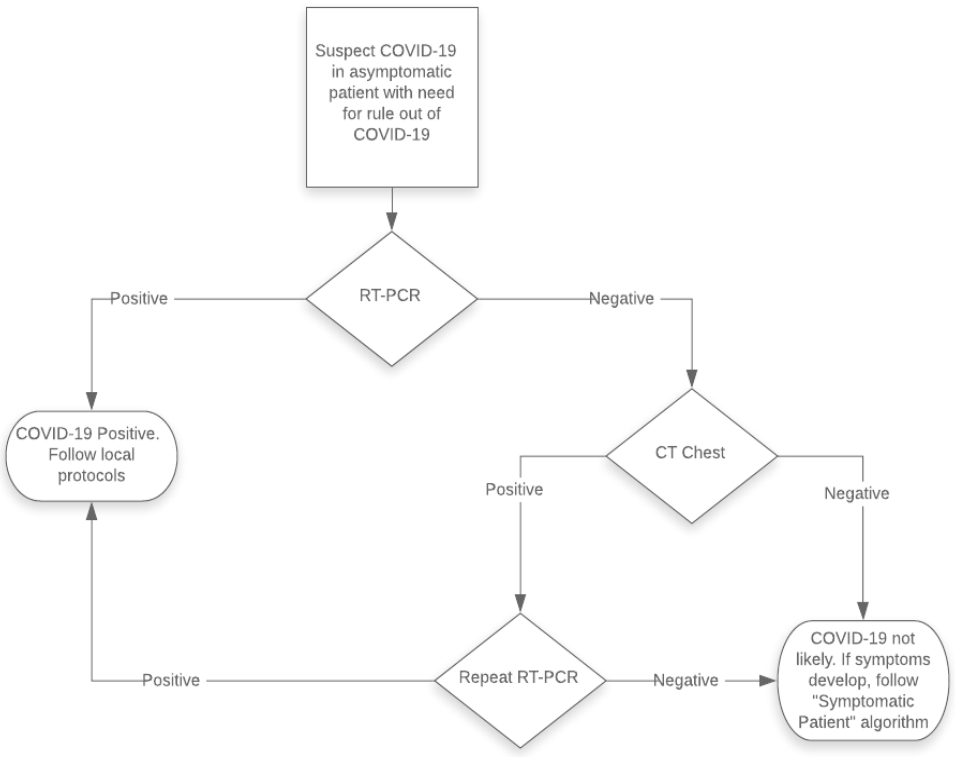
(-) = Pooled data not available

Table 9. Chest CT data.

Sensitivity Range (95% CI)		Specificity Range (95% CI)		PPV Range		NPV Range	
92% (86-96%)	99% (97-100%)	37% (26-50%)	46% (31.9-60.7%)	1.50%	30.70%	95.40%	99.80%

Discussion

Figure 2. Asymptomatic patient algorithm.



SUMMARY OF EVIDENCE

In summary, our comprehensive overview of meta-analyses concurs with the current use of RT-PCR as the first-line diagnostic test in screening for COVID-19 infection in both symptomatic and asymptomatic patients. When the sample is obtained from an upper respiratory source there is a high likelihood of obtaining a true positive result. However, in the event an asymptomatic patient with the need to rule out COVID-19 (i.e. a patient who is currently hospitalized, or an elderly patient in

a nursing facility, etc.) with an incidental finding that is suggestive of a COVID-19 infection (such as partial imaging of the lungs obtained on CT abdomen/pelvis that shows GGOs, for example) has a negative RT-PCR test, we offer guidance based on several factors. Chest CT has been shown to be highly sensitive for ruling out a COVID-19 infection, and the combination of a negative RT-PCR and a negative chest CT points away from COVID-19 as the diagnosis. However, if the chest CT following negative RT-PCR indicates COVID-19, we recommend repeating the RT-PCR, as there is still a roughly 1% chance for false negative. A subsequent positive RT-PCR would likely be a true positive, when correlated with a positive chest CT, whereas a second negative RT-PCR would likely point toward an alternate cause of the abnormal findings on chest CT (Figure 2).

Table 10. Quality assessment of included systematic reviews with AMSTAR tool.

Diagnostic Test	1	2	3	4	5	6	7	8	9	10	11
RT-PCR											
Böger et al. [2]	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y
Kim et al. [1]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y
Antibodies											
Bastos et al. [7]	Y	Y	Y	N	N	Y	Y	Y	Y	N	N
Böger et al. [2]	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y
Caini et al. [3]	Y	Y	Y	N	N	Y	N	N	Y	N	Y
Deeks et al. [5]	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N
Kontou et al. [6]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y
Zhang et al. [4]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	N
CT											
Adams et al. [9]	Y	Y	Y	N	Y	Y	Y	Y	Y	N	N
Böger et al. [2]	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y
Kim et al. [1]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y
Lv et al. [8]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y
Xu et al. [10]	Y	Y	Y	N	N	Y	Y	Y	Y	N	Y

AMSTAR criteria: (1) Was an 'a priori' design provided? (2) Was there duplicate study selection and data extraction? (3) Was a comprehensive literature search performed? (4) Was the status of publication (i.e. gray literature) used as an inclusion criterion? (5) Was a list of studies (included and excluded) provided? (6) Were the characteristics of the included studies provided? (7) Was the scientific quality of the included studies assessed and documented? (8) Was the scientific quality of the included studies used appropriately in formulating conclusions? (9) Were the methods used to combine the findings of studies appropriate? (10) Was the likelihood of publication bias assessed? (11) Was the conflict of interest included? N: no; Y: yes.

In the symptomatic patient, our findings point towards a slightly different diagnostic pathway. The first step, however, is the same. A positive RT-PCR in a symptomatic patient has an exceedingly high likelihood of being a true positive, whereas a negative result would require additional testing. The next step would depend on the duration of symptoms. If the patient has been symptomatic for less than 2 weeks, the next best test would be chest CT, like in our asymptomatic patient algorithm. Likewise, if the chest CT indicates COVID-19, we recommend repeating the RT-PCR for a final answer. If the chest CT does not indicate COVID-19, it is unlikely that COVID-19 is the culprit and we recommend investigating other etiologies. If the patient has been symptomatic for greater than 2 weeks, we recommend the use of serologic antibody testing. This option rivals chest CT in sensitivity, has far superior specificity, spares the patient from radiation, frees up a CT machine, and could even give faster results in the right setting. If the antibody test is positive, this could either mean the patient has an active infection, or they have recovered. Thus, we recommend repeating RT-PCR to differentiate between active infection and recovered status. If the antibody test is negative, there is a very low likelihood of COVID-19 being the cause of the patient's current symptoms, and other options should be explored (Figure 2).

There are limitations to this systematic review based on the lack of reported meta-analytical data on RT-PCR at the time of this publication. The current meta-analyses examining RT-PCR do not report specificities, as they tend to use RT-PCR as the reference standard to which other diagnostic testing modalities are compared. Therefore, the results of our systematic review are limited to only reporting sensitivities of RT-PCR. To combat this, we reached out multiple times to the authors of the meta-analyses in our systematic review for further data, however we either received no response or were informed that they had published all available data.

There is a risk for publication bias associated with component studies of the meta-analyses included in our systemic review. For example, there is a risk that component studies reporting more favorable outcomes (i.e. higher sensitivity and specificity of diagnostic tests)

were more likely to be published, thus potentially skewing the results of the meta-analyses and therefore our systematic review.

Conclusion

In conclusion, RT-PCR tests are most sensitive when the specimen is obtained from an upper respiratory source (sputum or nasopharyngeal swab/aspirate). Serologic antibody tests are most sensitive and specific when testing a patient that has been symptomatic for greater than 2 weeks for IgG or combined IgG/IgM antibodies using a chemiluminescent immunoassay (CLIA) method, with the combined NS antigens, from blood as the sample source. Finally, chest CT testing is sensitive, but shows very poor specificity for detecting COVID-19 based on features such as GGOs, "crazy paving", and other radiographic features. Based on these results, we created evidence-based COVID-19 diagnostic algorithms for symptomatic and asymptomatic patients in the hospitalized and ambulatory settings. We believe these algorithms can aid provider decision making in diagnosing COVID-19, as presented in the AMSTAR Quality Assessment Tool (Table 10).

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Desperate Times Call for Deliberate Measurement: A Review of COVID-19 Aerosol Barrier Devices and a Perspective from a Military Treatment Facility

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The threat of shortages of personal protective equipment have led to innovations in protective barriers to limit the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Those performing aerosolizing procedures such as endotracheal intubation have been designated by the Centers for Disease Control as increased risk of contracting COVID-19. Evaluation of aerosolizing containing barriers for intubation has been limited to date. Some have raised concerns about the universal use of these devices and their possible iatrogenic side effects. It is clear that in time periods of atypical practice that quality and outcome review are critical to addressing novel problems as they arise. An unusual set of injury patterns associated with videolaryngoscopy lead to further evaluation and reconsideration of these devices in our own military department. We review the current literature on this topic and provide a perspective from a single large academic military treatment facility.

The COVID-19 pandemic has impacted every aspect of the military healthcare system (MHS). Even routine procedures like endotracheal intubation for elective surgery could expose providers to SARS-CoV-2. Endotracheal intubation posed a particular risk to healthcare workers in previous health crises such as the severe acute respiratory syndrome epidemic in the early 2000s.[1] The high concentration of COVID-19 particles in secretions of the upper airway[2,3] raises further concerns about COVID-19 transmission to those instrumenting the airway during the pandemic. Current literature and expert opinions note that in addition to direct droplet and aerosol spread of the virus,[4,5] it persists in the aerosolized form and on surfaces for prolonged periods.[6,7]

The American Society of Anesthesiologists (ASA) recommends that procedures on patients with known or suspected COVID-19 infection be performed in a negative pressure airborne isolation room to prevent the spread of the virus,[8] but not all infectious patients exhibit symptoms of COVID-19.[9] Universal personal protective equipment (PPE) significantly decreases the risk of transmission of respiratory diseases,[10,11] but ongoing concerns for the availability of this equipment persist.[12] It has been suggested that physical barriers between patient and those preforming procedures that can generate infectious particles such as laryngoscopy for endotracheal intubation may limit exposure to aerosolized particles and thereby reduce the spread of COVID-19 to healthcare workers. These devices could additionally provide protection in the face of PPE shortages.[13,14]

The most commonly described solution to add another protective layer between the patient and those performing aerosol generating procedures is a ridged acrylic or clear plastic box.[15-18] Additional modifications to these boxes consisting of soft plastic bags and a frame could allow for more freedom of movement, less cost, may improve visualization and maneuverability during the procedure, and allow for suction to potentially evacuate any infectious particles that are produced within the barrier device.[19-21]

The effectiveness of these boxes to decrease exposure of laryngoscopists to SARS-CoV-2 remains unproven. The Anesthesia Patient Safety Foundation, ASA, and the American Association of Nurse Anesthetists do not have an official position on the use of these barriers and recommends local evaluation of such measures during the COVID-19 pandemic.[22] To date, qualitative evaluation of these devices using simulated patients rather than actual clinical use is most commonly cited as proof of efficacy. Simple evaluation of florescent particles from a simulated cough,[16] and the visualization of vapor trajectory within and around boxes have suggested that they could be

effective to decrease exposure to infectious material.[23] Analysis of air movement in these boxes using high-speed photography showed that with deep exhalation by the subject in the box air moved out of the box. This escaping respiratory effort and potential infectious agents were mitigated with additional draping over the open side of the box. Photography also documented air movement through the hand holes utilized by the laryngoscopist.[24]

More recent quantitative methods using particle detection devices have been used to evaluate aerosol limiting devices. A group of military otolaryngologists created a box that applied negative pressure using hospital wall suction within the frame of the device frame itself.[25] A decrease of aerosolized and smoke particles inside the device was observed over time. When a single working port was cut in the device there was not a significant increase in particles detected external to the device while suction was applied. However, when the device suction was turned off there were significantly more external particles compared with the system with the suction on. Simpson et al used a particle detector to determine the amount and size of particles near a larygoscopists head from a simulated cough every 30 seconds over a 5 minute period when either no barrier or 5 other variations of ridged boxes with openings, suspended plastic sheets, and a sealed box with rubber gloves incorporated into the wall of the box were used. There were no significant differences in aerosolized particles detected at the laryngoscopist's head between no barrier and the open boxes or the plastic sheet. There were fewer detected particles when the sealed box was used with suction applied through a viral filter when compared to no barrier. The aerosol box with hand holes was actually associated with an increase in some sizes of particles detected at the laryngoscopist's head at 300 seconds compared to no barrier. The authors felt that the arm holes allowed air and particles to move out of the box with coughing and to be directed toward the laryngoscopist and their assistants. A nearly complete seal with negative pressure greater than that created by standard hospital wall suction may be necessary to decrease respiratory particle exposure to the operating room.[26] Limitations in mobility within these sealed boxes made intubation essentially impossible.[3] The lack of a control for these experiments is notable and necessitates additional research before definitive determinations about the benefit or harm of these devices can be made.[27]

Some have raised safety concerns about aerosol limiting intubation boxes. The limitation of the larygoscopists movement could increase the risk of failed airway instrumentation.[28,29] Ridged acrylic boxes with hand holes for laryngoscopy have been shown to increase the time to successful intubation in simulated intubations on manikins when PPE is donned. PPE breaches were also common during these studies.[30] Limited vision from face shields, incomplete clarity of the barrier or plastic drape, the narrow view of video laryngoscopy view, less than ideal positioning due to decreased ability to manipulate the patients head and neck in the device, and limited space inside the device to maneuver the laryngoscope and endotracheal tube could all impact the ability to maneuver effectively when using these devices. In addition to the concerns with maneuverability, the risk of increased cognitive burden and decontamination needs for these devices and possibly the hospital suction system have also been cited as limitations.[24] Cognitive overload can lead to worse outcomes in airway management.[31,32] Sound methodology to evaluate these devices is critical. The risk of perceiving new technologies created to address a novel problem as beneficial when they are in fact not is well described.[30,33,34] In a pandemic where anxiety about the risk of infection remains high, empiricism must not be limited by the rapidity of this evaluation. The US Food and Drug Administration has acknowledged the importance of these possible risks and in particular the limitations of protective barrier enclosures without negative pressure to patients and those performing aerosol generating procedures in a recent letter to healthcare providers.[35]

Figure 1. Walter Reed Virus and Infection Risk Reduction Ultrafiltration System.

At Walter Reed National Military Medical Center (WRNMMC), an intubation box was improvised using a translucent bag with a drawstring placed over a PVC pipe frame (Figure 1). Holes cut in the bag allow

for access by the anesthesia circuit and the provider's hands. The Virus and Infection Risk Reduction Ultrafiltration System (VIRRUS) airway box is placed over the patient's head and shoulders, the anesthesia circuit is applied to the patient for pre-oxygenation, and the draw string is cinched over the chest. After rapid sequence induction, a video laryngoscope is used to facilitate intubation. Thanks largely to quality and patient safety monitoring efforts, injuries in two separate patients requiring inpatient admission were discovered within a two week period when this device was being used for all patients receiving intubation for general anesthesia as part of enhanced COVID-19 precautions. These injuries occurred in patients under 165 cm using a video laryngoscope. Both patients had radiographic evidence of injury in the deep neck tissues and mediastinum requiring antibiotic treatment and nil per os for 5 days. In the two years prior to these cases, there were no known deep structure injuries at our institution associated with video laryngoscopy. Universal use of these devices has essentially been abandoned at WRNMMC after review within our department regarding the injuries and further discussion with colleagues from other military treatment facilities (MTFs). After cessation of routine use of these boxes, we have had no deep structure injuries associated with video laryngoscopy. Anecdotal reports from other MTFs note that the devices were either never adopted or were used solely during the period of limitation of elective surgeries and have subsequently been abandoned due to concerns that they are cumbersome and an overall decrease in the perceived risk of COVID-19 infection with endotracheal intubation. Adequate supplies of PPE in MTFs and a resumption of elective surgical procedures with universal COVID-19 testing unavailable to many non-governmental institutions likely contributes to these perceptions. If these realities change it is possible that these barrier devices would receive renewed popularity.

Injuries associated with video laryngoscopy are well described. A recent review by Schwartz[36] succinctly and thoroughly reviews the recent literature on this topic. While rare, injury from video laryngoscopy is more common than from direct laryngoscopy.[37] Most of the injuries described occur in the right side of the pharynx and were localized to the soft palate.[38] The need for surgical repair was infrequent.[39,40] Rigid stylets are documented to play a role in injuring oropharyngeal tissue given the sharp angle and non-malleability.[41,42] "The blind spot" is a common theme described in literature.[36-38,40] During video laryngoscopy where the laryngoscope is placed in the oropharynx but the view of the glottis is not yet obtained, the exact location of the blade and styleted endotracheal tube are not known to the laryngoscopist. Direct visualization of the placement of the video laryngoscope and endotracheal tube into the pharynx are important steps in avoiding injury to the airway and other structures in the oropharynx. This is perhaps more difficult with aerosol containing boxes than without.

Most of the reported injuries associated with videolaryngoscopy involve the indirect view video laryngoscope.[43] The majority of these injuries were noted to be confined to the soft tissues of the oropharynx. This contrasted to the injuries at our institution where we noted deep neck and mediastinum impacts. While deep structure injuries are reported, they are less common.[44-46] The neck and mediastinum are at particular risk of infection with trauma to the airway and esophagus.[47,48] In the authors' experience it is not uncommon to place the blade too deep in the airway when the blade is not visualized into the oropharynx, obtaining a view of the esophagus or piriform sinus. Obscuration of the laryngoscopist's view by the aerosol barrier box may increase the frequency of an initial deep placement. The tip of the blade is somewhat more angulated than other video laryngoscopes, potentially changing the pattern of force on impacted tissues. The shape of the blade may make injury more common when the laryngoscope is placed deeply. The sense of being separated from the patient by the barrier may also play a role in the sense of urgency for the anesthesia providers to secure the airway leading to aggressive and deeper placement of the video laryngoscope.

In this moment of rapid change and adaptation, awareness of patient safety and patient outcomes is more important than ever. As an enterprise, military medicine prides itself on this rapid dissemination of experience to the benefit of beneficiaries. Detection of deviations from the expected course of care allows for changes and education which can positively impact patient safety.[49,50] This requires consistent measurement over time regardless of the practice environment.[51,52] The COVID-19 pandemic has highlighted the importance of this continued vigilance. Cooperation and information sharing has never been more important. The MHS should consider local and worldwide collaboration and experience distribution now more than ever. Detection of these events serves as an important reminder that when any new equipment is introduced focused training and follow up are necessary.

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Emergency Medicine Medical Director's Perspective: Preparation and Response to a Pandemic

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Introduction

As we look back to our preparation and response, it seems clear that there were distinct phases of the COVID-19 pandemic. Each of these phases brought changes, challenges, and opportunities to adapt and absorb the impacts. Many different hospitals in the US and abroad faced similar phases with different timelines and patient volumes, and dealt with them in a variety of ways. We believe there is no objectively right or wrong way to handle a situation like this, but there may be general principles that help individual institutions develop a response appropriate to their time and situation. The distinct phases of pandemics and the associated medical preparation and response has been described by the Centers for Disease Control and Prevention (CDC), which provides a helpful framework to describe our experience with regards to COVID-19 within our emergency department (ED) and hospital.[1]

Recognition

Our first recognition of the potential scope of COVID-19 came at a meeting of the South Texas Regional Advisory Council (STRAC) on 27 January 2020. The leaders at the meeting expressed their concern that this virus had the potential to cause a pandemic and have far-reaching impacts on the global health system. At the time it was difficult to comprehend how true that statement would come to be, but it was the first time there seemed to be a sense of real concern and urgency regarding COVID-19 in our local area.

Over the next several weeks, leaders from various departments at Brooke Army Medical Center (BAMC) (including Emergency Medicine, Pulmonary and Critical Care, Infectious Disease, Infection Control, Internal Medicine, Trauma, and others) began meeting regularly. We started to realize that no matter how severe the pandemic turned out to be, we would need to have a plan and make preparations to see numerous infected patients, worried-well patients, and continue to see the volume of non-COVID-19 patients we were currently seeing. Ultimately, we would see the very sick patients infected with the novel coronavirus similar to those being reported in endemic areas like Italy and New York City, but we would also have our resources, manpower, and fatigability tested by the large influxes of worried-well and possibly-exposed patients seeking testing and treatment.

We realized early on the severity of the novel coronavirus and the impact it could bring, but we also wanted to make it a priority to maintain the highest standard-of-care we'd worked hard to achieve for all of the other medical and traumatic emergencies that we treat every day such as heart attacks, strokes, sepsis, blunt and penetrating traumas, obstetric and pediatric emergencies, etc. We knew, however, that if the pandemic became pervasive, it would infiltrate our ability to treat all of these more common emergent conditions.

In early to mid-February 2020, we began to have regular email correspondence and in-person meetings with the various hospital departments and stakeholders. An interdisciplinary plan would be essential and we realized that one of the biggest challenges would be processing patients through the ED/hospital and preventing our facility itself from becoming a source of transmission. At this time, influenza was still prevalent and we knew it would be difficult to differentiate between influenza, COVID-19 and other viral illnesses without a rapid and available test for COVID-19, which was still several weeks to months away.

Initiation

In early March, we began to see confirmed cases of

COVID-19 in the US, so our preparation took on a new sense of urgency. Within the hospital, we worked to develop policies and protocols for the evaluation, treatment and admission of COVID-19 and non-COVID-19 patients. In order to approach the potential surge of infectious patients and prevent further spread of illness, we had to address how we moved patients through our ED, while the hospital leadership made plans for changes to patient and visitor flow within the hospital, and to ensure patient safety at BAMC and the associated outlying clinics.

The idea of redirecting patient flow during a pandemic is not new. In fact, there are several organizations that have references available to help facilities organize their workflow to accomplish safe movement in the ED and hospital. The American College of Emergency Physicians (ACEP) website has a practice management section with a working document called the COVID-19 Field Guide, which describes the split-flow emergency department model.[2,3] Our ED colleagues nationally and internationally have followed similar principles in the early phases of the pandemic to promote infection control and prevention.[4] We adopted the idea to create patient under investigation (PUI) for COVID-19 and non-COVID-19 zones of the ED, from the waiting room, to the patient care pods, and to disposition. Within the hospital, similar cohorting plans were being created for separating COVID-19 suspected patients from non-COVID-19 patients. These included plans for separate pathways for Xray/CT/MRI, hallways and elevators, and having separate care wards and ICUs. As mentioned above, we still needed to maintain our ability to see patients with emergencies not related to COVID-19, and those patients needed to be able to safely access emergency care in our facility without being at increased risk of being exposed to COVID-19 during their treatment.

The first re-organization of our workflow was to separate our entrance and waiting room into "PUI" and "non-COVID-19" pathways. At our entrances, we added signs about COVID-19 and our policies and made masks and hand-sanitizer available (and mandatory). We designated medical personnel (enlisted medics) at the entrance of the ED to cohort patients into PUI vs. non-COVID-19 groups. One novel idea we introduced at BAMC was a door-screening decisional support algorithm that was implemented via our medics at the two entrances to the ED. We developed a short screening protocol we called "eCOVID", which was a series of questions about COVID related exposure and symptomatology. Applying the protocol resulted in a score for the patient, with a lower score directing the patient to the non-COVID-19 pathway and a higher score directing them to the PUI pathway. The questions were developed using early data on likelihood ratios for certain types of symptomatology (e.g. exposure, fever, cough, anosmia, diarrhea, etc.).[5-9] While it is important to mention that this scoring system is not validated and did not perform perfectly, its benefits were that it gave our enlisted medics some standardized set of criteria, rather than their individual gestalt, to use in their initial triage of patients into the ED.

In the waiting room, we reorganized the seats to be at least 6 feet apart and gave the patients gloves and sanitizing wipes to clean their seats when leaving. We added plexiglass to our front desk to protect personnel at check-in. The hospital closed most entrances and restricted visitors, and we were able to keep two entirely separate entrances to the waiting room open for the two one-way pathways. In the ED waiting room, patients were triaged separately with our personnel wearing appropriate levels of personal protective equipment (PPE) depending on which population of patient they were treating. As COVID-19 increased in the population locally and we began to understand the widely variable presenting symptoms and prevalence of asymptomatic states, it became more challenging to keep the patients separated.

In a similar manner, the ED itself, which has historically been organized in pods, was partitioned into "PUI" and "non-COVID-19" zones. We utilized our Bravo pod for PUI's, which has clear glass doors for shooting portable chest-Xrays through, and easily visualized monitors from outside the room to minimize the number of times staff entered and exited the rooms. Additionally, Bravo pod has a negative pressure isolation room which we preferentially kept open for times when there was a particularly sick patient that would likely need an aerosol generating procedure such as nebulized medication, high flow nasal cannula, non-invasive ventilation, or intubation and mechanical ventilation. We instructed our staff to minimize the use of nebulized medication whenever possible, and to use a closed circuit ventilator with viral filters and a well-fitting mask if using non-invasive ventilation. High flow nasal cannula became our oxygen support mechanism of choice for hypoxic PUI patients. We developed a COVID-19 intubation tray that was kept in our negative pressure room which had all the necessary equipment to perform intubation in a manner that minimized risk of aerosolization of viral particles – fewest necessary staff in room, rapid sequence induction, video laryngoscopy use, avoid bagging and connect directly to closed circuit ventilator with viral filters in place. This arrangement seemed to work well, and we decided early on that any patient being intubated in the ED should be done in this manner once it became clear

that there was a substantial proportion of COVID-19 positive patients who were asymptomatic.

Similar to "eCOVID", we instituted another novel idea for directing admission flow from the ED to various areas of the hospital before rapid COVID-19 testing was widely available. This was another decisional support algorithm we called the "COVID" score. Rather than being based solely on symptomatology and exposure, it utilized lab and radiology data to assign a score to a patient being admitted as either "PUI" (and thus directed to a COVID-19 ward while confirmatory tests were pending) or "non-COVID-19" (and thus directed to a non-COVID-19 ward without further testing). The benefit of this algorithm was two-fold. First, it allowed us to use a standardized set of criteria to assign patients as low-risk "non-COVID-19" or high-risk "PUI" in order to keep flow in the hospital separate and transmission risk low. Second, this algorithm allowed us to move patients out of the ED before a confirmatory COVID-19 test result (which often took 6-8 hours early in the pandemic) and preserve ED throughput. Both the "eCOVID" and the "COVID" scores were developed during interdisciplinary team meetings with ED, Internal Medicine, Infectious Disease, and Pulmonary/Critical-Care and were agreed upon by all departments, based upon the available evidence-based literature, which helped ensure the protocols were followed from arrival at the door of the ED through arrival on the hospital ward.[5-11]

Acceleration

It should be noted that the dramatic changes to BAMC ED operations mentioned above were all done before there were a substantial number of cases in the local San Antonio, Texas area. Many people (ED Medical Directors included) were starting to wonder if the pandemic would reach us at all, and whether all of the effort was academic. Around that time, prevalence in the US rapidly increased in March to April, and although prevalence in Texas was still low, our planning and operational tempo rapidly changed. The majority of clinics converted to virtual appointments and the majority of administrative staff started teleworking. Elective surgeries were cancelled, but our facility still maintained its Level 1 Trauma capabilities. COVID-19 testing was made available in a tent outside of the facility, keeping many of the worried-well patients outside of our hospital and ED. This goal was supported by our hospital command which turned out to be crucially beneficial to maintain the ER's throughput and operational capability. Our available resources fluctuated throughout this process, including the available PPE, the laboratory testing capabilities, and the staff available due to exposure/quarantine, illness, and deployment taskings for COVID-19 response.

Regular communication with our staff became more vital than ever. The guidance from the CDC, Department of Defense and BAMC changed regularly in response to the information we were learning from China, Italy, New York, and Seattle. In addition to posting signs throughout the ED, we chose to send regular emails from a single source (Medical Directors) on all updates, pertinent research, policy changes, etc. Given our mission is 24 hours and it is not possible to always be present, we made sure our staff knew we were available at all times. We can't emphasize how important dissemination of information became and, with that, addressing any misinformation being circulated amongst the staff.[12]

Additionally, we wanted to ensure our staff felt that we were doing everything we could to keep them protected from occupational exposure. We set bi-level PPE standards (for all patients and PUIs) based on the best available CDC guidance, and regularly walked the ED to reinforce that guidance and make sure everyone knew the standards and were complying. We arranged N95 FIT testing for several brands of N95 masks, set up powered air purifying respirator (PAPR) training available to anyone who wanted it, and worked with Respiratory Therapy and Infectious Disease to ensure we minimized risks during any aerosol generating procedures (AGPs) by utilizing the proper equipment and training. We conducted simulation training regarding the treatment of hypoxic and coding PUIs. We also developed processes to safely reuse N95 masks.

At the end of May, our local government and state officials, as well as hospital leadership recognized that there was a low prevalence of COVID-19 cases in Texas, and the strains on the economy were evident. Restaurants, stores, gyms, parks, schools and small businesses started re-opening. Within the hospital, administrative personnel started to come back to work rather than teleworking, clinics started to have more appointments available, and elective surgeries restarted.

This coincided with the Memorial Day holiday and the re-opening of the economy, and San Antonio experienced a large spike in COVID-19 patients, becoming the third highest city-wide surge of COVID-19 cases nation-wide.[13] As a result there was a rapid draw-down of hospital facilities, non-essential workers, and elective surgeries. One unforeseen benefit of early recognition and preparation was that most of our processes were developed and field-tested during the early stages of the pandemic when the prevalence of disease was low, which afforded us the latitude to continue with our implemented processes and make adjustments as necessary

once the cases began to spike. Many people remarked that when our local case-burden spiked in June and July, we were so used to our processes by that time that it seemed less stressful than the initiation phase earlier in the pandemic.

Deceleration and the New Normal

Throughout the end of July and August, we have seen a decline in the new cases here in San Antonio, which we believe is the result of the widespread public health measures mentioned above. Disease detection, surveillance, and laboratory testing have improved greatly, and there are many promising signs in vaccine development.[14] Locally, our positivity rate has decreased and our hospital COVID-19 census has dropped in accordance. More recently our regional healthcare system stress scores have declined from Severe to Intermediate and briefly into the Normal range.

While we still have imminent concern of resurgence despite the community's mitigation measures, it is again time for our leaders to consider what our new normal will be within the hospital and community. Restaurants, stores, gyms, parks, schools and small businesses are re-opening. Within the hospital, elective surgeries have re-started. We anticipate administrative personnel coming back to their offices, and clinics will begin having more in-clinic appointments. Some level of resurgence is inevitable, and it will be important to avoid complacency, especially as the looming challenge of seasonal influenza is right around the corner, which will undoubtedly stress our system in ways we haven't envisioned yet.

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Rehabilitation Response to COVID-19: Optimizing Recovery and Social Reintegration for Military Beneficiaries

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Abstract

COVID-19 is a novel disease with complex primary and secondary health effects that may significantly impact the functional independence and quality of life of patients and their families. While the term "rehabilitation" is often associated with exercise, the interventions employed by rehabilitation professionals in both the inpatient and outpatient setting are much more complex and very relevant in caring for individuals hospitalized with respiratory infections. Since the start of the pandemic, the Department of Rehabilitation at Walter Reed National Military Medical Center has cared for over 85% of the military beneficiaries admitted to the hospital for COVID-19. In addition to providing acute inpatient occupational, physical, and recreational therapy to help maximize each patient's functional independence, the rehabilitation team has also developed a novel program to help facilitate the safe discharge and successful recovery and social reintegration for all patients with COVID-19. Using a holistic approach, a team led by Occupational Therapy has applied a needs-based assessment of each patient and developed an individualized treatment plan, which employs home monitoring, virtual health interventions, peer support, and augmentation to case management and behavioral health care. The overall acceptance and satisfaction of this program by the patients and staff has been excellent, with early evidence to suggest improved quality of life and possible mitigation of long-term complications. This article describes the development and essential elements of this unique rehabilitation program so that other military treatment facilities may consider implementing.

Introduction

COVID-19 is a novel disease with complex primary and secondary health effects that significantly impact the functional independence and quality of life of patients and their families.[1] While medical interventions for respiratory infections, including COVID-19, are largely centered on preserving and improving respiratory function during the acute phase of infection, serious complications may result from a secondary systemic hyper-inflammation and/or hyper-coagulation response, leading to end-organ damage, macro and microvascular infarcts or death.[2,3] From a rehabilitation perspective, severe impairment and subsequent disability may occur as a consequence of COVID-19 infection or the secondary complications often associated with severe respiratory infections. Conditions such as venous thrombosis, decubitus ulcers, joint contractures, muscle atrophy and cardiovascular deconditioning are common in patients requiring bed rest.[4,5] Similarly, peripheral neuropathies and systemic myopathies have been well described for critically ill patients.[6] Finally, mental health disorders, including post-traumatic stress disorder (PTSD), frequently occur with severe life-threating infections, particularly after ventilation.[7,8]

Although new information regarding the acute effects of COVID-19 emerge on a near daily basis, the intermediate and long-term effects on patients remain largely unknown. This is especially true for active duty military service members. Emerging evidence suggests that patients with COVID-19 may manifest a wide variety of symptoms affecting multiple organ systems.[9,10] More alarming, however, is that a significant number of patients recovering from infection will develop persistent symptoms.[11,12] In at least one study, more than one-third (36%) of Chinese patients diagnosed with COVID-19 experienced neurologic symptoms, including central

nervous system impairments (dizziness, headache, impaired consciousness, acute cerebrovascular disease, ataxia, and seizure), peripheral nervous system complaints (impaired taste, smell, vision, and nerve pain), and musculoskeletal pain.[13] Another study conducted by the Indiana University School of Medicine, characterizes the "50 most common Long Hauler symptoms" for COVID-19 survivors, reporting that more than one quarter (26.5%) of the symptoms were painful.[14]

To facilitate the safe discharge of military beneficiaries admitted to Walter Reed National Military Medical Center (WRNMMC) with a diagnosis of COVID-19, and to help better understand the persistent symptoms or unique challenges that each patient encountered, in April 2020, the Department of Rehabilitation began a telehealth interventional program for all discharged patients. Led by Occupational Therapy (OT), this program continues to foster and promote the ongoing holistic needs of this unique group of patients using an interdisciplinary care model approach, and has uncovered unique interventions to help facilitate recovery, maximize independence, optimize social integration, and hopefully mitigate long-term problems by providing early intervention.

This article describes the continuum of rehabilitative care provided at WRNMMC for patients with COVID-19, illustrates unique case examples of patients' lived experiences, reports the lessons learned through the inter-disciplinary team, and offers recommendations for developing similar programs at other military treatment facilities, including special considerations for service members returning to duty.

Inpatient Rehabilitation Innovations for Patients with COVID-19

Inpatient rehabilitation services played an important role at the onset of the pandemic in planning for the initial COVID-19 response. Working within interdisciplinary teams, physical therapists (PTs) and occupational therapists (OTs) met with critical care specialists, physicians, nurses and respiratory therapists to discuss how best to structure inpatient bed management and staffing so patient care could be preserved in all settings with maximal staff safety. It is widely accepted that early mobilization and rehabilitation of critically ill patients can reduce hospital lengths of stay and improve outcomes, although evidence is still emerging regarding SARS CoV-2 infections.[15,16] A unique challenge facing therapists, however, especially early during the pandemic was establishment of guidelines for the proper use of personal protective equipment (PPE). This was imperative to help limit patient and staff exposure, while still meeting each patient's therapy needs. Physical and occupational therapists have a relatively high exposed risk to patients with respiratory illnesses, as they frequently need to be in direct contact with patients over extended periods of time. Moreover, because therapists treat patients throughout the hospital, they may also be at a higher risk of acting as a transmission vector. While guidelines for PPE use were well-established for known COVID-19 patients, early during the pandemic only symptomatic patients were being tested, which potentially left patients and staff vulnerable to the spread from asymptomatic individuals. Given the high suspicion of possible asymptomatic spread, and out of an abundance of caution, inpatient therapists at WRNMMC were early adopters of PPE practices that assumed all patients were potentially infected and therefore started wearing masks, eye protection and gloves during all encounters, while also requesting patients and visitors to also wear facial coverings. This policy likely prevented the spread of virus among staff and patients, as data now clearly indicates the spreading of the virus can occur among asymptomatic individuals.[17] In addition, therapists also began limiting patient contact by coordinating visits with nursing staff, removing visitors from patient rooms whenever possible, and in some cases performing part of the assessments and treatment sessions from outside the patient room or through the use of mobile devices.

With access to proper PPE and management of workflow to reduce exposure, therapists provided uninterrupted services of COVID-19 and non COVID-19 patients throughout the hospital. Physical therapy (PT) interventions included basic bed mobility, respiratory muscle training, and functional transfers and ambulation with respiratory therapists to improve pulmonary function for patients on and off ventilators. Simultaneously, OTs assessed patient safety, engaged in training to improve independence in activities of daily living, and in collaboration with the recreational therapist, helped bridge communication between patients and their family members at home. While a comprehensive review of inpatient rehabilitation services is beyond the scope of this manuscript, listed below are some of the team's unique approaches to caring for COVID-19 patients.

- *Preserving the Work Force:* Armed with lessons learned from caring for combat casualties since September 11th, 2001, the rehabilitation team quickly adopted staffing schedules that would prevent burnout and allow continuous operation for an unknown period of time. This included the cross-training of outpatient therapists to rotate through inpatient to provide relief to the staff and meaningful backup in the event of any staff member becoming ill.

• *Maintaining Interdisciplinary Teamwork:* Fundamental to delivering the highest quality of rehabilitative care is the coordination of comprehensive, interdisciplinary, holistic care programs with a patient-centered approach early on in patients' hospitalization.[18,19] As COVID-19 cases increased in the intensive care unit (ICU), daily "COVID Rounds" were initiated as an extension to the medical intensive care unit (MICU) team's daily patient care rounds. The MICU COVID-19 team included interns, resident, fellow, and attending medical staff, anesthesiologists, infectious disease physicians, PT, OT, nutrition, social work, clinical researchers, the charge nurse, and each patient's direct care nurse. Extensive discussion and teaching was conducted during daily rounds with attention to ongoing advances in clinical trials, airway management, and prevention of pressure ulcers, joint contractions, and deconditioning. Family members were sometimes called during these rounds to receive updates and daily plans for their loved ones.

• *Early Introduction to Proning:* Evidence demonstrates that patients laying in the prone position are able to achieve greater oxygen saturation.[20] To help build patient tolerance and demonstrate effectiveness, therapists initiated staff training and encouraged patients to prone as much as possible during hospitalization.

• *Knowledge Sharing:* The Acute and Critical Care Rehabilitation Working Group, led by members of WRNMMCs rehabilitation team, shared more than 15 COVID-19 related training resources on its milSuite site to support training across the military healthcare system, reaching approximately 200 PTs and OTs. To further support the mission at WRNMMC, approximately 360 nursing staff members were trained in safe patient handling and progressive mobility. This training was particularly important, as it was unclear whether rehabilitation facilities would accept COVID-19 positive patients early in the pandemic.

• *Telehealth and Communication:* All aspects of telehealth were explored to augment rehabilitation. The early acquisition of iPads and tablets within the Department of Rehabilitation allowed patients to communicate more easily with their care team and families from whom they had been isolated from for days to weeks. This effort further allowed the team to preserve PPE and reduce unnecessary exposure of the inpatient staff. Phone lines in the MICU were activated to further enhance a patient's ability to communicate with the patient care team. To minimize exposure, PTs and OTs phoned into the room of non-intubated and non-sedated patients to gather subjective information from the patient prior to entering for their evaluations. If patients were intubated, therapists called patients' family members to gather prior level of function and home setup data.

• *Recreational Therapy Services:* Recreational therapists utilize recreational activities to help people with injury, illness, and disability participate in leisure activities to enhance their health, function, independence, and quality of life. Inpatient recreational therapy proved to be essential in mitigating the negative effects of isolation among COVID-19 patients by providing psychosocial and spiritual support, cognitive engagement, and physical activity. Interventions include connecting patients with family using tablet computers and smart phones, playing games, reading, listening to music, and using relaxation apps. The recreational therapist also provides patients with individual activity bags including small jigsaw puzzles, word puzzle books, Sudoku puzzles, Legos, adult coloring books and playing cards.

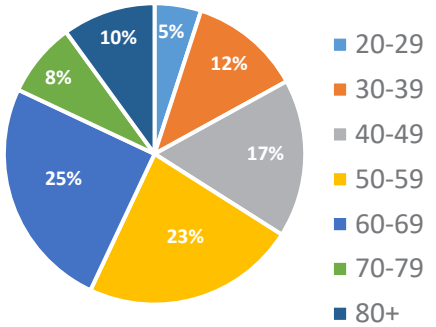
Outpatient Rehabilitation Innovations for Patients Discharged with COVID-19

The rehabilitation team quickly realized that COVID-19 patients discharged from the hospital would benefit from ongoing virtual or outpatient therapy, which could be augmented by an educational reference or guide. In response, a working group was established between PT, OT, Respiratory Therapy, Internal Medicine, Dietary Services, and Physical Medicine & Rehabilitation. Information was gathered from published reports and shared experiences to create the "WRNMMC COVID-19 Patient and Caregiver Guide", translated in both English and Spanish, and accessible at http://crsr.org/#/page/covid/patients. In addition to providing information about SARS-CoV-2 and COVID-19, the guide provides practical advice for setting up a successful home environment that prevents disease spread, while accommodating maximal functional independence. The guide informs the patient, as well as their caregiver, on techniques for preserving energy throughout the day, introducing self-relaxation and positive mental and behavioral health, monitoring physical and emotional symptoms, initiating phased approaches to exercise with clear precautions, recommended diet, and how to access supportive services. The guide is now distributed to all patients discharged from WRNMMC and has been shared with other military and civilian treatment facilities, as well as service members and families deployed overseas. It remains a useful resource for patients as they continue to recover from COVID-19 and is often referred to by therapists engaged with patients during tele-rehabilitation appointments.

In addition to the patients that the rehabilitation team was being consulted on within the hospital, members of the team became increasingly concerned about

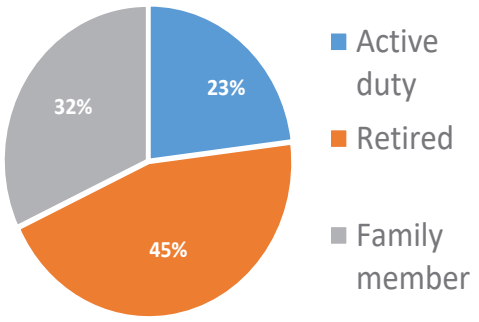
other patients discharged from WRNMMC who had not received inpatient rehabilitation consultations. In response, in April 2020, the Department of Rehabilitation instituted the Virtual Health Post-Discharge Follow-up Program for all patients discharged from WRNMMC with a diagnosis of COVID-19. Led by OT, this program involves an occupational therapist contacting every patient admitted to WRNMMC with a COVID-19 diagnosis within 48-72 hours of discharge home. Independent of the patient's age, length of stay, functional capacity or other co-morbidities, WRNMMC OTs perform a virtual health assessment with focused attention on the following functional domains: pulmonary health, mobility, self-care, diet, home safety, mental health, energy conservation, cognition, caregiver training/education, and access to follow-up care. Upon completion of the virtual assessment, OTs initiate individualized treatment plans for each patient addressing their unique needs. This includes developing goal-directed therapeutic interventions to enhance independence in self-care and energy conservation, monitoring of pulse-oximetry to facilitate safe aerobic conditioning, help in the acquisition of home equipment and home health services, as well as mental health support, education, and engagement with other medical and rehabilitation specialists to ensure comprehensive and holistic care as needed.

Figure 1. COVID-19 post-discharge beneficiary age.



Since initiating the virtual health post-discharge program, OTs have provided ongoing care for nearly all patients discharged with COVID-19 and have made a number of observations of this particularly vulnerable population. The patient demographics have ranged from young active duty services members with relatively short uncomplicated lengths of stay, to geriatric beneficiaries with multiple comorbidities, who required multiple-week intubation and artificial ventilation (Figure 1). Each patient was subsequently contacted one to three times per week, depending on their unique needs, until the patient demonstrated substantial recovery, including pre-morbid level of functioning. Approximately 50% of patients required ongoing skilled OT treatment beyond two weeks post-discharge. At present, approximately one third of the total patients who have been evaluated continue to receive virtual or outpatient OT services. Notably, while only approximately 23% of the hospitalized patients were on active duty (Figure 2), this group represents the individuals who continue to be followed by OT for the longest period of time post-discharge to help them return to full unrestricted duty.

Figure 2. COVID-19 post-discharge beneficiaries.



A more surprising finding of this program was the universal need for post-discharge care coordination services. Of the total patients evaluated by OT, 100% were determined to have ongoing care coordination and/or case management needs, with 37% requiring moderate to extensive case management needs. In August, a social worker from the Directorate of Behavioral Health joined the team and began conducting virtual assessments of these patients, as well. Table 1 lists common findings among most discharged patients, which are further illustrated in selected patient case examples.

Department of Rehabilitation Response to Patient Feedback

Based on trends and feedback received from patients treated with COVID-19, policies were put in place to have OT consulted on all patients admitted with COVID-19, to help not only with inpatient care, but to assist with discharge planning. Inpatient therapists continue to help ensure that each patient receives a comprehensive and holistic discharge plan along with a copy of the *COVID-19 Patient and Caregiver Guide*. OTs ensure that these plans are effectively communicated to both the patient and the patient's family through virtual health. In addition, the Department of Rehabilitation has also initiated the following programs to help address the ongoing challenges faced by COVID-19 survivors:

Table 1. Common findings among patients discharged from hospital with COVID-19.

Patients discharged without scheduled Primary Care Manager (PCM) follow-up	Uncertainty about how to receive profiles/limited duty chits
Challenges in attaining medical supplies/equipment (pulse oximeter, incentive spirometer, acapella device)	Anxiety about not knowing if they needed to be retested prior to reuniting with their families.
Exacerbation of symptoms, resulting in return to the emergency department (ED) or coordinating follow-up with other specialists	Questions about whether follow-up with other medical specialists (e.g. oncology, cardiology, pulmonary) was indicated
Uncertainty about when they could safely return to work/duty	Appetite impaired from loss of taste and smell, negatively impacting PO intake and nutrition
Feelings of stigma associated with disease, impairing reintegration with community and military units	Uncertain how to progression exercise, activity, and pulmonary status; no objective measure of oxygen saturation at home early on
Patient concerns about reintegrating with family following isolation at home	Difficulties and significant delays in receiving home health services
Patients and family caregivers requiring additional education on CDC recommendations including quarantine	Lack of instructions on how to return home O2 tanks

• *Issuing pulse oximeters and SpO2 education prior to home discharges:* As discovered in the feedback from patients, a significant amount of anxiety was created by patients not having objective guidelines for activity monitoring or progression of exercise. Moreover, since a number of patients had already experienced "silent hypoxia," or low blood oxygen saturation levels in comparison with their other vital signs, this only exacerbated their anxiety and reluctance to engage in home exercises. The Department of Rehabilitation secured, issued, and provided training on the use of pulse oximeters for every patient diagnosed with COVID-19 prior to discharge home. They also educated and trained patients on the use and cleaning of incentive spirometers. In addition, the rehabilitation team utilized the Borg Rating of Perceived Exertion scale and the Fifteen-Count Breathlessness Score as subjective measures of activity tolerance. This combination of actions has allowed patients and family members to log progress of recovery, and therapists to receive real-time feedback during virtual health treatment on each patient's pulmonary and cardiovascular recovery. Therapists continue to follow standardized guidelines (Table 2).

• *Cognitive and Brain Fog Interventions:* Many patients diagnosed with COVID-19 reported "brain fog" or cognitive changes associated with the virus. The patients' specific complaints included short-term and working memory deficits, "tip-of-the-tongue" phenomena/word-finding deficits, slower information processing speeds, difficulty concentrating, increased distractibility, and tangential and circumferential thinking and speech. Given the high prevalence of cognitive dysfunction reported by COVID-19 survivors, the OT team initiating screening of patients utilizing the Saint Louis University Mental Status (SLUMS) examination and the Montreal Cognitive Assessment – Blind (MoCA-Blind). These cognitive screens were selected due to their availability, brevity, ease of administration, and focus on verbal items rather than paper-and-pencil items. The overwhelming majority of those screened demonstrated at least some cognitive impairment or limitation, according to the scoring guidelines. When cognitive issues are identified, the virtual health OT team refers these patients to the National Intrepid Center of Excellence (NICoE) Brain Fitness Center, where specialists complete a battery of more refined cognitive testing, employ biofeedback sensors to help patients monitor their stress levels during daily activities, and introduce brain-training software accessible by smartphone.

• *Education and Coaching in Energy Conservation:* All COVID-19 patients treated at WRNMMC have demonstrated fatigue and significantly decreased activity tolerance during their hospital stay. The majority of them continue to report low energy and an inability to return to their prior level of functioning several months following diagnosis, regardless of age and presence of comorbidities. Therefore, energy conservation education, which is recognized as an important part of the recovery process for those with pulmonary conditions[21,22] emerged as a universal intervention employed by the OT team. Using the Person-Environment-Occupational Performance (PEOP) frame of reference and motivational interviewing strategies, OTs gain a holistic view of each patient and mutually collaborate on ways to implement energy conservation techniques that match his/her functional capabilities, environment, and goals. For example, in the early stages of recovery, a patient who enjoys cooking may choose to complete meal preparation tasks in a seated position to avoid overexertion. As the patient's recovery progresses and he prepares to return to work, he and his OT will discuss strategies such as scheduling more complex work tasks around the time of day he performs most optimally, and scheduling 10-minute breaks every hour. These treatment sessions have proved to be critically important for active duty service members who initially have difficulty with accepting and accommodating to a slower pace of life while recovering.

• *COVID-19 Survivors Peer Support Group:* Upon noticing common themes and trends among individual post-discharge patients, the OT team initiated a voluntary, virtual weekly peer support group for patients

diagnosed with COVID-19 in June 2020. The group is open to all COVID-19 survivors who were admitted to and discharged home from WRNMMC. Since its inception in June 2020, many COVID-19 survivors have attended. While all beneficiaries are invited to join, the majority of members are service members (mix of components) and retired military.

Table 2. Therapy/activity pulse oximetryguidelines.

Therapy should stop if either of the following two criteria are met:
1) The patient has a > 4% drop from basal O2 saturation
2) The patient's O2 saturation is ≤ 88% (but as above describes, once you get below 90% there is a potential steep drop, so therapists and patients need to be really careful.
Therapy should stop and patient should receive acute medical care if any of the following:
1) Sustained increased need for supplemental oxygen to maintain previous baseline oxygen saturation.
2) Sustained drop of ≥ 3% from baseline (i.e. at rest)
3) Sustained Shortness of Breath (SOB) after discontinuation of therapy
4) Any new Chest Pain or Productive Cough

• *Weekly Post-Discharge COVID-19 Multidisciplinary Rounds:* Rehabilitation specialists (PT, OT, Physical Medicine & Rehabilitation) engage in weekly patient virtual discussion rounds along with Internal Medicine, Social Work, and other adhoc members from nursing case management, behavioral health, and orthotics & prosthetics. During these rounds, team members share notes and brainstorm treatment plans and strategies to help address problems that patients have encountered at home or in the workplace since their discharge. The weekly support group and these weekly rounds have helped to uncover common findings among many COVID-19 survivors, especially those who continue to have protracted recoveries. These findings are as follows:

- *Pervasive social isolation/stigma* – Most members of the peer support group have described a feeling of being stigmatized once diagnosed with COVID-19. One group participant described his COVID-19 diagnosis as "like having HIV/AIDS in the 1980s." Other members mentioned feeling like a "leper" in their social groups. All group members shared that certain friends and family have left them out of gatherings or refused to visit them following their diagnosis. Many reported that they even felt stigmatized by medical staff providing their care. Half of them mentioned social media's profound impact on their mental health and regretted disclosing their COVID-19 positive status on a social media. They explained that they posted with the intent of warning others of the threat and promoting safety, but stated that they felt as if they had created a permanent record of their medical condition, and increased engagement with those promoting conspiracy theories/"COVID-deniers."

- *Physical changes and fear of the unknown* –The majority of group members reported feeling healthy, fit, and strong pre-infection and noted feeling surprised by the severity and duration of their symptoms. Many described persistent physical changes, including significantly decreased endurance and strength, lasting over two months. The same members discussed feelings of trepidation and anxiety around returning to their prior state of health. Their fears included how their symptoms would progress or resolve, their overall prognosis, and the long-term effects of COVID-19, given the reported pervasive multi-organ system damage the virus can cause. All group members have wondered if and when life, and their health status, might return to "normal."

- *Cognitive changes* – As mentioned above, many group members have described experiencing "brain fog," including problems with memory, attention, and concentration. Many group members related their experience of walking into the kitchen or grocery store for a simple item and returning with a different item each time. One member provided examples of tangential or circumferential speech. All described a pervasive need to compensate for the changes in memory and attention by using memory aids or taking increased time to perform more complex tasks. These cognitive issues resulted in patients experiencing difficulty in limited social settings. Patients cited feelings of embarrassment and social awkwardness when they were unable to follow a conversation and contribute meaningfully. Some patients had to ask others to repeat the question they had just asked, leading to stilted, slower social interactions.

- *Mood changes*: Many patients with COVID-19 diagnoses have complained of mood changes that impacted their personal relationships. These patients told stories of feeling tense, negative, hostile, critical of others, and impatient. Many reported that they had experienced increased interpersonal conflict and that they had chosen to distance themselves from friends or family members.

- *Trouble with return to work, return to duty*: Coupled with patient reported physical and cognitive fatigue, many survivors who were employed prior to their diagnosis have found it difficult to return to work. In fact, according to a recent study, 64% of US households in

which at least one member contracted COVID-19 experienced financial difficulties, such as reductions in pay or loss of employment.[23] Of those reporting financial concerns, patients with National Guard or Reserves status who had contracted COVID-19 while activated and were slated to return to the civilian workforce appeared to be the most concerned. Other service members feared that they would be unable to return to their positions or that they might be passed over for future promotions. Some were unsure whether they would be capable of passing their physical fitness tests. Aside from the financial concerns, most of the active duty patients also derived a sense of purpose and self-esteem from their occupations and feared losing this important role and piece of their identities. Finally, many were accustomed to the rigors and strict schedule of military life and felt demotivated without a routine.

Discussion

The goal of rehabilitation is to optimize the recovery of an individual suffering from an injury or illness in order to promote their safety, maximal functional independence, highest quality of life and meaningful social integration. Effective rehabilitation programs employ holistic assessments by specialized inter-disciplinary teams and develop treatment plans based on patient-centered goals. Rehabilitation specialists employ a variety of creative approaches to facilitate patient and family education, mitigate secondary injuries or illness, and improve cognitive, behavioral, and physical function through the use of therapeutic exercises, assistive technologies, counseling, and compensatory or facilitative techniques. These fundamental principles of rehabilitation can and should be applied to all conditions, including the novel disease associated with infection with SARS-CoV-2.

Although there have been increasing reports in the medical literature describing rehabilitation efforts for patients with COVID-1924,[25,26] this is the first report that describes rehabilitation practices in a military treatment facility and the unique challenges encountered by military beneficiaries, particularly active duty, reserve, and national guard service members. Similar to other reports, our rehabilitation team has observed significant challenges for patients recovering from COVID-19 related hospitalization. This has been especially true for patients, especially active duty service members, who were in previous excellent health prior to their infection. These patients often report persistent fatigue, cognitive fog, and stigma associated with their infection, which have negatively impacted their successful reintegration with their families and return to duty.

To meet the special needs of military beneficiaries with COVID-19, the Department of Rehabilitation at WRNMMC has observed the continued benefits of an OT led post-discharge virtual health intervention. Occupational therapists are uniquely skilled at performing comprehensive holistic assessments of patients with complex functional limitations, which can be effectively performed through current telehealth platforms. In addition, Army OTs serving within the Holistic Health and Fitness (H2F) System educate and coach soldiers on mental and physical performance strategies, including habit change, energy/arousal regulation, and breathing techniques to optimize performance and lethality, which have direct applicability to service members recovering from COVID-19, particularly as they prepare to return to duty. Similarly, military PTs with experience in treating combat casualties also possess unique skills in providing holistic assessments and innovative treatment plans to individuals with multisystem disease, injury and impairment. Together, as part of a rehabilitation interdisciplinary teams military OTs and PTs are uniquely qualified to meet the physical, psychosocial, and cognitive needs of a very heterogeneous group of patients with COVID-19.

In addition to traditional rehabilitation approaches, the team at WRNNMMC has also witnessed the added benefits of building patient resilience and recovery through unique programs such as peer support groups, frequent home monitoring by engaged and caring therapists, education and coaching on energy conservation and compensatory techniques. They provide necessary counseling to alleviate patient anxiety by normalizing frequently expressed constellations of physical, cognitive, and psychosocial symptoms experienced by patients with COVID-19, reassuring them that they are not "crazy." In fact, their symptoms are commonly seen, but will continue to improve with hard work, perseverance, and continued compliance with the established rehabilitation program.

Although it is premature to assess the full impact of the rehabilitation programs that have been developed at WRNMMC in response to COVID-19, early indications suggest of the program's success, as patients continue to report high satisfaction with the support they have received and continue to show functional improvements. Of the total patients seen since the end of April, 75% have been successfully discharged from the program because they have regained pre-infection functional levels. It is our team's experience that early rehabilitation intervention during the acute and subacute phase of COVID-19, especially during the inpatient to outpatient transition, is critical to successful recovery and may play a role in mitigating the risk of long-term complications.

Conclusions

While this descriptive report only represents a small cohort of patients that have been hospitalized in the United States with COVID-19, it is the first report of the unique challenges experienced by US military beneficiaries and service members, during the initial post-discharge convalescent period. We have demonstrated that a rehabilitation based post-discharge virtual health intervention, led by Occupational Therapy, is feasible to implement at a military treatment facility and has a positive influence on patient outcomes and experience. Further study is needed to assess the intermediate and long-term effects of acute rehabilitation interventions for patients hospitalized with COVID-19, including its influence on return to duty for military service members.

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Bench Building during COVID-19: Creating Capabilities and Training Teams

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Abstract

Background: Keller Army Community Hospital, a 12-bed community hospital located in the Hudson Valley of New York State, within the pandemic epicenter anticipated the surge of critically ill patients, which would overwhelm local resources during the coronavirus pandemic sweeping across the globe. In this facility, there were no Intensive Care Unit (ICU) beds and resources were mobilized in order to create a negative pressure Corona Virus Unit (CVU) consisting of seven ICU beds and two step-down beds. Although the creation of the CVU decreased the non-COVID inpatient capacity to five beds, the hospital also formulated a plan to expand overall bed capacity from 12 inpatient beds to 45 beds within 24 hours.

Objective: To create a ICU embedded within a CVU and implement a three day curriculum to prepare four mixed teams of critical care and non–critical care staff nurses to manage critically ill patients with the novel coronavirus disease 2019 (COVID-19).

Methods: Nursing leaders and hospital education staff developed a critical care curriculum utilizing Elsevier didactic, the DoD COVID-19 Practice Guide, and hands-on training for 34 nurses.[1,2] Nurses had varied scope of practice levels from licensed practical nurses to advance practice nurses, with diverse critical care expertise to non–critical care nursing staff from the primary care medical home (PCMH), all of which participated in the cross-leveling to the CVU unit during the pandemic response. Educational elements included PPE donning and doffing, mechanical ventilation, central venous catheter maintenance, arterial catheter management, hemodynamics, and critical care pharmacotherapy. A medical model skills station with common critical care equipment such as ventilators allowed for instantaneous feedback and 13 hands-on skills training.

Results: A fully functional ICU and CVU was created with thirty-four nurses who completed training within seven days with a didactic completing rate of 94.65 % and 100% hands-on skills. The program endures with monthly tailored re-fresher training to improve efficiency and maintain critical competencies. The team maintained operational readiness through the surge and remain resolute for the next surge.

Conclusions: On-going program execution and evaluation continues to develop new staff members due to permanent change of station, recent on-boarding, or because of evidence based clinical guideline changes. Training has continued, but shifted to include normal inpatient operations over the summer of 2020. Re-fresher classes covering the treatment and care of COVID patients continue with the anticipation of a second wave surge of COVID-19 cases emerges this fall based on epidemiology predictions.

Introduction

From the beginning, epidemiologists had predicted exponential increases in COVID-19 cases in New York State, due to the density of the population and the very nature of community spread. Their projections also came with an ominous warning that our current healthcare systems would quickly be overwhelmed. New York State government officials in response directed all hospitals to double their bed capacity in anticipation of the COVID-19 surge in cases and hospitalizations. The Army and Defense Health Agency also sent warning orders to be prepared to mobilize resources to defend in place.

Our facility, which had no Intensive Care Unit (ICU) beds, had to mobilize physical and human resources to establish a nine-bed Corona Virus Unit (CVU) and to increase the hospital bed capacity from 12 to 45 beds for potential mass casualty (MASCAL) of COVID related patients. To avoid cross contamination of the entire hospital, an independent seven-bed capacity ventilated

Intensive Care Unit within a negative pressure CVU was designed.

Nursing leaders along with the hospital's education department adapted existing competency methodologies for orientation and on boarding to maximize didactic training, track competency and hands-on skills training with daily updates and reports to show progression. The multidisciplinary team consisting of respiratory therapists, ER, and ICU nurses created and implement an abbreviated, focused ICU training program. Designated teams trained together within a controlled environment for hands-on practice in order to prepare the staff to care for the critically ill utilizing evidence based practice (EBP) and repetition of skills.[1,2] In less than 24 hours, a three-day curriculum was developed based on the Army Nurse Corps Critical Care area of concentration (66S) program with focused pulmonary, cardiac, and renal pathophysiology, pharmacotherapy treatment methodologies and incorporating the DoD COVID-19 Practice Guide and Elsevier critical care modules.[1,2]

Methods

Goals to optimize patient care and maintain the health of the workforce was a top priority for the command team.[3,4,5] Half of the 3rd floor of the hospital was converted to an area of negative pressure with controlled entry and exit points. The importance of a geographically separate isolation CVU/ICU allowed for the concentration and separation of personnel and supplies.[3,4,5,6] Logistical and physical modifications utilized unconventional, but effective infection control methods. The heating, ventilation, and air conditioning (HVAC) system was modified to ensure negative pressure flow, utilizing Infection Control Risk Assessment (ICRA) barriers normally used for construction projects. The former Obstetrics and Gynecology (OB/GYN) unit and Obstetrics (OB) operating room already utilized High Efficiency Particulate Air (HEPA) filters and were retested to ensure integrity and filtration by Industrial Hygiene prior to accepting patients. The former 3rd floor OB/GYN operating room, recovery areas, and OB/GYN unit quickly transformed into a negative pressure CVU, with embedded ICU, within days.[6]

Each ICU bed was equipped with a monitor and a mechanical ventilator, which also were transport capable. Dedicated x-ray and ultra sound machines, laryngoscopes, emergency crash cart, and IV and feeding pumps were also easily accessible in the CVU to decrease the amount of foot traffic within the CVU itself.[5,7] Internal communication barriers were overcome by using baby monitors for patients at the nurse's station and two-way radios for staff members in order to minimize exposure during patient care.

Field expedient education and training is embedded in the military culture, which required the training to be efficient and detailed, as well as adhere to non-pharmaceutical guidelines. Use of pre-existing training platforms and methodologies allowed for ease of maneuver. The conversion of the unoccupied space for the simulation laboratory for medical model hands-on skills, with rotation stations for training allowed for spacing of personnel and focused training. Nurses with advanced skill sets were able to "test-out" of training by completing didactic and return demonstration and/or proof of daily competency of the skill (eg. CRNAs and ventilation); whereas, those from non-critical care environments were grouped together and led by a highly skilled nurse who supervised their performance. Positive team training and re-enforcement allowed for the psychological safety of the novice critical care staff.[3] Training was scheduled for both day and night shifts to ensure training was conducive to learning and facilitated education.

Topics were reviewed with the hospital's command team, which consisted of a Certified Registered Nurse Anesthetist (CRNA) and an ICU Clinical Nurse Specialist (CNS), both of whom had access to the DoD's COVID-19 working groups and the Army Nurse Corps training programs.[8] Subjects for training were chosen based on the COVID-19 Practice Guide and the latest EBP clinical care guidelines with on-going evaluation of the disease process and shared understanding of complications, innovative treatments, and predicted disease course to include up to date care modalities.[2] Pathophysiology of the respiratory, cardiac, and renal systems were integrated with the divergent presentation of the illness from acute respiratory distress versus silent hypoxia, the development and recognition of hemodynamic shock, and resulting acute kidney injury were salient to a focus approach for training. The hospital education team utilized the Army's Critical Care Course and printed resource binders for reference on ICU care topics and COVID-19 for review of all classes covered; standard operating procedures were revised from other Army and Defense Health Agency (DHA) ICUs for our organization; multiple on-line resources through the hospital's internal public shared websites and electronic folders were also available. The pharmacy and CVU clinical manager created quick-reference "drip charts" for titration based on available in-patient formulary for continuous infusions for sedation and vasoactive drugs. The charts and training reviewed the expected routes, dosages/concentrations to include bolus and continuous, compatible fluids, and titration considerations.

Respiratory therapists and CRNAs provided instruction

Figure 1. Staff demonstrate donning and doffing of personal protective equipment (PPE) per the CDC standards.

on respiratory failure, acute respiratory distress syndrome, and ventilator management for modes of ventilation, inspiration to expiration ratios, oxygen concentration, ventilator setup and start-up of the machine, common alarms, and tips for troubleshooting of possible problems. CRNAs also provided Advanced Cardiovascular Life Support (ACLS) training that included the American Heart Association COVID-19 changes to ensure healthcare provider safety.[9] In addition, the hospital ethics committee reinforced the COVID-19 ethical guidelines as donning of PPE prior to entering a COVID-19 positive patent room was not intuitive and created moral distress for staff. Addressing these concerns were paramount to ensuring staff safety both psychologically and physically.[9,10]

The OR staff demonstrated donning and doffing of personal protective equipment (PPE) per the CDC standards in order to reduce the risk of cross contamination (Figure 1). Another station with former ICU, Post Anesthesia Care Unit (PACU) and ER nurses reviewed the pathophysiology of ICU patients, to include recognition and treatment of delirium, proning, and decubitus ulcer prevention awareness, pharmacotherapy to include neuromuscular blockade, sedatives, analgesics, and vasoactive drugs (cardiac and renal dose). A skills station with a medical model (Figure 2), which had breath sounds and bio-feedback capability, allowed for hands-on practice with common critical care equipment such as endotracheal and thoracostomy tubes, hemodynamic arterial and central venous monitoring catheters, and both tube-feeding and medication pumps. Documentation in the ICU modules of our Electronic Health Record (EHR) were also reviewed with add row features for lung fields, invasive lines, input and outputs for feeding and residuals, along with vasoactive medication monitoring and ventilator settings.

Results

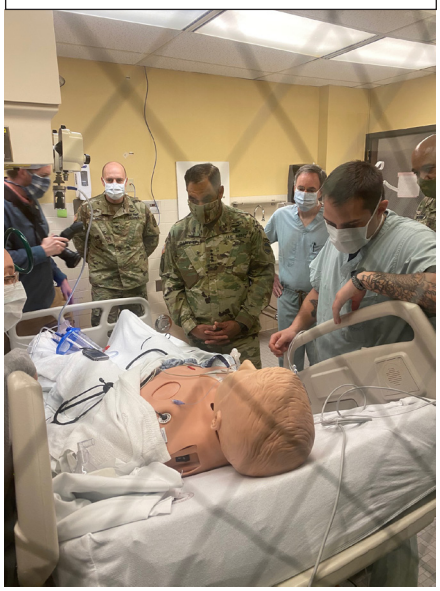
A total of 34 nurses completed the training within seven days. Over 25 skills were assigned by the end of the training with 94.65% completion rate. Staffing mix was based on the DoD COVID-19 Guidelines with teams formed based on ICU experience and skill types. The CVU was functional within one week and maintained operations until 6 June 2020. Currently, with the anticipated surge of coronavirus infections rising after Thanksgiving, the unit remains ready to re-activate again, when local hospitals begin to exceed 80% ICU fill rates. The staff are prepared with a five-day warning order to re-open the CVU once health protections levels increase. The program continues to undergo ongoing evaluation and refinement of the training in order to provide the latest evidence-based care and treatment modalities.

Discussion

This program trained nursing staff to augment a rapidly established CVU with an embedded ICU, integrate critical care focused knowledge and skills within established platforms, partnered experienced emergency room and critical care nurses as part of a cohesive team, while establishing an emergency operations staffing model to care for COVID-19 patients.

During the surge in New York State, we created seven operational ICU beds within the CVU and expansion capability from 12 inpatient beds to 45 beds within 24 hours. The development of the CVU was possible due to the ingenious use of ICRA barriers by facilities to create negative pressure to the former OB/GYN operating room and delivery space, cordoning off portions of the Same Day Surgery and PACU using zippered door barriers.

Figure 2. Staff participate in hands-on practice with common critical care.



Due to the initial lack of knowledge of the course of illness of COVID-19, the program initially focused on ventilated ICU care. As a better understanding of the disease progress developed over time to include the use of

self-proning and high-flow oxygen, the program has adjusted and adapted for equipment training and expected disease progression.[11,12] The timeline for implementing this field expedient program was hastened by the pressing surge of COVID cases in the local community healthcare system and was easily deployed due to the sharing of standard operating procedures, didactic resources, and on-going DoD wide working groups. These groups were able to collaborate and disseminate information quickly with sharing of best practices within the entire enterprise, not just the local organization. Eventually the Army deployed and stood up a COVID-19 field hospital/treatment center in the city of New York at the Javits Center, which allowed for our organization to disband the four CVU teams early in June 2020. The physical aspects of the CVU have not been dismantled as the unit has been placed in a temporary hold status, as our organization still anticipates another COVID-19 surge this fall. As the local healthcare community ICU bed capacity is nearly at 80% fill, we maintain a high level of operational readiness.

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Implementing Pool-Based Surveillance Testing for SARS-CoV-2 at the Army Public Health Center Laboratory and across the Army Public Health Laboratory Enterprise

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Abstract

With limited clinical resources, burgeoning testing requests from Army and other Service units to clinical laboratories, and the continued spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) throughout the military population, the Army Public Health Laboratory (APHL) Enterprise was tasked to establish surveillance testing capabilities for active duty military populations in an expedient manner. Following a proof-of-concept study conducted by Public Health Command-Pacific, Public Health Command-Europe was the first public health laboratory to offer the capability to assess for SARS-CoV-2 in pooled samples, followed closely by the Army Public Health Center (APHC) at Aberdeen Proving Grounds, MD, paralleling the spread of the SARS-CoV-2 virus from China to Europe to the continental US. The APHLs have selected pool sizes of up to 10 samples per pool based on the best evidence available at the time of method development and validation. Real-Time quantitative Reverse Transcriptase-Polymerase Chain Reaction (qRT-PCR) assays using RNA extracts from pooled nasopharyngeal swabs preserved in viral transport media were selected to assess the presence of SARS-CoV-2. The rapid development of initial surveillance testing capabilities depended on existing equipment in each laboratory, with a plan to implement full operational capability using additional staff and common high-throughput platforms. APHL Enterprise has successfully used existing resources to begin to address the changing and complex needs for COVID-19 testing within the Army population. Successful implementation of pooled surveillance testing at the APHC Laboratory has enabled more than 8,600 Soldiers to avoid clinical testing to date. The APHC Laboratory alone has tested over 10,000 samples and prevented approximately 8,600 soldiers from seeking testing with clinical diagnostic assays.

Introduction

The COVID-19 global pandemic is a result of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel coronavirus that was initially detected in Wuhan, China. The World Health Organization declared the outbreak a pandemic on March 11, 2020. The virus is primarily spread via nose and mouth secretions produced by coughing, sneezing, and talking.[1-3] COVID-19 is most contagious during the first three days after onset of symptoms; however, spread and shedding of the virus is possible even before symptoms appear. Asymptomatic carriers who do not show any symptoms may still spread the virus leading to further infections.[2-9] At the date of publication, there are currently no approved vaccines (although a number are in development), and there are only a limited number of effective treatments or therapeutic drugs available as treatment options, depending upon stage of illness. Expanding testing capabilities and the ability to rapidly diagnose SARS-CoV-2 is the critical first step in containing further spread of the disease and is a crucial public health priority.

The most widely used laboratory diagnostic tests for SARS-CoV-2 are Real Time quantitative reverse transcriptase polymerase chain reaction (Real Time qRT-PCR) based tests that are specific and sensitive to detect the presence of SARS-CoV-2-specific gene fragments.[6]

The starting template material for Real Time qRT-PCR is viral nucleic acid (RNA) extracted from human nasopharyngeal (NP), oropharyngeal (OP), or saliva specimens.

At the pandemic's outset, the Army possessed limited surveillance capabilities for detecting infectious diseases. These capabilities were primarily located in clinical laboratories and were insufficient to meet the global demands for COVID-19 pandemic surveillance tests. The Army has previously relied upon the clinical laboratories to provide diagnostic services as a method to monitor disease spread but these laboratories quickly became overwhelmed by the global demands for SARS-CoV-2 surveillance tests.[10] Traditional virus infection and incubation test methods were unable to keep pace with pandemic SARS-CoV-2 virus diagnosis and surveillance requirements.[5,7-9,11,12] The COVID-19 pandemic resulted in a high demand for SARS-CoV-2 testing, leading to global supply shortages of diagnostic test kits and reagents. To help address these shortcomings, the Army Public Health Laboratories (APHLs) set out to conduct pooled surveillance testing to identify asymptomatic individuals in military communities and isolate potentially infectious individuals to reduce further transmission and, thus, the clinical testing burden on military laboratories.

The Secretary of Defense established 4 tiers for surveillance testing within asymptomatic populations.[13] Tier 1–"Critical National Capabilities," Tier 2–"Engaged Fielded Forces," and Tier 3–"Forward Deployed/Redeploying Forces," and Tier 4–"Remaining Forces."[13] Sentinel surveillance of 1% of service members on installations or within their units will also be performed.[13] Following guidance from the Secretary of Defense, Army ;senior leaders mandated a surveillance testing program to identify asymptomatic individuals and isolate those who may spread SARS-CoV-2.

The APHL Enterprise moved to conduct pooled surveillance testing in order to conserve resources and decrease clinical testing burden. Sample pooling involves combining equal amounts of individual specimens collected from several people and conducting one laboratory test on the pool to detect the presence of SARS-CoV-2. This allows laboratories to increase throughput, reduce overall testing time, and utilize fewer materials. In areas of low disease prevalence, samples can be pooled to preserve reagents and test kits that are in short supply. However, pooling can result in sample dilution, leading to reduced sensitivity and false negatives depending on the number of samples used in each pool and the methods used for RNA extraction and testing.[14-16] The APHC laboratory designed and validated a pooling strategy which avoids such sample dilution and associated false negatives, as described in detail below. The goal of the APHL COVID-19 surveillance program is to implement standardized testing using common high-throughput instrumentation sufficient to support routine surveillance of the Army population as desired by senior leaders.

Implementation, Materials & Methods

Using a proof-of-concept study conducted by Public Health Command (PHC)-Pacific in March 2020, detailed below, two of the other APHLs (PHC-Europe and APHC) implemented pooled testing as of late July 2020. Based on the limited data available at the time of method development and validation, pool sizes of up to 10 were selected due to the presumed low prevalence of COVID-19 in the asymptomatic populations. Real Time qRT-PCR assays were implemented to detect SARS-CoV-2. Both laboratories chose to initiate initial surveillance testing using existing equipment including nucleic acid extraction systems and Real Time qRT-PCR machines.

Proof of Concept Study by PHC-Pacific: On March 17, 2020, two laboratory scientists from PHC-Pacific traveled to the Naval Health Research Center (NHRC) Satellite Laboratory at US Naval Hospital Yokosuka, Japan to bring clinical testing online for US Forces Japan. At the time, the US Food and Drug Administration (FDA) Emergency Use Authorization (EUA) protocol employing US Centers for Disease Control and Prevention (CDC) material was the only method authorized to conduct clinical testing and specified specific reagents and instrumentation platforms.[6]

The week after testing started, the laboratory team identified the first laboratory-confirmed case of COVID-19 in US Forces Japan. Less than 24 hours later, the laboratory received NP swab samples from 92 asymptomatic individuals aboard the USS Ronald Reagan. At this point in the pandemic, reagents were in high demand worldwide. To test these 92 asymptomatic patients individually would have used nearly all of the remaining reagent stock. Additionally, these 92 asymptomatic patients did not meet the stringent requirements for clinical testing as was written in the EUA at the time. Any testing of these samples had to be conducted as Research Use Only (RUO) testing to avoid violating the EUA. This RUO testing could not go directly into the patient's healthcare record.

To conserve the limited reagents available, the laboratory team developed a hasty pooling protocol similar to what the PHC-Pacific personnel had been using for vector-borne disease surveillance. Two factors were considered while developing the protocol: the number of samples that should be included per pool, and whether samples

should be pooled before or after nucleic acid extraction. The extraction protocol used by NHRC required manual extraction using a commercial silica membrane-based viral RNA kit to isolate viral RNA from cell-free body fluids with fast spin-column or vacuum procedures. At the time, the viral RNA extraction kits were the limiting factor for testing, so the team opted to pool samples before RNA extraction.

Three assumptions were made when calculating the number of samples to pool: (1) SARS-CoV-2 target cycle threshold (Ct) values would be higher (less virus in the sample) for asymptomatic patients, (2) prevalence of SARS-CoV-2 infection was low (<10%) in the asymptomatic population, and (3) Ct value would increase due to dilution. After consulting with NHRC's laboratory managers, a 1:5 dilution was determined to be acceptable. The approach involved pooling up to 5 samples prior to extraction of the nucleic acids followed by Real Time qRT-PCR. A serial dilution of a synthetic positive control extracted on a silica membrane-based spin column showed increasing Ct values which correlated with the appropriate dilution as expected.

The protocol created a chimeric sample while working in a Class II biosafety cabinet (BSC). To determine the optimal volume of sample to be taken from individual patient tubes, PHC-Pacific divided the volume of sample added to a silica membrane-based spin column under manufacturer instructions (100 µL) by the number of patients in the pool. The elution volume remained the same (100 µL), resulting in a 1:5 dilution. A surveillance pool that detected either the SARS-CoV-2 N1 or N2 gene would provide sufficient justification to subsequently test all samples in the pool individually under the EUA.

The 92 samples were divided into 19 pools of four or five individual samples to create a chimeric sample. Following manual RNA extraction of the chimeric pools, including a process control sample, samples were run on a Real-Time PCR System per the CDC EUA instructions.[6] The pooled sample reports contained disclaimers that the results were RUO-only and not for entry into individual medical records.

PHC-Pacific identified two SARS-CoV-2 N1 and N2 positive pools and ran EUA tests on all potential patients in the flagged pools. Ct values of the positive pools were compared with individually analyzed positive clinical samples (from the corresponding pool). The individual positive clinical sample resulted in a lower Ct, approximately 2 Ct units. This shift was consistent with the data for a 1:5 dilution of synthetic positive control. The extraction control target RNase P Ct values did not change appreciably between the pooled test and the EUA test. This result indicated the chimeric sample aligned well with individual samples. Although this study was on a small sample size (19 pools), it demonstrated that pooled surveillance was a viable means to conserve reagents and sustain higher sample throughput. The sample pooling method reduced the number of columns used to find the two positive individuals by 68% (19 columns for the pooled specimens plus an additional 10 columns for the two positive pools, versus 92 columns if run individually).

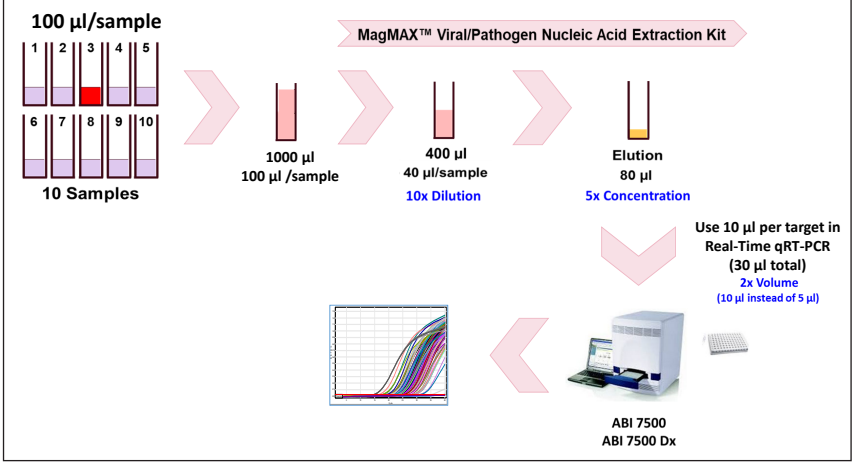
Testing Strategy Employed by APHC: On July 28, 2020, the APHC conducted the first iteration of pooled surveillance testing with the Office of Human Protections #20-848 *Army Public Health Center Lab Expansion of Capabilities to include Human Bio-specimens* protocol. The APHC Laboratory Sciences Directorate developed and validated a process for testing the virus in pools of up to 10 samples by using heat-inactivated SARS-CoV-2 as the positive control. The Limit of Detection (LoD) studies and subsequent workflow APHC has used to test over 10,350 Soldiers thus far is described below.

NP swabs collected from individuals by trained personnel were placed in tubes containing 2-3 mL viral transport medium (VTM). These specimen tubes were shipped on ice to the APHC Laboratory, and were used for pooling and subsequent testing. A specimen log was provided to APHC in advance of package receipt to enable APHC staff time to pre-log the samples into the lab's electronic enterprise laboratory information management system (ELIMS). Sample submissions were coordinated in a manner not to exceed capacity of the APHC Laboratory. The samples were collected on a staggered schedule from the units involved based on their operational planning. Samples were shipped overnight by commercial carriers to ensure arrival of the samples at the APHC Laboratory within 72 hours of collection, as recommended by CDC guidelines.[17]

All pooling and handling of the sample tubes were carried out in a Class II BSC, with appropriate personal protective equipment (PPE) and procedures. As depicted in Figure 1, pools were comprised of up to 10 samples each, and the samples comprising each pool were identified in advance by the submitting organization and packaged together. Samples were briefly vortexed before initiating pooling. From each specimen tube, an aliquot of 100 µL was collected into a 1.5 mL microcentrifuge tube. If fewer than 10 samples were included in a pool, VTM was used to supplement the pool to ensure the final volume after pooling was a uniform 1mL. A volume of 400 µL of the pooled sample was used for nucleic acid extraction on an automated magnetic bead-based nucleic acid extraction instrument using a corresponding viral/

pathogen nucleic acid isolation kit according to manufacturer's recommendations.All viral nucleic acid isolation reactions runs were conducted including a no template control (400 µL VTM) to rule out contamination, and a positive control containing 400 µL inactivated SARS-CoV-2 and human epithelial cell positive control material to ensure successful extraction of all genetic targets. The nucleic acid was eluted in a volume of 80 µL.

Figure 1. Sample pooling strategy.



Extracted RNA (10 µL) was used as the template and Real-Time qRT- PCR was performed on a Real-Time PCR System according to the instructions from the CDC Novel Coronavirus (2019-nCoV) diagnostic kit.[6] All runs included appropriate positive, negative, and extraction controls. Genetic targets were specific for the nucleocapsid gene of SARS-CoV-2 (N1 and N2) and the human RNase P (RP) gene. A sample was considered positive for SARS-CoV-2 if it showed exponential amplification for both N1 and N2 at a Ct value of ≤ 40. Inconclusive samples were positive for RP and either N1 or N2 but not both. Invalid samples did not show exponential amplification for the RP gene, indicating there were insufficient human cells in the sample, and the ability to detect the virus may have been compromised. Negative samples were positive for RP but negative for both N1 and N2.

Data was transferred from the Real-Time PCR instrumentation computers and entered into the ELIMS. Data were reviewed, verified, and reports were generated in ELIMS. Reports were sent to unit customers via email. Samples and the remaining volumes of pooled samples, as well as the elution plates were refrigerated during analysis to allow for subsequent analyses if retesting was required. All were stored at ≤-70C for 72 hours after reporting was completed.

Results of APHC Pooled Surveillance Testing & Validation Studies

As of September 16, 2020, the APHC Directorate of Laboratory Sciences had conducted surveillance testing on 10,350 samples in 1,123 pools (Table 1). Pools were categorized as positive, negative, invalid, or inconclusive based on the CDC definitions.6 Overall, 16.2% of samples were referred for clinical testing. Most sample pools were negative (83.8%), while 13.4% were positive and a small number were either inconclusive (1.6%) or invalid (1.2%). All members of the positive, inconclusive, and invalid pools were referred for clinical testing. Because of time constraints due to soldier travel schedules, the individuals that required follow-up tests were assessed in a clinical laboratory for resampling and testing. The pooled surveillance testing has saved 8,671 specimens from being run in a clinical laboratory with EUA material, thereby conserving limited reagents for the more critical diagnostic testing.

Table 1. Unit based pooling results.

Unit, State	Number of Samples	Pools	Percent Negative	Percent Positive	Percent Inconclusive	Percent Invalid	Number of samples referred for clinical testing
2-101st, KY	3774	421	80.0%	14.5%	2.6%	2.9%	756
1-101st, KY	3680	406	81.0%	17.7%	1.2%	0.0%	713
1-1ID, KS	2896	296	92.9%	5.7%	1.0%	0.3%	209

Pooling results vary based on prevalence of COVID-19. Based on qRT-PCR results, pools were determined to be positive, inconclusive, invalid, or negative. All individuals in the positive, inconclusive, and invalid pools were referred for clinical testing.

Prior to initiating surveillance testing, Limit of Detection (LoD) experiments were performed in two steps as recommended by the CDC in their EUA assay.[6] An approximate LoD was estimated in the first step using a series of dilutions of the reference SARS-CoV-2 virus (Figure 2). In the second step, the actual LoD was determined for the process using three different dilutions of the virus with each dilution having 20 replicates. All the required dilutions of the heat-inactivated reference SARS-CoV-2 virus (www.beiresources.org)

Table 2. Unit based pooling results.

Copies in the Original Sample	Copies in PCR & Ct (Mean ± SD)	Number of Positive Replicates (Out of 20 Replicates) & Ct Values (Mean ± SD)				LoD*
		Real-Time PCR Platform 1		Real-Time PCR Platform 2		
		N1	N2	N1	N2	
3162	15.8 Copies	20	20	20	20	Pass
	Ct (Mean ± SD)	35.06±0.72	36.89±0.66	35.30±0.64	36.91±0.73	
1000	5 Copies	9	14	10	3	Fail
	Ct (Mean ± SD)	N/A	N/A	N/A	N/A	
316	1.58 Copies	0	0	1	0	Fail
	Ct (Mean ± SD)	N/A	N/A	N/A	N/A	

*LoD is the concentration at which at least 19 out of 20 replicates are positive (≥95%). Based on preliminary LoD (Figure-2), LoD of our pooling based approach was determined using three dilutions of the SARS-CoV-2 virus, with 20 replicates each was used to extract viral nucleic acid and subsequent Real Time qRT-PCR. Our pooling based approach resulted in a LoD of ~15.8 copies/PCR using two Real-Time PCR instrument platforms. Ct values (Mean ± Standard Deviation (SD) provided for copies that are ≥95% positive. Calculations only include LoD Passed results. N/A=Not Applicable.

were carried out using VTM. This LoD effort covers the entire workflow starting from nucleic acid extraction as well as subsequent Real-Time RT-PCR using CDC recommended assays N1 and N2 for SARS-CoV-2. RNA extractions and Real Time qRT-PCR were performed as described above.

Pooling is highly beneficial in that it facilitates the analysis of many samples in a short time and saves reagent costs. However, pooling risks false negatives due to the dilution of a positive sample in the pool below the detection level.[14-16] The process developed overcomes this dilution effect by compensating for a 10x dilution at the beginning with a 10x concentration later in the process (Figure 1). This entire workflow involving sample preparation and Real Time qRT-PCR test achieved a LoD of about 15 copies/PCR (equal to 3000 viral particles/ml of specimen).These validation results indicate that the LoD achieved matches with the LoD achieved by CDC without pooling (3000 viral particles/ml of specimen)[6] suggesting no dilution effect due to sample pooling (Table 2). The validation data from this study has been evaluated by A2LA and the methodologies accredited to ISO 17025 standards.

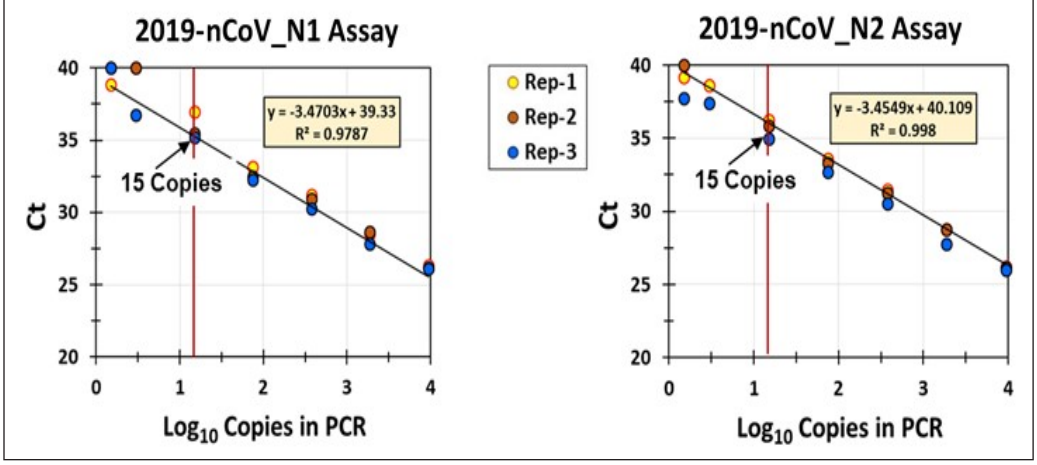
Discussion & Conclusion

Sample pooling is a useful approach to rapidly analyze low prevalence of disease specimen and conduct disease surveillance studies with tremendous time and cost saving benefits.[14-16] However, the practical benefits of sample pooling are dependent on a low infection prevalence in the population being surveilled, as well as the method by which samples are pooled. The number of samples in a pool and the resulting sample dilution may produce false negatives. In most cases, sample dilution is due to the volume constraints (input volume as well as elution volume) associated with the extraction kit being used. Most extraction methods use pre-determined volumes appropriate for individual samples for extraction and subsequent elution. In such cases, the sample would be diluted during extraction because of these restrictions on volume.

SARS-CoV-2 diagnostic test methods that received EUA from the FDA are intended for clinical decision making by healthcare providers, and are therefore intended for individual specimen testing in a clinical laboratory only. One of the earliest diagnostic tests that received EUA from the FDA is the CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time qRT-PCR diagnostic panel.[6] The CDC 2019-Novel Corona Virus Real Time qRT-PCR have been widely used in clinical laboratories in the US. Most of the extraction kits covered in CDC diagnostic test reflect a 1:1 correlation between the starting sample volume and the final elution volume.

Therefore, the original

Figure 2. Standard curve using serial dilutions.



specimen is neither diluted nor concentrated at the end of extraction process and 5 µL of such extracted RNA is used in a 20 µL Real Time qRT PCR reaction. This means that 5 µL of extracted RNA equals to 5 µL of original specimen. Under these conditions the CDC assay kit achieved a LoD of about 15 copies/PCR reaction which is equivalent to about 3000 viral particles/ml of the NP specimen in VTM (typically 2-3 ml of VTM). Our LoD validation study used the CDC detection strategy as a bench-mark for our pooling approach such that 10 µL of extracted RNA from a 10 sample pool equals to 5 µL of specimen from each individual sample of the pool. Hence the initial 10x dilution due to pooling is compensated with 10x concentration at the time of extraction and Real-Time qRT-PCR (Figure 1). In situations where the pool contained less than 10 samples, a fixed 100 µL volume of each sample was used with sufficient VTM added to ensure a final volume of 1000 µL to normalize samples.

APHC has successfully used this pooling strategy in our surveillance efforts to reduce the burden on the Army clinical laboratories. APHC has also positioned itself to continue to rapidly screen many samples to identify pools that require further confirmation by a clinical laboratory.

The application of pooled sample surveillance tests in APHLs has been effective at saving resources (i.e., time and cost) and at rapid identification of asymptomatic COVID-19 carriers for surveillance purpose. It is a valuable tool to preserve Army clinical laboratories for diagnostic resources and patient care.

Using a pooled surveillance strategy, the APHL Enterprise has been able to meet the Army's emerging test needs for identifying asymptomatic COVID-19 populations. In the future, the APHL Enterprise will add the capability to perform high-throughput surveillance testing using an automatic system platform to perform surveillance testing across the Enterprise.

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COVID-19: An Army Brigade Approach to Tracking, Management, and Treatment of Soldiers, US Army 18th Military Police Brigade

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Abstract

As SARS-CoV-2 spread throughout the world military units had to develop ways of combatting risk to ensure force health protection and deployability of their soldiers. Medical functions were impacted and solutions needed to be found in order to incorporate these items as functioning medical platforms. In the following article, we address one unit's individual response to the difficulties faced as a Military Police Brigade in Europe. Lessons learned from the initial wave of COVID-19 across medical operations, medical readiness, virtual health, and behavioral health initiatives can be utilized for better planning and response in the future.

Keywords: SARS-CoV-2, COVID, medical functions, medical operations, medical readiness, behavioral health

Introduction

As the SARS-CoV-2 virus (COVID-19) spread across the globe in early 2020, it directly affected individuals and societies. Not immune to this was the US military community and the 18th Military Police (MP) Brigade (BDE), who changed and adapted methods and operations in order to meet mission requirements while working to stop the spread of COVID-19. Planning a comprehensive response to COVID-19 was challenging across the 10 Medical Functions,[1] given the inherent uncertainty that comes with a pandemic brought about by a novel pathogen. The 18th MP BDE Surgeon Cell is the BDE medical cell consisting of one physician, one medical operations officer, one physician assistant, one senior combat medic, two behavioral health providers, and two enlisted behavioral health technicians. During the COVID-19 pandemic the Surgeon Cell faced significant challenges when first planning a response due to the BDE being geographically assigned across four European countries, with short and long term missions occurring in additional countries in Europe and Africa, and without comprehensive organic medical support. A "team of teams"[2] approach was taken in order to distribute work among the Surgeon Cell, based on expertise and experience, while maintaining a multi- focused approach to the pandemic response. Lessons learned from the initial wave of COVID-19 across medical operations, medical readiness, virtual health, and behavioral health initiatives can be utilized by the 18th MP BDE and other military units to more effectively plan and respond to future pandemics in order to preserve combat power.

Medical Operations

Challenges in medical operations and the lessons learned from those challenges during 18th MP BDE's initial COVID-19 response are most easily categorized into the medical logistics and medical mission command functions. The BDE Surgeon Cell (BDE Surgeon, Active Duty Operational Support – Reserve Component (ADOS) Physician Assistant (PA), Medical Operations Officer (MEDO), and Non-commissioned Officer In-Charge (NCOIC)) worked across multiple functions in order to source proper personal protective equipment (PPE), develop tracking mechanisms, and synchronize reporting efforts across the BDE. All challenges faced in these functions were solved primarily through coordination between staffs and open communication with subordinate units.

Initial Brigade Outreach: One of the first priorities for the Surgeon Cell was to provide education to the formation. This was done by educating leaders during medical portions of leadership meetings as well as producing fliers and handouts which were printed and posted throughout the BDE buildings and workspaces. These informational handouts were also posted on the BDE social media. Educational outreach continued throughout the initial COVID-19 response.

Medical Logistics: As COVID-19 cases began to rise in Italy in early to mid-March 2020, the Surgeon Cell and BDE Staff recognized a need to source PPE for soldiers in the formation. Military Police (31B) soldiers working law enforcement (LE) missions routinely interact with the general public, putting them at heightened risk to exposure to COVID-19. Lessons from Korea, where COVID-19 first impacted Department of Defense (DoD) forces, showed that soldiers, regardless of MOS, had been tasked to support installation gates for screenings to limit potentially infected personnel onto posts. There was a clear need to source and distribute PPE to 18th MP BDE soldiers. The BDE had little to no PPE on hand beyond a few hundred N-95 masks used for engineering operations and a few boxes of gloves for medics in each MP Company prior to the COVID-19 pandemic.

Two immediate challenges presented themselves in sourcing PPE. First, there was a need to determine type of PPE needed and the quantity required by each subordinate unit across the BDE based on respective missions. The BDE risked over or under-ordering without understanding these requirements. Second, there was a need to source the PPE required during a time of incredible demand from the DoD and private business from across the world.

Communication with the higher headquarters' Surgeon Cell was critical in resolving the first challenge. 21st Theater Sustainment Command (TSC) provided 18th MP BDE with a EUCOM "PPE Priority Matrix" to assist with prioritizing and determining quantity and type of PPE to order. The matrix created six groups of similar jobs/duty positions that had suggested quantity and type of PPE based off of their risk of exposure to COVID-19.

Coordination between and across staff sections was necessary once the matrix was completed. The BDE Surgeon and MEDO created a sheet for each type of unit in the 18th MP BDE and their required PPE based off of anticipated missions during the COVID-19 response. The Surgeon Cell NCOIC was then able to provide National Stock Numbers (NSNs) for all of these items and associated costs to coordinate funding with the S8 (resource management section). Each company senior medic was then provided the ordering sheet and ordered items through the Theater Enterprise-Wide Logistics System (TEWLS). In all, the BDE was able to conduct analysis and order PPE (N-95 masks, surgical masks, gloves, gowns and face shields) for a 45-day period of continuous need.

The second issue, that of sourcing the equipment, quickly became evident shortly after placing the PPE on order through US Army Medical Materiel Center- Europe (USAMMC-E). USAMMC-E continued to list PPE items as back-ordered for several months due to historic levels of demand. As a result, it was clear that the initial order would not arrive in enough time for soldiers in 18th MP BDE to utilize that equipment during the initial COVID-19 response. Regional Health Command - Europe (RHC-E) and Medical Department Activity-Bavaria (MEDDAC-B) both had contingency stocks of PPE, but attempts to earmark PPE for LE first responders from this stock were not supported given their need to conserve PPE for medical providers. Further challenging was the lack of a plan from Installation Management Command (IMCOM) and garrison commands to issue PPE to their respective LE units.

Overcoming this sourcing challenge again required coordination between the staff sections, particularly with the S4 (logistics). First, the Surgeon Cell decided to re-distribute a majority of the on-hand OSHA N-95 masks from 15th EN Battalion (BN) amongst the MP Companies. Leaving behind roughly 100 masks for the 15th EN BN, the additional 700 were better suited as contingency stock for roadable MPs given their first responder mission. In conjunction with BDE and BN S4 (logistics) sections, a distribution plan was developed to send those masks across Europe and to the companies. Last, government purchase card (GPC) purchases for basic cloth masks, gloves, and cleaning supplies were conducted with logistics section support and distribution to provide a stock of PPE until the items ordered through USAMMC-E arrived. While IMCOM would have ideally taken ownership of sourcing MPs serving in a Directorate of Emergency Services (DES) role, this internal solution did provide adequate protection to 18th MP BDE Soldiers during the COVID response.

The initial wave of COVID-19 in mid-March 2020 showed a need for the 18th MP BDE to order and maintain a reasonable amount of PPE, namely masks and gloves, in preparation for potential future waves to avoid waiting for back-ordered equipment. Coordination between staff sections and the higher headquarters to purchase and distribute locally sourced items demonstrated an acceptable alternative course of action in the event that the USAMMC-E backlogs. A stock of on-hand PPE

for first responders in the future will likely be the end result of this pandemic response.

Reporting, Battalion Medical Representatives, and Patient Tracking: While a medical logistics challenge was certainly the first visible issue during the BDE Surgeon Cell's response to COVID-19, medical mission command issues quickly took the bulk of the time and effort for the staff. Daily patient tracking reports for soldiers testing positive, tested for, or with potential exposure to COVID-19 became a requirement within the BDE and higher-level organizations as the pandemic more seriously impacted Europe. This information requirement brought about two specific challenges for the Surgeon Cell: how the BDE would receive patient information from units spread across Europe and developing a format in which that information would be reported.

The BDE had its first few patients that required tracking and reporting in mid-March. These soldiers did not have positive COVID-19 tests but did require tracking per US Army Europe requirements due to concerning symptoms. These first patients presented the initial medical mission command issue to the Surgeon Cell as pieces of information and reports of soldiers being tested were coming directly from company commanders to the BDE Surgeon, bypassing the BN assets who were often left in the dark. This ultimately led to incomplete or dual reporting that was confusing for multiple parties. Unlike a Brigade Combat Team (BCT), MP BNs lack BN MEDOs, Surgeons, and PAs, so communication between BDE medical assets and subordinate units often results in reaching directly to company senior combat medics. While unusual, this is normally an effective way to communicate and resolve routine issues. Given the constant need to update the BDE staff on new patients the practice was not effective during a pandemic.

With the assistance of the BDE S3 (operations), the BDE Surgeon Cell created a reporting matrix with seven specific Commander's Critical Information Requirements (CCIR) and COVID-Reporting requirements. This matrix provided clarity on when and to whom a commander needed to report a patient based on that soldier's situation, exposure, symptoms, and other situationally pertinent data. The creation of the reporting matrix was critical in the BDE's success in tracking and reporting accurate patient information during the COVID-19 response. It effectively established needed medical mission command procedures to standardize reporting criteria ensuring patient information flowed from a single source at the BN level.

A spreadsheet product was created enabling the BDE Commander (CDR) to visualize the number of patients currently being tracked (Figure 5). Anticipated return to duty (RTD) times were calculated giving the leadership visibility of the impact to LE power in each unit location. This tracker was published each morning at 0600 and 1700 to provide the BDE CDR with the most updated understanding of COVID-19's impact on his formation. Establishing those reporting times was important to create a steady battle rhythm in an uncertain time, and creating a robust product made it much easier to track the formation accurately.

Last in medical mission command lessons-learned from the patient reporting and tracking focus was the establishment of twice-daily medical syncs and BN-level "medical representatives." As COVID-19 became much more serious in late March and into April, the number of patients being tracked at the BDE level reached a point such that the receipt of COVID-19 Reports/CCIRs to the BDE was difficult to track by the Surgeon Cell alone. The typical medical administration function was not, at first, clearly defined below the BDE without BN MEDOS. The BDE began conducting twice daily teleconferences with BN medical representatives to receive the most accurate information from companies on the ground to fuel patient reports. These representatives (in 709th MP BN a senior combat medic and in 15 EN BN a Physician's Assistant) provided critical information to the BDE Surgeon Cell, ultimately ensuring that BDE and BN information was synchronized and patient's information was accurate. It will be critical that BNs identify these representatives to provide continuity of information during future waves.

Definitions: One of the most challenging aspects of medical mission command experienced by the BDE during the initial COVID-19 response was categorizing/defining soldiers based on their level of exposure to COVID-19. The multiple categories of tracked individuals included soldiers with positive COVID-19 test results, close contacts of positive individuals, those tested with negative results, as well as individuals with flu-like symptoms who were of low concern for COVID-19 due to exposure and travel risk. This variety of patient categorization was important to fully understand as each had a different set of guidelines for their mandated restriction of movement and, as will be later discussed, differing Return to Duty criteria.

Immediately, it was clear that the higher headquarters, RHC-E, and US Army Europe (USAREUR) lacked a standardized set of definitions for different types of patients. As a result, different garrisons, and more concerning, different units on the same garrison, had separate definitions and categorizations of patients impacted medically by COVID-19. In a BDE with units spread

throughout multiple garrisons in several countries, this made patient reporting very complicated.

Table 1. Definitions.

Quarantine	Isolation	Self-Isolation
Exposure without symptoms. Asymptomatic, but exposed to a known or suspected COVID-19 positive person	COVID-19 Confirmed Positive or an individual with a pending COVID-19 test. (referred to as a Person Under Investigation or PUI)	Flu-like symptoms (fever +/- respiratory symptoms) with no clinical indication for COVID-19.

The BDE Surgeon worked with 21st TSC to publish a set of definitions implemented for their subordinate units. These definitions were needed and provided clarity. In future waves of COVID-19 it will be critical for definitions to be standardized at a minimum at the theater/regional level in order to ensure the entire AO is operating with a shared understanding. The definitions utilized for the majority of the COVID-19 response are below. Given the conservative social distancing measures of any symptomatic person during COVID-19, the BDE implemented the "Self-Isolation" category to ensure that those individuals with flu-like illness without clinical indication for COVID-19 could still be tracked and placed in a restriction of movement (Table 1).

Return to Duty: Without information coming from higher headquarters, Public Health Emergency Officers (PHEOs), per the Senior Responsible Officer (SRO) for each Area of Responsibility (AOR), developed their own understanding of the Centers of Disease Control (CDC) guidelines. Each area developed slightly different internal protocols which became very confusing for a Brigade spread throughout the region. The most difficult situations revolved around individuals completing 14 days of isolation due to being a Person Under Investigation (PUI) and those individuals with a confirmed positive COVID Polymerase Chain Reaction (PCR) test.

An individual being isolated for 14 days with a negative test meant that there was a suspicion of a COVID infection due to symptoms and/or close primary contact. These individuals required a 14-day isolation period per USAREUR orders due to their potential risk to the population and formation. The confusion came from the different protocols per SRO area. For instance, one SRO may require retesting before return to duty, one additional retest or two depending on area, while another SRO may require 72 hours of no symptoms prior to release without a retest. There was one incidence where an area did not follow USAREUR guidance and released one family from isolation/quarantine with one negative test although all family members remained symptomatic.

The two ways a confirmed COVID positive individual could be released from quarantine was the test or no test methods. The test method required resolution of symptoms for 72 hours followed by two consecutive negative nasopharyngeal swabs 24 hours apart. The no test method required symptoms resolution for 72 hours and greater than 7 days since symptoms started. Both required a 14-day quarantine period. Although this was also SRO dependent, SRO areas utilized only these two methods. SRO protocols often changed due to testing capabilities based on supplies.

Maintaining communication with PHEOs in each SRO became critical to understanding a particular area's protocols for return to duty. This was accomplished through senior medic communication with local military treatment facilities and, more importantly, routine communication between the Brigade Surgeon and PHEOs throughout the USAREUR AOR. Remaining flexible and continuing communication between the Brigade Surgeon Cell with PHEOs as well as with subordinate commanders was key to success. The BDE implemented a COVID-19 RTD chart that was useful in organizing most RTD scenarios onto a single page.

Contact Tracing: The need for internal contact tracing was determined early in the process. Initial training for tracing at the unit level was performed by garrison PHEOs or their alternate. It was established, by local garrisons, that the PHEOs would run contact tracings of COVID positive individuals with the assistance of a small amount of individuals trained within units. It was quickly found that waiting to contact trace positive individuals increased the number of close contacts. Internal tracing of all symptomatic individuals tested was established internally. It was found that the initial training was not detailed enough to run proper internal contact traces. Internal training was performed through the Brigade Surgeon and a designated Brigade individual to subordinate Battalion and Company representatives. Tracing team procedures were developed to streamline the process and a questionnaire, modified from a USAG-Bavaria Public Health, publication was internally implemented.

Medical Readiness

As COVID-19 spread and the situation began to seriously impact Europe, it became clear that military treatment facilities (MTFs) would have to close for routine

care. The BDE Surgeon recognized a need to forecast potential negative impacts to unit medical readiness as a result of these closures while developing internal solutions to mitigate these negative impacts. The BDE medical personnel, personnel readiness impacts during COVID response, and finding a way to reach patients were all elements that needed to be understood to create and effective plan.

Understanding the need to be proactive was important due the lack of BDE medical assets. The 15 EN BN is the only BDE subordinate unit with an organic provider and accounts for approximately 25% of BDE authorizations. About 75% of BDE personnel are spread to multiple locations throughout Europe and belong to subordinate units that do not have an organic provider at the BN level. These soldiers have primary care managers (PCMs) assigned to MTFs and would be the most affected by MTFs closing to routine and readiness appointments.

In early March 2020, the Surgeon Cell performed a BDE-wide pull of Periodic Health Assessment (PHA) deficiencies through the end of June 2020. A by-name list was then provided to company's First Sergeant (1SG), the senior enlisted soldier, to schedule appointments directly with BDE medical providers. The BDE Surgeon, BDE PA, and 15 EN BN PA leveraged virtual health platforms to complete PHAs and Separation Physicians.

Utilizing virtual health platforms became critical in maintaining BDE medical readiness. As the BDE Surgeon and BDE PA were heavily occupied by COVID-19 medical operations a loose scheduling technique was utilized for mission completion. 1SGs were able to be flexible allowing the clinicians to reach out to soldiers between operational needs for PHA completion.

During COVID-19 response it was a known that negative impacts on readiness categories such as dental, audiology, labs, and immunizations could not be mitigated. The BDE Surgeon Cell worked with garrison MTFs throughout Europe for the planning of future readiness events as restrictions loosened. Building communication between outlying companies and their local MTFs was imperative to improving readiness when restrictions allowed.

Virtual Health

Finding a way to reach soldiers for encounters was the next step. The BDE previously used the RHC-E virtual platform to reach outlying soldiers for Behavioral Health needs. When COVID-19 occurred the RCH-E Virtual Platform became the primary source of communication due to familiarity. To determine the order of communication methods to be utilized the BDE established Primary, Alternate, Contingency, and Emergency (PACE) systems for use. The PACE Plan for virtual health (P: RHC-E Virtual Platform, A: Global Video Services (GVS), C: Other HIPAA Approved Platforms, E: Telephone) was then tested on BDE Headquarters and Headquarters Company (HHC) before expanding to the rest of the BDE. The PACE plan remained flexible as virtual platforms performed differently throughout the COVID-19 Response. For example, the RHC-E Virtual Platform performed well until it was overloaded during normal duty hours after Landstuhl Regional Medical Center began utilizing the system weeks into the response. Later, the RHC-E platform performed better while other HIPAA approved platforms struggled as civilian stateside clinics and hospitals increased their utilization of these platforms. Flexibility of the PACE plan remained key to virtual health encounters.

The use of virtual platforms overall was very successful. These types of encounters increased as BDE organic Behavioral Health Officers used these platforms while Behavioral Health clinics were closed. BDE providers also performed acute appointments, locally and at outlying locations, when MTFs could not see patients in addition to readiness appointments.

Behaviorial Health

From the beginning of the COVID-19 response it was understood that there would need to be changes to and even greater awareness of our soldiers and their interaction with the military Behavioral Health system. The pandemic situation brought on several new stressors from soldiers being at home more and at work less to soldiers already under treatment having less access to their clinician. The 18th MP BDE Behavioral Health team was already utilizing virtual health due to geographical spread of the unit and this became invaluable in reaching out to soldiers in our formation during this response. Treatment and evaluation, outreach, and limitations of each are keys to understanding how to better perform in future COVID-19 waves or other pandemic situations.

Treatment and Evaluation during COVID-19: Outside of the transition to virtual service delivery, Behavioral Health (BH) treatment remained similar during the COVID-19 pandemic. Treatment fell into one of three categories: ongoing therapy and new intakes; emergent command-directed evaluations; and routine evaluations. The majority of Behavioral Health appointments during COVID-19 were for established patients. Presenting issues for new patients were similar to those of existing patients, including occupational stress, relationship problems, reaction to severe stress/trauma, anxiety, and

depression. Of all new intakes during the pandemic, only one soldier reported a COVID-19 specific chief complaint. Several patients, approximately 23%, reported symptoms exacerbated by the secondary impacts of COVID-19 (e.g., restriction of movement, physical distancing) or by anxieties related to health concerns for themselves and others. For example, one individual sought treatment for ongoing separation from her eldest child. While the situation predated the pandemic, the uncertainty of when she would be able to see her child exacerbated her separation anxiety, which in turn led her to seek therapy.

Those reporting COVID-specific BH concerns were predominantly identified through outreach activities; consultation with commanders, chaplains, or other providers; or serious incidents. Those identified via CCIRs with BH concerns were directed to their respective area support clinics for face-to-face evaluation. All potentially high-risk soldiers were assessed face-to-face, with COVID-19 precautions in place (e.g., face masks, hand sanitizer before and after appointments, and sanitization after each patient).

Alternatively, routine evaluations, which include administrative separation and special duty assessments (e.g., recruiter, drill sergeant, CID agent, etc.), were conducted virtually. The 18th MP BDE had a virtual health evaluation policy in place prior to COVID-19, due to the geographically dispersed nature of the unit. Commanders completed the request for evaluation form. Soldiers completed a packet of administrative and screening items per Department of Defense Instruction 1332.143. Once soldiers returned the packets, they were scheduled for virtual appointments. If any safety concerns were noted in the packet, soldiers went to their area support clinics for face-to-face evaluations. At the conclusion of the assessment, in accordance with Department of Defense Directive 6490.14, commanders received documentation with appropriate recommendations via encrypted email. Overall, Behavioral Health treatment and procedures changed minimally during the pandemic. However, there were some limitations to providers' ability to deliver services.

Treatment Limitations: Both new and established patients engaged in telehealth therapy using the RHC-E virtual health platform. Traditional talk therapy, predominantly Cognitive-Behavioral Therapy (CBT), presented minimal logistical issues. However, some treatments required additional training, supervision, and creative implementation. For example, Eye Movement Desensitization and Reprocessing (EMDR) therapy requires the therapist to conduct movements within specific parameters. These parameters, while simple to adjust in person, vary greatly depending on internet speed and size of a patient's monitor, among other limitations. Another treatment, Prolonged Exposure (PE) therapy, involves patients engaging in "in-vivo" exposure (often shopping at busy stores, driving during high traffic hours, etc.). Given the need for physical distancing and stay-at-home orders, there were minimal opportunities for such engagement. Additionally, the risk/reward assessment for having patients leave home unnecessarily was in favor of caution. Other adjunctive therapies that require specialized equipment (e.g., biofeedback) were simply not available.

To address these limitations, Behavioral Health Officers recommended more accessible tools, such as cell phone applications (e.g., Breath2Relax5, Mindfulness Coach)6, handouts/worksheets, and online education programs. These tools also serve prevention and outreach functions.

Prevention and Outreach during COVID-19: The BH team focused on three major lines of prevention and outreach efforts to reach soldiers during the COVID-19 pandemic. They were BH screening of isolated soldiers, dissemination of psychoeducational materials, and physically distanced battlefield circulation. These efforts improved overall wellness of soldiers throughout the BDE and were met with positive feedback. Efforts continued beyond the end of stay-at-home orders due to soldier interest.

Behavioral Health prevention and outreach consisted of three specific lines of effort: BH screening of soldiers in isolation and quarantine; dissemination of psychoeducational and wellness materials; and physically distanced battlefield circulation. During their daily health checks, medics verbally administered the Patient Health Questionnaire-29 (PHQ-2, a brief screening tool for depression) to soldiers in quarantine and self-isolation. When scores exceeded the recommended cutoff (four), medics notified the BH Team. Additionally, the BH Team screened all soldiers on the COVID-19 tracker for BH history within the past year. They subsequently notified commanders of all significant concerns, as well as consistent, positive PHQ-2 screens. All soldiers, regardless of their PHQ-2 score and BH history, received various psychoeducational handouts. These handouts provided education and suggestions to manage isolation-related distress.

In addition to handouts, the BH Team collaborated with the BDE Public Affairs Office (PAO) to produce weekly resiliency videos. Videos ranged from 3-7 minutes; offered tips and education on how to remain resilient and healthy while physically isolated; and utilized multiple BDE staff sections (Equal Opportunities, Sexual

Harassment Assault Response Prevention (SHARP), Family Readiness Support Assistants (FRSA), and Unit Ministry Team (UMT)). Each week the BDE PAO posted a resiliency team video with a similarly themed brief yoga practice to BDE socila media. The BH team led these efforts, leveraging access to social media to ensure wellness during the pandemic.

Soldiers in essential positions continued to work during the pandemic. Their wellness needs were met via physically distant battlefield circulation. Utilizing safety precautions like facemasks, regular handwashing, and maintaining a minimum of 6 feet of space between people, allowed the BH team to visit soldiers in their work environments. Most circulation occurred around motor pools and company headquarters. During circulation, the BH team received first-hand accounts of soldiers' responses to COVID-19 restrictions. It also served as an opportunity to provide information and resources (e.g., stress balls, mindfulness coloring books, handouts) to soldiers.

Prevention and Outreach Limitations: The BH team developed creative methods to reach out to soldiers during the stay-at- home phase of COVID-19. However, there were some limitations. First, screening measures helped identify potential BH issues, yet they were not sufficient for thorough assessment. In addition, fliers, resiliency videos, and yoga videos were available only on the BDE social media page. This meant that only soldiers who followed the page would be able to access these resources. While some limitations existed, the outreach and prevention program was, overall, effective for combatting the negative BH impacts of COVID-19.

Conclusion

Utilizing a "team of teams"[2] approach was imperative to separating and maintaining focus on several different objectives simultaneously within the Surgeon Cell. This approach allowed the medical team to match expertise with correct tasks. This allowed the BDE Surgeon time to maintain contact with commanders and health experts at multiple different garrisons throughout Europe while overseeing Surgeon Cell operations and keeping the BDE Commander informed at all times. It further allowed for prevention and outreach services to all impacted to continue, minimizing secondary and tertiary effects. Through this method, the Surgeon Cell was able to have an impactful COVID-19 response while maintaining medical readiness so that the military policing and engineering capabilities remained viable in the European theatre of operation.

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Report of a Powered Air-Purifying Respirator and Its Use in the Dental Setting

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Abstract

Background: Respirators have received much attention since the outbreak of the COVID-19 pandemic. Due to a substantial shortage of the most commonly used respirator, the N95 Filtering Facepiece Respirator (N95), as well as the desire to have added protection while performing aerosol generating procedures (AGPs), dental healthcare personnel (DHCP) have considered alternative respirator options. It is well documented in the medical literature that the Powered Air-Purifying Respirator (PAPR) provides better protection against respiratory pathogens; however, there are no reported cases that describe the use of PAPRs in the dental setting. This survey report evaluates the use of a loose-fitting full facepiece PAPR by different dental providers.

Objective: To determine if a PAPR can be used in the dental setting and identify any potential barriers to use.

Methods: Eleven DHCP representing general dentistry, dental hygiene, pediatric dentistry, endodontics, orthodontics, oral and maxillofacial surgery and maxillofacial prosthodontics at Walter Reed National Military Medical Center (WRNMMC) and Naval Postgraduate Dental School (NPDS) were asked to wear the MAXAIR PAPR while performing an AGP. They then completed a 14-question survey.

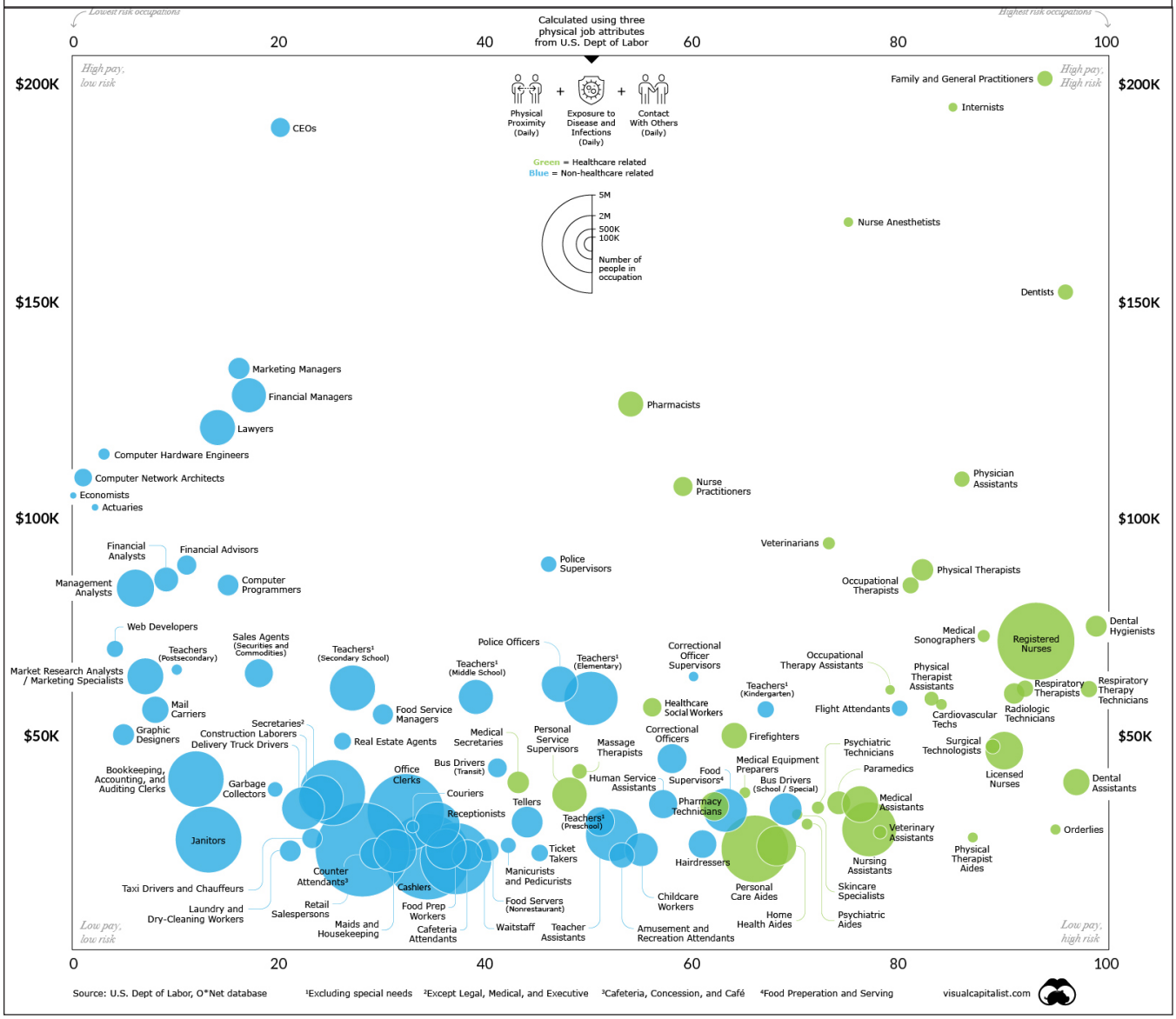
Results: There was a 100% response rate. All DHCP with the exception of the endodontist were able to successfully wear the MAXAIR PAPR for the duration of their procedure. All DHCP reported that the PAPR was more comfortable than expected. There were no reports of fogging or hindrance to visibility, breathing was unaffected or enhanced, and the noise level was tolerable. Average time to don and doff the PAPR was 5 minutes. All DHCP were able to wear loupes; some were not able to wear a headlight. Two DHCP reported a history of mild claustrophobia, and both were able to tolerate the PAPR without any issue. 44% preferred the PAPR over the N95.

Conclusion: This preliminary survey of a loose-fitting PAPR in the dental setting suggests there is a place for PAPRs in the dental community.

Dental healthcare personnel have one of the highest occupational risk for exposure to airborne and respiratory infectious diseases due to the location, duration, and nature of dental procedures (Figure 1).[1] Because of this, the outbreak of the COVID-19 pandemic paralyzed the dental community until enhanced guidelines for personal protective equipment (PPE) were developed. New guidelines published by the Center for Disease Control (CDC) placed a special emphasis on respirators in an attempt to ensure the safety of the DHCP. The new guidelines recommend the use of an N95 or a respirator that offers an equivalent or higher level of protection during AGPs when working in areas with moderate to substantial community transmission.[2]

There are four types of respirators: Filtering Facepiece Respirator (FFR), Elastomeric Half Facepiece Respirator, Elastomeric Full Facepiece Respirator, and Powered Air-Purifying Respirator (PAPR). PAPRs can be further divided into those that are tight-fitting and those that are loose-fitting. Loose-fitting respirators do not require fit testing whereas FFRs (i.e. N95s) and elastomeric respirators do. While FFRs are the most readily available and commonly used respirators by the health care professional (HCP), PAPRs provide the most protection against respiratory pathogens, with an Assigned Protection Factor (APF) between 25 to 1,000 compared to an APF of 10 for N95s and half facepiece elastomeric respirators.[3-5]

Figure 1. Dentists, dental hygienists, and dental assistants scored in the top four for highest occupation risk for COVID-19..



Due to a substantial shortage of N95s during the COVID-19 pandemic, the inaccessibility for the majority of DHCP to get properly fit-tested for a N95, and a desire for many DHCP to want increased respiratory protection, PAPRs have been considered as an alternative option to the N95 when performing AGPs such as dental hygiene, restorative dentistry, and surgeries during the coronavirus pandemic.

Methods

Demographics

Eleven DHCP working at Walter Reed National Military Medical Center (WRNMMC) and Naval Postgraduate Dental School (NPDS) were asked to participate in this survey:

(1) General Dentist
(1) Pediatric Dentist
(1) Orthodontist
(1) Oral and Maxillofacial Surgeon (OMFS)
(1) Maxillofacial Prosthodontist
(1) General Practice Resident (GPR)
(1) Endodontist
(4) Registered Dental Hygienist (RDH)

Each participant received generalized training on how to use the PAPR and properly don and doff it prior to use (Figure 2).

Armamentarium

The PAPR used in this survey was selected based on availability. WRNMMC had several MAXAIR PAPR units available from a previous purchase in 2014 in response to the Ebola outbreak and provided the equipment used in this survey (Figure 3).

1. Helmet (PN: 02531207)
2. Battery (PN: 01531032)
3. Battery charger (PN: 01432089)
4. Battery belt
5. Disposable comfort strips (ON: 2000-201)
6. Disposable hood (2 models: PN: 2000-25DMA, ON: 2272PB-07ML)
7. Duffel BAG (Not pictured)

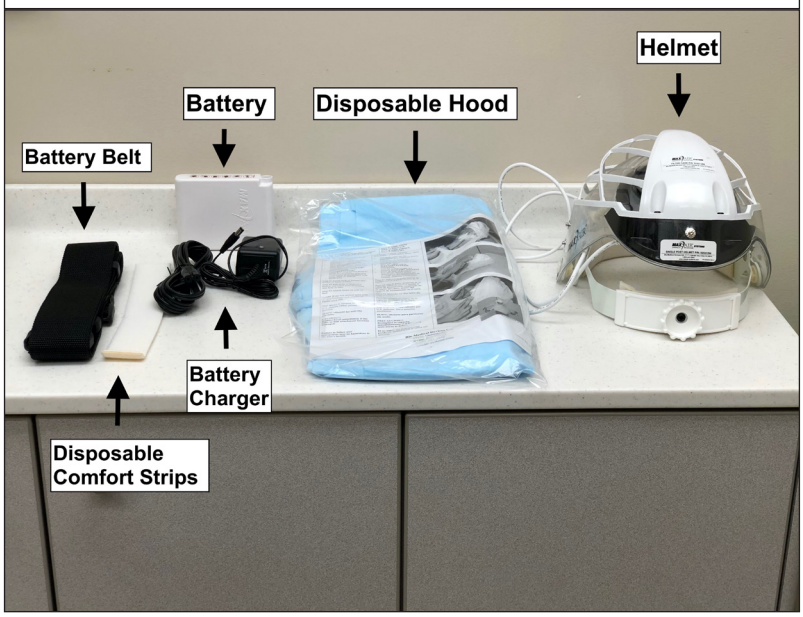
Survey Questions

Survey questions were developed based on questions and concerns raised by DHCP when discussing the potential to use the PAPR in the dental setting.

1. Overall comfort level (1 to 5, 5 being most comfortable)
2. Breathability (Increased, No effect, Decreased)
3. Did it fog? (Yes or No)
4. Visibility (Good, Partially obstructed, Obstructed)
5. Did it physically hinder you from performing your procedure? (Yes, No, Other)
6. Did you wear Loupes? (Yes, No)
   a. If yes, type (Through the Lens TTL, Flip up):
   b. If no, is it because it did not fit?
7. Did you wear a headlight?
   a. If yes, type?
   b. If no, is it because it did not fit?
8. Noise level (Quiet, Tolerable, Unbearable):
9. Time to don (0-5, 5-10, 10+ minutes):
10. Time to doff (0-5, 5-10, 10+ minutes):
11. Patient acceptance (Liked it, Little re action, No reaction):
12. Do you prefer an N95 or PAPR?
13. Is the PAPR better or worse than you expected?
14. Do you suffer from claustrophobia?
    a. If yes, were you able to tolerate the PAPR?

Figure 2. Participants had an opportunity to practice using the PAPR prior to engaging in patient care. *(In order to preserve PPE, the provider in this photo is not in full PPE during this non-aerosol generating training session.)*

Figure 2. Armamentarium used in this study.



Results

There was a 100% response rate (Table 1). All participants completed the procedure wearing the PAPR with the exception of the endodontist. As depicted in Figure 4, the pressure from the PAPR shield caused the microscope to drift and therefore the endodontist elected not to use the PAPR during the procedure. The results of his survey are omitted.

Overall, 100% of the participants reported the PAPR experience to be better than expected. 80% rated the PAPR to be a 4 or 5 for comfort (5 being the most comfortable). 100% reported no fogging, and either no effect or increased breathability.

In regard to performance, two participants reported their visibility was partially obstructed while wearing the PAPR. All providers who wanted to wear loupes were able to (7 of 10), and both "through the lens" and "flip up" styles were represented (Figure 5). Two providers wore a headlight with their loupes (one was detachable, one was built-in); one provider wanted to but was unable due to an improper fit under the PAPR hood. 44% of participants preferred to wear the PAPR rather than the N95.

The average time to don and doff the PAPR was 5 minutes. There was a 100% perceived patient acceptance rate with the majority of patients showing very

Figure 4.During training, it was discovered that the PAPR shield put pressure on the microscope causing it to drift. The endodontist elected not to use the PAPR during his procedure.

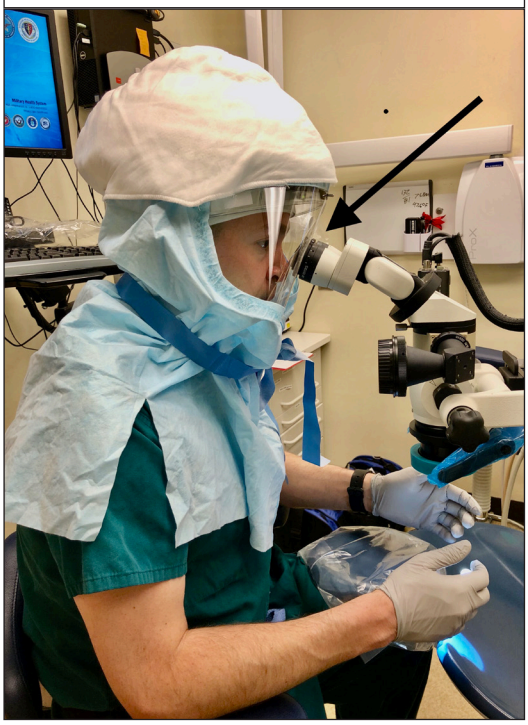


Table 1.Survey Questions and Responses.

	Pediatric Dentist	Orthodontist	Maxillofacial Prosthodontist	OMFS	General Dentist	GPR	Endodontist	RDH	RDH	RDH	RDH
1. Overall comfort level: (1 to 5, 5 being most comfortable)	4	3	4	3	4	4	*	4	4	5	4
2. Breathability: (Increased, No effect, Decreased)	Increased	No effect	Increased	No effect	No effect	No effect	*	No effect	No effect	No effect	Increased
3. Did it fog? (Yes, No)	No	No	No	No	No	No	*	No	No	No	No
4. Visibility: (Good, Partially obstructed, Obstructed)	Good	Good	Partially obstructed	Good	Partially obstructed	Good	*	Good	Good	Good	Good
5. Did it physically hinder you from performing your procedure? (Yes, No, Other)	No	No	No	No	No	No	Yes	No	No	No	No
6. Did you wear loupes?	No	Yes	Yes	No	Yes	No	*	Yes	Yes	Yes	Yes
If yes, type? (Through the lens TTL, Flip up)	n/a	TTL	TTL	n/a	TTL	n/a	*	TTL	TTL	TTL	TTL
If no, is it because it did not fit?	No	n/a	n/a	No	n/a	No	*	n/a	n/a	n/a	n/a
7. Did you wear a headlight?	No	No	Yes	No	Yes	No	*	No	No	No	No
If yes, type of headlight?	n/a	n/a	Detachable	n/a	Built-in	n/a	*	n/a	n/a	n/a	n/a
If no, is it because it did not fit?	No	No	n/a	No	n/a	No	*	No	No	Yes	No
8. Noise level: (Quiet, Tolerable, Unbearable)	Tolerable	Quiet	Tolerable	Tolerable	Tolerable	Tolerable	*	Tolerable	Tolerable	Tolerable	Tolerable
9. Time to don: (0-5, 5-10, 10+ minutes)	0-5	0-5	0-5	0-5	5-10	0-5	*	5-10	5-10	5-10	5-10
10. Time to doff: (0-5, 5-10, 10+ minutes)	0-5	0-5	0-5	0-5	5-10	5-10	*	5-10	0-5	5-10	5-10
11. Patient acceptance: (Liked it, Little reaction, No reaction)	No reaction	Little reaction	Little reaction	n/a (general anesthesia)	Little reaction	Little reaction	*	No reaction	Liked it	Liked it	Little reaction
12. Do you prefer an N95 or PAPR?	N95	N95	PAPR	N95	**	PAPR	*	PAPR	PAPR	N95	N95
13. Is the PAPR better or worse than you expected?	Better	Better	Better	Better	Better	Better	*	Better	Better	Better	Better
14. Do you suffer from claustrophobia?	Mild	No	No	No	n/a	n/a	*	No	Mild	No	No

little to no reaction to the additional PPE. Only two participants reported mild claustrophobia, and both were able to tolerate the PAPR without issue.

Discussion

This study was performed to determine if a PAPR can be used in the dental setting. Although there were not enough participants to perform a statistical analysis of the responses, the results of this preliminary study suggest that there is a place for PAPRs in the dental community.

The loose-fitting PAPR has many benefits when compared to the N95. For one, a fit-test is not required and therefore is an option for any personnel not able to get fit-tested or who has failed the fit-test.[3-5] One participant in this study failed multiple N95 fit-tests and therefore has been wearing a PAPR for all AGPs since the start of the pandemic. PAPRs also increase the overall respirator quantity and can be worn if a DHCP's N95 size becomes unavailable.

PAPRs are more protective than N95s. With an APF ranging from 25 for loose-fitting PAPRs up to 1,000 for tight-fitting PAPRs, many participants in this study, the hygienists in particular, preferred to wear the PAPR for both the actual and perceived added protection. Hooded PAPRs like the one used in this study offer limited to significant splash protection for the hair, face, eyes and neck and reduce the need for additional PPE such as bouffants, goggles, and surgical masks.[3-5]

From a comfort perspective, all participants reported that the PAPR was "better than expected." Although

Figure 6.The PAPR was worn while treating a patient under general anesthesia.

Figure 5. The comprehensive dentist is able to wear both loupes and headlight under the PAPR.

data on the type and length of procedure was not included in the methods or results, the information was collected from each participant. Procedures ranged from 20 minutes (Orthodontist) to 5 hours (OMFS) and were performed in both the operating room (OMFS and pediatric dentist) as well as the clinic setting (Figure 6). While it cannot be statistically confirmed in this study that length of procedure inversely correlates to comfort level, many of the participants' comments did state that the PAPR became heavy after wearing it for a period of time and wished for something a little more lightweight. However, PAPRs may be less taxing from a physiological and breathing resistance perspective than other respirators which was suggested in this study.[6]

Many DHCP wear loupes when treating patients. There have been questions raised by the dental community as to whether or not loupes can be worn with the PAPR. There are many different types of loupes and PAPRs on the market, but all providers in this study who wanted to wear loupes were able to (Figures 2 and 5). Two participants did report a partially obstructed view when not looking directly through the loupes, one due to the distortion placed on the hood by the attached headlight and one due to the limited downward vertical field of view of the PAPR hood. Another provider was not able to wear a headlight due to inadequate spacing between the light and

hood. There was no fogging reported in this study that is often experienced when wearing an N95 with a face shield and/or other eye protection.

Communication is key when performing safe and reliable care. The noise level was tolerable by all participants in this study, however, some reported that communication was difficult between the dentist and assistant when the PAPR, suction, and handpiece were all on at the same time. In contrast, in the absence of an N95 and face shield or goggles, the PAPR allows an unobstructed view of the provider's full face which could improve non-verbal communication such as a smile. This is an important aspect when meeting patients for the first time and trying to establish rapport. There were two non-sedated pediatric patients treated during this study, and neither had any adverse reaction to the additional PPE.

Only two participants responded that they have mild claustrophobia, and both were able to tolerate the PAPR without issue. More trials should be conducted to determine if those who suffer from claustrophobia can tolerate a PAPR.

While there are advantages to the PAPR, there are limitations and factors that may affect its use in the dental setting. This study revealed a potential problem for endodontists or anyone who uses a microscope. While the actual visibility was not altered by the PAPR, the physical pressure that the hood placed on the microscope caused it to drift (Figure 4). More trials should be conducted to determine if this is a consistent problem. An alternative to the PAPR and N95 in this case may be an elastomeric half facepiece respirator.

Another factor to consider is time. This study looked at the time it took to don and doff the PAPR. Though the average time was only 5 minutes, in a high-volume practice, this time adds up. One intraoperative nuance that was reported was the inability to dim the built-in headlight that was attached to the loupes. Minor inconveniences can lead to inefficiency and ultimately to provider burn-out. In this study, several participants reported that they preferred the N95 for its simplicity and convenience.

One major factor that was not addressed in this study but cannot be overlooked is cost. PAPRs have an initial start-up cost ranging from $1,000–$1,500 USD. Many PAPRs use a disposable hood which is an additional $35–$50 USD per use. Cost alone can be a deterrent for many DHCP to consider using a PAPR.

This study suggests that PAPRs can be a viable, if not necessary, addition to any dental clinic's respiratory protection plan. As more DHCP start using PAPRs, it would be prudent to collect a database of the different types of PAPRs that are being used in the dental setting and identify if there are any that are more conducive to the unique DHCP's needs than others. Note: Some of the components of the PAPR model used in this study are no longer available. Compatible, updated versions are available.

Conclusions

Prior to the COVID-19 pandemic, respirators were not commonly used in the dental profession. Today, they have become a part of the "new normal." While N95s are the most commonly used respirator by the DHCP, there is a need for an alternative option for personnel who do not fit an N95. A loose-fitting PAPR may be an option for those personnel.

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Risk Mitigation Strategies to Prevent Transmission of COVID-19 in the Military Classroom Setting: A Case of a Symptomatic SARS-CoV2 Positive Student without Apparent Spread to Classmates

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Introduction

Since the onset of the COVID-19 pandemic in late 2019, the world community has responded with ever-evolving measures to reduce the spread of SARS CoV-2, the virus that causes COVID-19 (Coronavirus Disease 2019)[1]. One particular area of interest is understanding the risk of the in-person classroom setting and if any mitigation efforts are effective in preventing the spread of disease in that setting. In this paper, we present a case study of a US Army Advanced Individual Training (AIT) course/classroom wherein a student was diagnosed with COVID-19, and there was no apparent spread to others in his classroom. We discuss the mitigation efforts put in place that appear to be, in this case, effective in preventive onward spread of the virus. These are social distancing, face coverings/masks, and hygiene practices including hand washing and sanitation of surfaces.

Case Study

On 1 June, 2020, an active duty soldier, enrolled in the Licensed Practical Nursing Course (LPN) at Joint Base Lewis-McChord (JBLM) tested positive for the SARS CoV-2 virus. He had presented the previous day for testing. Beginning on 27 May, he developed symptoms of headache, chills, and cough.

Contact tracing was undertaken. It was determined that the student attended class for 4 days while possibly infectious (26-29 May). Ten close contacts (within 6 feet for 15 minutes or longer) were identified and placed in quarantine. All affected students were able to continue class remotely. No close contacts reported any symptoms. All close contacts were tested for COVID-19 and all were negative. All close contacts were tested again on day 12 of quarantine, and again, all tests were negative. This case was diagnosed during a period of increasing COVID-19 transmission in the local community, following a lull with low transmission in May associated with the Washington State Governor's stay at home order.

The soldier was enrolled in a course with 49 other students and 9 instructors/staff. All students and staff were in a single, large classroom together for about 8 hours per day. Details of the classroom follow. Efforts were made to maximize social distancing; however, many students were slightly less than 6 feet away from their nearest classmate, with distancing ranging between 4.5-5.5 feet (1.37-1.68 meters).

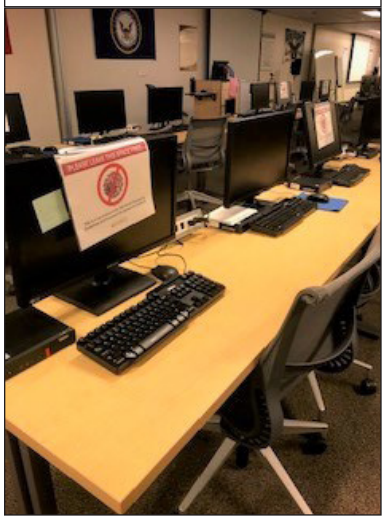
In order to assess the seroprevalence of COVID, as well to assess the class for possible transmission of COVID-19, COVID antibody testing was offered to all staff and members of the LPN training course on 15 Jul. 41 participants chose to participate and have their blood tested for antibodies (32 students and 9 faculty/staff). No participant in the study showed antibodies to COVID, including the index case.

Interventions/Prevention Measures

Social Distancing: The six-foot or 2-meter distance between individuals has become the standard to help guide individuals on the minimum social distancing required to prevent the spread of infection. These distances are certainly not absolute and evidence suggests SARS-CoV-2 can travel more than 2 meters in certain situations. Furthermore, distribution of viral particles is affected by numerous factors, including airflow, and multiple factors affect risk, including ventilation, occupancy, and exposure time.[2-5]

In 2017, one group of researchers examined social distancing as a way for schools to reduce the transmission

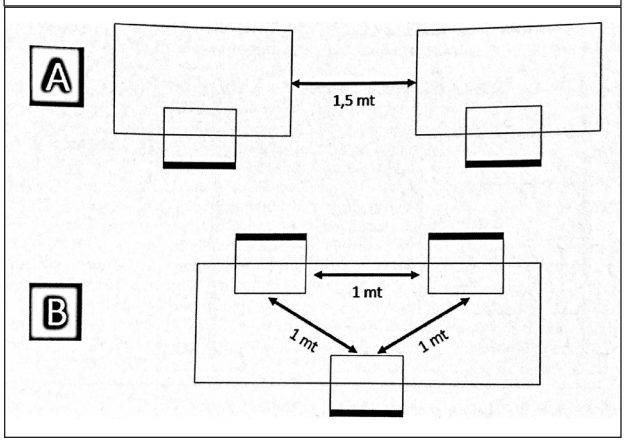
Figure 1. Staggered classroom seating.



of influenza during a pandemic.[6] The research illustrated the complex nature of social distancing, for example, that social distancing is challenging to enforce and can have negative consequences to include impacts on mental health and increased resource requirements.[6]

Seating arrangements within the classroom can be reconfigured to maximize space between students. The suggested checkerboard seating pattern recommends separating desks 1.5 meters apart, and if multiple chairs are to be placed at a table, they should be staggered to achieve distance between seated students of 1 meter (Figure 1).[7] Attention should be placed on layout of the classroom, flow of movement within the classroom and between the classroom and other sites, ensuring adequate airflow, and creating processes and visual cues that support physical distancing.[7] Of note, in the case study described above, the seating arrangements were placed in a checkerboard pattern (Figure 2) and were at least 4.5 feet apart between seats at the same table or between seats of adjacent rows (Figure 3). Although the social distancing of 6 feet could not be achieved between most of the seats in this classroom, the distancing and checkerboard patterning did incidentally follow the recommendations outlined in most cases.[7]

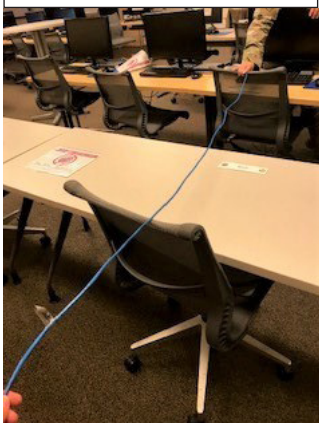
Figure 2. Checkerboard seating pattern.



Furthermore, areas that are used for gatherings, especially where personal protective equipment (PPE) is not mandatory (such as eating areas), should be avoided and individuals encouraged to either eat foods brought from home within the classroom or eat outside.[7] A space that promotes congregation and removal of face masks increases risk. In this case, the break area was open for use and could be utilized when eating without the use of face masks. However, efforts were made to reduce use by limiting the number of places that one could sit and eat.

Face Masks: Even before the COVID-19 pandemic and the socialization of mask-wear to prevent the spread of COVID-19, the use of face masks was shown to reduce the spread of respiratory viruses and decrease the odds of contracting respiratory infection in systematic studies. Furthermore, these studies showed that protection against infection from such viruses could occur for both the mask-wearer and contacts of mask wearers.[1] One example during the pandemic highlighted no evidence of virus transmission when mask wear was enforced in many individuals exposed to symptomatic COVID-19 hairdressers who also wore masks.[8]

Figure 3. Distances ranged 4.5-5.5 feet between seats at the same table or between seats of adjacent rows of tables.



In the case presented, mask wear was mandatory for all students and staff. Per discussion with class leaders, students and staff were mostly compliant with mask wear, though there were times when students congregated briefly without wearing masks (e.g. meal time, smoke breaks).

Hygiene Practices: Uncertainty exists about whether handwashing can reduce the spread of coronaviruses between humans.[9] It is, however, a well-known method to reduce the spread of multiple illnesses. Some studies have suggested that handwashing in conjunction with mask-wear have reduced the spread of respiratory viruses such as the seasonal influenza virus.[10] However, it was noted by the authors that studies support that once a surgical mask is removed, "the effect of hand hygiene became insignificant."[10] In our described case study, frequent handwashing and use of alcohol-based hand sanitizer were encouraged, and all common surfaces were disinfected daily.

Discussion

In the case described above, multiple measures were implemented. Frequent handwashing with an alcohol-based hand sanitizer was encouraged, wearing of face masks was mandatory, and all common surfaces were disinfected daily. Social distancing of six feet could not reliably be ensured and ventilation could not be maximized given that the classroom was without windows. However, social distancing within the classroom was still maximized as much as feasible to achieve at least 4.5 feet between classroom participants using a checkerboard pattern of seating described above. Additionally, a shared eating space where masks were not used while eating occurred for those students who chose to stay in the facility to eat lunch, but was limited in seating.

Despite these issues, we have no evidence that any classmate in the vicinity of the infected student subsequently became infected themselves with COVID-19, either with regards to clinical symptom development or on confirmatory testing. The consistent use of face masks in both students and faculty, handwashing, and disinfecting efforts, and an effort to change seating patterns to create a checkerboard or alternating seating pattern to maximize the space between students may have been associated with the absence of transmission in this situation.

The findings of this report are subject to limitations. First, while all close contacts were tested for SARS CoV2 at the start and end of their quarantine and at approximately the end of the incubation period, this was only a subset of those who may have been exposed. Second, although antibody testing suggests no virus transmission, not all individuals infected with COVID-19 will produce detectable antibodies and false negatives are not uncommon.[11]

This study provides information that can inform decisions in safely executing classroom training, particularly in the military and healthcare training settings. Non-pharmaceutical interventions are important to prevent the transmission of COVID-19. It is possible that combining strategies may be helpful when some mitigation efforts cannot be carried out ideally. For example, the fact that handwashing, mask wearing, staggered seating arrangements, and regular disinfection of surfaces occurred concurrently in the classroom of the student described above, may have helped to offset the fact that social distancing of 6 feet could not be realistically achieved between students in the classroom and that class members may have had time when they were together without masks (e.g. in the breakroom). In an effort to guide classroom planning efforts during the current pandemic and in the future, it is important consider combining multiple simple interventions to prevent the spread of infection whenever possible. These actions in conjunction with further research examining which combinations of interventions will best prevent the spread of respiratory illnesses may help us continue classroom-based training to ensure continued operational readiness.

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COVID-19 MEDEVAC Best Practices: The Development of a Standardized Medical Operating Guideline

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Introduction

COVID-19, a highly infectious virus, presents self-evident problems with regards to aeromedical transportation. Droplet size, proximity of caregiver from the patient, severity of upper and lower respiratory symptoms, personal protective equipment (PPE) and turbulence of airflow are factors which may influence the transmission of any biological agent aboard an air transport platform. Given the relatively confined space of rotary-wing MEDEVAC helicopters and the lack of structural barriers between flight crew and passengers, transmission risk is high, particularly when close contact under these conditions last beyond 15 minutes.[1] Some authorities strongly recommend against the rotary-wing evacuation of COVID-19 patients when ground or fixed-wing transport is available due to the high risk of transmission.[2,3]

Nonetheless, MEDEVAC transportation is an important contingency for COVID-19 positive or suspected COVID-19 patients who are decompensating in far forward areas where fixed-wing access is impossible. Rotary-wing transport is an important consideration for the US Army given its dedicated MEDEVAC mission, yet the preponderance of literature pertaining to medical evacuation of COVID-19 patients addresses fixed-wing evacuation, particularly with regard to mass repatriation efforts early in the pandemic.[4-8] Comparatively, there is a dearth of literature pertaining to rotary-wing evacuation of COVID-19 patients,[9,10] with only a single rotary-wing evacuation standard operating procedure (SOP) described in the literature to date.[9] Contributing to a future MEDEVAC Standardized Medical Operating Guideline (SMOG) is a compilation of international surveys and SOPs regarding best practices—the aim of the present process improvement project.

Methods

A 24-item voluntary process improvement survey project was deemed exempt from Institutional Review Board review by the US Army Aeromedical Research Laboratory Determination Official. Volunteers completing the survey had the option of providing personal information to facilitate follow-on questions and to enable final report distribution, but otherwise the survey was anonymous. In a preliminary assessment of best COVID-19 rotary-wing MEDEVAC practices, our team collected 55 SOPs, photographs, lessons learned, phone interviews, and surveys between 1 May, 2020 and 8 September, 2020. Data was received from 20 authorities spanning Australia, Israel, New Zealand, Spain, Sri Lanka, the United Kingdom, as well as military services and civil helicopter organizations across the US and outside the contiguous US. Solicitation for SOPs and survey completion occurred through North Atlantic Treaty Organization (NATO) COVID-19 Aeromedical Evacuation Work Group participants, the US Army Air Evacuation Enterprise telephone conference, the US Navy En Route Combat Casualty Care Sub-Community Meeting and a series of e-mails and phone calls to leaders in aerospace medicine across the international community. Calculation of the survey response rate was not reliable due to the nature of solicitation e-mails forwarded from one subject matter expert (SME) to others within commercial enterprises and military services. Although a formal analysis by a panel of SMEs has yet to occur, some potential best practices have been elucidated by our project team.

Results

Pre-flight procedures are an important aspect of readiness for the safety of the rotary-wing en route care mission. Best practices include the following:

- Preparing a staging area for disposal of PPE prior to flight;
- Communicating with receiving medical treatment facility about a potential COVID-19 patient, enabling health care providers at the destination to don the appropriate PPE;

- If possible, static loading of COVID-19 patients, using litter bearers outfitted in appropriate PPE;
- Transport to the nearest medically appropriate treatment facility;
- Enclosing survival gear in a bag in order to protect it during the decontamination of life saving equipment process;
- Limiting the number of people in the aircraft to only those required to render medical care and to safely fly the aircraft;
- Placing patients as far as possible from the flight crew;
- Avoiding packing any unnecessary gear that would present more risk for contamination;
- Ensuring all patients are screened for COVID-19 symptoms, to include patients presenting with non-COVID-19 symptoms or injuries;
- Training for 'first pass success' intubations;
- Intubation on the ground if there is concern regarding in-flight decompensation;
- Ensuring passengers are provided with a bag for any potential emesis in order to reduce transmission risk, and treating this bag as contaminated;
- Ensuring double eye protection for all medical crew;
- COVID-19 symptom screening of entire flight crew at the beginning of duty day through a cell phone application using employee number; and
- Website portals for posting the latest COVID-19 related policies and resources of the organization.

Patient transfer presents a high risk of transmission to receiving and handling personnel as well as a time of potential disruption to ventilator support systems. Best practices include the following:

- Keeping MEDEVAC equipment transferred into hospital with patients to a minimum;
- Ensuring that pilots glove if involved in patient loading; and
- Hand washing.

In flight patient management includes the follwing:

- Maintaining an altitude as low as possible in order to limit risk of hypoxia;
- Using standardized COVID-19 'run sheets';
- Using bacterial/viral filters for all patients requiring ventilation support;
- If possible, moving infected and non-infected patients via separate aircraft during multi-ship formation flight;
- Ensuring that patients wear a surgical mask or use a non-rebreather mask if oxygen supplementation is required;
- Avoiding any aerosol generating procedures such as bag valve mask use;
- Using high dose neuromuscular blocking agents for rapid sequence intubations; and
- Assuming all patients could be COVID-19 positive and managing them as such.

Post flight procedures involve decontamination of personnel, equipment, and the airframe. Best practices include the follwing:

- Using a standardized, airframe-specific decontamination procedure;
- Compiling lessons learned and after-action reviews, which are shared at aeromedical evacuation forums;
- Decontaminating safety equipment using non-flammable disinfectant;
- Immediate doffing and washing of the flight uniform;
- Supervision of flight crew doffing by the medical crew whenever possible;
- Using a standardized checklist for decontamination procedures;
- Validating the training for all personnel involved in decontamination;
- Deferring fueling and maintenance until after decontamination;
- Regularly rehearsing decontamination procedures;
- Ensuring protocols for managing potentially exposed crew members are followed; and
- Using cell phone QR code-enabled protocols to determine crew member risk following suspected exposure.

Discussion

Divergent practices that need to be critically analyzed prior to universal military application include the use of flammable biohazard suits, which may present unacceptable risk. For this reason, the curtains used to separate pilots from the rear crew are not uniformly used. The maxillofacial shield, not available for use in civilian rotary-wing aviation, is used by some US Army MEDEVAC units and presents a structural barrier not afforded to civilian flight crews. For this reason, some US Army MEDEVAC local policies identified on the survey included a mandate for visor-down positioning of the helmet. Some non-US militaries advise a facial mask in lieu of the facial shield in order to limit the amount of equipment that needs to be decontaminated following every patient transport.

There is controversy about the safety of nebulizer use within the rotary-wing community, with some authorities

recommending against this therapy while others deem it to be explicitly non-high risk. The authors were unable to identify a validation study that assessed nebulizer use in the context of rotary-wing air turbulence and are thus unable to ascertain the acceptability. It is important to note that the use of a nebulizer could potentially prevent the need for an intubation, an undeniably high risk procedure for contamination. At least one military MEDEVAC unit is practicing with patient isolation units; such isolation units do not appear to be commonplace in the civilian rotary-wing sector. However, a US Army flight medic noted limitations in patient access when using an isolation unit in the confined space of the aircraft. A research engineer at the US Army Aeromedical Research Laboratory involved in the testing of patient isolation units also noted that space constraints would be challenging, especially if critical medical equipment has to be used during air transport.[11] Finally, isolation units were noted by intensivists to potentially exacerbate patient breathing difficulties while not affording any additional protection for ventilated patients.[12] Civilian rotary-wing companies engage in a higher level ultraviolet (UV) decontamination of the aircraft following COVID-19 patient transport, potentially due to liability risk, the availability of UV decontamination systems, as well as the availability of greater funds that often accompanies commercial for-profit status.

Project limitations include a relatively small sample size and an intuitive, rather than rigorous, assessment of best practices to date. A follow-on project will culminate in a best practices SMOG for military operations following a formal assessment of project data by a panel of SMEs. Ultimately, a SMOG can be validated through a trial of aerosolized fluorescein dye application throughout an aircraft cabin during flight in order to assess the degree of contamination that a flight crew and their equipment receives as a course of their pre-flight and in-flight procedures. Residual dye assessment can also be quantified following a best practice decontamination technique. In this manner, an interim SMOG can be compared to other procedures that the SMEs felt may have merit but were not incorporated into the interim SMOG.

Importantly, many of these best practices often transcend aviation and are applicable to ground evacuation platforms as well. During Joint All Domain Operations and Large Scale Combat Operations, ground evacuation will become increasingly important and must harness the lessons learned of aviation. Following resolution of the current pandemic, our military and those of our allies still require standard ways to evacuate infectious patients.

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Conducting Virtual Global Health Engagement (GHE) activities in the Midst of the Global COVID-19 Pandemic: Considerations for the Department of Defense GHE Enterprise

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Introduction

The global COVID-19 pandemic resulted in restriction of non-essential travel across the globe, as seen in the Office of the Under Secretary of Defense Memorandum, "Force Health Protection Guidance (Supplement 4): DoD Guidance for Personnel Traveling During the Novel Coronavirus Outbreak" (11 March 2020). This resulted in the suspension of most, if not all, Department of Defense (DoD) security cooperation (SC) programs, including DoD Global Health Engagement (GHE) activities.[1] One such program is the African Peacekeeping Rapid Response Partnership (APRRP), which relies heavily on face-to-face interactions with select African Partner Nations (PNs), and which was significantly impacted by the inability to conduct in-person training with key partners. In light of these restrictions and suspended activities, the Uniformed Services University of the Health Sciences' (USU's) Center for Global Health Engagement (CGHE), in support of the US Africa Command (USAFRICOM) Office of the Command Surgeon, explored virtual means to execute DoD GHE activities to continue engaging its APRRP PNs, pending return to in-country activities.

To mitigate these challenges, USU's CGHE, in close coordination with the Office of Security Cooperation (OSC), US Embassy Accra, designed a virtual engagement for the Ghana Armed Forces (GAF), which consisted of a series of training modules on Critical Care and COVID-19 Patient Management (CCPM) using Zoom, a globally-recognized virtual platform. When in-person SC activities cannot be conducted due to a global pandemic or other crisis, DoD GHE planners and executors need alternative solutions to remain on target with meeting GHE program objectives. This article proposes key recommendations to assist DoD GHE planners and executors in developing and implementing relevant virtual engagements which, for the APRRP program, served to supplement postponed medical training activities while strengthening the established partnerships with each APRRP country.

Beyond technological issues, one of the primary obstacles that GHE planners face when pitching a GHE virtual medical training concept is getting the right audience, such as key PN leadership and decision makers, to the table. This makes already established partnerships critical to the successful planning and execution of virtual training engagements. Existing relationships increase the chances for executing GHE in foreign countries, while having no relationship with a country would potentially limit GHE activities at least until such a relationship could be established.

Background

Michaud et al. reflected that, "Many militaries see value in health training and capacity building efforts because they can create and strengthen international relationships, help partners become more resilient, and provide training opportunities for their militaries' own personnel."[2] The APRRP program, noted in the Defense Security Cooperation Agency's Security Cooperation Programs Handbook (Revision 19.1, updated February 2019), which is funded by the Department of State and

executed by USAFRICOM, aims to build the capacity of African PNs to rapidly deploy peacekeepers by developing capabilities in the areas of logistics, engineering, medical, and command, control, and communications.[3] The program supports PNs that have shown a willingness and demonstrated ability to support United Nations (UN) and African Union peacekeeping missions by increasing their capability to rapidly deploy to any situation that may threaten regional stability. APRRP defines rapid deployment using the UN definition in which unit(s) are prepared to deploy within sixty days of a request issued by the Secretary-General.[4] USU's CGHE supports the USAFRICOM Office of the Command Surgeon in executing the medical component of APRRP for four African PNs: Ghana, Rwanda, Senegal, and Uganda. USU's CGHE coordinates and delivers tailored training courses to each country based on identified capability needs, which are designed with the goal of enabling African PNs to rapidly deploy, sustain, and redeploy a UN Level 2 hospital (L2H) for peacekeeping operations or emerging crises on the African continent.

Prior to the last APRRP medical or GHE activity conducted in March 2020, USU's CGHE had conducted 13 of 29 GHE activities planned for calendar year 2020: 4 out of 9 in Ghana, 3 out of 8 in Senegal, 4 out of 7 in Uganda, and 2 out of 5 in Rwanda. This initial plan quickly changed due to the travel restrictions and public health measures implemented to flatten the curve and prevent further spread of COVID-19. The USU's CGHE team immediately reassessed all planned GHE activities for the year and developed a new plan to support the APRRP PNs. USU's CGHE developed this new APRRP Medical COVID-19 Program Plan after reassessing the needs and priorities of the PNs, formulating the specific actions necessary to continue PN support while maintaining program timelines as much as possible in light of a global pandemic situation. In addition, anticipation of the APRRP PNs to likely deploy one of their US provided UN L2Hs to support a domestic COVID-19 response propelled USU's CGHE to devise a plan which would include the development of a series of virtual training modules focused on the topic of CCPM as a starting point.

DoD defines security cooperation as "All Department of Defense interactions with foreign security establishments to build security relationships that promote specific United States security interests, develop allied and partner nation military and security capabilities for self-defense and multinational operations, and provide United States forces with peacetime and contingency access to allied and partner nations."[5] DoD GHE activities can serve as a security cooperation tool; promoting, building, and reinforcing new and already established relationships between the United States and partner countries. Current relationships with APRRP PNs, Ghana, Rwanda, Senegal, and Uganda remain stronger today due to the continuous interaction and execution of medical activities accomplished through the APRRP program. Since 2016, the USU's CGHE team coordinated and conducted over 40 APRRP medical activities which trained over 1,000 PN personnel, contributing to the successful deployment of four L2Hs as part of each APRRP PN's domestic COVID-19 response. Among the four APRRP PNs, only Ghana and Senegal provided care and treatment of patients as part of the response. The GAF deployed their L2H to provide health care services to COVID-19 positive patients while the Senegalese Armed Forces provided health care services for overflow patients from a city outside of the capital. Several months after the deployment of the L2Hs, USU's CGHE began discussing the possibilities for conducting virtual training related to COVID-19 with respective Embassy Country Teams.

In today's technological environment and considering the current circumstances, e-learning or virtual training plays a significant role in enhancing partnerships and maintaining communications with our partners. For instance, in an analysis of the evolution of online learning in the US, Kentnor argued that, "As developments in technology continue to advance, the ways in which we deliver and receive knowledge in both the traditional and online classrooms will further evolve."[6] Due to the APRRP PNs' trust and confidence in USU's CGHE, the GAF welcomed the idea of receiving training using virtual means. By leveraging technology and pursuing virtual training, SC and GHE objectives can still be achieved using modified approaches to training and education of partners while strengthening alliances and partnerships. Utilizing a method such as virtual training to support major SC programs like APRRP aligns directly with the National Defense Strategy's objectives to "strengthen alliances and attract new partners."[7] The CCPM Virtual Engagement series conducted through APRRP demonstrated a training approach which contributed to continued partnership building with the GAF while enhancing the GAF's medical capabilities.

The Training Plan

When conceptualizing and designing the virtual engagement training plan, USU's CGHE grappled with a major question: How can training best be delivered in a resource-limited environment for courses that are typically skills-based? This question posed particular challenges for the APRRP Critical Care Course, because as a new line of effort, a predeployment site survey

(PDSS) would typically be conducted to assess a Partner's capabilities and information obtained during the PDSS would then be used to customize the course to be conducted. However, due to COVID-19, an in-person PDSS did not occur, which led the team to develop a different training plan involving e-learning. Ruiz et al. stated "E-learning is also called web-based learning, online learning, distributed learning, computer-assisted instruction, or internet-based learning. e-learning is the use of internet technologies to enhance knowledge and performance. In diverse medical education contexts, e-learning appears to be at least as effective as traditional instructor-led methods such as lectures. Students do not see e-learning as replacing traditional instructor-led training but as a complement to it, forming part of a blended-learning strategy."[8] Although COVID-19 halted execution of in-person activities, finding other ways to continue medical training for APRRP PNs remained a priority.

USU's CGHE developed a three-pronged approach in response to this question. This approach included (1) conducting a brainstorming call with critical care subject matter experts to determine requests for information (RFIs) and discuss potential training topics; (2) developing a survey of critical care practices and COVID-19 deployment experiences; and (3) working closely with subject matter experts, USU learning resources experts, and GAF points-of-contact to plan course delivery logistics, based on evidence-based best practices and resource availability at the GAF's 37th Military Hospital located in Accra, Ghana.

First, USU's CGHE conducted a brainstorming call with the US instructors who had served on the pilot Critical Care Course held in Uganda in 2019-2020. The initial goal for the call was to determine both their availability to lead a virtual training engagement in Rwanda and Ghana, and how their experiences in COVID-19 intensive care units (ICUs) could best be leveraged to help the PNs develop baseline critical care capabilities. During the call, instructors considered whether instruction should emphasize core background knowledge for the Critical Care Course (e.g. basic electrocardiogram interpretation and advanced cardiac life support algorithms), or whether it should build a foundation in specific critical care topics, through applied instruction on COVID-19 topics. As discussions continued, the virtual engagement training plan began focusing on the GAF more specifically since the first series of virtual training had been offered to the GAF. Instructors had been heavily involved in creating the DoD's COVID-19 Practice Management Guide, Clinical Management of COVID-19, dated 30 July 2020,[9] and decided this would be a more timely and effective way to introduce fundamental topics like airway management, while building trust and confidence with GAF implementers and preventing a scenario in which the in-person Critical Care Course had participants with inconsistent medical skills backgrounds (i.e. GAF leadership could be encouraged to nominate the virtual trainees who received these critical care background materials through the virtual series to attend the in-person course rather than nominating those who had not attended virtual training).

Based on the call, USU's CGHE developed overarching goals for the CCPM series: to use the Clinical Practice Guidelines to instruct on COVID-19 patient management in an austere ICU context; to build a strong foundation between the team of US instructors and PN medical instructors in advance of the in-person Critical Care Course; to reinforce the PN's baseline knowledge of airway management and ventilation; and to gain contextual knowledge of the 37th Military Hospital's critical care practices to guide customization of the planned in-person Critical Care Course. Five progressive modules were developed, in line with these goals (Figure 1).

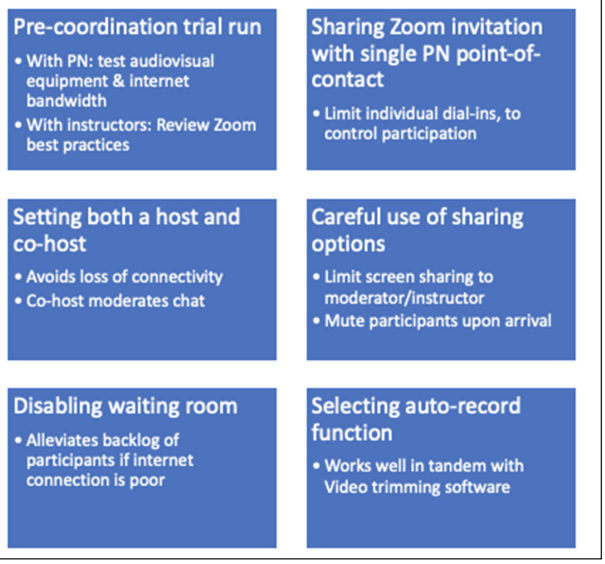
Figure 1. CCPM modules and primary learning objectives.

Module	Title	Learning Objectives
1	**Hypoxia in COVID-19 patients and early steps of supplemental oxygen**	-Define basic principles of dyspnea and control of breathing -Review causes of hypoxemia in COVID-19 pneumonia -Describe the mechanism of silent hypoxemia -Outline the escalation of oxygen therapies for hypoxic COVID-19 patients -Recognize patients at high risk for clinical deterioration
2	**Emergent airway management**	-Review basic airway skills (jaw-thrust-chin lift, oropharyngeal airway, nasopharyngeal airway, bag-valve-mask use) -Discuss non-invasive intubation methods, total intubation methods, and airway adjuncts (bougies, video laryngoscopy) -Describe indications for failed algorithms and emergent surgical airways (cricothyrotomy) -Review COVID-19 era precautions for airway procedures
3	**Basic principles of mechanical ventilation in COVID-19 patient management**	-Review basic principles and indicators for mechanical ventilation -Compare and contrast invasive and non-invasive positive pressure ventilation -Outline initial settings for mechanical ventilation for the Level 2 Hospital ventilator -Discuss initial troubleshooting of elevated peak pressure
4	**Management of acute respiratory distress syndrome (ARDS)**	-Describe definitions and classification of ARDS -Review COVID-19 specific ARDS phenotypes -Describe lung protective strategy ventilation -Discuss appropriate use of proning and neuromuscular blockade in COVID-19 patients
5	**Lessons learned in resuscitation of COVID-19 patients and therapeutic recommendations**	-Review evidence base for COVID-19 therapies, including disinformation and when to change practice -Review re-use protocols for personal protective equipment -Discuss the current evidence base for use of therapeutics, including: corticosteroids, remdesivir, convalescent plasma, anticoagulation, awake proning, invasive mechanical ventilation, extracorporeal membrane oxygenation, and hydroxychloroquine

Second, USU's CGHE worked closely with the US subject matter experts to develop a survey of critical care practices at the GAF, which it then shared with the OSC in Accra. This survey included sections on personnel (e.g. typical staffing of ICUs), programming (e.g. preferred hours for the course), training (e.g. familiarity with L2H ICU equipment), and institutionalization (e.g. preferences for integrating the course into existing training activities). At the time of initial virtual course development, the GAF had not yet returned this survey, but its creation provided USU's CGHE with clear RFIs for the virtual training, and will be instrumental in planning for the in-person course while ensuring it is tailored to the deployable L2H setting. During the COVID-19 era, such detailed surveys, particularly when channeled through the OSC or a similar agency, can serve as a proxy for a formal PDSS which would typically be the means for obtaining the answers necessary to shape training engagements.

Third, by working closely with the GAF coordinator, OSC, and subject matter experts to pre-coordinate for delivery of the virtual series, USU's CGHE ensured most participants were able to attend the live sessions and those who could not were able to view a recording previously approved by the GAF. A recording of the lecture and question & answer session allowed participants to review the information presented at a later time and reinforce the training they received during the live virtual training. Drawing on experiences delivering the in-person Critical Care Course in late 2019 and early 2020 in Uganda, USU's CGHE determined an optimal lecture time was approximately 45 minutes, and live question & answer sessions were vital to guide nuanced comprehension of applied topics. The team then carefully considered platforms and delivery specifications for each module, within two major logistical areas: knowledge management and facilitation. Based on a review of existing knowledge management platforms and their use in the PN context, USU's CGHE selected a web-based creation tool (see below for an outline of the steps in this selection process). This web-based creation tool provided the means for a custom-built website to be created which served as a private platform on which to share resources about L2H equipment (e.g. ventilator guidelines) and vetted critical care resources from military and professional societies (e.g. Walter Reed's COVID-19 Toolkit and the Society for Critical Care Medicine's Surviving Sepsis Campaign). By establishing this custom-built website for access only by the GAF, the OSC, and USU's CGHE, this kept the program equities and information relevant and limited to APRRP stakeholders. It also served as a location to upload recorded lectures and allowed APRRP to reduce overlap with other online training programs, by providing links to these programs (e.g. Harvard University's Mechanical Ventilation for COVID-19 edX course). USU's CGHE then selected Zoom Video Communications as the delivery platform, due to the GAF's familiarity with its use. Details about the recommended specifications for virtual delivery are provided in Figure 2.

Figure 2. Recommended Zoom pre-coordination & settings.



Recommended Practices for Virtual Training Engagements

Obtaining Support from Relevant US Leadership: All SC activities must be routed through the OSC for approval before any coordination or execution of training events can occur in the respective country. As such, the OSC plays both an approving and coordinating role in activities such as the launch of GHE virtual series in PNs, and it is essential to build in time for any required vetting of participants and materials through official channels. For instance, more than a month in advance of the anticipated launch of the virtual training, USU's CGHE presented the concept for conducting the virtual series to the OSC Accra, Ghana and requested approval to conduct the series by submitting a formal memorandum to the embassy. This official memorandum requested permission to conduct the virtual series with the GAF and included a course description (with titles and learning objectives for each module, projected dates, and an overview of 37th Military Hospital facility requirements) as an appendix. The OSC obtained buy-in from GAF leadership and received a roster of nominated participants. Subsequently, USU's CGHE was able to formally engage with GAF local coordinators about audiovisual equipment and date finalization.

Ideally, any slides accompanying planned lectures should be submitted at least a week before the planned engagement, for editing and relevant approvals. Due to the substantial responsibilities of course instructors (who are critical care physicians) during the COVID-19 pandemic, USU's CGHE did not receive the CCPM slides as early as ideal. However, when obtained, slide decks were submitted to USU for approval, to obtain permission to conduct the lectures and ensure that materials were in compliance with DoD and USU guidance.

Considerations When Selecting a Learning Management Platform: Knowledge management platforms can bolster USU's CGHE virtual training course capacities because they capture evolving training documents (inventory templates, L2H equipment resources, the latest versions of guidelines, etc.). They can also allow dissemination of customized resources for PNs and foster controlled access to these resources. USU's CGHE chose the web-based creation tool to create a customized website which served as its knowledge management platform based on several levels of deliberations. Based on experiences with this customized website during the CCPM, USU's CGHE recommends that organizations considering a learning management platform for a GHE virtual training apply a four step methodology to identify a platform that meets their needs.

Step 1—A careful review of the PN's existing use of platforms at universities and by the military or medical communities is necessary. For the CCPM, USU's CGHE researched the largest universities in each country, and determined which platforms they used for online education. Popular internet search engines were well-known and used throughout each of the four countries.

Step 2—Virtual engagement planners should carefully identify their top criteria for execution feasibility, and rank these in terms of 'must haves' and 'good to haves'. For example, USU's CGHE determined the training platform criteria for the CCPM—and other lines of effort for which virtual training would be conducted—and then ranked these criteria in terms of importance for achieving the most successful outcome. The key criteria included pricing, administrative burden, learning curve, precedent, compatibility with local information technology (IT) infrastructure, mobile phone compatibility, long-term sustainability (i.e. no restrictive limits on course end dates), and languages supported.

Step 3—Planners should identify any appropriate educational liaisons at their organizations, to determine if there are internal requirements or recommendations for learning platforms. In the case of the CCPM, USU's CGHE contacted the USU internet technology (IT) office to discuss the educational platforms that were supported by USU and could be utilized to conduct virtual training with partners. At that time, the customized website along with a few other platforms were all supported and compliant with USU security standards, while other platforms required a paid subscription for use. In addition, USU's CGHE consulted with USU medical curriculum development point-of-contact to discuss the aforementioned criteria and their platform recommendations. This led to the determination that, while no platforms met every 'good to have' criteria, the website creation tool which was used to create the customized website would be the most sustainable platform, because it is free to use, has simple administrative controls and user interfaces, and is easily accessed on mobile devices. These criteria seemed to be the most likely to achieve execution feasibility with APRRP PNs and hence USU's CGHE elected to use this popular web-based creation tool to tailor a website best suited for the APRRP PNs.

Step 4—It is essential to recognize the limitations of the selected platform, to promote reflexivity during (and after) its roll-out. In the case of this custom-built website, identified limitations included permission access and PN internet bandwidth constraints. For example, the utilized web-based creation tool requires permission for website access, and USU's CGHE had three options for sharing the site with PN participants, with varying levels of access control. These included publishing the site publicly (which establishes no access control); publishing the site privately with users logging in through specific types of email accounts; and publishing the site privately with users accessing the site through a shared link (which does not require specific types of email accounts but does not allow administrators to restrict access if the link is shared more widely than intended). USU's CGHE would have preferred an intermediate access control option, in which participants logged in with the option of a non-specified email account, but was able to compromise by sharing links with the GAF point-of-contact to a private site. This approach would not have been appropriate if the site contained more sensitive material, and underscores the importance of carefully thinking through platform limitations before their roll-out. Other continual limitations such as PN participants' limited internet bandwidth continue to be persistent issues. USU's CGHE plans to continue monitoring the utility of its customized website platform, through a combination of embedded products (which allow for anonymous feedback and evaluations) and continued PN point-of-contact engagement.

Recommendations for Facilitating GHE Modules on

*Zoom Video Communication*s: If compliant with COVID-19 social distancing best practices, USU's CGHE recommends that participants gather in a single location, or a few designated locations, for each virtual module. This increases the chances of having adequate audiovisual and internet capabilities, and makes it more likely that question & answer and skills-based practicals will receive full participation. For example, in CCPM modules one and two, all 12 PN participants met in the same room with masks. The GAF local coordinator organized the room and technical equipment, and moderated the live question & answer session. Each question & answer session ran for approximately 30 minutes due to the high level of participant engagement. In contrast, during modules three, four, and five, the GAF organizer was not able to organize a single location for participants. PN participants therefore joined the Zoom session from their personal computers and respective locations. This created issues with participant drop-off due to unstable internet connections, made it challenging to create clear participant rosters, and made the question & answer sessions less interactive (lasting approximately ten minutes each).

USU's CGHE found Zoom Video Communications to be an appropriate delivery platform, and experimented with several different features during each module. This experimentation revealed several recommendations for using Zoom Video Communications as a virtual engagement platform for GHE (Figure 2).

It should be noted that the CCPM series went smoothly because it was intended to be more lecture-based, rather than skills-centered. For a session in which it is necessary to verify an acquired skill, such as the planned APRRP Clinical Ultrasound virtual engagement, much more pre-coordination with PN points-of-contact will be required. During module three of the CCPM, for instance, USU's CGHE attempted to pre-coordinate to have the L2H ventilator available for an informal mechanical ventilation practice activity, but the GAF was unable to make the ventilators available during the virtual engagement. This complication did not significantly impact the execution of the module, as the instructor skipped over the ventilator activity portion after the lecture, and reverted to showing compiled ventilator pictures during the presentation (ventilator training videos were also placed on the customized website). For future skills-heavy virtual engagements, USU's CGHE anticipates that additional local coordinators, pre-coordination sessions, and audiovisual equipment to support multiple skills stations will be required.

Next Steps

USU's CGHE plans to roll-out additional virtual engagements in support of the APRRP program in late 2020 and early 2021, to provide continuity in PN instruction and strengthen relationships between USU's CGHE, instructor teams, and PN medical professionals. The CCPM will be delivered in Rwanda, Uganda, and Senegal during this time period, and Field Sanitation modules will be offered in each of the four PNs. The three-hour, single module Clinical Ultrasound virtual engagement is planned for Ghana, Rwanda, and Senegal, which will emphasize eFAST and vascular access, and will contain designated skills stations for hands-on practice with the L2H ultrasound systems.

As USU's CGHE continues to plan for these virtual engagements, several new strategies for knowledge management and facilitation will be piloted with other APRRP countries. For CPPM series in the upcoming PNs, USU's CGHE is designing a short pre- and post-knowledge assessment, which will be delivered through a form embedded within the series' country-specific custom-built website. This assessment will serve the dual purpose of determining whether key learning objectives were met, and identifying topics that may require further engagement during the planned in-person Critical Care Course. For the Clinical Ultrasound virtual line of effort, USU's CGHE is working closely with more than one local GAF point-of-contact to pre-coordinate for multiple training rooms (each with audiovisual equipment) and transportation of ultrasounds from the L2H storage facility. This course will require multiple trial runs, to experiment with the usefulness of having a single Zoom session, with break-out rooms for skill station rotations.

Conclusion

One of the ways in which the global COVID-19 pandemic's impact on the DoD SC and GHE communities can be measured is by calculating the number of engagements canceled due to travel restrictions around the world. Several months of inactivity due to the COVID-19 aftermath, especially by APRRP program execution teams, clearly took a toll on the progress of building capacity and capability in APRRP PNs. SC and GHE planners need to explore beyond the typical methods of executing activities, especially when outside circumstances, such as a global pandemic, drastically change countless months of planning and coordination of strategically important activities intended to build PN capabilities. Although APRRP PNs were deeply immersed in their own country's domestic COVID-19 response, the relationship between USU's CGHE and each of the APRRP PNs did not falter thanks to the strong relationship and continued communication with each country

prior to the pandemic. When USU's CGHE offered the opportunity to conduct virtual engagements, including medical training, both the OSC and the PN welcomed the opportunity since there was no indication as to when in-person activities would resume, while it was increasingly clear that the need to engage with our partners was a rising demand by all parties. Virtual training engagements are viable alternatives to in-person training but cannot replace them. The value of conducting virtual training engagements enhances partnerships by maintaining communications and connection with the PNs in light of the circumstances. SC and GHE planners should take into consideration alternative solutions such as conducting virtual training engagements when planned SC or GHE events cannot be conducted for whatever reason in order to keep existing relationships and increase trust and confidence between the US and its allies. Maintaining these relationships and continuing to support our allies and partners in times of crisis enables one of the three pillars of our National Defense Strategy, which aims to strengthen the US global network of allies and partners in the face of a growing great-power competition.

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COVID-19 in a Role I Evacuation: A Case Series

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Introduction

Since December 2019, the novel SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2) became an emerging infectious disease pathogen that led to a global pandemic with over 43 million cases reported worldwide and more than 1.1 million global deaths (as of 26 Oct 2020, from https://coronavirus.jhu.edu/map.html). Commonly known as coronavirus disease 2019 (COVID-19), this pathogen presents with a broad spectrum of disease progression and manifestations (no symptoms to acute respiratory distress syndrome leading to severe complications and death).[1,2] Multiple publications have reported risk of disease and co-morbidities to include select underlying medical conditions and risks: older age (≥65 years), hypertension (HTN), cardiovascular disease, smoking, chronic respiratory disease, cancer, diabetes (DM), obesity (BMI≥30 kg/m2), and male sex.[2,3,4,5,6,7,8] In one study, researchers found severe obesity (BMI≥35 kg/m2) associated with intensive care unit (ICU) admission alone.[8] Nonetheless, risk factors for severity of the disease are determined by the pathogen, host, and environment.[9]

As a result, additional research on racial/ethnic health disparities was conducted, which concluded a disproportionate burden of COVID-19 related health outcomes among minority groups.[2,10] Reviewing the data, it appears the most pervasive inequities in COVID-19 related morbidity and mortality occur among African-American, Native American, and Latino populations.[2,10,11,12] Although the mechanisms of these health disparities may not be clear, social determinants of health and multiple underlying co-morbidities may be the significant contributing factors.[13,14,15] Furthermore, occupational and workplace characteristics may also pose as risk factors due to the nature of close contacts with one or multiple persons posing as the nexus of disease transmission.[16] Notably, military occupation in a deployed setting also presents as a plausible risk for infectious diseases such as COVID-19.[17] In one study describing the number of military medical air evacuations between 2001 and 2013, non-battle injuries accounted for 31-34% of the total number of casualties.[17] Although there is published literature from the US Navy describing COVID-19 medical evacuation in a deployment,[18,19] there is insufficient data relating to the medical evacuation of COVID-19 patients from an Army Role I platform. This paper aims to describe a case series of COVID-19 positive cases that will further explain the capabilities and challenges in a far forward medical unit in a deployed setting.

Case Series

These data represent a six-patient case series of symptomatic COVID-19 positive individuals from a single austere location within the US military's Central Command (CENTCOM) Area of Operations (AOR). These patients were seen and treated between 16 May and 03 Aug 2020, at a US Army Role I medical treatment facility. The patients were all males and ranged from 39-64 years of age (Table 1).

Polymerase Chain Reaction (PCR) testing for SARS-CoV-2 was utilized to determine the causative agent of illness. The patients presented to care with new-onset, primary respiratory complaints. The most commonly reported symptoms were a frontal headache, fevers, shortness of breath, and debilitating fatigue (Table 2).

Table 1. Patient characteristics.

Cases:	Gender:	Age:	Race/Ethnicity:	Status:	Occupation:	Comorbidities:
Case 1	Male	51	Caucasian	Active Duty	Force Protection	Elevated BMI
Case 2	Male	40	Hispanic	Active Duty	Land Forces	None
Case 3	Male	61	African-American	Contractor	Contract Management	HTN, HLD
Case 4	Male	59	Caucasian	Contractor	Contract Management	Elevated BMI, Type 2 DM
Case 5	Male	39	Caucasian	Active Duty	Land Forces	Asthma, Allergic Rhinitis, Gout
Case 6	Male	64	Middle Eastern	Contractor	Logistics Support	Elevated BMI, Type 2 DM, HTN

*BMI-Body Mass Index, HTN-Hypertension, HLD-Hyperlipidemia, DM-Type 2 Diabetes Mellitus.

All patients further developed significant symptomatic coronavirus disease. Although these cases were all between the ages of 40 and 65, the majority were male, had potential interaction with local nationals, hypertension (HTN), Type 2 Diabetes Mellitus (DM) and elevated body mass index (BMI).

Table 2. Symptoms chart.

Symptoms:	Fever/Chills	Headache	Cough	Shortness of Breath	Rhinorrhea	Myalgias	Fatigue	GI Complaints
Case 1	X	X	X	X		X	X	
Case 2	X	X	X			X	X	
Case 3	X	X		X		X	X	
Case 4		X	X		X	X	X	
Case 5		X		X			X	
Case 6	X			X	X		X	X

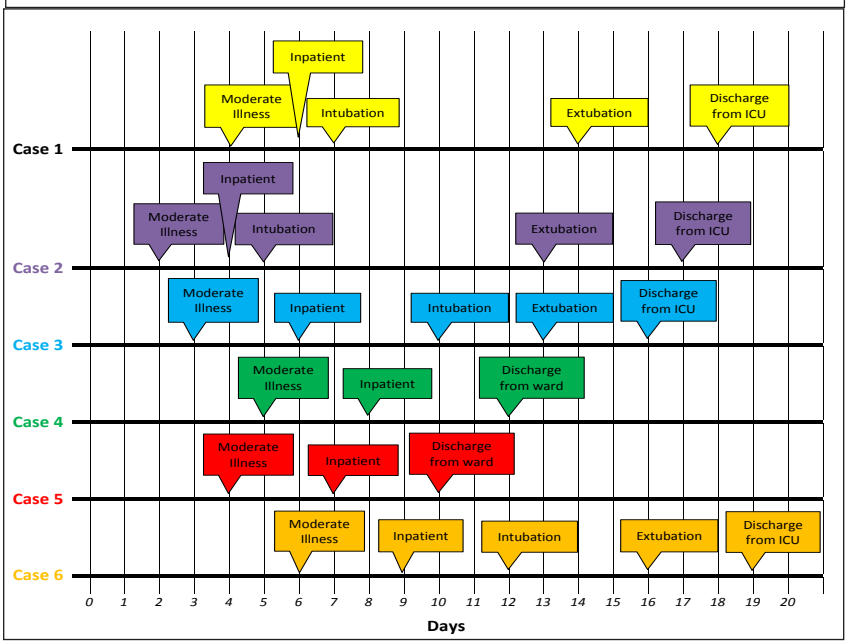
*GI-gastrointestinal

Four of the six patients required mechanical ventilatory support. All mechanically ventilated patients also received both Dexamethasone and Remdesivir per an open-label Department of Defense (DoD) investigational drug protocol. All patients were evacuated from a Role I facility using a variety of evacuation platforms to include ground ambulance and rotary-wing MEDEVAC. The patients were initially transferred to a nearby flight line while awaiting movement via the Patient Movement Request (PMR) process. Ultimately, all patients were successfully air-evacuated via the DoD's new biocontainment transport medium, the Negative Pressure Conex (NPC) system. Once out of the theater, evacuees were transported directly to LRMC (Landstuhl Regional Medical Center) via the assistance of TPMRC-E (Theater Patient Movement Requirements Center-Europe). All patients survived then discharged (Figure 1).

Discussion

It is now well understood that COVID-19 presents with a wide variety of clinical manifestations ranging from the asymptomatic carriage of the virus to fulminant illness with severe complications, including permanent disability and death. This case series highlights the challenges of dealing with the manifestations of illness due to COVID-19 in a single austere location within CENTCOM. As the infection progresses and the patients' clinical conditions worsen, one of the primary obstacles to care associated with the CENTCOM AOR is the difficulty in evacuating patients, specifically, from a Role I facility with limited medical resources to a higher echelon of care in an expeditious manner. CENTCOM guidance, at the time of the initial outbreak, called for the evacuation of all symptomatic COVID-19 positive service members, government service personnel, and DoD contractors to definitive care at LRMC via the PMR evacuation process. The rapid clinical deterioration of some patients posed a significant challenge, as evacuation timelines commonly exceeded 24 hours. Additionally, the Role I facility was unable to rely on host nation medical facilities as the COVID-19 pandemic had severely degraded local hospital facilities. This confluence of factors placed tremendous pressure on a Role I facility to provide advanced life support measures to critically ill COVID-19 patients.

Figure 1. Timeline of illness.



While the US military's active-duty population tends to be younger, healthier and possesses higher levels of physical fitness compared to the population of the US at large, these factors alone are not enough to guard against infection with COVID-19, nor do they preclude a service member from becoming seriously ill. Before deploying to CENTCOM, all personnel undergo a medical screening process per MOD 15 of AR 40-501 to ensure minimum standards of fitness for deployment to the area of responsibility

are met. During the pandemic, this update to the medical readiness standards was released in April 2020. One of the primary changes this revision introduced was the addition that the service member is less than 65 years of age for the duration of the deployment. This recommendation was congruent with emerging data, which indicated that the severity of illness from COVID-19 was strongly correlated with increasing age. While this was beneficial for preventing individuals with the potential to become seriously ill from entering theater, it did little for those already active in the AOR.

Pre-existing medical conditions and co-morbidities played a large role in our case series. Elevations in BMI, Type 2 Diabetes Mellitus (DM) and Hypertension (HTN) were the most commonly observed among critically ill patients from this location. Environmental and occupational factors unique to the authors' location included the mission-essential need to work on a nearly continual basis with host nation mission partners. Our data indicates that those with the most serious levels of illness worked to the greatest extent in host nation military occupational environments, in an advisory capacity.

A Role I medical facility provides a certain amount of capability to a commander on the battlefield. That capability includes a medical provider who can extend human life until a patient can be transferred to the next higher level of care. During a pandemic on a military base, the Role I medical facility delivers the same life-extending capability.

We experienced that the progression of illness for COVID positive patients can become critical within a few days of showing symptoms. The command received continuous updates on the status of all positive patients on the base to help determine when a patient could no longer be treated by the Role I. The timing for submitting an air medical request to extract a patient to a Role IV was critical. Not having a Role II or III within proximity places a high risk for continuing treatment of COVID-19 positive patients on the base. At that time, there were no higher echelons of adequate hospital care that could render COVID-19 patient management. This placed a higher emphasis on making a timely decision as to whether a patient will be evacuated to a Role IV or stay on the base to recover.

Conclusions

During the COVID-19 pandemic, limited Role I capabilities in an austere environment creates challenges during a medical urgent MEDEVAC scenario. Identifying risk factors to include co-morbidities is critical to successful patient outcomes. Although this case series had an age group younger than 65 years of age, other co-morbid risk factors (HTN, DM, obesity, male gender and occupational risk exposures) were identified. Appropriate screening of individuals before deploying into the CENTCOM AOR is vital to prevent high morbidity and mortality in the theater. Further, command priorities focused on a medical operational lens will synchronize the leadership into a main effort directed toward treating and evacuating patients. Dedicated resources are essential for the timely and productive medical care of a critically-ill patient requiring extraction to a higher level of care. This case series remains a sober reminder to commanders and military medical providers that infectious diseases in the deployed setting are a top priority for Force Health Protection.

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Alternative Immunization Clinics to Improve Vaccination Access during the COVID-19 Pandemic

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Abstract

The United States declared a national emergency on March 13, 2020, in response to the rapidly spreading COVID-19 pandemic after all 50 states reported laboratory-confirmed cases.[1] The demand for ambulatory medical care in the US fell by almost 60% and immunization encounters at Walter Reed National Military Medical Center decreased by 76% as patients became concerned about the risk of coronavirus exposure within a clinic or hospital setting.[2] Our vaccination initiatives aimed to increase our pediatric and adult immunization rates through offering two alternative immunization platforms aimed to reduce patient concerns about COVID exposure.

Our facility implemented seven weeks of multidisciplinary alternative vaccination access through an After Hours Immunization Clinic which transitioned to a Drive Up Immunization Clinic. Almost 600 adult and pediatric patients received immunizations at the After Hours and Drive Up immunization clinics, which boosted our overall vaccination status from 23% to 78% from early April to June 2020, when compared to baseline 2019 Immunization Clinic encounters. The number of encounters served as a surrogate marker for vaccination rates. This innovative Immunization Clinic could serve as a rapidly deployable model to facilitate future vaccinations during the continued COVID-19 pandemic, annual influenza vaccine drives, or other future biological crises.

Background

Over the course of several weeks, the novel coronavirus SARS-CoV-2 traveled from its site of origin in Wuhan, China, and emerged as a global pandemic. Despite our previous knowledge of other similar viruses, it spread rapidly in our ever-expanding and richly connected world, and the World Health Organization officially declared a pandemic on 11 March 2020. This prompted a swift response by many countries who shut down cities and towns to try to prevent additional spread of the virus. The US followed suit when the president declared COVID-19 a nationwide emergency on 13 March 2020, the effects of which continue as many regions of our nation still remain in a state of partial or total shutdown.[3]

Governor Larry Hogan, Jr declared a state of emergency for the state of Maryland, which included Walter Reed National Military Medical Center (WRNMMC) in Bethesda, on 5 March 2020. State government immediately offered guidance for social distancing, including avoiding large gatherings, which transitioned to an official stay at home order for Maryland residents on 30 March 2020.[4,5] Residents were allowed to travel only to obtain healthcare, necessary supplies, or participate in activities essential for one's health and safety. On 15 May 2020, limited businesses, organizations, and establishments including religious facilities, retail establishments, and outdoor recreation reopened with restrictions to maintain safety, but many others remained closed with no guidance on a reopening date. The state of emergency remained in place even as cautious phased reopening still continues.[6]

The WRNMMC Immunization Clinic is adjacent to the Allergy/Immunology Clinic and Pediatric Clinic. In our hospital, the Immunization Clinic is available

on a walk-in basis, without scheduled appointments. Many of our vaccination visits are for pediatric patients, with pediatrics immunizations coordinated with scheduled pediatric appointments, but also include routine adult, travel, or military deployment vaccines. Wait times can be slightly unpredictable due to a constant influx of walk-in patients, who also share a central waiting area with other Allergy/Immunology Clinic patients.

A recent report in *Morbidity and Mortality Weekly Report* from May 2020, showed routine vaccine rates in children ages 0-24 months declined from roughly 66% during the COVID-19 pandemic to less than 50%.[1,7] This trend was observed in all the milestone age cohorts with the exception of the birth-dose hepatitis B vaccine, which is generally given while infants are still inpatient after birth. In our own Immunization Clinic, we also noticed a striking decline in pediatric and adult vaccination encounters during a similar short period of time.

Our facility's alternative Immunization Clinic began as an idea to improve patient access to vaccinations during the COVID-19 pandemic after the Pediatric and Immunization Clinic waiting areas remained unoccupied for weeks. Demand for in-person ambulatory care in the US declined nearly 60% by early April, due to patient concerns about exposure to coronavirus within the hospital.[2] Our Pediatric Clinic rapidly transitioned to telehealth encounters much like the rest of the country to meet patient demand, but immunizations still required a face-to-face clinic visit which many families were reluctant to complete.

By mid-April, the WRNMMC Immunization Clinic had a decrease in total encounters of over 2,000 encounters that grew by more than 60 per day when compared to the same time period in 2019. Weekly average immunization encounters were 76% lower as patients explained they did not want to come into the hospital for routine vaccinations due to the risk of COVID-19 exposure. This is concerning due to the potential outbreak of vaccine-preventable illnesses such as pertussis or measles when immunization rates fall to less than 90-95% within a population.[7] Immunization encounters served as a proxy for vaccination rates due to the complexity of tracking patients across an ever-changing military healthcare system. Our vaccination initiatives aimed to increase our immunization rates through offering two additional immunization platforms intended to reduce patient concerns about COVID-19 exposure.

Design/Methods

Our working group consisted of clinicians and staff from pediatrics and allergy & immunology, organizational leadership, public affairs, facilities, infection control, and military base support staff who developed two possible courses of action to improve vaccination access. The first involved the expansion of the Immunization Clinic's regularly scheduled weekday hours and allowed families to schedule staggered appointment times. The second was an alternative Immunization Clinic to administer vaccinations in a separate location from the hospital clinic. As the group discussed, planned, and determined timelines for operating either of the options, the underimmunized population continued to grow as daily immunization encounters remained low. Additionally, our Pediatric Clinic noticed many parent-measured inaccurate heights, weights, and head circumferences or inability to obtain measurements at home during virtual visits.

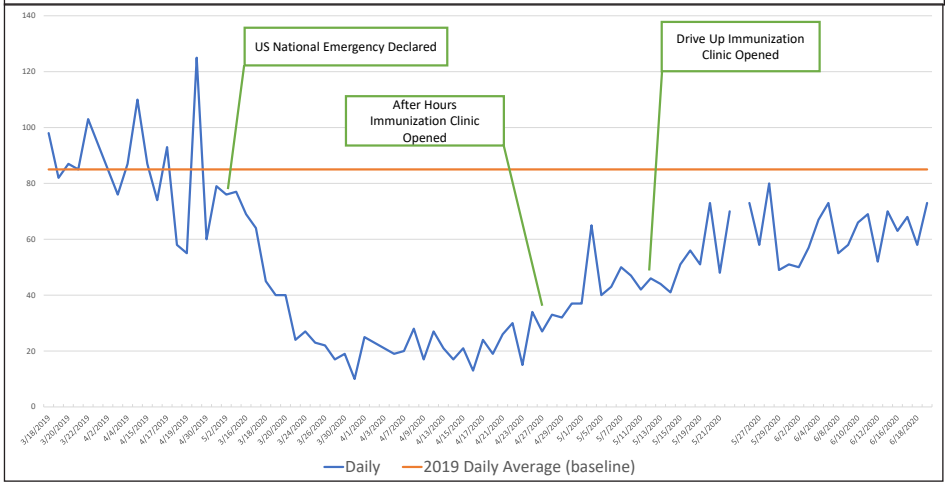
The planning team developed an information paper with workflow diagrams, staffing requirements, and supply/equipment lists for expanded daily hours of the Immunization Clinic which became known as the "After Hours Immunization Clinic." Usual daily Immunization Clinic hours were 0730-1600 and the After Hours Immunization Clinic offered appointments and walk-in vaccinations 1600-1900. Additional screening of pediatric patients under age 17 included height, weight, and head circumference (for children under 2 years of age) immediately prior to administration of the age-appropriate vaccinations. These measurements were entered into a separate electronic medical record and reviewed by pediatricians to ensure patients tracked along their appropriate growth curves.

While the After Hours Immunization Clinic opened, the working group simultaneously planned an alternate location Immunization Clinic. The hospital Director approved the After Hours Immunization Clinic as an interim solution once the large scope of the added site clinic was fully realized. This After Hours Clinic utilized already-established pediatric screening rooms, immunization rooms, staff, and supplies; it required no expanded funding. All required staff operated on an alternative duty schedule and the only required training was the workflow and concept of the clinic. Public affairs and the involved clinics announced the details for the newly established After Hours Immunization Clinic via social media, flyers, and direct patient communication using a secure messaging system.

The second course of action launched an out-of-hospital

Immunization Clinic using either a field mobile tent or hard-sided, commercial temporary structure. Planning for this clinic occurred concurrently with the opening of the After Hours Immunization Clinic. The hospital already had a large climate-controlled military tent, but required additional coordination with the military base, facilities, and hospital operations to determine location and supporting infrastructure needs. A temporary commercial trailer quickly exceeded available funding and lacked the needed configuration capabilities without expensive modifications.

Figure 1. All immunization encounters.

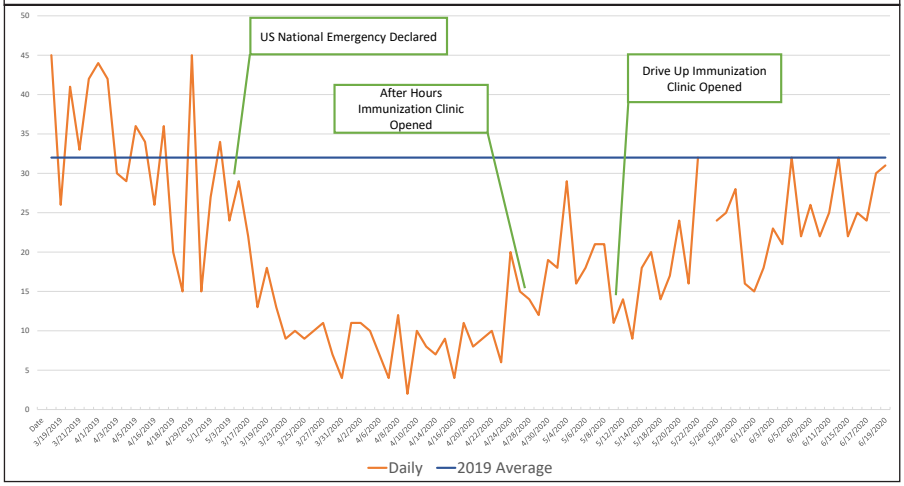


The tent-based operation moved forward with additional supply, staffing, and other planning needs determined over the next week. The hospital director approved the Drive Up Immunization Clinic with a planned opening one week later, approximately two weeks after initiation of the After Hours Immunization Clinic. Public affairs again notified patients about the change from the After Hours Immunization Clinic to the newly established Drive Up Immunization Clinic through the hospital website, immunization information phone line, and social media.

The ideal location for the immunization tent was in a parking lot across from the hospital building that housed the Pediatric and Immunization Clinics where supplies and staffing were easily available. Hospital COVID emergency funding paid for rental of a generator, a shade canopy, and road signage. Families entered the base, followed signs to the parking lot, and were screened for COVID-19 symptoms before being directed to park in a designated area adjacent to the tent. They remained in their vehicle while a screener took their information, determined appropriate vaccines, and escorted them from their vehicle to the tent where pediatric patients had height, weight, and head circumference obtained. Patients then received immunizations in one of three available bays, walked back to their vehicles, and were released after 15 minutes of monitored time in their individual cars. There were two pediatric staff and four to eight immunization staff working in the tent during normal weekday operations.

The number of immunization encounters served as a surrogate marker for vaccination rates due to the complexity of data manipulation within the confines of our medical record system. The After Hours Immunization Clinic saw 90 patients during the two weeks it was open and the Drive Up Immunization Clinic had 503 encounters over the five weeks it was operational. We calculated baseline Immunization Clinic numbers using a weekly average number of encounters from the prior year (March to May 2019).

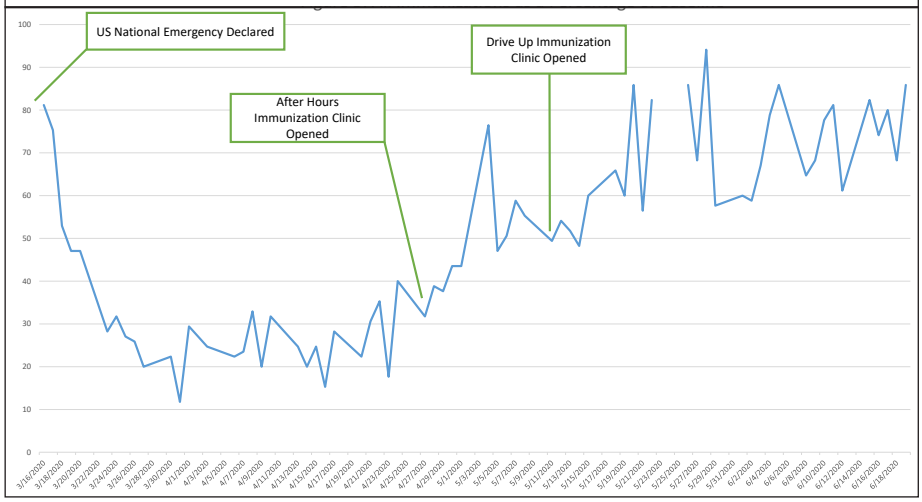
Figure 2. Pediatric immunization encounters.



Results

Our vaccination initiatives aimed to increase the number of immunizations through offering a minimal contact detached location to

Figure 3. All immunizations as a percentage of baseline.



patients with fear of COVID exposure. During the seven combined weeks of After Hours Immunization Clinic and Drive Up Immunization Clinic, almost 600 patients received immunizations through these alternative means. These initiatives met patient desire for an alternative immunization location not co-located with the clinics inside of the hospital.

Another important impact from our initiatives included increased rates of vaccinations as we improved our overall number of daily immunization encounters when compared to baseline from a low of 23% during early April to 78% at time of closure of the Drive Up Immunization Clinic in the middle of June. Our pediatric numbers reflected the same trend with an improvement in baseline encounters from a low of 22% also in early April to 83% at closure of the immunization tent.

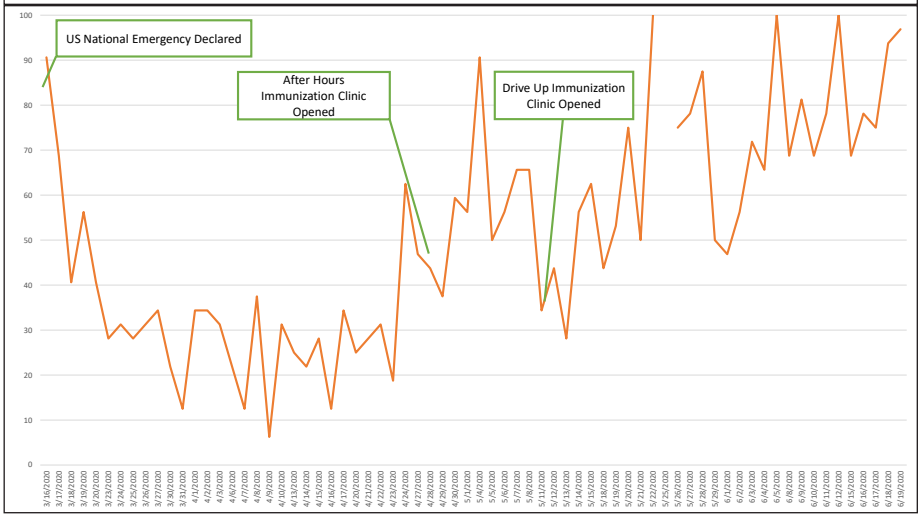
Lastly, the innovative immunization offerings had a significant positive impact on patient satisfaction which families provided on clinic feedback. Patients remarked that they had "the best experience possible" and "appreciated the fact that they did not have to enter the hospital" in order to get their necessary vaccinations. All Pediatric clinicians reported parents were happy to have the ability to ensure their children stayed up to date on their immunizations while maintaining distance from the perceived risk of COVID exposure at the hospital.

In order to track the data, the senior noncommissioned officer from the Immunization Clinic manually counted the number of encounters daily and added them into a tracker spreadsheet. Initial metrics tracked from 2019, included date and encounters divided by age (adult and pediatric [age 17 years and younger]). Metrics from 2020 included the same data, but expanded to include the percentage of baseline encounters.

The immunization spreadsheet was electronically tracked after daily closure of the expanded clinic by the hospital Director, Director for Medical Services, and leadership from both the pediatric and immunology departments. Trends and numbers of encounters were discussed at various hospital level leadership meetings down to individual department meetings. Patient feedback was discussed during leadership meetings and daily Immunization Clinic huddles.

Data analysis yielded positive trends for total numbers of encounters after both phases of the initiative as well as the percentage of encounters when compared to baseline. Figure 1 demonstrates the run chart with specific points annotated for our overall immunization numbers with Figure 2 showing our run chart for pediatric immunization encounters. Figure 3 also shows a run chart for immunization encounters as a percentage of baseline for both our overall numbers, while Figure 4 is a picture of the same for our

Figure 4. Pediatric immunization encounters as a percentage of baseline.



pediatric patients.

The data obtained from our expanded vaccination initiatives showcases that the additional Immunization Clinic opportunities had a positive impact on the overall immunization status of the facility's beneficiaries. The goal of the phased initiatives was to increase the number of immunizations given to our patient population, which was accomplished when almost 600 patients received vaccinations during those seven weeks of operational time. Our overall number of immunization encounters increased and the daily immunization encounters grew closer back to 78% of baseline when compared to 2019. The expanded access vaccination initiatives were completely patient-centered and focused on their safety and quality of the care experience. The positive comments from patients and families confirmed the success of our operation in addition to the more straightforward improved metrics.

We did encounter minor difficulties in rolling out the initiatives; these were fairly easy to overcome, and could be attributed to the rapid timeline from planning to implementation of the alternate site Immunization Clinic. The initial plan was to start with operations in the Drive Up Immunization Clinic, but we quickly realized the depth and breadth of such an operation required more than two weeks. The After Hours Clinic became a stopgap measure to help expand operations as we continued to plan and develop the offsite location. Our hospital leadership gave full support to the project as it represented a much needed and patient-centered expanded service during unprecedented times. One further limitation we identified was the dissemination of information to our large patient population about the Immunization Clinic changes but the public affairs office provided key assistance. Moreover, our beneficiaries remain ever-resilient even in the face of COVID-19, and changing site locations or other minor details about where and how they receive these protective vaccines did not prove to be a significant issue.

Conclusion

The objective of our expanded access Immunization Clinic was to increase the number of vaccinations our beneficiaries received in a patient-centered environment. The After Hours Immunization Clinic and Drive Up Immunization Clinic successfully achieved this purpose for almost 600 patients. The risk of potential COVID-19 exposure during a hospital-located clinic encounter frightened many patients who were willing to postpone critical medical needs to stay away from the hospital. The patient-centered initiatives anticipated the risk of an underimmunized patient population and found a novel solution to expand vaccine access in a non-hospital setting.

The overall practical usefulness of the Drive Up Immunization Clinic cannot be underestimated in the uncertainty facing our healthcare system during the current pandemic. It could serve as a model for expanded vaccination access in a nontraditional environment due to ongoing barriers to care. This could be extended to cover seasonal flu vaccinations or converted to provide basic ambulatory care if needed. Our facility now has a verified standard operating procedure which other installations could use if they chose to establish a similar clinic.

Our clinic ran extended hours for two weeks within the facility and then transformed into a five week drive up alternative site. Immunization encounters increased and were trending toward baseline when we closed the tent due to patients returning to clinic-based care, staffing issues, upcoming flu drive preparation, and decreasing coronavirus cases in our area. Continuation of the Drive Up Immunization Clinic throughout the summer and possibly into fall/winter season would provide additional data about patients' preferred immunization location. Comparison of our facility's utilization of alternative vaccination sites with other military treatment facility's alternative vaccination sites could show a regional trend, which may fluctuate depending on current coronavirus case numbers.

Our expanded access vaccination clinic has the potential for replication within the military healthcare system as it does not require significant additional personnel, equipment, or a large budget. It is relatively quickly set up and operational if the facility has a tent or shelter available and an open area to place the independent clinic. Given the uncertainty of the current pandemic and our goal of military readiness, the alternative Immunization Clinic could represent the future of immunization operations.

Preoccupation with failure by anticipating risk and finding a solution perfectly encompasses the expanded access vaccination clinic through the domain of patient-centeredness with focus on patients' safety and quality of care experience. The entire operation is based on the patient experience and desire to seek care in a separate and easily accessible location in order to maintain optimal health despite the ongoing COVID-19 pandemic. There is an inherent exposure risk in entering a healthcare facility during a biological crisis and our facility met patient request for healthcare delivery in a safe environment to counter

the risk of an underimmunized population. The alternative Immunization Clinics offered expanded patient access to a vital healthcare component and could serve as an innovative model to facilitate vaccinations during the continued pandemic or other future biological crises.

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Using Real-Time Google Search Interest as a Predictive Tool for COVID-19 Cases in the United States

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Abstract

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is an ongoing global pandemic with over 23 million associated cases and 800,000 associated deaths. There is a surplus of proposed predictive models (n>145) for COVID-19 that have emerged in academic literature; however, many of these predictive models have proven unreliable or biased.[1] Several studies have looked at Google Trends data as a possible predictive tool in the last months.[2–12] In this retrospective study, we looked at the predictive value of the Google Trends Tool as it applies to COVID-19 Cases and Reported Onset of Symptoms in the US. We looked back at Google Trends data for search interest of common COVID-19 search terms: "coronavirus" and "covid-19" from January 2020 through mid-June 2020 and compared that data to Centers for Disease Control (CDC) data on COVID-19 Cases Reported and Reported Date of Initial Onset of Symptoms.[13] Google Trends is a free online tool that allows a user to quantify the search interest for a keyword or phrase over time.[14] Significant strong positive correlation was found between CDC Reported Date of Initial Symptoms for Cases data and Search Interest for both terms "covid-19" and "coronavirus." Google Trends is a free and easy to access tool that may have utility as a predictive instrument with regards to the current COVID-19 pandemic. The Google Trends Tool may offer new insight and predictive value for medical decision making during current and future outbreaks in near-real time at a very granular level allowing states, cities and military bases to prepare.

Introduction

A PubMed search for "forecasting covid-19 cases google trends" returned 31 results with eight of the resulted papers analyzing Google Search Interest data to COVID-19 case data.[2-5,7-10] None of the reviewed articles looked specifically at CDC reported date of symptom onset or CDC reported case data within the US. Statistically significant correlation between Search Interest and COVID-19 Case date for multiple countries including Italy, Spain, France, Germany, the United Kingdom, China, Iran and India.[3,7-10] Relative Search Volume has been found to be a reliable tool to help monitor outbreaks showing a peak in interest 11.5 days before a peak in new cases.[3] Many of these studies focused on search interest related specifically to terms like "covid-19" or "coronavirus" while others looked at search interest for symptom related terms such as "loss of smell" or "GI symptoms."[6,12]

SARS-CoV-2 became a global pandemic after initial cases in Wuhan, China, occurred in December of 2019.15 It was originally named the 2019 novel coronavirus (2019-nCoV) but was later changed due to further classification as part of the species severe acute respiratory syndrome-related coronavirus by the Coronaviridae Study Group of the International Committee on Taxonomy of Viruses.[16] As of 24 August 2020, the World Health Organization reports over 23 million cases and 800,000 deaths.[17] The origin of the outbreak has been suggested to be the Huanan Seafood Wholesale Market, where the patients from the first four cases identified had worked. These patients were all admitted to the hospital on 29 December 2019, and by the following day the China CDC was notified.[18] The first symptoms of coronavirus were recorded earlier on 8 December 2019.[15] It is likely that a bat was the original host that spread the virus to humans. The virus Bat CoV RaTG13 has an almost identical genome sequence, which suggests they have the same ancestor.[19] The first reports outside of China

were in Thailand, Japan, and Republic of Korea.[18] On 11 March 2020, the virus had spread to dozens of countries and was declared a global pandemic by the World Health Organization.[15]

Clinically, COVID-19 presents as pneumonia that has several clinical manifestations.The most common manifestations are fever, cough, and dyspnea. The most prevalent laboratory results among positive cases include decreased albumin, high C-reactive protein, high lactate dehydrogenase, lymphopenia, and high erythrocyte sedimentation rate.[20] For human-to-human transmission, coronavirus spreads through droplets, respiratory secretions, and direct contact. Due to results from studies finding the virus in fecal swabs, it could be spread through the digestive tract as well but this has not been confirmed and requires more research. Coronavirus has an incubation period of 1-14 days and is contagious during this time. It has a low infectious dose and is highly contagious. Acute respiratory distress syndrome, respiratory failure, multiple organ failure, and death can all be outcomes of a severe case. Severe outcomes occur most often in cases where patients are elderly or have underlying disorders which may affect their ability to recover.[19]

COVID-19 Predictive Modeling

As more academic literature regarding different projection models is being published, it is important to identify the utility of predictive studies in identifying long-term outlook of COVID-19 versus the possible risks associated of placing too much weight on predictive mathematical calculations. Taking these risks into consideration, predictive models provide insight into potential trends of this unprecedented pandemic.

In the April 2020 study by Benvenuto et. Al., the auto regressive integrated moving average (ARIMA) model was applied to the Johns Hopkins epidemiological data to predict the epidemiological trend of the prevalence and incidence of COVID-19.[21] They concluded that although the number of confirmed cases is still increasing, the spread of the virus seems to be slightly decreasing and the incidence is decreasing. Also deduced from the information is that seasonality does not appear to be influencing the incidence or prevalence of COVID-19.

Within Brazil, short-term forecasting of COVID-19 cases using the Holts exponential model was conducted by Martinez et al.[22] This model does not account for seasonal components. Data from April 26th 2020 through May 3rd 2020 was compared to forecasts from the Holt's method (95% prediction intervals) and demonstrated good short-term predictive value; however, it also underestimated the number of observed cases. As stated by the authors, logarithmic models in general have low sensitivity for predicting the peak of the COVID-19 outbreak or for providing long-term predictive forecasts.

As the total number in cases reaches new heights globally, predictions regarding the prevalence, mortality and outlook, can often be skewed. Multiple factors can contribute to this; lack of government transparency (in cases such as China and Iran), relatively low percentage of the overall population having been tested, using self-reported symptoms as "positive" case definition in predictive models, and the high risk of bias given the catastrophic social, economic, domestic and geopolitical impacts of a global pandemic. It is imperative that accurate real-time data, coupled with expertise of professionals specializing in epidemiology and infectious disease and social consideration such as increased individual mobility (with or without easing of travel restrictions) in combination with this calculated data to best understand outbreak dynamics and prepare for the future.

Methods

Google Trends is a free online tool that allows a user to quantify the search interest for a keyword or phrase over time.[14] It serves as an index to gauge search volume relative to peak popularity of a keyword or group of keywords. It does not give actual search volume, rather a comparative view making it an ideal means of comparison of two or more separate terms or a single terms popularity over time. We utilized the Google Trends tool to quantify interest over time. In this retrospective study, we looked back at Google Trend data within the United States from January 2020 to June 2020 for the keywords "covid-19" and "coronavirus."

Following this search, we pulled the publicly available CDC Covid-19 case report data from the week of January 5th, 2020 to the week of June 14th, 2020 for comparison.[13] All data was pulled during the week of June 23, 2020. Specifically, we analyzed the January 2020-June 2020 CDC Data for "Number of COVID-19 Cases, by Date of Illness Onset" and CDC Data for "Number of COVID-19 Cases, by Date Reported." The "Number of COVID-19 Cases, by Date Reported" data set was created by taking the "Total Number of COVID-19 Cases, by Date Reported" and subtracting a day's total from the prior day's total to yield the difference or number of new cases. Data was analyzed within the Google Trends user interface and a standard spreadsheet software. Statistical analysis was completed utilizing to assess correlation, regression, and statistical significance.

Google explains that a value of 100 represents a peak

popularity for the search term relative to all other search terms over the given time period and region. A value of 50 means that the term is half as popular. A value of 0 or <1 indicates that there was not enough data for that term per Google Trends.[14] Google Trends also allowed for sub-regional (state/metro/city) interest to be evaluated.

Results

The most profound discovery from this study was a significant ($p = 1.17E-05$) strong positive correlation (r=0.90) between Search Interest for "covid-19" and CDC Reported Date of Illness Onset for Cases. Furthermore, we found significant (p<0.001) strong predictive value (R2= 0.81) between the search interest for "covid-19" and CDC Reported Date of Initial Symptoms for Cases.

A significant (p=0.0005) strong positive correlation (r=0.81) was also found between search interest for "coronavirus" and CDC Reported Date of Illness Onset for Cases. Furthermore, we found significant (p=<0.001) moderate predictive value (R2=0.65) between the Search Interest for "coronavirus" and CDC Reported Date of Initial Symptoms for Cases (Table 1).

A significant (p=0.015) moderate positive correlation (r=0.52) was found between search interest for "covid-19" and CDC Reported Cases. Furthermore, we found significant (p<0.05) very weak predictive value (R2=0.27) between the search interest for "covid-19" and CDC Reported Cases. A very weak positive correlation (r=0.01) was found between search interest for "coronavirus" and CDC Reported Cases, however, it failed to achieve statistical significance (p=0.95) (Figure 1).

Search interest (SI) for the term "coronavirus" was present from the first week of January 2020 (SI=1), peaked the week of March 15th 2020 (SI=100) before tapering to an SI of 9 the week of May 31st, 2020, and saw a slight increase the week of June 21st 2020 to an SI of 11. SI for the term "covid-19" was present from the February 9, 2020 (SI=1), peaked the week of March 22nd 2020 (SI=100) before tapering to an SI of 28 the week of May 31st 2020 then saw an increase over the next two weeks to an SI of 41. CDC Number of COVID-19 Cases, by Date of Illness Onset data started the week of Jan 12th 2020 with 9 cases, peaked the week of March 29th 2020 before the CDC ceased reporting this metric two weeks later. CDC Reported Case data started with 6 cases the week of January 26th, 2020 and peaked the week of April 5th, 2020 at 220,878 cases reported.

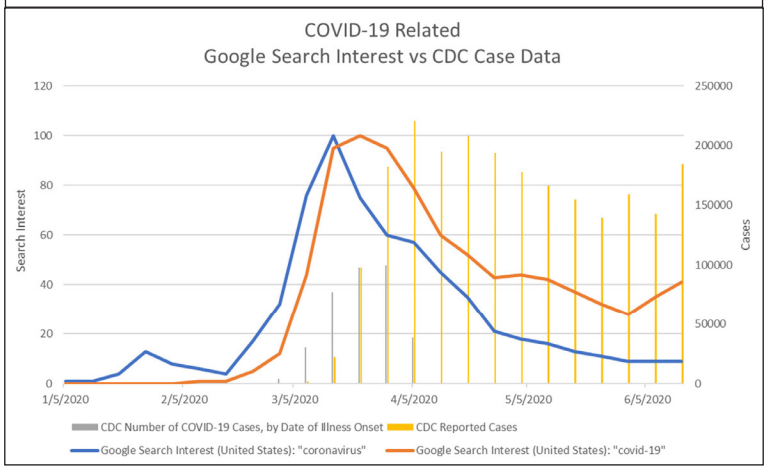
Table 1. A summary table of the regression statistics for search interest for the terms "covid-19" and "coronavirus" and CDC Data for Cases Reported and Cases by Reported Date of Illness Onset.

Regression Statistics				
	"covid-19" : DOIO	*"coronavirus" : DOIO*	*"covid-19" : cases*	*"coronavirus" : cases*
Multiple R	0.90	0.72	0.53	0.32
R^2	0.81	0.52	0.28	0.10
Observations	14	14	21	21

Discussion

The most significant findings in this study were the strong positive correlations between the CDC Reported Date of Initial Symptoms for Cases and Search Interest for both search terms ("covid-19" and "coronavirus"). It is interesting to note that both search terms shared stronger correlation with the CDC Date of Symptom Onset data than they did with the CDC Case data. This indicates that there is a higher volume of searches for these COVID-19 related terms as symptoms are first starting to appear. This data is available days or weeks before cases are actually reported and could serve as an early indicator. The benefit of an early predictive model lays in early detection and increased awareness.

Figure 1. Graphic depiction of Search Interest for the terms "coronavirus" and "covid-19" (represented by blue and orange line graphs respectively) and CDC Reported Cases (yellow bars) as well as CDC Cases Reported by Date of Illness Onset (gray bars).



Google Trends provides real-time data which would allow for early detection of increases in COVID-19 related SI and early alerting of the public which could lead to decreased exposure. E.g. An individual may monitor SI in real-time, and upon

seeing an increase, decide to increase social distancing or forego a trip to the grocery store that week. This increased awareness would likely lead to a higher suspicion and decreased lag time until testing and diagnosis. This in turn would reduce the lag time between exposure and diagnosis, leading to decreased proliferation and a decreased burden on contact tracing resources and medical treatment facilities.

We analyzed Google Trends data at the national level, however, the data is available at a much more granular level. State, metro and city level is available. Google has leveraged this real-time, granular reporting dubbed "nowcasting" in the past to combat Flu and Dengue.[23] This level of reporting would allow for state, local, military installation or hospital leaders to make more informed decisions with minimal data lag.

Conclusion

Significant strong positive correlation was found between CDC Reported Date of Initial Symptoms for Cases data and Search Interest for both terms "covid-19" and "coronavirus." Google Trends is a free to use and easy to access tool that may have utility as a predictive instrument with regards to the current COVID-19 pandemic. Further research into correlation and predictive value at the state and metro level would likely be beneficial in establishing relevance as a real-time predictive tool for local or state governments and non-governmental organizations.

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Nutrition, Immune Function, and Infectious Disease

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Abstract

Consuming a diet meeting energy demands and providing essential nutrients promotes a healthy immune system. Suboptimal nutritional status, resulting from either under- or overnutrition, disrupts immune health and compromises resistance to, and recovery from, infections. Multiple micronutrients contribute to immune health, for example vitamin D, iron, selenium and zinc. Inadequate intake and suboptimal micronutrient status have been observed in military personnel, which potentially increases the risk of acquiring, and recovering from, infectious diseases and may compromise readiness and lethality. This manuscript briefly reviews the relationship between nutrition, immune function, and infectious disease, and provides resources and future research directions.

Keywords: immune function, obesity, energy intake, micronutrients, vitamins, minerals, respiratory tract infections, COVID-19

Introduction

Consuming a diet meeting energy demands and providing essential nutrients promotes a healthy immune system.[1-3] Under- and overnutrition have been associated with immune dysfunction. In the context of immune function, undernutrition is characterized as inadequate intake of energy and/or specific nutrients that support immune health. Overnutrition refers to excess energy intake which can induce obesity and the associated chronic inflammatory state. Suboptimal nutritional status, resulting from either under- or overnutrition, negatively impacts immune health and compromises resistance to, and recovery from, infections.[3]

Under Consumption of Energy, Macronutrients, & Immune Health: Under consumption of energy and/or protein has a profound effect on both innate and adaptive immunity.[3] Innate immunity is the first line of defense against pathogens, consisting of physical barriers and substances in the blood and immune cells that mount a defense against foreign pathogens. In contrast, adaptive immunity is a second line of defense against pathogens that elicits a targeted response to invading organisms. The impact of inadequate intake on immune function has been documented in both civilian and military populations.[3-7] For example, soldiers attending Special Forces Assessment and Selection School experienced ~4% weight loss and decrements in immune function due to moderate energy deficit over 19 days. Notably, the immune decrements were attenuated with the provision of a twice daily beverage containing a variety of essential vitamins and minerals.[5]

Micronutrients & Immune Health

Multiple micronutrients contribute to immune health, for example, vitamin D, iron, selenium, and zinc. The function of white blood cells, which ingest bacteria and other foreign cells, is compromised by poor iron and zinc status. Poor zinc status also impairs barrier function which allows pathogens to enter the body. Poor iron and zinc status also compromise certain aspects of adaptive immunity.[3] From a clinical standpoint, inadequate micronutrient intake decreases resistance to infections.[8-13]

Vitamin D contributes to immune function through a number of mechanisms, including support of the physical barrier which serves to prevent pathogens from infiltrating the body, stimulating production of antimicrobial compounds that fight infection, and by regulating the production of proteins to modulate inflammation.[3]

These mechanisms are of clinical importance. For example, higher incidence of respiratory tract infections (RTI) is associated with vitamin D deficiency, in addition to multiple other micronutrient deficiencies, in older adults;[9] and vitamin D deficiency increases the risk of RTI.[9,14-16] Additionally, an observational study in the US indicated that higher levels of serum vitamin D were associated with a two-fold reduced risk of respiratory tract infections;[17] and individual studies and meta-analyses have demonstrated that vitamin D supplementation reduces the risk of RTI, especially in individuals who are deficient.[15,16] Evidence suggests that vitamin D status becomes even more important during times of psychological and physiological stress. For example, a marker of innate mucosal immunity was positively associated with vitamin D status and vitamin D supplementation during Marine Corps basic training.[18]

In addition to weakening the immune response, nutritional status can influence the genetic makeup of a viral pathogen that may contribute to the emergence of new pathogens. For example, insufficient intake of selenium is associated with oxidative stress and inflammation, leading to increased viral damage and mutations and, subsequently, more pathogenic viral strains.[19] This remarkable observation has been replicated in animal models with regard to influenza and coxsackie viruses. Ongoing research in this area may lead to the development of tools to predict and reduce the health burden of outbreaks of new infectious diseases such as the current global COVID-19 pandemic.

The effect of inadequate intake of nutrients and suboptimal nutrient status is relevant to military personnel. For example, a study conducted during Army Basic Combat Training suggests that recruits under consume certain micronutrients that are important for immune function, such as vitamin D and iron (females only),[20] and a decline in iron status during initial military training (IMT), to include iron deficiency with and without anemia, is well documented in the IMT environment.[9,14-16,21,22] Further, data compiled over the recent decade indicate that approximately 30% of Army, Marine and Air Force military trainees are vitamin D deficient and 13% of females are iron deficient at the start of IMT.[23]

Insufficient intake of nutrients during military training and operations increases the risk of acquiring, and recovering from, infectious diseases. This risk is further compounded by immune decrements secondary to the psychological and physical stressors of training and the abundance of risk factors that promote the spread of pathogens (e.g., crowding and infrequent hand washing/bathing). Indeed, infectious diseases are a common problem in training and operational environments. For example, between 25-80K military recruits experience an estimated 36-100K medical encounters related to respiratory tract infections (RTI) per year, which accounts for up to ~27K lost training days and up to ~3K days of hospitalization annually.9 Recently, the SARS-CoV2 has emerged as a highly contagious and virulent viral RTI agent with a high mortality rate. The severity of disease that SARS-CoV2 causes, known as COVID-19, has created a tremendous public health burden and, along with other viruses causing RTI, potentially threatening the readiness and lethality of military personnel.[5,9] Optimizing nutritional status could be a cost-efficient approach for reducing disease burden.

Obesity & Infectious Disease

Obesity is relevant to military personnel,[23] and in general, is a consequence of excess energy intake. However, inadequate intake of micronutrients, some of which are important to immune health (e.g., iron and zinc), is also quite common in individuals with obesity.[14] Thus, the impact of obesity on immune health is multifactorial, that is, the chronic inflammatory state caused by excess body fat is coupled with the immune impairments associated with inadequate micronutrient intake. Compared to healthy normal weight individuals, those with obesity are at greater risk of contracting infectious diseases, may experience more severe infections, and demonstrate reduced vaccine responsiveness. For example, non-responsiveness to hepatitis B vaccination was more than 8 times greater in individuals with obesity as compared to those with normal body weight. Immune impairments in individuals with obesity is relevant to military personnel, given that approximately 15% of military personnel have obesity (BMI > 30 kg/m2), ranging from 6.4% in the Marine Corps to 18.0% in the Army.[24]

Large population studies indicate that the risk for hospital-acquired infections is greater in individuals with obesity as compared to those without obesity.[25] Further, obesity has been identified as an independent risk factor for increased morbidity and mortality following the flu,[22] and the risk for hospitalization with respiratory infections during flu season is greater in persons with obesity.[3] Additionally, obesity is associated with greater risk for viral and bacterial infections.[3]

Most recently, evidence suggests that obesity is a major predictor of morbidity and mortality related to COVID-19. Among US patients under 60 years old, those with obesity were twice as likely to require hospitalization for COVID-19 and had a higher probability of requiring acute and critical care.[21] Similarly, other reports indicate that disease severity increases with body mass index (BMI).[15] For example, those with a BMI > 35 kg/

m2 (class II and III obesity) had a more than sevenfold increased risk for requiring mechanical ventilation compared to those with BMI < 25 kg/m2 (normal weight), independent of age and other factors;[15] and patients with obesity had twice the risk of severe pneumonia compared to those with normal BMI.[16]

The deleterious effects of obesity on COVID-19 outcomes may be attributed to a variety of factors including impaired immune responses secondary to inflammation, altered ventilation from compression of the diaphragm, and fibrous deposits in the bloodstream that limit the circulation of oxygen.[15] A recent study posits that adipose tissue in persons with obesity may be a breeding ground for viral spread due to increased shedding, immune activation, and a more pronounced inflammatory response.[26]

Conclusions & Relevance to COVID-19

While the data are not yet conclusive with regard to nutrition status and COVID-19, the existing evidence has important practical implications. Maintaining a healthy body weight and optimizing nutritional status by consuming adequate intake of energy and nutrients are important factors for promoting immune health and overall readiness. As detailed above, suboptimal nutrient status increases the risk of acquiring, and recovering from, infectious diseases (including COVID-19). Individuals with obesity appear to be at high-risk with regard to the severity of COVID-19 infections, and may be considered a vulnerable population. In support of healthy body weight management and nutritional health, Army Regulation 600-9[27] implements Army body composition standards and presents guidance for achieving and maintaining those standards and AR 40-25[28] outlines military dietary reference intakes (MDRIs) to meet nutrient requirements and optimize Warfighter performance.

Optimal nutrition is perhaps more relevant now than ever considering the health burden of COVID-19. Future research to further characterize the relationship between nutritional status and infectious diseases (including COVID-19) in the context of the military environment are warranted. Studies conducted by the US Army Research Institute of Environmental Medicine (Natick, MA) with Department of Defense and other US government agency partners are underway to characterize immune responses to strenuous military training, and identify individual factors (i.e., sex, nutritional status, dietary behaviors, metabolic health, gut microbiome, physiologic responses) associated with resilience or susceptibility to diminished immune function. Additionally, research to investigate the association between nutrition-related factors (e.g., nutritional status, diet quality and body mass index) and COVID-19 vaccine responsiveness (when available) is planned. Altogether, findings will better inform the development of interventions and policy that mitigate illness and infection risk during and after military training and operations.

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A Comprehensive Overview of the US Army Dentistry Response to COVID-19

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Introduction

The historic outbreak of the novel coronavirus (SARS CoV-2) sent concern and even panic around the world due to the unknown nature of this disease. As a result, the US implemented a whole-of government approach to tackle the outbreak of this deadly virus. The national and global impact of an uncontrolled COVID-19 outbreak, threatens the US healthcare system and our way of life with potential to cause riveting economic and national security instability. As a result of the health impact on American society, the US military must also take precaution to preserve and defend our nation's fighting force. This charge has created a unique opportunity for military medicine to take the lead at the front line to combat this biologic viral threat.

Army Dentistry represents one of the front line professions in the fight against COVID-19. "The oral cavity is the window to the body and is often the area where systemic disease first presents itself."[1] Once in the human body, SARS-CoV-2 replicates in nasopharyngeal and salivary secretions of affected patients, and spreads predominantly through respiratory droplets.[2] Clinical symptoms of COVID-19 directly associated with the dental profession include: persistent sore throat, cough, fever, dyspnea (wheezing or shortness of breath), dysguesia (abnormal taste sensation) and hyposmia (reduced sense of smell).[3]

The Army Dental Care System has adapted to the present day crisis through evaluating lessons learned from past health crisis and epidemics by incorporating stringent infection control protocols to decrease community spread within the dental clinical setting. The Center for Disease Control and Prevention (CDC) and Occupational Safety and Health Administration (OSHA) lists the dental setting as an environment of highest risk to healthcare personnel. This is because clinical dentistry involves the use of rotary dental and surgical instruments, such as hand pieces, ultrasonic scalers and air-water syringes which create potentially infectious aerosols containing particle droplets of water, saliva, blood, microorganisms, and debris. Scientists assert that this pandemic will remain a concern until a vaccine is found. While we await a vaccine, Army Dentistry follows protocols to maintain the safety of patients and providers while working to ensure the readiness of the force. These protocols include following OSHA and CDC guidelines, implementing preventive measures, applying treatment protocols, and documenting best practices.

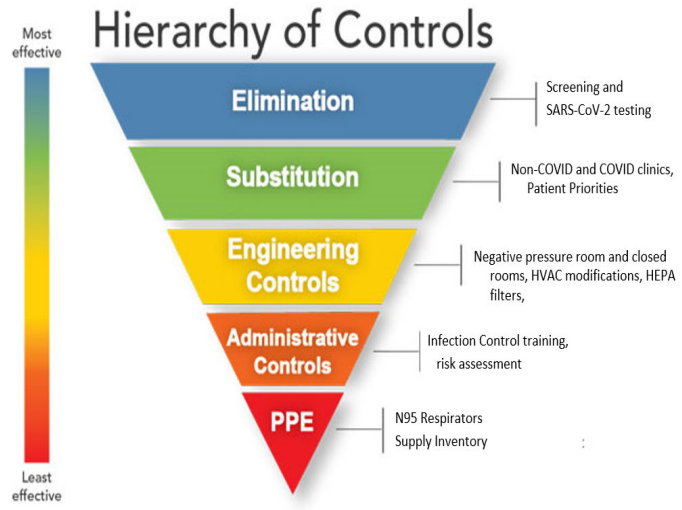
OSHA updates and CDC guidelines: Army Dentistry has adapted to specific mitigation protocols to help keep the dental team and patients safe through prevention of cross-infection. Most of the implemented infection control, joint commission, and patient safety protocols come from dental, medical, and public health organizational standards. In March 2020, the CDC recommended dental settings prioritize urgent and emergency visits and delay elective procedures to protect staff and preserve supplies.[4] While state dental boards are the approving authority for dental practice guidelines, the level of authorized care during the coronavirus pandemic in Army dental clinics are determined by coordination between US Army Medical Command (MEDCOM), the Regional Health Commands and Combatant Commands.

Infection control protocols call for all patients to be treated as though they are infected with infectious diseases such as Hepatitis B, HIV, and now COVID-19. "Since transmission of airborne droplets is considered the main routes of infection spread, application of personal protective equipment (PPE), such as masks, protective goggles, gowns, helmet, gloves, caps, face shields, and shoe covers, is strongly recommended for all health care personnel."[4] OSHA requires that workers must be protected from exposure to blood and body fluids that may contain blood borne infectious agents. There are standards for bloodborne pathogens, personal protective equipment and respiratory protection.

Usage of the N95 respirator mask is the standard of care when treating patients in the COVID-19 environment in part due to the ability to filter out at leader 95% of airborne particles. Users must perform a seal check

each time the respirator is put on allowing for minimal leakage around the edges when the user inhales. The N95 respirator is traditionally a one-time use mask.[5] Limits to the supply of N95 respirators, required the adoption of "contingency" and "crisis" measures to extend the use of N95 respirators as long as they were not damaged or soiled and continued to function properly. In certain crisis situations where supplies were significantly constrained, some dental clinics utilized vaporous hydrogen peroxide (VHP) decontamination to further extend the life of N95 respirators until supply lines could be restored.

Figure 1. The Hierarchy of Controls categorized by level of effectiveness.



Patients with suspected coronavirus infection should not be treated in a regular dental setting. If the treatment needs are emergent, the dental care team should use specialized protective gear and equipment such as the NIOSH-certified, disposable N95 filtering face piece respirator. Treatment should take place in a negative pressure room with appropriate suction devices. When cleaning and disinfecting, routine cleaning procedures are critical to protecting against cross contamination of SARS-CoV-2 by applying EPA-registered, hospital-grade disinfectant to frequently touched surfaces or objects."[5]

Dental treatment facilities and military installations also required and encouraged individual level responsibilities to help reduce community spread. The CDC recommends practicing hand hygiene with an alcohol-based hand rub or handwashing with soap and water for at least 20 seconds when hands are visibly soiled, before eating, or after using the restroom. Alcohol-based hand rubs should contain at least 60-95% alcohol in healthcare settings. All personnel entering any medical treatment facility to include dental clinics are required to wear masks to help reduce exposure. Wearing a mask helps in the prevention of respiratory droplets traveling in the air when a person coughs, sneezes, or speaks. The use of a mask is extremely important in areas where social distancing of at least a six foot distance is difficult to maintain.

Preventive Measures: Prevention is key to limit the spread of the coronavirus. To mitigate risk, the Army Dental Care System implemented the hierarchy of controls (elimination, substitution, engineering controls, administrative controls, and PPE) categorized by level of effectiveness (Figure 1).[6] Traditional Army dental clinics have an open bay design with large open waiting rooms. This open concept design is not conducive to preventing community spread of contagions and presents challenges when attempting to control and remove potentially infectious aerosols from the air.

Elimination Controls: Pre-screening and testing: To help decrease community spread, Army dental clinics have limited the number of personnel in the clinic at any given time. Only patients receiving care are allowed into the clinic. During Health Protection Condition (HPCON) Level Charlie, where significant community spread of the virus exists, emergency care is performed by mission essential personnel only and limited to patients requiring Class 3 treatment due to a deployment. The Dental Team incorporates teledentistry capabilities to screen patients via telephone, text, or email prior to their visit. In some clinics, patients received COVID-19 testing prior to treatment to rule out infection. At Force Generating platforms such as Fort Benning, where First Term Dental Readiness is a priority, the Maneuver Center of Excellence took an aggressive approach towards in-processing basic training recruits. Recruits received multiple coronavirus tests as well as quarantine for at least 14 days to ensure they were not contagious with the coronavirus prior to entering the dental clinic for care.

Substitution Controls: Patient Flow & Social Distancing: To account for the additional time needed to properly screen patients and properly disinfect the operatory after patient care, clinic operations extended appointments. Management of schedules and patient flows maximized social distancing. Staff members organized the waiting room to allow for appropriate distancing between seating. If social distancing was not logistically

possible, patients were directed to wait in their vehicle and received a text notification to return to the facility when their operatory was prepared to receive them.

Army dental clinics resorted to use of rotational schedules dividing staff into groups to help decrease the potential for clinic spread. Some Dental Health Activities (DENTACs) designated clinics as Non-COVID or COVID clinics to help reduce risk. During HPCON level Charlie and Delta, only mission essential personnel reported to the clinic to continue patient treatment.

Clinics also eliminated providing elective procedures during HPCON Charlie and Delta to help reduce aerosol production and preserve PPE. Hygienist decreased the use of the ultrasonic scaler and resorted to hand scaling instruments to decrease aerosol production. If there was a need to perform emergent aerosol producing care, providers used protective rubber dams and/or Isolite systems to prevent the mixture of contaminant saliva and water being aerosolized.

Army Dentists incorporated the use of pre-procedural mouth rinses containing oxidative agents such as 1.5% hydrogen peroxide or 0.2% povidone-iodine to help reduce the microbial load of oral cavity fluids.[7] High volume evacuation (HVE) is one of the most important mitigation measures available to control dental aerosols at the source, before they can spread. So called "4-handed dentistry" was employed even for dental hygenists to ensure aerosols were minimized during necessary treatment. Providers and assistants also limited air-water syringe use to prevent excess spray, splatter, or aerosol creation.[8] Additionally, clinics allotted 15 minutes of time for aerosol settling between patients and before thoroughly cleaning operatories per OSHA and CDC guidelines.

Engineering Controls: Engineering controls represent a preventive measure to help protect against exposure to SARS-CoV-2. Decontaminated physical barriers or partitions which help to isolate patients and staff can protect from aerosol exposure. Local exhaust ventilation help capture and remove mists or aerosols.[9] Directional airflow also helps ensure that air moves through staff work areas before patient treatment areas. Consultation and collaboration with industrial hygienist or ventilation engineers helps ensure ventilation removes workplace hazards. Negative pressure rooms are not common in the standard Army dental treatment facility (DTF) and are commonly referred to as Airborne Infection Isolation Rooms (AIIR). Positive pressure rooms are much more common and help to keep infectious organisms out, similar to operating rooms. DENTACs are currently researching ways to create negative pressure environments and HVAC modifications to create an atmosphere more conducive to protecting patients and staff against COVID-19.

Administrative Controls: In order to ensure all staff feel prepared to provide dental care during a pandemic, leadership reinforced infection control, patient safety, and PPE training. For example, the Hawaii DENTAC developed and provided a Tri-Service COVID-19 infection control and PPE training program to over 100 dental health care personnel, as well as training with the Tripler Army Medical Center Intensive Care Unit and Tuberculosis (TB)/Ebola team. According to the Army Techniques Publication (ATP) No. 5-19 on risk management, a risk assessment is performed to "estimate the probability of a harmful event from a hazard, estimate the expected severity of an event, and determine the level of risk for the estimated probability and severity."[10] Through the use of the risk assessment matrix and the Department of Defense (DD) Form 2977, Deliberate Risk Assessment Worksheet, DENTACs were able to adequately assess risk levels and document risk management. This practice is the standard for the majority of Army operations.[10]

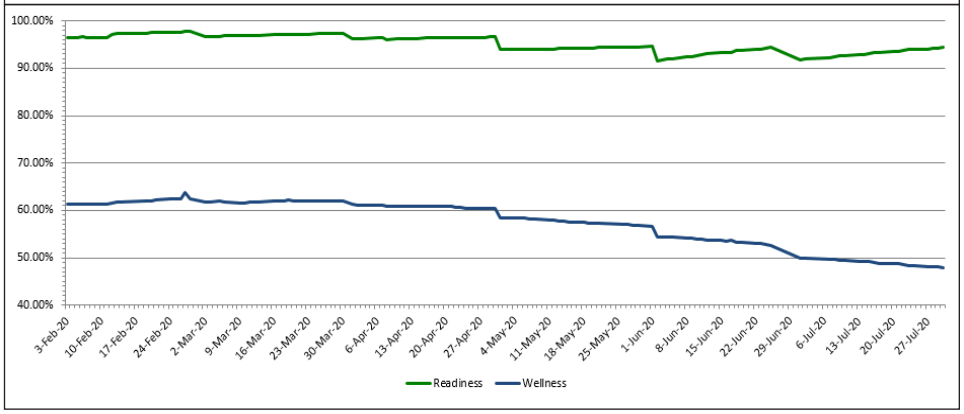
PPE/Supply Management: Supply management presented as a critical issue during the on-going COVID-19 pandemic. Acquiring the appropriate amount of PPE and maintaining adequate stocks became a challenge. Many DENTACs listed their supply technicians as mission essential to ensure an adequate supply storage on hand. Reassessment and prioritization of the type of dental care helped reduce the burn rate of PPE. Additionally, the N95 respirator represented a critical supply item needed by the DENTACs. Critical supplies, including N95 respirators, were thoroughly tracked to predict future need.

Dental Readiness & Best Practices

Dental Readiness and Wellness: Despite the need to adjust protocols to promote a safe environment, DENTAC leadership did not ignore the importance to maintaining readiness as an Army priority. At the beginning of the pandemic, many clinics resorted solely to providing emergency care, but as the curve began to stabilize and flatten, readiness exams were added to the available treatment list. Prior to the pandemic, dental readiness rates averaged 96% Armywide. Due to the need to limit procedures to help preserve PPE and limit unnecessary exposure, clinics limited exams causing a drop in readiness to an average of just above 90% by July 2020 (Figure 2).[11] The decrease in non-emergent procedures decreased wellness by over 10% during the quarter.

The decrease in available dental appointment inversely affected the Class 3 and 4 Dental readiness levels (Figure 3).[11] Patient with these dental readiness classifications (DRC) are considered not medically ready because they either require an annual readiness exam or expedited treatment to prevent a probable dental emergency.[12] DENTACs created their return to care plan based on local levels of community transmission, and most clinics resumed dental exams by June 2020.

Figure 2. Dental Readiness and Wellness percentages during the height of the pandemic.



PPE Ingenuity: Strategic communication and messaging allowed all DENTACs to learn the correct policies and procedures to create a safe healthcare environment throughout the pandemic. The Dental Directorate released a Dental Concept of Operations (CONOP) providing guidance based on rapidly changing national infection control guidance. They also hosted weekly briefings to assess the situation in each region and discuss key topics and best practices to share throughout the dental enterprise. The Fort Sill engaged hands-on education during the pandemic to focus on real world problems faced in Army Dentistry and the profession. Shortages of PPE and implementation of extended-use practices under crisis presented unknown risk for dental providers. As a result, the Fort Sill Advanced Education in General Dentistry (AEGD) residency program used this real world problem, combined with the digital learning management system, to reinforce military decision making processes and allow residents to exercise their disciplined initiative to think "outside the box." They participated in approximately 16 hours of literature review on virology, infection control, and policy affecting PPE utilization and strategy.

One best practice shared by the Fort Sill residency provided practical protective gear during a time of national PPE shortages. At the onset of the COVID-19 pandemic, the face shields on-hand in local dental clinics did not allow for wear of loupes or lights due to their size. Through innovation and creativity, members of the Fort Sill AEGD team configured dental face shields from a clear banister guard, zip-ties, a paper template, and a hold punch or scissors (Figure 4). This product was a locally constructed, affordable dental face shield that could support the wear of dental loupes. The design was shared for a use as needed throughout the dental enterprise.

The Oklahoma Mask is another example of thinking outside of the box to accomplish the mission during the pandemic when supplies were scarce. The Oklahoma Mask is a digitally designed and 3D printed mask which leverages supplies and skill available in the dental clinic through dental technology. A 3D Computer Aided Design-Computer Aided Manufacturing (CAD-CAM) software along with rapid prototype thermoform molds, ASTM (American Society for Testing and Materials) level three masks and intravenous tourniquet straps combined to show how dental professionals can leverage technology to create a safe, reusable alterative to the disposable level 3 masks (See Figure 5). While the Oklahoma mask is a potential alternative method of PPE, the Army did not use it during the pandemic

Figure 3. Dental Readiness Classification levels 3 and 4 during the height of the pandemic.

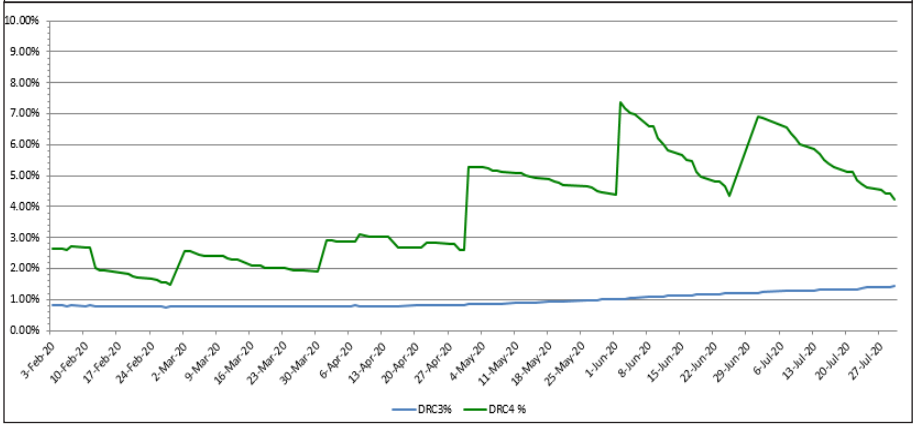


Figure 4. Fabrication of the locally constructed face shield.

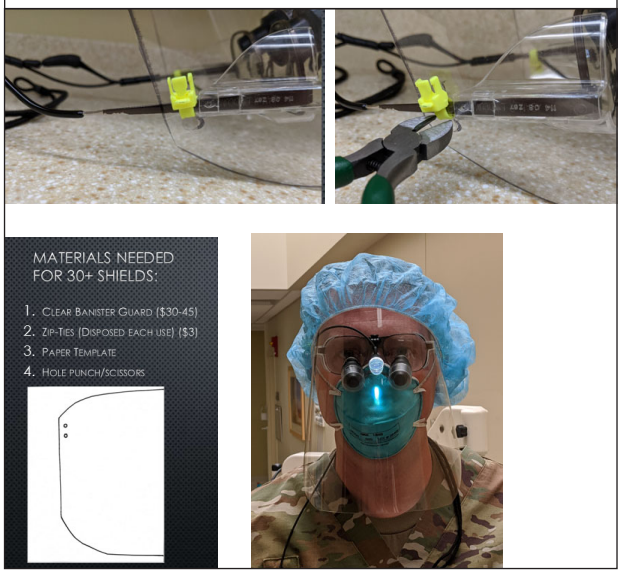
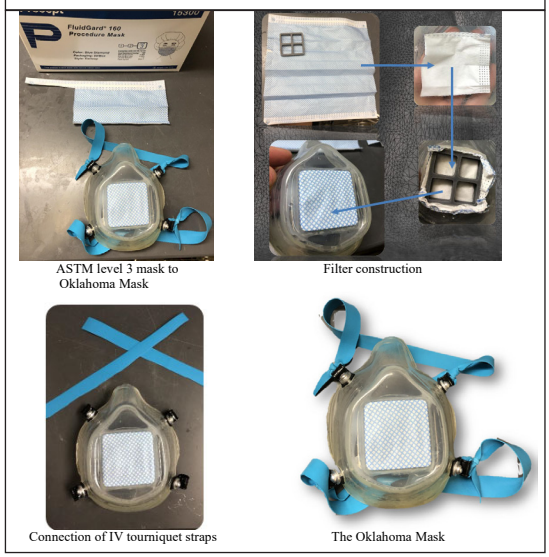


Figure 5. Fabrication of the Oklahoma Mask.



because it is not FDA approved. It is an example of a way to address supply shortages during times of crisis.

Dental Education: The COVID-19 pandemic has put a halt on many forms of education we have become accustom to in the military. Local continuing education (CE) officer must become creative in providing avenues to keep their providers on top of current evidence-based best practices. As in any operational environment, our best laid plans never survive first contact with the enemy and the fog and friction of the environment only reveal uncertainty. So how can we continue to grow professionally during COVID-19?

Dental residents at Fort Sill helped create the One-year AEGD Virtual Short Course as a solution to deliver quality education across the enterprise in the COVID-19 environment. Along with the tireless effort of the Graduate Dental Education staff, the residents researched relevant evidence-based topics with a comprehensive approach, recorded their findings and published them for the American Dental Association Continuing Education Recognition Program (ADA CERP) lecture credit. The online tool, offered to the field, helped guide the Army Dental Care System through the "friction" of the current operational environment where many do not have access to a Common Access Card (CAC) enabled computers.

In the military we often live by the proverb *Mater artium necessitas* or "necessity is the mother of invention." Understanding that, we can utilize our constructs of military theory and navigate these trying times, much like Carl von Clausewitz. He describes the fog, friction, and uncertainty that surround the battlefield to develop solutions that will prepare us for global engagements and disasters while staying ready and prepared as a professional dental force.[13]

Technological Advancement: The US Army Corporate Dental System (CDS) created a screening assessment that was sent to all dental patients 48 hours before and after their appointment as recommended by the CDC. This system contacted patients by text/email and sent a report to the respective dental clinic. This helped identify symptomatic and suspected COVID-19 patients before coming to the dental clinic, and protected staff and other patients by identifying potentially infectious but asymptomatic individuals after a dental appointment.

The Tri-Service Encounter Module (TEM) was released and helped providers become more efficient during this pandemic and beyond. The TEM is a module in the Corporate Dental System (CDS) which allows users to capture patient information, health metrics, risk assessments, digital charting, and diagnostic and treatment information for data mining, workload and Dental Readiness Classification (DRC).[14] During a pandemic, utilization of the TEM will help prevent community spread by removing the need for a paper record in the operatory during treatment.

Currently, the patient record is obtained by the front desk, retrieved by the dental assistant, provided to the patient for update of medical history and consent signatures, and finally given to the dentist for exam or treatment documentation. The TEM system allows CDS to

request patient health history information prior to the appointment. The feature also has a 2D barcode which allows the user to scan the patient's CAC to begin the TEM encounter and provide patient information. The system also allows providers to update a patient's dental readiness classification and treatment needs using the charting tool, odontogram, and charting grid. Overall, the TEM and other new CDS features will help to enhance infection control which is critical during this time. The Army Dental Care System began phasing in the TEM in August 2020 with a full Tri-service implementation in November 2020.

Figure 6. Left: Reverse flow HEPA scrubber; right: HEPA scrubber mounted above the ceiling grid for DTR.

Expeditionary Dental Airborne Infectious Isolation Room: The Joint Base San Antonio DENTAC led the way in incorporating an engineering control through its introduction of the Expeditionary Dental Airborne Infectious Isolation Room (EDAIIR). This room allows dental providers to safely provide procedures which generate COVID-19 aerosols. Leaders at Rhoades Dental Clinic worked with the Defense Health Agency Facilities Operations Branch and Engineering team to design and test a temporary negative pressure dental treatment room (DTR). Design teams created the EDAIIR as a short term fix (< 12 months) to allow safer dental treatment of symptomatic or suspected COVID patients requiring an emergency procedure or other procedures that produce the heaviest aerosols. The room design featured magnetically closing door flaps, plastic walls, HEPA filtration, and negative pressure created by ducting the filtered air outside the room (Figure 6).

The EDAIIR required self-sealing doorways that do not require handling of zippers to get in and out of the room quickly and cleanly without the use of hands (Figure 7).[15] The DTR needs to achieve at least 12 air changes per hour to ensure the virus is diluted to safe inactive levels per the CDC MMWR 2005 guidelines (Table 1).[15] It also requires digital sensing equipment to confirm that the room has negative pressure. A pressure indicator is mounted outside the EDAIIR to reflect the pressure difference between the DTR and the outside space. Rhoades Dental Clinic incorporated the use of two EDAIIR systems in late July 2020 for aerosol generating procedures and sick call screenings. Additional EDAIIR plans were sent to dental facility teams in the Army, Navy, and Air Force.

Figure 7. Left: Rhoades Dental Clinic DTR doorway; right: EDAIIR with self-sealing door.

Conclusions

Just as the COVID-19 pandemic surprised the world, it had the same effect on Army Dentistry. While some private practice dental clinics were required to close as a result of state board requirements, Army Dental Activities and dental clinics curtailed patient care but did not fully close. To help limit viral spread, preserve personnel protective equipment and support the hospital effort at the beginning of the pandemic, many clinics stopped providing aerosol producing procedures. Staff trained for and implemented infection control protocols provided by OSHA and the CDC to protect patients and themselves, as well as prevent community spread. Dental leadership also incorporated risk mitigation practices such as pre-screening, teledentistry, appropriate social distancing in clinics, engineering controls, and supply management to continue to operate during the COVID-19 pandemic.

Through effective communication and strategic messaging the Army Dental Care System helped share best practices

Table 1. CDC Morbidity and Mortality Weekly Report (MMWR) Guidelines 2005 assumes: perfect mixing, perfectly clean air.

Dilution (Fly in Room)

ACH	Minutes required for removal of 90%	Minutes required for removal of 99%	Minutes required for removal of 99.9%
2	69	138	207
4	35	69	104
6	23	46	69
8	17	35	52
10	14	28	41
12	12	23	35
15	9	18	28
20	7	14	21
50	3	6	8

*ACH-air changes per hour.

amongst the dental team. Communication at all levels, from the dental providers at the clinic level to the Tri-Service Defense Health Agency, made the difference in effectively supporting the broader medical mission. Notable best practices included ways to innovatively construct PPE to help treat patients and technological enhancements which help with infection control and dental education. Finally, despite the need to adapt to the current medical crisis, Army Dentistry kept its focus on maintaining dental readiness. The Army Dental Care System remains resilient in the mist of the fight and will remain focused to continually adapt to any challenge brought our way while helping preserve the fighting force.

Acknowledgements

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1ST Cavalry Division Forward's Defender Europe 2020 Plus: Lessons Learned Fighting in a Biological Contested Environment

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Abstract

The 1st Cavalry Division Forward (1CD FWD) along with Polish ally, subordinate brigades, adjacent supporting commands, and the 7th Army Training Command successfully executed large scale combat operations training in the Defender Europe 2020 Plus (DE20P) exercise in a biologically compromised environment. The coronavirus 2019 (COVID-19) presented many unique challenges and opportunities across all warfighting functions. Still, it proved that it is possible to train in a large-scale multinational exercise while effectively mitigating the contraction and contamination of COVID-19. Through behavioral policies, screening, and testing, the 1CD FWD was able to conduct a high-quality multinational training event, while preserving force health protection and preventing the spread of COVID-19 within the host nation. The 1CD FWD executed a qualitative focus group study and learned that fighting in a pandemic is challenging but manageable and sustainable. The overall protective measures associated with the training exercise did have shortfalls; there were populations that had the potential to bring outside vectors in the training area. Units must create their codified policies, communicate, train, and resource their behavioral and movement systems. Leadership and individual involvement with accountability enforced. COVID-19 tests must be comprehensive, continuous, focused, and targeted as described in the 1CD FWD's ready to fight guide and concept. Recommend one point of restriction of movement and coronavirus test upon reception, staging, on-ward movement, and integration (RSOI) into the European theater.

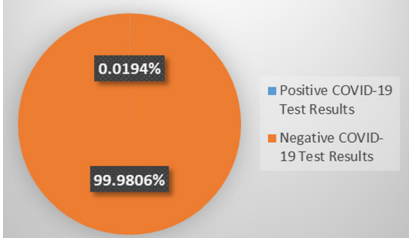
Six months into the first pandemic of the 21st century, the coronavirus 2019 (COVID-19) infected 17.8 million people and increased daily with 685,178 deaths, and 10.6 million recovered cases as of 2 August 2020.[1] COVID-19 created a new challenge in an unknown environment for military leaders, soldiers, and families. This virus is a multifaceted adversary that threatens our forces at large and has an enduring effect that has impacted all training. The 1st Cavalry Division Forward (1CD FWD) trained in this austere environment and developed lessons learned from the Defender 2020 Plus (DE20P) military exercise. The 1CD FWD executed DE20P, a large scale ground combat operations (LSGCO) exercise from 8-23 June 2020 in Poland, by mitigating COVID-19 contraction and contamination with behavioral policies, screening, and testing. The 1CD FWD found the implementation of behavioral conditions to prevent the COVID-19 contagion improved with screening and testing. The following is a brief background followed by lessons learned from behavioral policy implementation, screening, and testing, underpinned by a focus group qualitative analysis study.

Background

1CD FWD executed three methods to prevent the contraction of and contamination from COVID-19 via behavioral policies, screening, and testing. First, it implemented the Center for Disease Control's (CDC) policies such as wearing face masks, social distancing, routine hand washing, and restriction of movement. Second, 1CD FWD health care providers medically screened individuals for signs and symptoms by taking infrared temperatures and asking a series of medical screening questions. For example, "Have you been in contact with someone who has tested positive with COVID-19," and "Have you been exposed to COVID-19?"[2] Finally, COVID-19 genetic tests executed on every member of the 1CD FWD team (Figure 1). The 1st Cavalry Division Forward (1CD FWD) used genetic testing via polymerase chain reaction (PCR) to test for the coronavirus to ensure health protection and safety of those who participated

in DE20P. The 1CD FWD tested personnel for COVID-19: soldiers, service members, and civilians from the US and Poland from the start of the Defender Europe 2020 Plus (DE20P), 8-23 June 2020. Overall, 99.98% tested negative throughout DE20P.[4]

Figure 1.Polymerase chain reaction (PCR) test samples.



Individuals with positive signs and symptoms of COVID-19 during the initial screening were immediately quarantined, tested, and isolated if found coronavirus positive. Additionally, 1st Cavalry Division (1CD) created means and ways to trace and clean suspected COVID-19 cases via contact tracing and cleaning teams, following the Centers for Disease Control (CDC) guidelines.[3] 1CD effectively executed team trace and team clean during the redeployment of the 1CD's headquarters from Germany back to Fort Hood, Texas, in March 2020. Overall, these three methods ensured individuals free of the virus remained healthy by maintaining the restrictive tactical area (RTA) of health protection and not allowing any virus contamination or contraction. RTAs defined as teams, crews, squads, and task-forces who are free of COVID-19 and underwent quality assurance and checks, i.e., behavioral policies, screening, and testing. Moreover, individuals within RTAs have limited access to areas outside of training and only with specific authorization to exit or enter (penetrate) the group. Soldiers preserved their training integrity, or RTAs, by abiding with the United States Army Europe's (USAREUR) policies. Some examples of USARER systems include the above mentioned behavioral policies, screening, quarantine procedures, and testing pre and post-move from country to country or training area to another.

Table 1.Participant demographics.

Demographics	# of Personnel
Total	30
Male	26
female	4
Age 18-25	4
Age 26-30	5
Age 31-35	7
Age 36-40	9
Age 41-45	3
Age 46-50	1
Age 51-55	1
Age 56-60	0
Enlisted E1 to E4	4
Enlisted E5 to E7	4
Enlisted E8 to E9	1
WO1 to WO5	1
Officer O1 to O3	12
Officer O4 to O5	6
Officer O6 to GEN	0
GS13-SG14	1
Rank not specified	1
Education - GED	1
Education - High School	6
Education - Associates	1
Education - Bachelors	6
Education - Masters	13
Education - Doctorate	1
Ethnicity - Black (African American)	4
Ethnicity - Caucasion (White)	16
Ethnicity - American	1
Ethnicity - Hispanic (Latino)	3
Ethnicity - Polish	4
Ethnicity - Pacific Islander / Asian American	1
Ethnicity - No Answer	2
Military Service - US Army	23
Military Service - US Air Force	2
Military Service - Polish Army	4
Government Services - US Civilian	1

After implementing the above three standards and ensuring soldiers and civilians were free of COVID-19, additional measures taken to sustain health protection. Cohorts free of the virus were able to train and operate in their protected RTAs. Cohorts also were protected by using 'fire breaks,' such as the Drawsko Pomorskie Training Area's (DPTA), Poland Life Support Areas (LSA).

The 7th Army Training Command (7ATC) describes 'fire breaks' in their 7ATC COVID Playbook. One, fire breaks are physical distancing measures or a specific protocol in place for entering or exiting groups. Second, fire breaks are the boundaries formed by these "fire breaks" must delineate prohibited areas, procedures to prevent a breach of these protected areas and groups, and what level approves breaching of the boundaries." 1CD FWD implementation of "fire breaks" was controlled by military police checkpoints and individual behavioral policies such as hand washing and social distancing. Individuals within the RTA remained free of COVID-19 by limiting contact and contamination from anyone outside of their training. Vectors are individuals who have designated to leave the safety RTA for mission requirements, and their influences were taken into account.

Methods

1CD FWD used a qualitative focus group method to create lessons learned in how to fight and train in a biological contested environment. The problem statement for the study: The 1CD FWD developed lessons learned to prevent contamination and contraction of COVID-19 in a large scale ground combat operation (LSGCO), the Defender 2020 Plus (DE20P), mitigating future risks to force and mission during military training exercises. The hypothesis used to create the focus group questionnaire and survey: Implementation of behavioral conditions to prevent the COVID-19 contagion is improved with screening and testing.

This qualitative study focused on a small sample of more than 5,000 DE20P participants. Thirty volunteers sampled from the DE20P units participated in this study: to include soldiers, airman, and civilians from the Polish 12th Mechanized Division, 12th Mechanized Brigade; the US 2nd Armored Brigade Combat Team, 3rd Infantry Division; the Polish 6th Airborne Brigade; the 1CD FWD; the 3rd Combat Aviation Brigade, 3rd Infantry Division; and the 7th Army Training Command. Demographics of participants included age, sex, education, ethnicity, military or government service, and rank or civilian grade (Table 1). Personally identifiable information(PII) was not requested to ensure privacy, anonymity, and

integrity with an increased probability of candor, quality, and openness of answers.

Additionally, the focus group studies questionnaire and survey included open-ended questions, scaled surveys, and built-in redundancy to capture qualitative and subjectivity of answers (Figure 2). Redundancy of questions asked in a different manner, such as question number 1 and 3, allowed for analysis of the open-ended responses, qualitative answers, and differences within each scaled survey comprehensively.

The following describes the focus group survey. Six questions asked in the study with four scaled response choices.

- Item 1, describe your environment, and how safe it is from COVID-19? Please rate how safe your environment is: (1) not safe at all, (2) less safe, (3) safe, and (4) absolutely safe.
- Question 2, how safe do you feel moving from your unit from the Drawsko Pomorskie Training Area (DPTA), Poland, and back home? Please rate how safe your movement was from point to point: (1) not safe at all, (2) less safe, (3) safe, and (4) absolutely safe.
- Question 3, how safe is the DPTA environment from COVID-19? Please rate how safe does you feel at DPTA: (1) not safe at all, (2) less safe, (3) safe, and (4) absolutely safe.
- Question 4, what measures were taken into effect to keep you safe from COVID-19, e.g., training, living conditions, and travel?
- Item 5, what are your thoughts about the COVID-19 tests; was this sufficient to prevent you from COVID-19 exposure? Please rate how sufficient was your COVID-19 Test: (1) not sufficient, (2) less sufficient, (3) sufficient, and (4) absolutely sufficient.
- Question 6, how would you improve the process to prevent the contraction and contamination of COVID-19?

Continuing with the qualitative focus group methodology, lessons learned from this study were binned into four categories: (1) behavioral policies, (2) screening, (3) testing, and (4) recommendations. Answers from the six survey questions were placed into the above four categories, understanding that some answers overlapped with others and were comprehensive. These four categories will be described independently and sequentially, first with a re-introducing the category. Second, a brief background as to what developed to mitigate contraction and contamination for that category. Third, findings from the focus group questionnaire and survey. Finally, lessons learned and the "so what" for that category.

Figure 2. Behavorial policies COVID-19 focus group survey results.

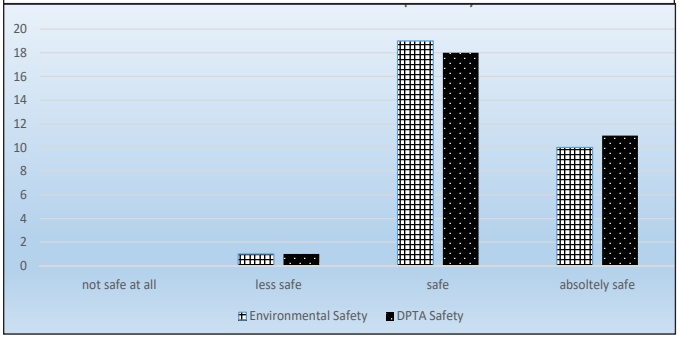
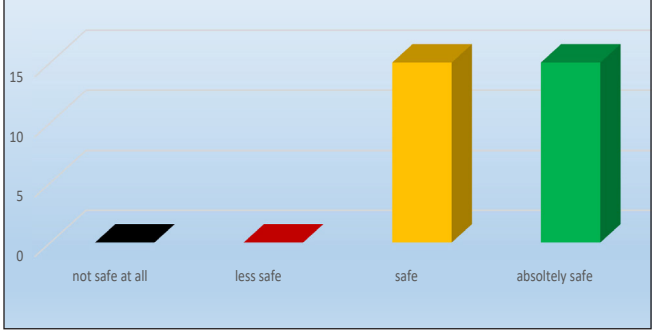


Figure 3. Moving safety COVID-19 focus group survey results.



Results

Starting with category one, question 1 and 3 asked the behavioral policies questions: describe how safe your environment and DPTA is from COVID-19? Now, for a brief background about what the Department of Defense (DoD) to what 1CD FWD implemented to protect the force health sustainment and mission. 13 March 2020, the Secretary of Defense Mark Esper enacted a stop movement for all DoD personnel as the coronavirus (COVID-19) pandemic developed.[4,5] The DoD sustained readiness through social distancing and leveraging technology to work distributed. 1CD FWD implemented the European Command's 7th Army Training Command COVID-19 playbook. The Playbook executed allowed for a titrated means and ways to train and fight, e.g., behavioral systems such as restriction of movement, routine hand washing, and wearing personal protective equipment like masks, gloves, and eye protection.

Category one continued, findings revealed 29 of 30 individuals felt safe to absolute safety from COVID-19 in their environment to include the DPTA, Poland (Figure 3).[4] One person reported being less safe in their environment and DPTA, from COVID-19. A volunteer's description of how secure their situation was, "We were briefed by our intelligence officer that Poland has had a limited amount of cases of COVID and that in the country, all required to wear a facemask. It has felt very safe·

Also, knowing that everyone on the base is required to test negative for COVID before entering, the whole post felt safe from COVID." Another individual who felt less safe in their environment reported, "I live in a tent with ten people and work in a tent with 30; no one wears masks." This individual also believed DPTA is occupied with "4,000 plus people in very close contact with the host nation and civilian allies are not ideal!"

Transitioning to category one's lessons learned and the "so what," volunteers overall expressed feelings of their environment, and DPTA was safe while executing behavioral policies. 1CD FWD created and codified a COVID-19 system to keep soldiers and civilians safe. Units must create their codified procedures, communicate, train, and resource their behavioral policies. Individuals must abide by the rules, such as wearing their masks, routine hand washing, maintain social distancing, and maximize distributed telework.

Moreover, individuals must report any violations, on-the-spot correct violations, and develop recommendations for their leaders to fix. Leaders must communicate, reinforce, and hold subordinate leaders with individuals accountable to prevent the contraction and contamination of the virus. Leaders must ask soldiers and civilians at all levels what they understand as the units' COVID-19 behavioral policies. If individuals do not know, then use that opportunity to train the individual and maximize the opportunity to allow non-commissioned officers to train subordinates. Finally, leaders must reinforce the codified behavioral policies via on-the-spot corrections.

Category two screening with questions 2 and 4: how safe do you feel moving from DPTA and back home; what measures taken to keep you safe from COVI-19, e.g., training, living conditions, and travel? DoD and 1CD FWD implemented background actions to protect the force on movement from continental US (CONUS) to the European theater and safely into individual's area of operations. DoD implemented travel restrictions and quarantine procedures pre- and post-movement from point to point or country to country. Moreover, with DoD's travel restrictions and point to point quarantine procedures, units and individuals were challenged and constrained with their freedom of movement and action. Restriction of movement (ROM) was essential to our force health protection, as the coronavirus lifespan is two weeks. 1CD FWD effectively prevented the contraction and contamination of COVID-19 with the First Team's soldiers redeployment from Germany and Europe to Fort Hood, Texas, in April via mandating two weeks of quarantine. USAREUR allowed and supported 1CD FWD's courses of action to move units and individuals into Europe following the exception to policy guidelines. 1CD FWD successfully deployed leaders and soldiers into Poland by May 2020, following the pre and post quarantine ROMs. Additionally, the military police implemented screening questionnaires and took temperatures upon entry control points as fire-breaks, which protected COVID-19 free personnel and groups of RTAs.

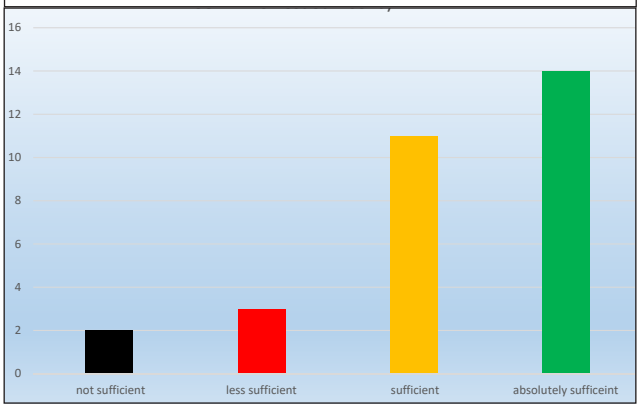
Category two findings revealed 30 of 30 individuals felt safe to absolutely safe from COVID-19 during movement from their units to the Drawsko Pomorskie Training Area (DPTA), Poland. Fifteen volunteers felt safe while the other fifteen felt absolute safety during their move from their groups to DPTA and back.[4] One volunteer described their movement as "safe, we are all tested again before we leave since multiple training RTAs mixed during the exercise." At the same time, another described, "safe, as the process of screening before entering the general population allows identifying service members with possible symptoms." "Safe, moving from RTA to RTA."

Category two's movement lessons learned and the "so what" demonstrated volunteers felt safe moving from country to country and training area to another; the overall protective measures associated with the training exercise did have shortfalls. Foreign military, local national vendors, and contractors remained a population that had the potential to bring outside vectors into the training area RTA. Also, individual travelers who broke away from the RTAs have a higher susceptibility to contamination, e.g., personal travel for emergency leave such as the birth of a child or death of a family member who was more susceptible to COVID-19. As of current, there are numerous points of entry and exits in Europe, which increase the chances and complexity of controlling and sustaining ROM sites. 1CD FWD recommends one single location of reception site to manage individual and unit infiltration and exfiltration operations.

Additionally, units must enforce quarantine, isolation, and ROM policies. Units must establish, ready, and activate their team trace and team cleans, as required. Unit leaders must empower, enforce, quality assurance, and quality checks for their personnel at entry control points and fire breaks. Entry control personnel must understand their standing operating protocols to manage, reject, hold, and report through the chain of command for immediate action upon identifying any individual who is positive with COVID-19 signs and symptoms. Moreover, units must create, codify, communicate, train, resource, and implement reporting procedures to protect personnel within COVID free RTAs.

Category three's testing question 5: what are your thoughts about COVID-19 tests; was this sufficient to prevent you from COVID-19 exposure? As background about what the DoD and 1CD FWD implemented to protect the force executing coronavirus tests, the DoD immediately looked for means and ways to test for the novel virus. Still, it was limited to research and developers, but once an approved test was available, DoD immediately deployed resources and scientists to test. The 1CD FWD tested DE20P participants for the coronavirus with polymerase chain reaction (PCR) genetic Test. During the DE20P training exercise, 8-23 June 2020, personnel tested for COVID-19. One US service member tested positive, immediately quarantined, retested, and isolated months before the start of DE20P.4 The test resulted in 99.98% negatives with one positive throughout DE20P (Figure 1).[4]

Figure 4. COVID-19 test sufficiency group survey results.



Category three findings resulted in mixed feelings about the COVID-19 testing sufficiency: 14 felt absolute sufficient, 11 sufficient, three less sufficient, and two not sufficient (Figure 4).[4] An individual scored the COVID-19 Test safely and described its sufficiency, "It was thorough, but I believe following the prevention guidelines (ROM, social distancing, proper hygiene, etc.) helps reduce the risk of being exposed to COVID-19." Another volunteer described how the Test is not sufficient, "No, the false positive rate and the false-negative rate is high with the Test. If we are not exhibiting symptoms, there is no medical reason or requirement, especially if we quarantined prior." An absolute sufficiency rater describes, "Test does not prevent me from COVID-19 exposure. The measures such as quarantine, screening, ROM, and work from home limits my exposure."

Category three's COVID-19 testing lessons learned and the "so what" show there were many entry points where COVID-19 tests executed, such as the living support areas (LSA) in Konotop and Trezbien, Poland, and the deployment processing center at Kasserine, Germany. COVID-19 testing site(s) requires logistical health sustainment, medics to collect patient samples, microbiologists and technicians to execute the PCR test, and systems to ground or aerial transportation samples. Currently, transportation of samples move from the multiple locations to the Landstuhl Regional Medical Center's laboratory for a theater level confirmatory test. The 21st Theater Sustainment Command, USAREUR, and 1CD FWD are working on synchronizing, streamlining, and revising current testing protocols. 1CD FWD recommends a single point of entry during reception, staging, onward movement, and integration (RSOI) at the reception point to add a 14-day ROM and COVID-19 testing upon arrival and at day ten of the ROM.

Finally, moving to the last category, recommendations with question 6: how would you improve the process to prevent the contraction and contamination of COVID-19? Maintain procedures and standing behavioral policies, screening, and testing. Continue to execute targeted vector testing with random testing. "Maintain social distancing, mask-wearing, and reduce personnel at dining facilities." Current protocols for dining facilities are no more than 2 to 5 personnel to a bench, depending on which post and how large the dining facility. "I would integrate unit time slots at the dining facilities to reduce the number of soldiers at any given time." "Fewer people in a sleeping area, where there are small sleeping areas with five to one room double-bunked." "Publicize what measures taken with local nationals working on the base." All bases have pictures of how to limit COVID-19 exposure, with handwashing stations outside

Figure 5. The United States Army Europe (USAREUR) COVID-19 lexicon includes four terms.

- **Diagnostic Testing**: clinically indicated testing of individuals who are symptomatic or thought to be at increased risk of COVID-19 infection due to known contact. Diagnostic testing is done at the direction of a health care provider and conducted at a military treatment facility (MTF) or host nation health care facility. Diagnostic testing is referred to as "tier 0 testing" and is the highest priority for use of testing resources.
- **Screening**: a risk mitigation method to evaluate a population during a pandemic. Screening may include an interview or questionnaire about COVID-19 symptoms, signs, exposure factors, protective factors, and relevant existing medical conditions, IAW CDC and DOD force health protection (FHP) protocols.
- **Screening with Asymptomatic Testing** for operational risk reduction: a risk mitigation method to evaluate a population in order to prevent a widespread outbreak of COVID within the population. Screening with asymptomatic testing may include testing entire deploying and/or redeploying units, and may be done in conjunction with a restriction of movement.
- **Sentinel Surveillance**: population level testing strategy that provides data about the prevalence of disease in a population through random sampling of asymptomatic individuals within a unit or installation.

public buildings and dining facilities, including wearing masks and proper protective equipment. "Keep implementing the same rules until COVID-19 is normalized"

Comments

The 1CD FWD created a 'Ready to Fight' in a COVID-19 environment guide concept. This guide is focused towards a goal of twenty-one days from start to a ready-to-fight or train, and sustain a fighting timeline that protects while sustaining the force's health. The starting point occurs when a higher headquarters directs its warning order to its subordinates units.

Day one directs subordinate units to execute screening with asymptomatic testing, which means 100% of the personnel is tested for COVID-19. The US Europe (USAREUR) Commander, Lt. Gen. Christopher Cavoli's staff created, defined, and clarified COVID-19 terms, such as diagnostic testing, screening, screening with asymptomatic testing, and sentinel surveillance (Figure 5) for COVID-19 lexicon. Moreover, the ready to fight guide details the personnel, equipment, training operations, and COVID-19 test requirements by days. For example, established at sixty days prior to RSOI: personnel for team trace and clean; required personnel protective equipment (PPE), medical supplies or class VIII supplies required on-hand; and a unit codified COVID-19 policy established with a COVID-19 test standing operating procedure (SOP).

Conclusions

The 'new normal' to mitigate COVID-19 is sustaining behavioral policies, screening, and testing. Moreover, the implementation of behavioral conditions to prevent COVID-19 contagion is improved with screening and testing. Behavioral strategies include quarantine, isolation, routine handwashing, mask-wearing, social distancing, and telework distributed. Screening to include entry control point questions of COVID-19 signs and symptoms verified with temperatures taken. COVID-19 PCR tests with limiting virus-free RTAs and groups away from non-tested individuals. Activation of team trace and clean as required to prevent further spread of COVID-19.

In conclusion, the 1CD FWD proved that it is possible to train and fight in a large scaled ground combat operation with DE20P. We learned that fighting in a pandemic is challenging but manageable, accomplishable, and sustainable. The overall protective measures associated with the training exercise did have shortfalls. Foreign military, local national vendors, contractors, and individual travelers remained a population that had the potential to bring outside vectors in the training area RTA. Units must create their codified policies, communicate, train, and resource their behavioral and movement systems. Leadership and individual involvement with accountability enforced. COVID-19 tests must be comprehensive, continuous, focused, and targeted as described in the 1CD FWD's ready to fight guide and concept. Recommend one point of ROM and coronavirus test upon reception during RSOI into the European theater. There is still a lot to learn from how the military fights and operates in a biological contested environment.

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The COVID-19 Army Rapid Assessment Tool (CARAT) for Management of COVID-19 in the Deployed Setting

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Abstract

The COVID-19 pandemic poses unique challenges within the austere clinical setting, and the time between patient presentation and deterioration is a critical opportunity for intervention. In some cases, this may be a life-saving transfer to a higher level of care. US Central Command (CENTCOM) has provided valuable guidance for COVID-19 management in the operational environment,[1] and has proposed the National Early Warning System 2 (NEWS2) scoring tool as a useful adjunct to gauging illness severity. NEWS2, however, does not consider co-morbidities, such as diabetes or chronic cardiac disease, which could worsen the clinical course of SARS-CoV-2 patients. Thus, NEWS2 fails to address such factors during the risk stratification of patients to a higher level of care. To address this concern, June 2020, 3rd Medical Brigade, Operation Spartan Shield (OSS) developed the COVID-19 Army Rapid Assessment Tool (CARAT) with inputs from clinicians and researchers (The Team). The CARAT is a clinical scoring system, modified from the NEWS2, which combines the effects of co-morbid disease with the current physiological condition of a COVID-19 patient. The Team obtained clinical data for 105 patients from the CENTCOM area of responsibility (AOR), who presented to a military treatment facility (MTF) symptomatic for, and testing positive for SARS-CoV-2, during the time period of June to mid-August 2020. Each patient was retrospectively assigned a CARAT score based on his or her initial presentation. Preliminary review of data suggested a CARAT value of 4 or greater was an indicator for risk of further deterioration. Patients were then grouped into two categories: patients who received transfer to a higher level of care, versus "stay-in-place" supportive care. Results showed that 100% of patients with a score ≥4 had been transferred to a higher echelon of care, compared to 2% of patients with scores <4. A Fisher's exact test demonstrated a statistically significant difference between these two groups ($p<0.001$). Interestingly, when compared with the NEWS2 score, the CARAT identified 9 individuals for transfer to a higher level of care, of whom only one patient was identified by the NEWS2, clearly underscoring the significance of CARAT despite small sample size. We therefore recommend that CARAT be further validated in predicting disease severity and need for emergent evacuation in larger patient settings.

Introduction

The COVID-19 pandemic has claimed over 187,000 lives in the US since the initial impact of SARS-CoV-2 became known in late 2019, with almost 7 million confirmed US cases at the time of this publication.[2] Throughout this time, the US DoD has prioritized maintaining a maximally ready fighting force while minimizing SARS-CoV-2 exposures and mitigating COVID-19 syndromes outside of continental US (OCONUS).[1] Accordingly, early recognition of patients requiring evacuation from theater is of critical importance, particularly in Role 2 and Role 3 settings (Table 1).

US CENTCOM has provided valuable guidance for COVID-19 management in the operational environment,[1] and has advocated the NEWS2 as an adjunct to gauging illness severity. The NEWS2, however, does not consider co-morbidities during risk stratification of patients, which might improve our patient-care guidelines

by identifying patients who would benefit from transfer to a higher level of care.

Table 1. General capabilities of various levels of military treatment facilities (MTF) (adapted from "Clinical Flow," Medical Communications for Combat Casualty Care).[4] OCONUS: outside continental US; CONUS: continental US.

Military Roles of Care		
Role	**Level of Care**	**Components**
Role 1	**Aid Station**	1 physician, 1 PA, 3-6 medics
Role 2	**EMT, Dental, and Patient Hold**	Physicians, physician assistants, dentist, dental tech, medics
Role 2	**Forward Surgical Team**	General surgeons; orthopedic surgeon; anesthesia providers; OR, ER, and critical-care nurses; emergency physicians
Role 3	**Combat Support Hospital**	Emergency physicians, surgeons, anesthesia providers, other specialty providers, ER / critical-care nurses, full clinical-support complement
Role 4 (OCONUS)	**Regional Medical Center**	Full medical staff
Role 4 (CONUS)	**DoD Medical Center** **VA Hospital**	Full medical staff

June 2020, a team of clinicians and researchers from 3rd Medical Brigade, OSS, was identified to develop and assess the CARAT for its ability to address risk stratification and guide medical decision making for transfer of COVID-19 patients who present in theater. The CARAT is a modification of the NEWS2, combined with specific comorbidities chosen from Centers for Disease Control and Prevention (CDC) guidance known to further complicate clinical course.[3] In this project, we have retrospectively applied this score to a multicenter series of patients residing in an austere environment to observe for a correlation of their CARAT score with early clinical deterioration and evacuation status. We have further compared the CARAT to the NEWS2 for its ability to identify patients who might best be managed by transfer to a higher role of care.

Background

A number of recent publications have explored clinical-risk scoring systems to identify early clinical severity in SARS-CoV-2-positive patients, in order to guide medical decision making.[5-14] The majority of these studies have sought to predict need for rapid deterioration and/or intensive care unit (ICU) admission.

The Modified Early Warning Score (MEWS) is a prospectively validated tool developed to identify patients who are clinically declining and at-risk for ICU admission and/or death.[5] The MEWS has taken on a number of variations. The National Early Warning System (NEWS) is a modified version of MEWS, first published by the Royal College of Physicians of London (2012) as an aggregate scoring system to identify patients in need of prompt critical-care intervention.[15] Physiologic parameters of the NEWS include: respiratory rate, oxygen saturation, systolic blood pressure, heart rate, level of consciousness and temperature (Table 2). December 2017, the NEWS was further modified to the NEWS2,[16] providing weighting to vital sign parameters.[16,17] In DoD guidance put force April 2020, NEWS was highlighted as a "potentially useful tool for the initial categorization of clinical severity" of COVID-19.[1]

Current DoD-proposed algorithms suggest early evacuation based on emergent symptoms appropriately combined with clinical gestalt.[1] In an effort to aid in this decision, members of the 3rd Medical Command collectively developed the CARAT to evaluate patients for evacuation from resource-limited settings. The CARAT is a clinical scoring system, modified from the NEWS2, which combines the effects of co-morbid disease with the current physiological condition of a COVID-19 patient (Table 3). The intent of the CARAT is to improve upon the NEWS2 in guiding clinicians as to which patients need to be emergently evacuated to a higher echelon of care. This higher role could be a Host Nation facility, or it could be the nearest Role 3 MTF.

Table 2. National Early Warning Score (NEWS) (image adapted from Matos, Chung).2 *A=Alert, V=Verbal, P=Pain, U=Unresponsive.

PHYSIOLOGICAL PARAMETERS	3	2	1	0	1	2	3
Respiration Rate	≤ 8		9-11	12-20		21-24	≥ 25
Oxygen Saturation	≤ 91	92-93	94-95	≥ 96			
Any Supplemental Oxygen		Yes		No			
Temperature	≤ 35.0		35.1-36.0	36.1-38.0	38.1-39.0	≥ 39.1	
Systolic BP	≤ 90	91-100	101-110	111-219			≥ 220
Heart Rate	≤ 40		41-50	51-90	91-110	111-130	≥ 131
Level of Consciousness*				A			V, P, U

Methods

Population: A multi-center cohort was retrospectively obtained from the time period of June–mid-August 2020, of service members from the CENTCOM AOR, who presented to an MTF symptomatic for, and testing positive for SARS-CoV-2 on the initial visit. Civilians eligible for military healthcare in theater were included in this study if they satisfied the aforementioned criteria. RT-PCR was used for all SARS-CoV-2 testing. Additional inclusion criteria are indicative of the predominant patient population in our setting: age ≥ 18 years and with a traceable clinical course within our electronic health record (EHR) system, Theater Medical Data System (TMDS), and Joint Legacy Viewer (JLV).

Table 3. COVID-19 Army Rapid Assessment Tool (CARAT). *A=Alert, V=Verbal, P=Pain, U=Unresponsive.

COVID-19 ARMY RAPID ASSESSMENT TOOL (CARAT)

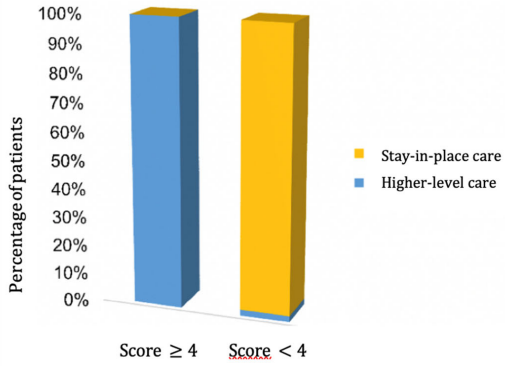
PHYSIOLOGIC PARAMETER	PATIENT SCORE	SCORE						
		3	2	1	0	1	2	3
RESPIRATORY RATE (breaths/min)		≤ 8		9-11	12-20		21-24	≥ 25
OXYGEN SATURATION (%)		≤ 91	92-93	94-95	≥ 96			
SUPPLEMENTAL OXYGEN			YES		NO			
TEMPERATURE (C)		≤ 35		35.1-36.0	36.1-38.0	38.1-39.0	≥ 39.1	
SYSTOLIC BLOOD PRESSURE (mmHg)		≤ 90	91-100	101-110	111-219			≥ 220
HEART RATE (bpm)		≤ 40		41-50	51-90	91-110	111-130	≥ 131
LEVEL OF CONSCIOUSNESS*					A			V,P,U
CO-MORBIDITY								
AGE		≥ 65	60-64	50-59	≤ 50			
BMI		≥ 40	36-40	31-35	≤ 30			
CURRENT SMOKER				YES	NO			
CHRONIC RESPIRATORY DISEASE				YES	NO			
CHRONIC HEART DISEASE				YES	NO			
CHRONIC KIDNEY DISEASE				YES	NO			
DIABETES				YES	NO			
TOTAL SCORE								

Data Collection: Clinical data satisfying the CARAT parameters were able to be obtained for 105 patients who met the above inclusion criteria. These patients were then anonymized and entered into a working database.

Score Calculation: A single provider retrospectively calculated and assigned a CARAT score for each anonymized patient using TMDS and JLV, based on available clinical data at the time of initial patient encounter.

Data Analysis: Patients were grouped into two categories: those with a CARAT score ≥4 , and those with a CARAT score <4 (Figure 1). Patients within these two groups were further categorized as receiving transfer to a higher level of care, versus "stay-in-place" supportive care. Results showed that 100% of patients with a score ≥4 required transfer to a higher echelon of care, compared to 2% of patients with scores <4. A Fisher's exact test demonstrated a statistically significant difference between these two groups ($p<0.001$). For the purposes of this study, "transfer to a higher level of care" referred to patient transfer from a Role 1 aid station or greater (which included our clinical isolation facility), to any higher level of care, up to Role 4 (Landstuhl Regional Medical Center). "Supportive care" referred to routine interventions such as rest, oral hydration, and OTC medications such as anti-inflammatories or anti-emetics, as needed. In all cases, the decision to transport was made based on clinical status of the patient at the presenting facility.

Figure 1. Graph showing distribution of COVID-19 patients with the care needed.



N=105	Higher-level care	Stay-in-place care (supportive)
Score ≥ 4	9	0
Score < 4	2	94

Fisher's exact test, $p<0.001$

Discussion

While the immediate impact of COVID-19 has primarily involved urban communities, individuals in rural and austere environments face a unique set of challenges related to the potential for rapid deterioration and limited resource availability. While the NEWS2 has been helpful in risk-stratifying COVID-19 patients in theater, we have proposed the CARAT as a modified tool to enhance

Table 4. Summary of patients who were transferred to higher echelon of care. HR: Heart Rate, O2: Oxygen Saturation, HTN: Hypertension, BMI: Body Mass Index, DM: Diabetes Mellitus, RR: Respiratory Rate, Temp: Temperature and BP: Blood Pressure. Score Index: +1, +2, and +3.

Patient ID	Age	Gender	CARAT score	Underlying Characteristics									
				Age	HR	O2	HTN	BMI	DM	RR	Smoking	Temp	BP
7	22	M	1										
10	37	M	0										
12	54	M	9										
15	55	F	5										
19	42	M	0										
21	37	M	4										
37	54	M	4										
62	45	M	4										
103	56	M	7										
104	61	M	6										
105	52	M	6										

patient care. To do so, our team applied the CARAT to our patient population and compared its performance to the NEWS2. A CARAT score was retrospectively applied to a cohort of 105 service members and civilians eligible for military healthcare within CENTCOM AOR. The cohort was characterized by patients who presented to MTFs with symptoms of COVID-19 and had a positive RT-PCR on the initial visit. NEWS2 uses a score of 5 or greater as an indicator of a patient's need for greater care. Review of data revealed that a CARAT score ≥4 upon arrival for medical treatment consistently correlated with illness severity and subsequent evacuation, ($p<0.001$) Figure 1). We have determined that the CARAT has demonstrated potential to better identify patients in need of transfer to a higher echelon of care (Table 4). To that fact, a comparison of patients' scores who received higher echelon care was performed between NEWS 2 and CARAT (Table 5). The former only identified one patient to be transferred while latter identified 9 individuals for transfer to a higher level of care, respectively clearly underscoring the significance of CARAT score in providing intervention at an early stage of treatment (Table 3). The Fisher's exact statistic value obtained for observation between NEWS2 and CARAT is 0.0019, which is significant at $p<0.05$.

Several recent studies have been conducted to examine previously established predictive scoring tools for applicability during the COVID-19 pandemic. Meylan et al[6] conducted a data review to explore the Early Warning Score19 as a predictor of ICU admissions in patients with COVID-19 and suggested its utility. Myrstad and colleagues[7] sought to evaluate NEWS2 as a decision tool for providers of COVID-19 patients. They reported that a NEWS2 score ≥ 6 on admission predicted severe disease with 80% sensitivity and 84.3% specificity.[7] Greenhalgh and colleagues suggested that NEWS and NEWS2 lack consideration for age and other independent predictors of survivability in COVID-19 patients.[18]

The CURB-65 is a severity score that is widely used to predict mortality in community acquired pneumonia (CAP) and as a predictive tool for the guidance of inpatient versus outpatient management of (CAP).[8] Nguyen et al[8] retrospectively evaluated the CURB-65 to determine applicability as a predictor of poor outcome in COVID-19 patients, and concluded there were limitations in using this tool to guide inpatient versus outpatient management.

The Rapid Emergency Medicine Score (REMS), initially developed to gauge mortality of non-surgical patients presenting to the ED, incorporates heart rate, blood

Table 5. Comparison of NEWS2 and CARAT for patients who were transferred to higher echelon care.

Patient ID	NEWS2	Level of Care	CARAT	Level of Care	Agreement
7	0	Supportive	1	Supportive	Yes
10	0	Supportive	0	Supportive	Yes
12	5	Higher	9	Higher	Yes
15	3	Supportive	5	Higher	No
19	0	Supportive	0	Higher	No
21	4	Supportive	4	Higher	No
37	1	Supportive	4	Higher	No
62	3	Supportive	4	Higher	No
103	4	Supportive	7	Higher	No
104	4	Supportive	6	Higher	No
105	4	Supportive	6	Higher	No
NEWS2: Scores > 4, transfer to higher care			CARAT: Score ≥ 4, transfer to higher care		

N=11, patients received higher care		NEWS 2		
		Supportive	Higher	Total
CARAT	Supportive	2	0	2
	Higher	8	1	9
	Total	10	1	11

The Fisher's exact test statistic value is 0.0019. The result is significant at $p<0.05$.

pressure, respiratory rate, Glasgow Coma Scale (GCS), and age.[9] Hu et al[9] compared The REMS and MEWS and reported that both demonstrated acceptable use as risk-stratification tools.

May 2020, Liang and colleagues[10] proposed the COVID-GRAM Critical Illness Risk Score, internally validated, to predict the risk of critical illness in hospitalized COVID-19 patients. Clinical predictors include chest-radiograph abnormality, age, hemoptysis, dyspnea, unconsciousness, number of comorbidities, cancer history, neutrophil-to-lymphocyte ratio, lactate dehydrogenase (LDH) and direct bilirubin.[10] Notably, neutrophil-to-lymphocyte ratio, LDH, and direct bilirubin may not be available in theater due to limited lab capabilities, making this score less ideal within the austere setting.

Challenges to healthcare within the deployed environment include limited resources, isolation, and difficulties with accessing higher echelons of care. For the COVID-19 patient, these challenges are further compounded by the potential for rapid deterioration which is prevalent in patients with certain comorbidities.[1] The CARAT, a tool modified from the NEWS2, was designed to address COVID-19-specific challenges in austere environments. Our performance-improvement project has suggested the CARAT may be useful in facilitating efficient decision making and thus improving patient outcomes.

Limitations

We faced a number of limitations in the implementation of our project. First, our application of the CARAT was retrospective. Furthermore, the CARAT was applied to a rather homogenous population of relatively young, healthy soldiers within the US military, although our study also accounted for civilians eligible for military healthcare, as long as they met inclusion criteria. The decision for patient evacuation was based on clinical presentation in real-time, and may have been somewhat dependent upon subjectivity of the transferring provider and clinical gestalt. Finally, our data collection was limited by a short time period and relatively small sample size.

Conclusions

At present, there is limited guidance to aid in the triage and transfer of COVID-19 patients presenting to facilities in austere settings. Our performance-improvement project suggests that the CARAT may be more useful than NEWS2 in predicting which patients are most at-risk for rapid deterioration and in-need of prompt evacuation to a higher level of care. The CARAT is worthy of further study, which might include a prospective evaluation and validation study within a more heterogeneous population.

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Deployment of the 1st Area Medical Laboratory to South Korea in Response to the COVID-19 Pandemic

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Initial Response & Deployment

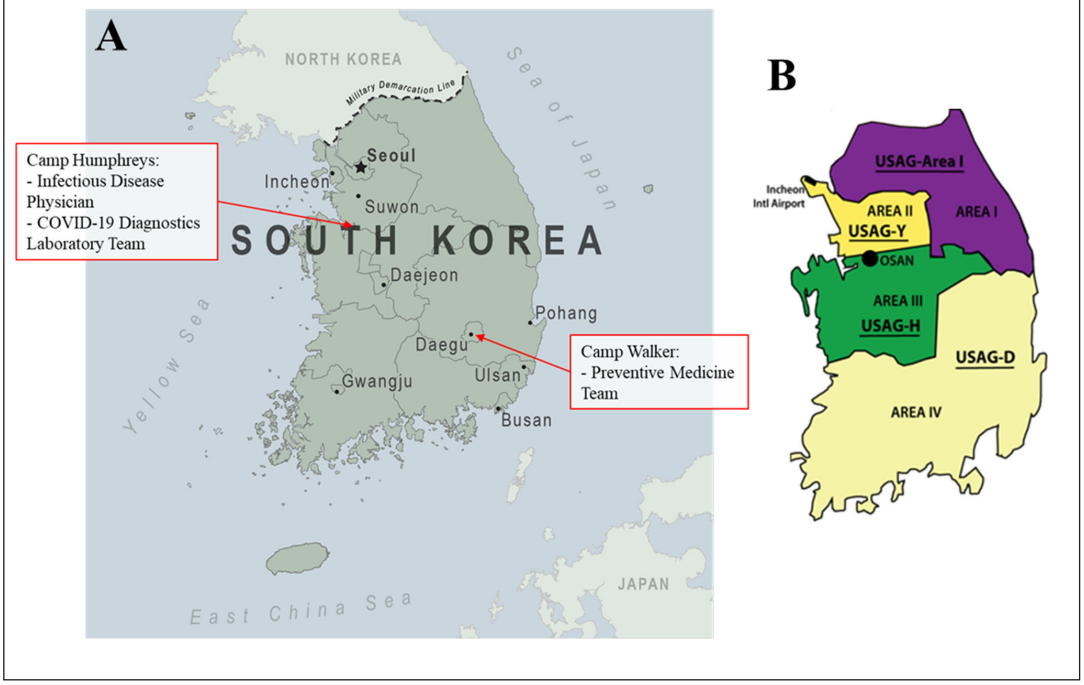
In December 2019, an outbreak of pneumonia caused by a novel coronavirus, severe acute respiratory syndrome (SARS)-CoV-2, occurred in Wuhan city, Hubei province, China.[1] South Korea saw its first confirmed Coronavirus Disease 2019 (COVID-19) case on January 20, 2020, when an infected woman from Wuhan, China arrived in S. Korea via Incheon International Airport.[1] By mid-February, SARS-CoV-2 was rapidly spreading in the southern city of Daegu, S. Korea in proximity to three US Forces Korea (USFK) military installations. COVID-19 cases continued to increase during the following weeks, reaching a peak of nearly 1,000 confirmed cases per day by the end of February. As cases surged dramatically, over 28,000 USFK service members, family members, and Department of Defense (DoD) employees were at a risk of exposure to COVID-19. On February 24, clinicians diagnosed the first confirmed case in the USFK population, a 61 year-old widow of a retired service member. This individual, who experienced a mild illness, was the spouse of a retired US military veteran living in S. Korea. The retiree and his spouse both had access to military posts in S. Korea, and the spouse tested positive after she had been on one of the military bases in Area IV (Figure 1). The following day, USFK reported its first confirmed case in a service member, which was the triggering event for the 1st Area Medical Laboratory (AML) to deploy to S. Korea.

While daily confirmed cases of COVID-19 were exponentially increasing in S. Korea, the 1st AML received deployment orders from USFK requesting personnel with expertise in preventive medicine, infectious disease, and laboratory diagnostics. The 1st AML is the US Army's only deployable laboratory for theater level validation of Chemical, Biological, Radiological and Nuclear (CBRN) and health hazard threats. A variety of the Army's specialized biomedical professionals are assigned to the 1st AML, and the unit maintains a high level of force readiness for mobilizations under a Prepare-to-Deploy Order (PTDO). Nearing its 90th year as the Army's deployable laboratory, the 1st AML is currently configured to include a headquarters element and three specialized modular teams: Alpha Team, the Occupational/Environmental Health section; Bravo Team, the Endemic Disease/Biological Warfare Assessment section; and Charlie Team, the Chemical Threat Assessment section. Upon receiving the USFK support request, the 1st AML mobilized a multidisciplinary task force of 12 Soldiers on February 28, 2020, including physicians, laboratory science officers, and medical technicians to S. Korea, to help establish clinical management protocols and manage the COVID-19 diagnostic laboratory (Figure 2). Despite the short mobilization window of less than two weeks, the task force team quickly organized to deploy, meeting medical readiness and immunization standards, training and documenting the technical competencies required to perform clinical diagnostic testing. In addition, team members coordinated with USFK medical personnel for operational planning, and rapidly integrated three MAP (Modification Table of Organization and Equipment (MTOE)-assigned personnel) officers into the task force team.

Although the primary mission of the 1st AML is to assess CBRNE threats in a forward deployed setting, the 1st AML's most recently deployed to Liberia in 2014-2015 for a humanitarian mission. Their four teams of the 1st AML soldier scientists from the Bravo and Charlie teams (cross-trained to perform on Ebola diagnostic testing) supported Operation United Assistance (OUA).[2] As with OUA, the 2020 COVID-19 response mission to South Korea also capitalized on 1st AML's modularity,

deploying an ad hoc team of microbiologists, lab technicians, preventive medicine (PM) specialists, and physicians pulled from all three sections and cross-trained to support testing, treatment, and contact tracing missions. In addition to highlighting the strengths of the task force response, this article highlights lessons learned and makes important recommendations on how these elements of organizational planning, training, and personnel readiness can be incorporated throughout the Army Medicine community.

Figure 1. (A) Deployed locations of the 1st Area Medical Laboratory Task Force Teams in South Korea. (B) USFK functional areas, Area I – IV. Maps adapted from wwwnc.cdc.gov and https://8tharmy.korea.army.mil.

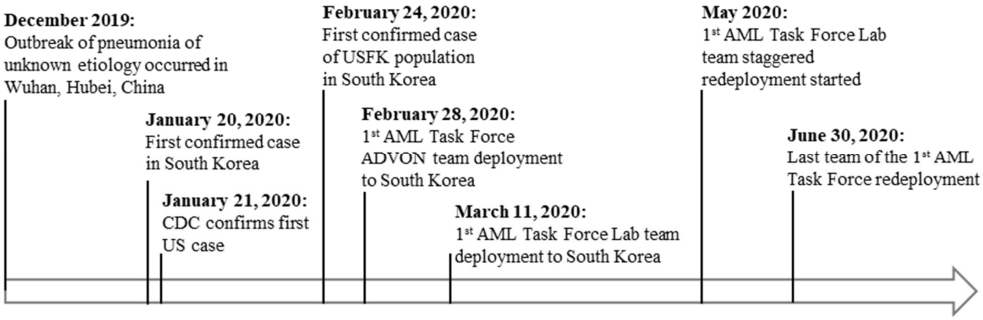


Infectious Disease Advisory & Support Mission

The Brian D. Allgood Army Community Hospital (BDAACH) support staff in Camp Humphreys expedited the in-processing of the Army infectious disease (ID) physician from the 1st AML, completing the ID physician's credentials packet within two days of his arrival. This was hastened by a temporary duty credentialing packet from Ft. Belvoir, the primary site of the physician's credentials before arrival. During his two months on-site, the ID physician was able to provide clinical consultation, both onsite and via telemedicine, for the USFK-related COVID-19 patients throughout the Korean peninsula. He provided new clinical interventions and treatment strategies, visited the COVID-19 isolation barracks in Camp Humphreys for rounds and diagnostic sample collections, and facilitated a public health assessment project between Walter Reed Army Institute of Research (WRAIR) and BDAACH. In addition to COVID-19 consultation, he also consulted on complex infectious disease cases and provided expert advice for general hospital infection control policy.

The 1st AML team supported BDAACH's infection control and occupational health teams in a number of ways. First, they developed a monitoring plan in accordance with Centers for Disease Control and Prevention (CDC) guidelines for providers seeing COVID-19 patients. Next they provided decision support for personal protective equipment (PPE) usage, equipment sterilization, and other COVID-19 infection control questions

Figure 2. Timeline of the 1st AML deployment in response to the COVID-19 pandemic.



that arose. Finally, the ID physician coordinated a public health investigation between USFK, BDAACH, 1st AML and WRAIR's Emerging Infectious Diseases (EID) branch. This collaborative effort 1) correlated viral kinetics and host immune responses with the course of clinical illness, 2) investigated the effect of quarantine and other non-pharmacologic interventions on COVID-19 infection rates in USFK forces, and 3) developed actionable outbreak models to inform force health protection for USFK.

The public health assessment consisted of several subprojects: immune marker and viremia study of COVID-19 subjects, which characterized the immune response by correlating cytokine patterns with illness severity, timing of infection, molecular and serologic diagnostic patterns during infection. The second subproject involved sequencing SARS-CoV-2 isolates from USFK subjects. The sequencing analysis indicated that what initially appeared to be one local outbreak cluster was instead caused by two separate point sources of infection (one local strain and one imported from overseas). The third study was a serology-based assessment of healthcare workers at BDAACH. This occupational health-based project evaluated risk factors for healthcare workers with a high probability of work-related COVID-19 transmission. The healthcare workers were stratified by their risk of COVID-19 exposure, healthcare specialty, and the efficacy of PPE.

Contact Tracing & Preventive Medicine Response

The 1st AML Task Force team members initially deployed to S. Korea in late February of 2020 with minimal operational guidance, and very little experience or historical perspective to draw on due to the nature of this public health emergency. The Task Force team worked with USFK epidemiologists, laboratorians and physicians, as well as parallel medical professionals from the S. Korean CDC, to quickly develop practicable courses of action. The Task Force team started with an assessment of existing preventive medicine measures to do determine what was working well, and whether any aspects of the action plan could be improved.

In making recommendations to the leadership, the Task Force members relied on the Public Health Emergency Management instructional guide, DoDI 6200.03.[3] One of the first concerns that was identified, and a common finding in the overall epidemic response, was that the leadership occasionally issued directives which were not necessarily in concert with published public health guidance. As such, the team learned to creatively match the commander's stated intent with published guidance and public safety best practices in order to execute the mission. Using the commander's guidance, the Task Force strategically insured that consistent and sound protocols for quarantine, isolation, and management of exposed and infected persons were developed.

The desired end state from the Commander was as follows:

1. All DoD personnel and their dependents were provided with vetted and accurate public health information and messaging,
2. All DoD personnel and dependents who required surveillance, quarantine or treatment received said treatment in compliance with defined standards of care,
3. Disease transmission was contained, or was significantly reduced.

With the hard work and dedication of everyone involved in the effort, the Task Force was able to achieve what it set out to accomplish. The 1st AML team entered a pandemic battlefield that was poorly defined and unfamiliar, yet performed in an exemplary fashion. Familiar roles within the preventive medicine community were stretched due to the many unique facets of this mission. In particular, the preventive medicine specialists performed tasks that were well outside of their defined areas of expertise, but they accomplished these tasks with enthusiasm, professionalism and precision. Their positivity was infectious to all with whom they worked, and their contributions were invaluable to the overall success of the COVID-19 Task Force team efforts.

Laboratory Response

When the 1st AML team arrived in Camp Humphreys, Korea, the laboratory team of the Department of Pathology (DPALS), BDAACH was already spearheading the effort to establish diagnostic capability to test COVID-19 under the CDC guidelines with the US Food and Drug Administration (FDA) Emergency Use Authorization (EUA) approved testing kit and Polymerase Chain Reaction (PCR) platform. One Army pathologist and three microbiologists from BDAACH initiated the establishment of an auxiliary laboratory facility in Camp Humphreys for the COVID-19 testing mission. Having conducted planning meetings with BDAACH in advance of mobilizing, the 1st AML laboratory team arrived nearly fully compliant with the regulatory and technical standards of the College of American Pathologists (CAP) standards for conducting the high-complexity molecular diagnostic testing. Fortuitously, the

1st AML's Biological Threat Assessment Team uses the same diagnostic platform at its home stations which was the instrument available at the COVID-19 testing lab in Korea. Thus, the team's prior experience and expertise with the diagnostic platform positioned them to meet BDAACH's testing demands quickly and with relative ease.

In the early days of the pandemic, the CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel protocol was the only FDA-EUA approved assay. The CDC protocol stipulated that sourcing for the RT-PCR primers and probe sets come from the International Reagent Resource (IRR), and limited the number of extraction kits and methods. Reagent shortages and a lack of variety of diagnostic methods became a serious challenge to most SARS-CoV-2 testing clinical laboratories including the laboratory in Camp Humphreys. As a result, the integrated BDAACH and 1st AML diagnostic teams faced significant difficulties in obtaining reagents and supplies. In addition to the narrowed options for reagents and kits, the team also dealt with limited oversea supply channels from both Defense Logistics Agency (DLA) and commercial vendors, despite efforts to remain proactive in ordering and maintaining disciplined supply chain management.

The dedication of the BDAACH and 1st AML teams allowed expansion of their SARS-CoV-2 laboratory testing support outside the USFK area of responsibility (AOR) to the US Indo-Pacific Command (USINDOPACOM) AOR, including the Navy's 7th Fleet aircraft carriers, USS Theodore Roosevelt and USS Ronald Reagan, and the US naval hospitals of the US Forces Japan (USFJ). Gradually increasing its capacity to perform diagnostic, screening, and surveillance support for USINDOPACOM, the lab team handled this high volume of samples with a surprisingly fast turnaround time (TAT) of less than 24 hours in most cases. By the end of the 1st AML's four-month deployment, the COVID-19 Task Force processed nearly 45,000 clinical specimens from the USFK AOR and sixteen different DoD medical facilities and military units within USINDOPACOM AOR.

In order to provide large scale and sustainable COVID-19 testing support, the Task Force leveraged the capabilities of the Seoul Clinical Laboratory (SCL), a CAP-accredited host-nation clinical reference laboratory in South Korea, a partner of the BDAACH laboratory for over 25 years. The reference lab provided high throughput and fast TAT of 24 hours that allowed BDAACH and 1st AML teams to support the high volume of COVID-19 diagnostic, screening, and surveillance testing requests.

Redeployment

Case activity in the USFK's area of operation (AO), which is divided into 4 functional Areas from the north to the south of the peninsula (Area I– IV), a shifted over the course of the deployment. The trigger to redeploy PM assets was based on both a sliding scale of case loads in the AO and the transition from Health Protection Condition (HPCON) C to B. At the beginning of the deployment, most cases were in Area IV, but as the spring turned into summer, the majority of cases were occurring in Area II, a region which is supported by a large military medical center, the Korean CDC and robust ancillary support capabilities. By late April, case numbers had stabilized and preparations to redeploy some of the PM support staff and PM physicians began. The PM team redeployment required a methodical hand-off of information and responsibilities to the organic team in Areas II and IV. By early May, the 1st AML ID physician and two of the PM specialists were redeployed to the US In mid-May, the transition from HPCON C to B was formally declared, and the remaining PM personnel were redeployed. Eventually, the organic staff stationed in S. Korea had resumed full control of the COVID-19 operations by mid-June 2020.

To meet the steadily increasing USFK COVID-19 testing demands resulting from expanded screening and surveillance algorithms and ensure continuation of the COVID-19 testing mission at BDAACH, the laboratory team had to carefully transition its responsibilities to organic laboratory personnel. US Army Medical command's (MEDCOM) distribution plan for replacing the time- and labor-intense the manual RT-PCR diagnostic platform with automated, high capacity COVID-19 testing eased the 1st AML transition plan. By the end of June 2020, DPALS, BDAACH was in receipt of multiple automated RT-PCR diagnostic platforms. With the brunt of the labor demands lifted, half of the 1st AML laboratory team was able to redeploy in mid-June, with the remaining team members following near the end of June after the successful transition of the COVID-19 sample and data management responsibilities to the DPALS, BDAACH.

Discussion: Lessons Learned & Recommendations

Overall, the broad range of subject matter expertise and modularity of the 1st AML allowed for support of the USFK COVID-19 Response mission in a number of ways: treatment, laboratory diagnostics, contact tracing, and public health knowledge generation. The ability of the healthcare providers to establish credentialing

before arrival was essential to rapid integration of these assets into the response effort. Pre-credentialing should be considered a best practice in any future outbreak response where medical care or preventative medical services will be provided. The 1st AML Bravo team has both next generation sequencing capabilities and contact tracing expertise. If these capabilities were leveraged in real time (24-48 hours), then sequence data could potentially enhance the contact tracing efforts in future outbreak responses by identifying the highest risk activities for transmission. Although the public health assessment project obtained actionable data about the clinical course and modifiable risk factors for COVID-19 infections, a fully realized research study would have generated more rigorous data. For the next pandemic, a predesigned research study protocol for a generic pathogen with regulatory approvals in place would both hasten the data gathering and improve the quality of the results. A pre-approved research plan is possible because there are universal data points that need to be characterized regardless of the actual etiologic agent. These include risk factors for acquisition and poor outcome, performance of molecular and serologic diagnostics, risk factors for severity, mode of transmission, and efficacy of PPE. If the 1st AML's capabilities are expanded to have pre-approved research protocols (with 1st AML soldier scientists as protocol investigators) bolstered with well-coordinated, pre-arranged reach-back support from Army research facilities, then the 1st AML could have decision-guiding data generated within weeks of arrival. This coordination between the 1st AML and Army research facilities during a pandemic could also be further extended to perform clinical trials for therapeutics or vaccines. This capability would require significant good clinical practice training for any AML personnel involved in studies or trials and potentially create a need to add clinical research coordinators to the 1st AML's MTOE.

In summary, the following are recommendations for improving the effectiveness of 1st AML preventive medicine capabilities for future public health emergency deployments:

1. The Army has in its inventory many well trained, capable, hard-working and highly skilled professionals. While it is clear that the COVID-19 pandemic is unlike any battle the 1st AML team has ever fought, it is important that outbreak response leadership takes full advantage of the talents available to achieve success of mission. We recommend a mission command structure on the front end that recognizes and respects the value and expertise that all team members bring to the operation. A comprehensive public health response requires coordination by public health officers with local public health organizations, hospitals, critical care and clinic assets. A command structure which allows medical experts a space to fully assert their skillsets and assure the best public health outcomes greatly benefits future outbreak response.

2. Another critical piece to an effective public health response to an infectious disease public health emergency is the capacity to provide reliable and efficient testing, results acquisition, quarantine, isolation and shelter-in-place functions. Until all of these components are fully deployed, it is very difficult for any public health response to have a significant impact.

3. Finally, effective public health messaging is imperative in outbreak management. There are several historical examples of how ineffective public health messaging has compromised the success of a public health response effort. Utilizing the skills and expertise of public health officers to develop, shape and deliver an accurate, science-based and consistent public health message to the public is key.

The 1st AML mission's requires adaptable and agile analytic capability. The team places heavy emphasis on training its Soldiers in Tactics, Techniques, and Procedures (TTPs) that are relevant to current technological advances in the healthcare system and ensures that they maintain competency in diagnostic testing. Therefore, it is critical to meticulously review and update the unit Medical Equipment Set (MES) to the Army Medical Department of Excellence. Comprehensive training opportunities such as the Field Identification of Biological Warfare Agents (FIBWA) course and unit training exercises are also key to developing the technical proficiency of soldiers.

Building relationships and maintaining close collaborations with the host nation entities are important for mission success. At the beginning of the pandemic, COVID-19 testing support by Korea CDC allowed the USFK to focus on establishing its own COVID-19 diagnostic capability at Camp Humphreys. Later, when high volumes of testing were required for screening of incoming personnel to S. Korea and surveillance testing for the populations within the installations, the USFK leveraged the existing contract with the host nation reference laboratory to manage high-volume capacity with a short TAT. Lastly, sharing the experiences with the counterpart of the US AMEDD, the Republic of Korea (ROK) Armed Forces Medical Command (AFMC) via virtual conferences promoted the cooperative preparedness on such public health crisis and the military alliance between the two countries.

The 1st AML is a unique organization with vast capabilities to respond to a broad variety of public health threats. From patient management, to diagnostic testing , to regulated research capabilities, to public health response implementation and beyond, when all available talents within the 1st AML are fully utilized, there is no barrier too high, and no problem too complex.

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