Hawaii National Guardsman assigned to Task Force Hawaii administers COVID-19 vaccine to Department of Education employee at Kealakehe High School, March 6, 2021, Kona, Hawaii (U.S. Army National Guard/John Schoebel)

Health, Pandemic Preparedness, and Multidomain Operations

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Historically, infectious disease has been one of the most significant threats to U.S. Servicemembers on the battlefield, constituting the largest source of mortality through World War I and a significant source of casualties and nonbattle injury through the present day.[1] During World War II, General Douglas MacArthur famously expressed his frustration with malaria's operational impact: "It's going to be a very long war if for every division I have facing the enemy, I have one sick in hospital and another recovering from this dreadful disease."[2] More recently, David Matson, an infectious disease clinician, vividly described the impact of diarrheal disease: "I expect that our imaginations cannot fathom the problems attendant from the absolute urgency for relief

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from explosive vomiting and diarrhea when experienced within an armored vehicle under fire and at ambient temperature of >40°C."[3]

To manage infectious disease domestically, the United States developed a robust public health system that supported sanitation, water treatment, and vaccinations, effectively reducing the risk for the population. The inadvertent consequence of these successful efforts is that the modern American warfighter is at an immunological disadvantage in certain locations; Servicemembers do not necessarily share the acquired immunity to endemic diseases that locally based forces may, creating a gap in force health protection.

Besides traditional diseases, some emerging infectious diseases pose an even greater danger to Servicemembers and local communities. Poor understanding of disease transmission mechanisms, unknown durability of immunity, and a dearth of effective diagnostics or countermeasures can stress medical systems to a breaking point—as has been the case during the COVID-19 pandemic, which has had broad impacts on military operations, ranging from altered training schedules to the diversion of the USS *Theodore Roosevelt* to Guam due to a shipboard outbreak.[4]

Even limited epidemics of emerging diseases can cause significant disruption. In 2012, Middle East respiratory syndrome coronavirus (MERS-CoV), a cousin of SARS-CoV-2, led to outbreaks in Saudi Arabia and South Korea, resulting in a fatality rate of nearly 40 percent of those infected.[5] Critically, these outbreaks could have spread to the thousands of U.S. Servicemembers deployed to both areas. Moreover, to date, there is still no approved vaccine against MERS-CoV.

Viral infections such as SARS-CoV-2 are not the only threats; bacterial infections can significantly complicate recovery from wounds sustained during combat. Traumatic combat injuries alter human physiology by disrupting the body's first line of defense—skin—and inducing contamination, significantly increasing the risk of infection. When combat injury is sustained in the context of blast exposure, the immune response is also suppressed and may limit the efficacy of antibiotics.[6] Already a major concern during previous conflicts, the risk of combat wound infection is forecasted to grow during future conflicts and multidomain operations (MDOs) as antibiotics grow increasingly ineffective due to multidrug-resistant organisms. Moreover, the anticipated difficulty in battlefield evacuation limits treatments options.

In the MDO environment, Servicemembers will likely not be able to follow traditional health guidelines, such as quarantining, regular handwashing, physical distancing, and receiving advanced medical care. These limitations heighten the risk of sickness and underscore the necessity of pathogen surveillance, new countermeasure development, and low-tech strategies to enable Servicemembers to remain in the fight.

Additionally, military assets are sometimes called on to respond directly to infectious disease crises. While these noncombat missions afford greater opportunity for the use of appropriate risk-mitigation strategies, Servicemembers are still at risk when deployed to these environments. Servicemembers are playing an active role in the response to COVID-19, supplementing civilian medical infrastructure and supporting mass vaccination campaigns in addition to facing exposure to the virus at Department of Defense (DOD) installations and hospitals.[7] This support is not unique to COVID-19. In 2014, approximately 2,500 Servicemembers deployed to West Africa as part of Operation *United Assistance*. As part of their work to construct treatment units, train healthcare workers, and provide laboratory testing capacity, these individuals were at risk from not only the ongoing Ebola outbreak but also endemic diseases, notably malaria.[8]

A Perpetual Challenge

Countless factors indicate that the threat of infectious disease will only worsen, underscoring the need for a robust military capability to address outbreaks and ensure force health protection. One major factor driving this increased threat is climate change, which was listed in a 2019 DOD report as a national security issue with potential impacts to missions, operational plans, and installations.[9]

Both climate and weather are significant factors regulating the life cycles of mosquitoes, ticks, and other vectors of diseases such as Lyme, dengue, yellow fever, or Zika. Warmer conditions could increase the geographic range and number of months in the year where diseases and vectors are viable, allowing infection to spread more freely.[10] Consistent with this concern, a recent study found that a broad range of insects can migrate hundreds of kilometers on wind currents—potentially spreading disease while they travel.[11] Diarrheal disease, listed as the Military Infectious Disease Research Program's number-one infectious disease threat to deployed Servicemembers, is also likely to worsen because of climate change. Higher temperatures will create more favorable conditions for disease-causing agents, and more extreme weather events, such as severe rainfall or hurricanes, can damage or overwhelm water treatment systems, raising the risk of contaminated water.[12] As David Matson has described, diarrhea has the potential to wreak havoc on small military teams operating in confined environments.[13]

Beyond climate change, many emerging infectious diseases originate in animals. The H1N1 influenza outbreak of 2009 (the so-called swine flu) originated from pigs; certain coronaviruses, such as SARS-CoV-2 and MERS-CoV, are often traced to bats.[14] New pathogens can emerge in areas with limited public safety, health care, and regulatory infrastructure, spreading from a local emergency to an international disaster. Though medical countermeasure development is ongoing at government, academic, and industry laboratories around the world, this process can be slow. Vaccines typically require 7 to 10 years for design, preclinical and clinical testing, and Food and Drug Administration approval. A massive investment of time and more than $15 billion at the beginning of the COVID-19 pandemic shortened this timeline, with the government accepting financial risk to manufacture millions of doses before

Servicemembers converse between treatment of COVID-19 patients at monoclonal infusion site in St. George, Utah, November 4, 2021 (U.S. Army/ Timothy Hughes)

clinical trials proved vaccines safe and effective.[15] Though this gambit yielded three vaccines within approximately 1 year, a global end to this pandemic is expected to take several years.

In the absence of any incentive, however, industry and academia often focus on diseases with the largest potential customer base—typically treatments for chronic health conditions. Even when developing countermeasures for infectious disease threats, researchers may not factor in the unique needs of the warfighter unless they are working directly with a military medical laboratory. Given that the far-forward warfighter needs to deploy rapidly to and operate in any context—including dense urban and subterranean environments, jungles, forests, and other locations that could serve as disease reservoirs—tailored strategies are needed. Even effective vaccines can require time or multiple injections to induce a protective response. For example, the vaccine against yellow fever, a disease commonly found in South America and sub-Saharan Africa, requires approximately 10 days to induce an immune response. A Servicemember who must deploy prior to that 10-day period risks infection.

Thus, military medical research institutions around the world are working to identify, prevent, and overcome known and unknown disease threats to ensure force health protection. In particular, the Walter Reed Army Institute of Research (WRAIR) and Naval Medical Research Center address disease threats globally through surveillance, medical diplomacy, partner capacity-building, and product development. These DOD assets include WRAIR's overseas directorates in Southeast Asia (Armed Forces Research Institute of Medical Sciences), Africa (U.S. Army Medical Research Directorate–Africa), and Europe (U.S. Army Medical Research Directorate–Georgia). These laboratories are strategically positioned to support international efforts to develop medical countermeasures that address established and emerging diseases.

Protecting the Joint Force

In the absence of medical countermeasures, what strategies can leaders and warfighters employ to help safeguard force health? Sleep and psychiatry researchers at WRAIR, working alongside nutrition and performance researchers at the U.S. Army Research Institute of Environmental Medicine, have identified that the strategies used to ensure units are fit and deployable can also help mitigate risk of infection. These strategies are an integral part of readiness and include "domains" of adequate sleep, physical activity, healthy diet, and stress management. Indeed, in explicit recognition of the importance of leveraging these factors collectively, the Army has developed Holistic Health and Fitness (H2F), a comprehensive system to optimize Soldier and unit performance by integrating best practices in these physical and nonphysical domains.[16] These same integrated strategies may also help mitigate risk of infection.

Physical Activity. Physical fitness is a basic requirement for military service and can be the difference between life and death in contested operational environments. Underscoring its importance, a growing body of evidence suggests

that regular physical activity can be beneficial to the immune system. For example, higher levels of physical activity are associated with a 10 percent lower risk of COVID-19 infection; similarly, physical inactivity prior to the pandemic period was a strong risk factor for severe COVID-19.[17] While physical activity is not a panacea, it can provide at least some force health protection when considered at the population level.

After a single bout of exercise, the body experiences a marked increase in immune system activity. Researchers believe this increase marks the movement of elements of the immune system to the body's frontlines (the lungs, gut, and so forth) to meet and overcome invading pathogens.[18] Similar data exists for long-term training, with one study demonstrating that athletes show lower rates of upper respiratory tract infections compared with more sedentary individuals.[19] While a range of factors associated with exercise governs and complicates the immune response, including type (endurance, resistance, stretching) and character (intensity, duration, frequency, recovery), the majority of evidence points toward a positive effect.

It is important to note that, just as overtraining or excessive exercise—a common occurrence during military training—can cause musculoskeletal injury, overtraining has also been linked to a *suppressed* immune system.[20] Maintaining appropriate exercise regimens that are vigorous, challenging, and sustainable is one way that military leaders can support fitness, readiness, and resilience in the warfighter.

Sleep. Responding to the growing understanding of sleep's role in military performance, Major General William Burleson, director of operations for U.S. Forces Korea, coined the saying, "Sleep is ammunition for your brain." For decades, studies have demonstrated that sleep loss negatively affects emotion regulation, psychological resilience, learning and memory, judgment, cognitive performance, and reaction time. In one study, after 3-day field exercises the ability to identify and accurately target the enemy decreased by 220 percent, while errors in decisionmaking increased by 86 percent and reaction time worsened by 22 percent.[21]

Recent evidence also suggests that sleep is just as important for healthy immune function and the ability to fight off infection. In one study, volunteers without previous exposure to the common cold were exposed to a live cold virus. Researchers found that no variable predicted whether a participant would fall sick better than sleep duration—not even age or stress level.[22] In other words, those who habitually slept less were more likely to fall ill with a cold virus. A follow-on study identified a "sleep threshold," noting that individuals who slept less than 6 hours per night were at significantly greater risk of cold infection compared with those who slept 7 to 9 hours.[23] In addition, there is now limited but compelling evidence from preclinical studies using animal models that suggests sleep not only helps protect against initial infection but also plays a direct role in aiding recovery from infectious illness and response to immunization.[24]

Despite the importance of sleep in keeping Servicemembers healthy, studies show that approximately 62 percent of Soldiers get less than 6 hours of sleep per night.[25] While mission requirements do not always allow for a full 7 to 9 hours of sleep, there are strategies to mitigate performance decrements associated with inadequate sleep. Sleep banking, or increasing sleep prior to a period of limited sleep, builds resilience to the negative effects of sleep loss.[26] Other warfighter-focused strategies have been developed to mitigate the risk of performance decline during nocturnal operations, high-altitude missions, and long-distance travel.[27] Under garrison conditions, it is also critical that leaders allow Servicemembers time to get enough sleep or recover from sleep loss due to mission requirements. These strategies that promote sleep may in turn benefit Servicemembers' immune systems.

Diet. Not only is proper nutrition a critical component to military readiness, but it is also a significant contributor to a healthy immune system. Undernutrition is a critical threat: The absence of key nutrients can directly limit the body's ability to protect itself from pathogens. A lack of vitamin D can limit the production of antimicrobials and compromise the skin, the primary barrier against infectious disease. A lack of iron and zinc directly threatens the function of white blood cells, which include the body's "first responders" against pathogens.[28] Poor nutrition can even increase harm from infectious disease—one study found that low levels of the nutrient selenium caused viral mutations resulting in a more damaging infection.[29]

Obesity can also stress the immune system. Obesity is one of the most pressing challenges to military readiness because it significantly hampers performance. As of August 2019, approximately 17 percent of military personnel were considered obese, with the highest rates in the Navy, at 22 percent.[30] Studies have identified a greater risk of hospital-acquired infections, more severe respiratory infections, and a greater overall risk of viral and bacterial infection for individuals with obesity.[31] Furthermore, individuals with obesity are still at risk of missing critical nutrients from their diets, further compounding potential health risk.[32]

These factors make it all the more critical that leaders and individuals take a balanced, healthy diet seriously. Efforts to improve readiness should consider the nutritional composition of operational rations and meal options available in garrison and at home. Foods provided by the Services, including operational rations and garrison meal plans, must meet the standards for nutritional requirements described in Army Regulation 40-25, *Nutrition and Menu Standards for Human Performance Optimization*.[33] These requirements are based on the Dietary Guidelines for Americans, with adjustments to accommodate increased energy expenditure and other operational demands of military service.[34] That said, military personnel consume the majority of meals outside of military dining facilities. Current efforts are thus focused on improving the nutritional quality of foods offered at on-post locations, such as commissaries, restaurants, and recreational facilities. Harmonizing standards for food and nutrition in all locations serving

Electrician's mate 3rd class Maggie Flatt plays violin during mental health awareness event on mess decks of aircraft carrier USS *Ronald Reagan*, Philippine Sea, September 27, 2021 (U.S. Navy/George Cardenas)

military personnel and their families will be paramount for ensuring optimal immune health and readiness.

Mental Stress. Mental stress can manifest in a range of ways, from lack of engagement with one's job to behavioral health problems. During Operation *Iraqi Freedom* and Operation *New Dawn*, behavioral health problems constituted 12.1 percent of medical evacuations; during Operation *Enduring Freedom*, 10.1 percent.[35] Even for those who were not necessarily evacuated during deployment, 23 percent of Servicemembers report post-traumatic stress disorder after returning home.[36] Not only does mental stress result in diagnosable conditions, but it can also impede performance during combat. Soldiers in combat may become so mentally stressed that they are unable to function for a period of time. In two studies, more than 40 percent of Soldiers who experienced a combat-related event reported encountering team members with an acute stress reaction.[37]

Mental stress may also impact the immune system. One study found that self-reported stress best predicted whether volunteers exposed to the influenza virus would show symptoms.[38] Another study found that individuals who reported high levels of mental stress for at least a month were two to three times more likely to develop colds compared with those reporting less stress when challenged with a cold virus.[39] In addition, mental stress also can worsen disease. Stress may increase the likelihood of a disease becoming symptomatic (as opposed to mild, asymptomatic infection) or more active (some viruses, such as herpes, can lay dormant after infection, with symptoms recurring over time in response to stress).[40]

Efforts have also tracked the COVID-19 pandemic's impact on Soldier mental health. The first iteration of this study linked pandemic concerns to behavioral health symptoms—Soldiers reporting more fears and concerns about the pandemic were up to four times more likely to screen positive for depression or anxiety.[41] These results informed the development of resources to help units address and overcome a range of behavioral health concerns related to the COVID-19 pandemic.[42]

Healthy Lifestyles and Vaccine Efficacy

A healthy lifestyle requires balancing activity, sleep, diet, and stress. Indeed, all four are intrinsically linked to one another. High stress may result in difficulty falling asleep, poor diet (for example, consuming excess alcohol or eating fast food), or lack of motivation to exercise. Poor nutrition can result in diminished physical and cognitive performance and sleep disturbance. Not only can a holistic approach such as H2F support military performance, but

it can also be important in protecting Servicemembers from infectious disease. Likewise, just as leadership is critically important in promoting components of H2F, it is critical that leaders consider and address these elements together when combating a pandemic.

Such factors are particularly important given that sleep, exercise, nutrition, and stress can significantly impact vaccine efficacy. One study found that nonresponsiveness to hepatitis B vaccination was more than eight times greater in individuals with obesity than in those at a healthy body weight.[43] Studies have shown that both acute and chronic stress can impair the production of antibodies, the body's means of flagging invaders for attack by the immune system.[44] Six months after receiving a hepatitis B vaccination, individuals who slept fewer than 6 or 7 hours the night prior to vaccination were at significant risk of being unprotected compared with those who slept more than 7 hours.[45] Both acute and prolonged exercise prior to vaccination can actually enhance the immune response as a result of vaccination.[46] Collectively, such research suggests that a healthy force may help reduce the threat of infectious disease.

Research at WRAIR, the U.S. Army Research Institute of Environmental Medicine, and elsewhere is aimed at identifying how healthy lifestyle changes can improve immune response. Identifying and implementing these healthy behavioral changes can provide the military with an additional edge in combatting infectious disease and support force readiness.

Leadership and Unit Adoption

Leaders are key to implementing and sustaining these changes, with numerous studies documenting their role in health-related outcomes. For example, one study found that, when Soldiers view their officer and noncommissioned officer leadership as effective, there is a near fourfold reduction in risk of psychological problems.[47]

Other studies, conducted in settings from deployment to mandatory quarantine, found that specific leader behaviors

On January 6, 1777, following the Battle of Princeton, George Washington ordered beginning of yearlong mass inoculation of Continental Army forces against smallpox; George Washington and Marquis de Lafayette on horseback during winter quarters at Valley Forge, Pennsylvania, oil painting by John Ward Dunsmore, 1907 (Library of Congress)

are associated with a range of positive outcomes, including increased resilience, better mental health, increased engagement in stress-mitigating activities, and better attitudes toward preventive health measures.[48] Most recently, Soldiers who reported their immediate leaders engaged in COVID-19 leadership behaviors (for example, following COVID-19 health guidelines, acknowledging the stress of the pandemic) also reported fewer mental health symptoms and greater adherence to COVID-19 health guidelines.[49] Importantly, in each study, the benefits of specific leadership behaviors were found even when controlling for overall leadership ratings.

At every level, military leaders can create a culture that supports exercise, sleep, nutrition, and stress mitigation through encouraging healthy behaviors in their units and following their own recommendations. These lifestyle factors can directly impact health outcomes and the ability of their units to reduce the threat of infectious disease.

Conclusion

Infectious diseases have altered the course of history. Smallpox nearly ended the Revolutionary War in 1776, leading to an order from George Washington's headquarters beginning, "The General has nothing more at heart, than the Health of the Troops."[50] More than two centuries later, infectious disease remains one of the most consequential threats to Servicemembers, capable of compromising units in combat or before they even reach the battlefield. In particular, during MDOs when small teams are expected to function effectively with limited support, every casualty represents a significant threat to the overall effectiveness and survival of the team.

In a world with dozens of known diseases without safe, reliable countermeasures and the potential for new pandemics to emerge at any moment, leader support for positive lifestyle choices can improve the resilience of the force to disease, potentially improving their odds of remaining safe, healthy, and in the fight. **JFQ**

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