The human intestine harbors trillions of microorganisms that are essential to human health. Collectively referred to as the **gut microbiome**, this complex ecosystem consists of commensal archaea, eukarya, bacteria, viruses, and fungi that facilitate the anaerobic oxidation of complex carbohydrates to promote digestion and nutrient absorption. The composition of the microbiome varies dramatically from person to person and depends on numerous factors, including diet, age, gender, the presence of stressors, and geographic location [1].

Military personnel deployed to areas of the developing world often experience gastrointestinal illnesses from exposure to environmental bacteria that take up residence in the gut and cause dysbiosis [2]. Interestingly, the microbiome influences an array of physiological processes well beyond the intestinal tract and the U.S. Department of Defense (DoD) is actively engaged in research efforts to exploit the microbiome to optimize warfighter health and performance [3-5].

**A Gut Shield System to Prevent Enteric Infections**

Acute enteric infections and diarrheal illness—also known as disease non-battle injuries—afflict approximately 30% of warfighters per month during deployment to parts of the developing world [2]. Enteric infections may be underappreciated and viewed as more of an inconvenience rather than a formal injury; however, they result in lost duty days, decreased performance, and healthcare costs [6]. One strategy to mitigate this disease burden is to deliver cross-reactive antibodies to the gut that bind toxic non-commensal bacterial proteins, creating a **gut shield system** within the warfighter [5].

To this end, researchers at the Naval Medical Research Center recently partnered with Immuron Limited to evaluate the efficacy of an antibody-containing supplement to prophylactically combat bacillary dysentery in non-human primates [7]. The orally administered antibody protected against clinical shigellosis in 75% of animals compared to placebo—supporting the use of targeted antibodies for the prevention of enteric disease.

**The Microbiome’s Impact on Vaccine Efficacy**

Microbial metabolites produced in the gut enter circulation where they directly impact the immune response, the perception of pain, inflammation, and other aspects of human health in ways that are not well understood [8]. For instance, some reports suggest a link between microbiome composition and the efficacy of certain vaccines [9, 10]. In infants and adults, a higher relative abundance of the phylum Firmicutes is associated with higher humoral responses to oral vaccines [9]. Interestingly, the bacterial protein flagellin, which is abundantly present in the gut, is necessary to activate mammalian toll-like receptor 5 (TLR5) and stimulate the production of antiviral antibodies following influenza vaccination [11]. In contrast, germ-free mice deficient in TLR5 had poor serological responses to influenza vaccination.

It’s apparent that the microbiome and the humoral immune response develop in parallel and it’s possible that seemingly innocuous genetic variances may have complex immunological consequences due to different interactions with bacterial products produced in the gut. The DoD recognizes the significance of these reports and has a keen interest in developing high-efficacy vaccines that synergize with the microbiome to protect military personnel from high-risk pathogens.

**Military Stressors and Microbiome Composition**

In 2018, Dr. J. Philip Karl of the U.S. Army Research Institute of Environmental Medicine announced a collaborative research effort at the 1st Annual DoD Gut Microbiome Informational Meeting to characterize the relationship between...
military stressors, gut microbiome composition, and warfighter performance [5]. Dr. Karl and collaborators demonstrated that prolonged exposure to physiological stress led to changes in microbiome composition and increased intestinal permeability in young adults [12].

Increased intestinal permeability has been linked to the development of cardiovascular disease [13], psychiatric disorders [14], autoimmune disease [15], inflammatory bowel disease [16], and a host of other health complications. Fortunately, the microbiome is a malleable target that can be manipulated with a fiber-rich diet to build resiliency toward military stressors like sleep deprivation, exposure to environmental extremes, and prolonged physical activity. Diet was the primary tool identified by Dr. Karl and his team that will be used by the U.S. Army to manipulate the gut microbiome in future studies relating to inflammation, innate immunity, and gut permeability.

**Conclusion**

The gut microbiome is a dynamic and highly complex entity that engages with multiple aspects of human physiology and influences the efficacy of certain vaccines. Poor gut health is intimately tied to a menagerie of disease states, such as enteric infections and intestinal permeability, that can dramatically impact warfighter health and performance. Regular consumption of probiotics and nutritional prebiotics may help mitigate the health consequences associated with military stressors, although further work is required to establish the efficacy of this approach. Looking ahead, synthetic biology and genetic engineering may provide a novel means toward manipulating the intestinal microbiota and advance DoD efforts to improve warfighter health both on and off the battlefield.

**REFERENCES**


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**Spotlight**

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**Figure 1. A select number of anatomical sites influenced by the gut microbiome (Source: U.S. Department of Veterans Affairs)**

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