SPECIAL REPORT

MILITARY MEDICINE, 180, 6:626, 2015

Operation United Assistance: Infectious Disease Threats to Deployed Military Personnel

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ABSTRACT As part of the international response to control the recent Ebola outbreak in West Africa, the Department of Defense has deployed military personnel to train Liberians to manage the disease and build treatment units and a hospital for health care volunteers. These steps have assisted in providing a robust medical system and augment Ebola diagnostic capability within the affected nations. In order to prepare for the deployment of U.S. military personnel, the infectious disease risks of the regions must be determined. This evaluation allows for the establishment of appropriate force health protection posture for personnel while deployed, as well as management plans for illnesses presenting after redeployment. Our objective was to detail the epidemiology and infectious disease risks for military personnel in West Africa, particularly for Liberia, along with lessons learned from prior deployments.

INTRODUCTION

The ongoing Ebola outbreak in West Africa is requiring an international response to curb the regional epidemic which, as of January 13, 2015, has led to over 21,373 cases with 8,468 deaths.[1] The Department of Defense (DoD) has deployed approximately 3,000 personnel under the direction of United States Agency for International Development (USAID) to train Liberian and international health workers to manage Ebola virus disease, to build Ebola Treatment Units for Liberians and a 25-bed hospital for health care volunteers, and to establish Ebola laboratory testing facilities to ensure a more robust medical system and augment Ebola diagnostic capability within the affected nations.

As the U.S. military has done for other larger deployments around the world, a key aspect of preparing for the deployment of military personnel is to determine the infectious disease risks of the region.[2–8] This allows establishment of appropriate force health protection posture for those in country, as well as management plans not only in the area of deployment, but for illness presenting after returning home. This review details the epidemiology and infectious disease risks in West Africa, with an emphasis on Liberia. Lessons learned from prior U.S. deployments in Africa and Liberia are also summarized.

HISTORICAL MILITARY DEPLOYMENT RELATED TROPICAL INFECTIOUS DISEASES EMPHASIZING OPERATIONS IN IRAQ AND AFGHANISTAN

Prior to World War I, the ratio of deaths due to disease versus battle injury was approximately 10:1, which decreased to 1:1 during World War I and 0.01:1 during the Gulf War.[9] During the Vietnam War, there were 1,253 in-hospital deaths among a total of 132,996 military hospital admissions. Of which, 91 (7.3%) were nonsurgical and the result of common infectious disease causes, including malaria (12 deaths), hepatitis (4 deaths), and encephalitis (4 deaths).[10] As an example of the impact that can occur, in 1970 alone during the Vietnam War, there were 167,950 lost work days from malaria, 70,800 from acute respiratory tract infections, 85,840 from viral

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doi: 10.7205/MILMED-D-14-00691

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hepatitis, 45,100 from diarrheal diseases, 3,700 from venereal disease, and 205,500 from fever of undetermined origin. In comparison, there were 10,444,750 lost work days resulting from battle injury and wounds.[11] Overall, diarrhea and respiratory tract infections have the most substantial impact on morbidity and lost days of work during deployment, which should be consistent in future operations. Both malaria and dengue also contribute a significant portion to morbidity and lost work days and the impact of these diseases on multiple military operations (i.e., Spanish–American War, Korean War, Vietnam War, Operation Restoring Hope in Somalia, and Operation Enduring Freedom [OEF] in Afghanistan) have been recently reviewed.[12,13]

During the last 13 years, the U.S. military's primary focus has been the operations in Iraq and Afghanistan, which have greatly influenced combat casualty care. Similar to prior military operations, disease and nonbattle injury (DNBI) are the most common causes for evacuations out of theater. Specifically, there were 23,719 medical evacuations for the period of October 2001 through December 2012, of which 232 cases were because of infectious and parasitic diseases (ranked 14th of all evacuation causes).[14] In addition to diarrhea and respiratory tract infections, malaria,[15,16] leishmaniasis,[17,18] multidrug-resistant (MDR) bacteria and invasive fungal infections of combat-related wounds,[19,20] and transfusion transmitted infections with whole blood use represent other emphasized infectious diseases.[21,22] Rickettsial infections were frequently noted during British operations in southern Afghanistan, likely highlighting the challenges with preventing exposure during military operations.[23] At times, assistance is required through remote teleconsultation with clinicians for major infectious disease issues, such as tuberculosis, methicillin-resistant *Staphylococcus aureus*, leishmaniasis, malaria, human immunodeficiency virus (HIV), and viral hepatitis.[24,25] As another clear example of the significant impact of infectious diseases in the deployed setting, a norovirus outbreak nearly closed a military medical treatment facility in Afghanistan and in Iraq.[26,27] A case of Crimean-Congo hemorrhagic fever (CCHF) acquired in a U.S. soldier while deployed to Afghanistan resulted in his death, along with prophylaxis of a number of health care personnel with ribavirin after nosocomial exposure.[28]

Further studies of our military forces in southwest Asia have demonstrated that up to 75% of military personnel suffer from at least one episode of diarrhea during a deployment.[29] Data collected from deployments in Iraq and Afghanistan (2003–2004) revealed that 45% of soldiers with diarrhea reported a decrease in job performance (3 day average), 61% sought medical attention, and 17% were confined to their bed for an average of 2 days.[29] In an additional study of soldiers serving in Iraq and Afghanistan, a similar decrease in job performance (2 days in half of the diarrhea cases).[30] On occasion, patients developed reactive arthritis from their gastroenteritis, and some developed chronic persistent diarrhea.[31–34]

Along with diarrheal disease, Q-fever and respiratory infections were also observed during the Iraq and Afghanistan deployments. A study of vector-borne disease 2000–2011 at Army and Navy medical facilities revealed 136 cases of Q-fever among military personnel. In 2008, the number of cases peaked at 48, and is likely reflective of transmission in Iraq.[35] Fewer cases of Q-fever were noted in Afghanistan, which might be related to doxycycline malaria chemoprophylaxis. This is plausible, as the British military had high rates of Q-fever in Helmand Province while using malaria prophylaxis regimens with no rickettsial activity.[23,36]

Regarding respiratory tract infections, a survey of nearly 16,000 personnel deployed to Iraq and Afghanistan (2003–2004) reported that 69% experienced respiratory illness and 17% required medical evaluation related to acute respiratory disease.[30] In addition, 50% experienced two or more respiratory illnesses, and 3% developed pneumonia. Limitations in individual performance related to respiratory illness were reported by 14%, and 9% reported decrease in unit performance during combat operations. Self-reported data from Operation Iraqi Freedom (OIF) and OEF in 2009 reflected similar findings, with 15 episodes/100 person-months reported.[37]

During operations overseas, sexually transmitted infections (STIs) have been commonly encountered. In addition, the rates of gonorrhea and chlamydia were assessed in Iraq and were higher among deployed personnel when compared to their U.S.-based counterparts, which is consistent with risks in previous wars.[38–41]

PREVIOUS MILITARY TROPICAL INFECTIOUS DISEASE LESSONS LEARNED IN SOMALIA AND LIBERIA

The transition away from combat focused operations in Iraq and Afghanistan toward support of USAID and humanitarian assistance in Liberia brings new challenges to military medicine. The operations in Africa are notably different than Iraq and Afghanistan as these two regions were categorized as low risk for infectious diseases, whereas Liberia is classified as high risk per the National Center for Medical Intelligence (NCMI), along with the type of operation (combat operations versus humanitarian assistance). The last operation with large numbers of troops in Africa was in Somalia (Operation Restore Hope), during which more than 30,000 U.S. troops deployed in support of humanitarian relief efforts. Although many of the lessons below are relevant to the approach to managing endemic diseases, the specific disease threats are different across Africa, with considerable variability for West versus East Africa. Medical intelligence assessment before the operations highlighted many standard deployment threats, but as typical of a tropical medicine deployment to Africa, malaria took center stage. Although it was initially determined that malaria was unlikely to be present in Mogadishu because of the city's advanced development, these historical data did not take into consideration the detrimental impact of civil war on public health measures

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and infrastructure.[6–8] The risk of *Plasmodium vivax* was also thought to be low and primaquine antirelapse therapy (PART) was not initially recommended. From December 1992 to May 1993, 48 cases of malaria were detected, of which 41(85%) were *Plasmodium falciparum*.[42] A major issue identified was inconsistent adherence with personal protective measures and malaria chemoprophylaxis. Initially, service members took both mefloquine and doxycycline in nearly equal numbers, and then all of the troops on doxycycline were switched to mefloquine to "ensure operational uniformity." Service members did not receive loading doses of mefloquine to account for the short half-life of doxycycline and long half-life of mefloquine. About half of the population overlapped doxycycline and mefloquine by 1 week, which was likely inadequate, as mefloquine drug levels effective for prophylaxis may require 4 weeks of drug administration. There was also a peak malaria attack rate in the first 5 weeks before force health protection measures were firmly established. A subsequent study in Somalia revealed 112 cases of malaria in 106 Marines, with *P. vivax* accounting for 97 cases and *P. falciparum* 8 cases (mixed infection noted in 6 cases).[43] The lack of PART among troops likely impacted the occurrence of this disease. A subsequent study revealed *P. vivax* treatment failures with the 15 mg base dose of primaquine for 14 days, leading to the introduction of 30 mg base dosing for 14 days even though occasional failures occurred with this dosage.[44] Although traditionally failures were blamed on patient nonadherence or parasite resistance, treatment failures may occur because of a genetic component instead.[45]

The lessons regarding malaria in Somalia were also encountered in 2003 when U.S. Marines were deployed to augment security at the embassy and international airport in Monrovia, Liberia. Despite prescribed mefloquine chemoprophylaxis (which was not administered by directly observed therapy), an outbreak of febrile illness ensued within 11 days of landing. Ultimately, many cases were diagnosed as *P. falciparum* malaria and others were treated empirically, with an estimated 44% malaria attack rate in 69 of 157 Marines that spent the nights ashore, and 80 of 290 (36%) for those who went ashore during the day only.[46,47] Diagnosis was delayed due to lack of rapid diagnostics shipboard, resulting in five cases which required intensive care unit admission for severe malaria. In 2009, a naval mobile construction team was again in Monrovia, Liberia where 7 of 24 (24%) persons developed malaria, including one who died of cerebral malaria after medical evacuation.[48]

In addition to malaria, other diseases remained an issue during military operations in Africa. Hepatitis E and dengue has also been reported in connection with military operations in Somalia. In particular, the U.S. military deployed a diagnostic laboratory for infectious diseases to Mogadishu, Somalia, in support of Operation Restore Hope.[49] Testing of patients with acute hepatitis revealed that hepatitis E was the leading cause of hepatitis among 39 people evaluated, including two relief workers, whereas hepatitis A was identified in one relief worker. The relief workers reported eating the local food and drinking untreated well water. There was no evidence of infection with malaria, yellow fever or hepatitis B in the samples tested. Regarding dengue, a seroepidemiology study revealed a 7.7% prevalence of dengue IgM among 530 troops with fever.[50] In an assessment of 289 hospitalized troops with fever, 129 (45%) had no initial identified cause; however, dengue was later identified in 41 of 96 by cell cultures (39 DEN-2 and 2 DEN-3). An additional 18 of 37 culture-negative cases had IgM antibodies. No dengue hemorrhagic shock or dengue shock syndrome was reported.

In addition to malaria, viral hepatitis, and dengue, diarrheal disease occurred among troops in Somalia, albeit at low levels because of the military-provided supplies of safe food and drinking water. An 8-week assessment of 20,859 U.S. troops revealed a mean of only 0.8% (range 0.5–1.2%) personnel seeking care for diarrhea each week, with <3% of troops experiencing a diarrheal illness each week.[51] Various bacterial, viral, and parasitic pathogens were identified from specimens, and antimicrobial resistance was commonly observed.[49]

A major lesson learned during every deployment experience into malaria endemic regions is that there is a challenge associated with enforcing adherence with personal preventive measures (i.e., uniform policy, application of DEET, sleeping under permethrin-treated bed nets, and malaria chemoprophylaxis). Among the Marines that developed malaria in Liberia in 2003, 45% reported using insect repellent, 12% treated clothes with permethrin, and none used issued bed netting.[47] Reported adherence with weekly mefloquine was 55%, although drug level data indicated that the true percentage was likely lower. This remained true among Rangers that developed malaria in Afghanistan, 52% took their weekly chemoprophylaxis, 82% had permethrin treated clothes, and 29% used insect repellent.[15] An interesting study regarding postdeployment chemoprophylaxis adherence explored a randomized trial of short message service (SMS) reminders among French military returning from Cote d'Ivoire; however, no increase in adherence occurred.[52] In contrast, some utility has been shown with SMS by U.S. military personnel in Liberia.[53] It is unclear why the discrepancy occurred between these studies, but this could be an option if directly observed therapy is not undertaken in the country and there is adequate SMS service throughout Liberia.

Many of the lessons learned in previous deployments can be applied to Operation United Assistance (OUA), including the impact of civil war on local health care infrastructure, which may increase disease exposure and underestimation of disease threat assessment. Furthermore, there may possibly be delays and inaccuracies in diagnostic capabilities, especially for malaria, challenges with changing malaria chemoprophylaxis medications if patients become intolerant of the recommended agent in Liberia, and difficulties with ensuring both malaria chemoprophylaxis and personal protection measures (PPM) adherence.

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TROPICAL INFECTIOUS DISEASES IN WEST AFRICA AND LIBERIA: CIVILIAN TRAVEL EXPERIENCE

Numerous civilian studies have evaluated travel-related infectious diseases across Africa. The GeoSentinel Surveillance Network assessed 5,899 travelers to West Africa (1997–2011) and reported six deaths from infections (five from severe *P. falciparum* malaria and one from *Mycobacterium tuberculosis* with pulmonary and extrapulmonary presentation).[54] The top three causes of illnesses were malaria (25%), viral syndrome without rash (7%), and acute unspecified diarrhea (6%). Other diagnosed illnesses included schistosomiasis (83 cases), strongyloidiasis (64 cases), hepatitis A (13 cases), typhoid fever (25 cases), bite wounds requiring rabies prophylaxis (22 cases), dengue (48 cases), tuberculosis (31 cases), and acute HIV (14 cases). Among those with fever upon return from travel (2,607), nearly 70% were diagnosed with malaria. Another study assessing all fevers from sub-Saharan Africa noted *P. falciparum* malaria in 1,527 of the 2,633 West Africa cases.[55] Other common infections included typhoid fever, paratyphoid fever, leptospirosis, and relapsing fever.

A European survey of 6,957 travelers reported three deaths, which included one from severe malaria in Liberia.[56] Moreover, a total of 1,832 traveled to sub-Saharan Africa with 319 (17%) having acute diarrhea and 85 (5%) having chronic diarrhea. Acute diarrhea pathogens included 38% unspecified, 34% *Shigella* spp., 15% *Giardia lamblia*, 6% *Salmonella* spp., 5% *Campylobacter* spp., and 2% *Entamoeba histolytica*. Of the 602 persons with febrile illnesses, there were 241 cases of *P. falciparum*, 82 other malaria species, 36 rickettsiae, 9 dengue, 8 chikungunya, and 6 cases of salmonellosis. Other common infectious disease related complications included 79 individuals with schistosomiasis, 63 with bacterial infections, 37 with arthropod bites, 28 with larva migrans, 12 with myiasis, 10 with STIs, and 7 with rabies postexposure prophylaxis (PEP).

Overview of Liberia

Liberia began as a colony of freed slaves from the United States in the early 1820s, naming the capital Monrovia after President James Monroe. By 1847, Liberia declared its independence from the United States and was established as a republic. In 1980, authoritarian rule was established following a military coup and lasted nearly a decade until a rebellion began in 1989. The civil war lasted until 1997, but resumed in 2000 until a peace agreement was signed in 2003.[57] Along with impacts on the economy, government, and society, the civil war also caused a breakdown of Liberia's health infrastructure, which has yet to fully recover and is likely due to corruption and lack of adequate financial support or leadership.

Presently, Liberia has a population of 4.2 million with a gross national per person income of approximately $580, a life expectancy of 62 years, and literacy rate of 60%.[58] There are approximately 2.6 physicians and 12 midwives per 10,000 individuals, which is inadequate for appropriate medical care, especially during extreme epidemics such as Ebola. Overall, the climate is tropical, hot year-round, and humid. Specifically, the winters are dry, with hot days and cool nights; summers are wet and cloudy with frequent heavy showers (heavy rainfall from May to October with a short break in mid-July to August).[57] From November to March, dry dust-laden harmattan northeasterly winds blow inland. The terrain is mostly flat to coastal plains rising to rolling plateaus with low mountains in the northeast (max elevation 1,380 m) with 579 km of Atlantic coastal waters. Liberia borders Guinea, Cote d'Ivoire, and Sierra Leone. Vectors are common in the region, and include ticks and various genera of mosquitoes including *Culex*, *Aedes*, and *Anopheles*.[59,60]

TROPICAL INFECTIOUS DISEASE THREATS IN LIBERIA TO DEPLOYED PERSONNEL IN SUPPORT OF OUA

The following sections highlight the epidemiology and mechanism of acquisition of key pathogens likely encountered during a deployment to Liberia, augmented with analysis from the NCMI, the Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO) country analysis,[58] the United Kingdom Fit for Travel site (http://www.fitfortravel.nhs.uk/home.aspx), and published literature in the National Center for Biotechnology Information PubMed database (http://www.ncbi.nlm.nih.gov/pubmed). Emphasis was placed upon reports from Liberia specifically, but if data were not available, then information from surrounding countries or West Africa in general was discussed. The six sections based on transmission patterns are food-borne and waterborne (Table I); vector-borne (Table II); water contact (Table III); STIs (Table IV); aerosolized dust, soil contact and animal contact (Table V); and respiratory/person-to-person (Table VI). A brief summary of the currently directed personal protective measures for those deployed to Liberia is also provided.

Pathogens are assessed by mechanism of transmission, highlighting risk to those deployed, severity of illness, attack rate/month without countermeasures, incubation period, transmission mechanism, and presentation. The sections are in order of risk, which is detailed in the supporting tables. Overall, the risk period for all diseases is year round, except for two diseases having peak periods of transmission: Lassa fever between November and April and meningococcal meningitis between December and April.

Food-Borne and Waterborne Diseases

Diarrhea, Bacteria, and Protozoan

Although rarely fatal, diarrheal illness threatens deployment missions by consuming medical resources and causing shortages in personnel. During OIF/OEF, a predeployment survey

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TABLE I. Food-Borne and Waterborne Diseases

	Risk[a]	Severity[b]	Potential Attack Rate/Month Without Countermeasures	Incubation (Days)	Exposure History	Presentation
Diarrhea						
Bacterial	H	M	100%	Avg 1–3	Consuming local food, water, or ice. May have person-to-person spread.	Acute diarrhea (with or without low-grade fever), nausea, abdominal distension, and anorexia.
Protozoal	H	MD	1–10%	Avg 7–28 Min–Max 3–90	Consuming local food, water, or ice. Outbreaks possible with *Cryptosporidium*.	Acute diarrhea (with or without low-grade fever), nausea, abdominal distension, greasy stools, and anorexia.
Cholera	I	MD	<1%	Avg 2–3 Min–Max 1–5	Requires large inocula associated with ingestion of heavily contaminated food or water.	Onset of painless watery diarrhea become voluminous and followed by vomiting.
Hepatitis A	H	S	<1%	Avg 28–30 Min–Max 15–50	Consumption of food, water, or ice on the local economy or from non-approved sources. Raw or undercooked foods are particularly high risk, but contamination with fecal pathogens may occur in a wide variety of food items. Occur through direct person-to-person contact with a hepatitis A patient.	Loss of appetite, nausea, abdominal discomfort, jaundice, dark urine, and clay-colored stool. Hepatitis A is clinically indistinguishable from acute hepatitis B, C, or E.
Hepatitis E	I	S	Present, unknown	Avg 26–42 Min–Max 15–64	See hepatitis A. Although uncommon, exposure also can occur through direct person-to-person contact with a hepatitis E patient.	Loss of appetite, nausea, vague abdominal discomfort, and ultimately, jaundice, dark urine, and clay-colored stool. Frequently is severe and fatal during pregnancy.
Typhoid, Paratyphoid Fever	I	MD	<1%	Avg 8–14 Min–Max 3–30	As above or contact with a person with typhoid.	Abdominal pain, nausea, diarrhea, constipation, sore throat, and cough. Blanching maculopapular lesions 2 to 4 mm in size ("rose spots") on the abdomen or chest and sometimes on the extremities.
Brucellosis	I	S	<0.1%	Avg 30–60 Min–Max 5–90	Consumption of dairy products that may not have been pasteurized, including milk, cream, cheese (particularly soft cheese), ice cream, coffee creamers, etc. Exposure also can occur through direct contact with infected livestock.	Acute or insidious infection may include nonspecific symptoms of fever, sweats, loss of appetite, headache, arthralgia, myalgia, and weight loss. Chronic infection may present with symptoms referable to a site of persistent infection, e.g., bone, liver, spleen, or other organs.

[a]H = high: potentially high impact on operations because disease affects large percentage of personnel or causes severe illness in smaller groups; I = intermediate: disease affects smaller number of personnel or causes mild symptoms or diseases present at unknown levels that could degrade operations under some conditions. [b]M = mild: less than 72 hours in sick quarters, limited duty, no hospitalization; MD = moderate: 1 to 7 days of inpatient or supportive care, followed by return to duty; S = severe: hospitalization or convalescence over 7 days, typically evacuated.

of deploying providers revealed a knowledge gap in the management of travelers' diarrhea (TD).[61] The World Bank estimates that more than 30% of Liberians living in rural areas do not have access to acceptable drinking water and only 20% of the population has access to acceptable sanitation facilities.[62] Areas affected by natural disasters, famine or political instability are vulnerable to disease, specifically diarrhea from consumption of contaminated water. Furthermore, the current Ebola outbreak has caused significant strain on the medical and public health systems, contributing to more unfavorable water and sanitation resources. During 2001–2002, after a decade of civil war, diarrhea was responsible for 19% of deaths in Liberian refugee camps. In the summer of 2003, Monrovia's internally

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TABLE II. Vector-Borne Diseases

	Risk[a]	Severity[b]	Potential Attack Rate/Month Without Countermeasures	Incubation (Days)	Exposure History	Presentation
Malaria	H	MD	11–70%	Avg 10–14 Min–Max 7–30 (*P. ovale* relapses up to 5 years)	History of bite by (or exposure to) *Anopheles* species mosquitoes, typically at night in rural areas. The patient may be unaware of mosquito bites. NOTE: Delayed cases of relapsing malaria can occur from previous exposure to endemic areas months to years earlier.	Consider in any patient with fever and potential exposure to mosquitoes. Fever patterns in malaria may be episodic, constant, or without a pattern. May present with a wide variety of nonspecific symptoms that might suggest other diagnoses and include headache, chest pain, abdominal pain, arthralgia, myalgia, nausea, vomiting, and diarrhea. Rash is uncommon. Chemoprophylaxis can alter the presentation.
Dengue Fever	H	MD	1–50%	Avg 4–7 Min–Max 3–14	History of bite by (or exposure to) *Aedes aegypti* or *Aedes albopictus* mosquitoes, typically during daytime in peridomestic environments. Risk is highest in areas with small water containers (such as flowerpots, debris, tires, and gutters) that can serve as breeding sites. An outbreak in the local population raises risk significantly.	Dengue fever includes fever, headache, retro-orbital pain, musculoskeletal pain, rash, nausea, vomiting, sore throat, conjunctival injection, and facial flushing. Symptoms can progress to the more severe dengue hemorrhagic fever, with hypotension, shock, fluid build-up around the lungs and in the abdomen (that can lead to breathing difficulties), and frank bleeding, usually occurring at the time the fever resolves.
Yellow Fever	H	VS	1–10% (Epidemic Potential)	Avg 3–6 Min–Max 3–6	Sylvatic (jungle) exposure: history of bite by forest-dwelling *Aedes* species mosquitoes. Village or urban exposure: history of bite by *Aedes albopictus* or *Aedes aegyptii* mosquitoes, typically during daytime in peridomestic environments with small water containers such as flowerpots, debris, tires, and gutters that can serve as breeding sites.	75–80% are self-limiting, nonspecific febrile syndromes. For severe cases that develop into classic yellow fever, additional features may include nausea; back pain; knee pain; low heart rate; congestion and erythema of the face, tongue, and conjunctiva; jaundice; renal failure; and hemorrhage.
Chikungunya	I	MD	1–50% (Epidemic Potential)	Avg 3–7 Min–Max 2–12	See Dengue fever	Fever and polyarthritis (distinct from simple arthralgia). Also myalgia, headache, nausea, vomiting, and maculopapular rash primarily on the trunk. Joint pain may be severe and persist for weeks to months in some cases.
Rickettsiae						
Rickettsioses, tickborne (Spotted Fever Group)	I	MD	Present, Unknown	Avg 2–14 Min–Max 2–14	History of bite by (or exposure to) ticks, including *Rhipicephalus* species (associated with dogs) or *Ixodes* species (associated with rodents or other mammals). Patient often does not recall tick bites, which may indicate bites from small larval or nymphal stage ticks.	Generalized skin rash (maculopapular, petechial, occasionally vesicular-pustular) or localized eschars at bite sites may be present, but not in all cases. Severity can range from mild to fatal, depending on the specific rickettsial agent. Also nausea, vomiting,

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TABLE II. Continued

	Risk[a]	Severity[b]	Potential Attack Rate/Month Without Countermeasures	Incubation (Days)	Exposure History	Presentation
						abdominal pain, fatigue, and regional lymphadenopathy. Severe cases may manifest obtundation, hepatomegaly, coagulopathy, and acute renal failure.
Typhus-murine (Flea-Borne)	L	MD	Present, Likely <0.1%	Avg 12 Min–Max 7–14	History of exposure to peridomestic rats and their fleas. Flea bites seldom are recalled.	Nausea, vomiting, diarrhea, abdominal pain, jaundice, and cough. Some may have a generalized macular or maculopapular rash, and rarely petechiae. Neurologic symptoms occur rarely, including confusion, stupor, seizures, ataxia.
West Nile Fever	I	MD	Present, Unknown	Avg 3–12 Min–Max 3–12	History of bite by (or exposure to) *Culex* species mosquitoes. Infection can occur in both rural and urban environments. Bird die-offs can be an indicator of active West Nile circulation and may be a proxy for increased human risk.	Fever may be of abrupt onset. Also nausea, vomiting, diarrhea, retro-orbital pain, rhinorrhea, sore throat, and cough. Some have generalized rash or, more rarely, lymphadenopathy. Neurologic manifestations occur in approximately 1% of infections (usually age > 60) and may manifest as either meningitis or encephalitis.
Leishmaniasis						
Cutaneous	I	M	Present, Unknown	Avg 7–180	Transmitted by sandflies, typically bite at night and breed in dark places rich in organic matter, particularly rodent or other animal burrows or leaf litter, rubble, loose earth, caves, and rock holes. Potential reservoirs include humans, wild rodents (e.g., African grass rat), marsupials, and domestic dogs. Sandflies may be common in peridomestic settings. Stables and poultry pens in peridomestic areas may also harbor sandflies.	Multiple lesions starting as nodule ulcerates to wet or dry appearance. No systemic symptoms. Secondary bacterial infection occurs. Spontaneous healing over 2–12 months with scarring.
Visceral	L	S	Present, Likely <0.1%	Avg 60–180 Min–Max 10–180	See cutaneous Leishmaniasis.	Abrupt onset of fever and chills with subsequent abdominal enlargement and weight loss. Subacute or chronic cases present with gradual onset of fever, weakness, loss of appetite, and weight loss that can either resolve slowly or, if immunocompromised years later, can lead to full-blown infection.
Crimean-Congo Hemorrhagic Fever	I	VS	Present, Likely <0.1%	Avg 3–7 Min–Max 1–12	History of bite by (or exposure to) *Hyalomma*, *Boophilus*, or *Rhipicephalus* species ticks. Other exposure mechanisms include direct contact with blood or body fluids of infected livestock (sheep,	Sudden onset of fever associated with nonspecific features of chills, severe headache, dizziness, neck pain and stiffness, myalgia (especially in the lower back), eye pain, photophobia, sore throat, nausea, vomiting,

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TABLE II. Continued

	Risk[a]	Severity[b]	Potential Attack Rate/Month Without Countermeasures	Incubation (Days)	Exposure History	Presentation
					camels, goats, or cattle) or an infected human.	abdominal pain, flushing of the face and neck, and conjunctival redness. Hemorrhagic manifestations (petechiae, bruising, and nosebleeds) typically do not occur until after several days of fever.
Trypanosomiasis-Gambiense (African)	L	S	Present, Likely <0.1%	Avg 90 Min–Max 60–365	History of bite by (or exposure to) riverine species of tsetse flies found in rural areas with dense vegetation along rivers and in forests. Distribution of tsetse flies tends to be focal, related to suitable habitat and the availability of blood meals from infected human hosts in the local population, many of whom may be relatively asymptomatic.	Painful chancre may develop at the site of the tsetse fly bite weeks before fever begins. Fevers may be episodic, with long periods between bouts. Transient edema of the face, weight loss, asthenia, cervical lymphadenopathy, and generalized pruritus. In advanced infections, central nervous system symptoms of somnolence, behavioral changes, or psychosis may develop.
Sindbis (and Sindbis-Like Virus)	L	MD	Present, Likely <0.1%	Avg 3–11 Min–Max 3–11	History of bite by (or exposure to) *Culex* mosquitoes found in primarily rural areas.	Pronounced arthralgia, myalgia, headache, nausea, vomiting, and maculopapular rash, primarily trunk.
Typhus-murine (Flea-Borne)	L	MD	Present, Likely <0.1%	Avg 12 Min–Max 7–14	History of exposure to peridomestic rats and their fleas. Flea bites seldom are recalled.	Nausea, vomiting, diarrhea, abdominal pain, jaundice, and cough. Some may have a generalized macular or maculopapular rash, and rarely petechiae. Neurologic symptoms occur rarely, including confusion, stupor, seizures, ataxia.
Rift Valley Fever	L	S	Unknown, Environmental Conditions Suitable	Avg 3–6 Min–Max 3–12	History of bite by (or exposure to) *Aedes* species found in close proximity to livestock, typically in rural settings. During epizootics, multiple species including *Aedes*, *Culex*, *Anopheles*, and other biting arthropods may become infected and can transmit infection to humans on an explosive scale. Exposure also can occur through direct contact with blood or body fluids of infected livestock.	Self-limited, nonspecific febrile syndromes. Up to 10% may develop retinitis, which may lead to blindness. 1% of infections become severe, with hemorrhagic manifestations such as epistaxis, hematemesis, melena, and ecchymoses, or encephalitis leading to brain damage, death.

[a]H = High: potentially high impact on operations because disease affects large percentage of personnel or causes severe illness in smaller groups; I = intermediate: disease affects smaller number of personnel or causes mild symptoms or diseases present at unknown levels that could degrade operations under some conditions; L = low: minimal impact on operations because of low likelihood of cases. [b]M = Mild: less than 72 hours in sick quarters, limited duty, no hospitalization; MD = moderate: 1 to 7 days of inpatient or supportive care, followed by return to duty; S = severe: hospitalization or convalescence over 7 days, typically evacuated; VS = very severe: intense or tertiary care required, significant morbidity or mortality or delayed mortality.

displaced population (IDP) faced a cholera epidemic affecting nearly 17,000 people.[63] A study conducted in Liberia by researchers from Johns Hopkins showed that flocculation-based water disinfectants, chloride and improved water storage reduced incidence of diarrhea by 90% among IDP camps.[64] Access to clean water can significantly reduce rates of diarrhea, morbidity and mortality.

Diarrheal illness not only affects the local population, but can have a significant impact on the health of travelers. Based on a study conducted on German travelers to tropical countries, the risk of developing TD was highest in travelers returning from West Africa.[65] The study identified entero-aggregative *Escherichia coli* (EAEC) as the most common cause of diarrhea (isolated in 45% of people), followed by

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TABLE III. Infections Associated With Water Contact

	Risk[a]	Severity[b]	Potential Attack Rate/Month Without Countermeasures	Incubation (Days)	Exposure History	Presentation
Schistosomiasis	H	MD	1–10%	Avg 14–42 Min–Max 14–42	History of skin exposure to lakes, streams, or irrigated fields contaminated with human waste. Presence of snails with cercariae that penetrate the skin	Itchy rash at the site of parasite penetration often precedes fever by 4 to 8 weeks. The fever associated with acute schistosomiasis (Katayama syndrome) begins abruptly. Fever may be accompanied by abdominal pain, bloody stools, cough, lymphadenopathy, and hepatosplenomegaly. Gastrointestinal symptoms often are delayed until 6 to 12 weeks after initial infection.
Leptospirosis	I	MD	Unknown	Avg 4–19 Min–Max 4–19	History of skin or mucous membrane contact with surface water, moist vegetation, or mud in rural or urban areas. Skin abrasions raise the risk of infection.	Fever may begin abruptly. Rash (maculopapular, erythematous, or purpuric), nausea, vomiting, sore throat, cough, conjunctival suffusion, and myalgia. Symptoms of aseptic meningitis occur in up to 80% of cases, with severe headache and sometimes delirium. 10% of cases, severe symptoms develop, including liver failure, acute renal failure, hemorrhagic pneumonitis, cardiac arrhythmia, and circulatory collapse.

[a]H = high: potentially high impact on operations because disease affects large percentage of personnel or causes severe illness in smaller groups; I = intermediate: disease affects smaller number of personnel or causes mild symptoms or diseases present at unknown levels that could degrade operations under some conditions. [b]MD = moderate: 1 to 7 days of inpatient or supportive care, followed by return to duty.

TABLE IV. Sexually Transmitted Infections

	Risk[a]	Severity[b]	Potential Attack Rate/Month Without Countermeasures	Incubation (Days)	Exposure History	Presentation
Hepatitis B	H	S	<1%	Avg 60–90 Min–Max 45–180	History of sexual contact, direct exposure to blood or body fluids of a potentially infected individual, household contact with a hepatitis B carrier, needle sharing or reuse, tattoos, exposure to reused razor.	Loss of appetite, nausea, abdominal discomfort; jaundice, dark urine, and clay-colored stool.
Gonorrhea/ Chlamydia	I	M	1–50%	Avg 2–21	History of sexual contact.	Painful urination, cloudy urine, abnormal vaginal discharge in women or penile discharge in men; may be asymptomatic.
HIV/AIDS	I	VS	<0.1%	Seroconversion Within 3 Days of Exposure	History of sexual contact, direct exposure to blood or body fluids of a potentially infected individual, needle sharing.	Influenza-like illness within 4 weeks of seroconversion, including symptoms such as fever, pharyngitis, and/or rash; may be asymptomatic.

[a]H = high: potentially high impact on operations because disease affects large percentage of personnel or causes severe illness in smaller groups; I = intermediate: disease affects smaller number of personnel or causes mild symptoms or diseases present at unknown levels that could degrade operations under some conditions. [b]M = mild: less than 72 hours in sick quarters, limited duty, no hospitalization; S = severe: hospitalization or convalescence over 7 days, typically evacuated; VS = very severe: intense or tertiary care required, significant morbidity or mortality or delayed mortality.

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TABLE V. Aerosolized Dust or Soil Contact and Animal Contact

	Risk[a]	Severity[b]	Potential Attack Rate/Month Without Countermeasures	Incubation (Days)	Exposure History	Presentation
Lassa Fever	H	S	<1%	Avg 6–21 Min–Max 6–21	Exposure to dwellings or other structures infested with *Mastomys* mice. Acquired through inhalation of aerosols of rodent excreta, direct contact with infected rodents, or consumption of food or water contaminated by rodents. Person-to-person transmission can occur in health care settings through contact with blood or body fluids, contaminated parenteral injection equipment, and (in some cases) aerosols.	Sore throat, retrosternal chest pain, and proteinuria. Other symptoms include back pain, vomiting, diarrhea, conjunctivitis, facial edema, and abdominal pain. A minority of patients progress to mucosal bleeding from the nose, mouth, urinary tract, or intestinal tract; subconjunctival hemorrhage; and petechial or purpuric rash.
Soil-Transmitted Helminthes[c]	I	M	1–10%	Avg 7–21 Min–Max years	Direct skin exposure to soil contaminated with human or animal feces (including sleeping on bare ground, walking barefoot).	Skin symptoms typically are minimal. Systemic symptoms of fever, cough, abdominal pain, nausea, and diarrhea may develop weeks to months after initial infection.
Rabies	H	VS	Risk Among Highest in the World	Avg 21–56 Min–Max 9–1,500 90% of cases, incubation is less than 1 year, rarely 7–19 years	Exposure to virus-laden saliva of an infected animal, typically through bites or scratches or mucous membranes. Rarely, transmitted by the respiratory route in caves with large numbers of infected bats. Human-to-human transmission through saliva is theoretically possible, although rarely documented. Dogs, cats, and bats are the principal sources of human exposure. Coyotes, foxes, jackals, marmosets, mongooses, raccoons, skunks, and wolves also may transmit infection to humans. Chipmunks, livestock, mice, opossums, rabbits, rats, and squirrels can also be infected with rabies but rarely, if ever, transmit the infection to humans.	Paresthesia, pain, or intense itching at the inoculation site is pathognomonic for rabies. Fasciculations, priapism, and focal or generalized convulsions.
Q-Fever	I	MD	Present, <0.1%	Avg 14–21 Min–Max 14–21	History of contact with infected livestock or exposure to environments such as barnyards or fields where animals are concentrated. Infective aerosols also may be associated with contaminated materials such as straw, hay, or wool. Cases may occur through indirect exposure to infective aerosols, which can be carried downwind for long distances and cause human infection miles from the contaminated source.	Self-limiting fever is the most common presentation. Some develop Q-fever pneumonia, with or without cough. Progression to hepatitis, aseptic meningitis, or encephalitis can occur.
Anthrax	L	S	<0.1%	Avg 1–7 Min–Max 1–60	Occupational-type exposure to livestock or wild herbivores, or hides or wool products from these species, as well as handling or consumption of undercooked meat. The risk of naturally acquired inhalation (pulmonary) anthrax is remote. Inhalation cases raise the possibility of weaponized agent.	Cutaneous anthrax includes small blisters or bumps that ulcerate and form black center. Oropharyngeal anthrax lesion starts as a swollen area that becomes necrotic and forms a pseudomembrane. Sore throat, dysphagia, respiratory distress, and oral bleeding along with soft-tissue edema and cervical lymph node enlargement occur. Intestinal anthrax has abdominal pain and fever, followed by nausea, vomiting, malaise, anorexia, hematemesis, bloody diarrhea, and, occasionally, watery diarrhea. Pulmonary anthrax includes nonspecific symptoms, low-grade fever and a nonproductive cough, which can progress to hemorrhagic mediastinitis.

[a]H = high: potentially high impact on operations because disease affects large percentage of personnel or causes severe illness in smaller groups; I = intermediate: disease affects smaller number of personnel or causes mild symptoms or diseases present at unknown levels that could degrade operations under some conditions; L = low: minimal impact on operations because of low likelihood of cases. [b]M = mild: less than 72 hours in sick quarters, limited duty, no hospitalization; MD = moderate: 1 to 7 days of inpatient or supportive care, followed by return to duty; S = severe: hospitalization or convalescence over 7 days, typically evacuated; VS = very severe: intense or tertiary care required, significant morbidity or mortality or delayed mortality. [c]Hookworms, strongyloidiasis, and cutaneous larva migrans.

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TABLE VI. Respiratory and Person-to-Person Transmitted Diseases

	Risk[a]	Severity[b]	Potential Attack Rate/Month Without Countermeasures	Incubation (Days)	Exposure History	Presentation
Respiratory						
Meningococcal meningitis	I	VS	<0.1%	Avg 3–4 Min–Max 2–10	Meningococcal meningitis can occur without a specific exposure history but close contact with a known or suspected case or close contact with the local populace in areas where a community outbreak is occurring increases the likelihood of infection.	Most cases demonstrate classic headache, meningeal signs, and alteration in consciousness. Petechial, purpuric, and ecchymotic rash is common, sometimes preceded by maculopapular lesions.
Tuberculosis	I	M	High for Exposed Individual	Avg 60–180 Min–Max 60–365 Possibly years	Requires prolonged indoor exposure to local populations with high tuberculosis incidence rates.	Cough, weight loss/anorexia, fever, night sweats, hemoptysis, chest pain, fatigue.
Person-to-Person						
Ebola hemorrhagic Fever	L	VS	<0.01%	Avg 2–21 Min–Max 2–21	History of contact with blood or body fluids of a severely ill or recently deceased patient or the carcass of a dead or dying primate.	Features that may precede hemorrhagic manifestations include nausea, vomiting, abdominal pain, chest pain, shortness of breath, cough, and conjunctival injection. Frank hemorrhage may or may not be present.
Monkeypox	L	S	<0.01%	Avg 12 Min–Max 7–17	Sustained in ground squirrel reservoirs in rainforest habitat, humans infected through close contact with animal reservoirs, butchering and consumption of infected carcasses. Infection results from the deposition of aerosolized virus on respiratory or oropharyngeal membranes. Human-to-human transmission requires prolonged household contact; secondary attack rate in close contacts is 8%.	Prodrome or pre-eruptive stage (lasts 1–10 days), fever with chills, drenching sweats, severe headache, backache, myalgia, malaise, anorexia, prostration, pharyngitis, shortness of breath, and cough (with or without sputum). Lymphadenopathy appears within 2–3 days after the fever. In the exanthem (eruptive) stage, rash within 1–10 days after the onset of fever starting on the face and then spreads to the rest of the body. It persists for 2–4 weeks until all lesions have shed the crusts.

[a]I = intermediate: disease affects smaller number of personnel or causes mild symptoms or diseases present at unknown levels that could degrade operations under some conditions; L = low: minimal impact on operations because of low likelihood of cases. [b]M = mild: less than 72 hours in sick quarters, limited duty, no hospitalization; S = severe: hospitalization or convalescence over 7 days, typically evacuated; VS = very severe: intense or tertiary care required, significant morbidity or mortality or delayed mortality.

enterotoxigenic *E. coli* (ETEC). In a study of 45 travelers to neighboring Benin, 87% (39/45) developed TD, of which 85% experienced moderate to severe symptoms requiring the use of antibiotics. Using polymerase chain reaction methodology, enteropathogenic *E. coli*, EAEC, and ETEC were identified in 77%, 59%, and 56%, respectively, of people with TD. Moreover, multiple pathogens were identified in 79% of the cases. Among the asymptomatic travelers, more than 50% also had diarrhea-causing *E. coli* in their stool. *Shigella* spp. and *Salmonella* spp. were found in symptomatic cases only (16% and 2%, respectively). There were no cases of *Campylobacter* spp.[66] These data are consistent with military studies on TD, which also identified *E. coli* as the most common pathogen associated with TD.[61] Regarding Liberia, cryptosporidiosis has been previously reported as a common cause of diarrhea among children.[67] Furthermore, pathogens seen in the Navy operations in West Africa, including Liberia in the late 1980s, included giardiasis, cryptosporidiosis, rotavirus, and Norwalk virus.[68]

Antimicrobial resistance of enteric pathogens has been examined in West Africa and the vast majority of these reports are from the more industrialized nation of Nigeria.

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There are no reports on the status of enteric isolates from Liberia. In general, fluoroquinolone resistance has not been commonly reported in West Africa, except with Gram-negative enterics. In particular, one Nigerian analysis found that 34.5% of *E. coli* isolates were quinolone nonsusceptible by 2009.[69] Moreover, the spread of the fluoroquinolone-resistant *Salmonella enterica* serovar Kentucky has been noted in Nigeria and other African countries.[70,71] In a study from Senegal, a significant increase in the prevalence of resistance to amoxicillin (0.9% in 1999 to 11.1% in 2009) and nalidixic acid (0.9% in 1999 to 26.7% in 2009) was reported with nontyphoidal *Salmonella* serotypes.[72] An additional Nigerian study involving blood cultures collected from patients with suspected enteric fever found that *Enterobacter, Citrobacter, Escherichia, Klebsiella,* and *Shigella* isolates were resistant to ceftriaxone, cefuroxime, ampicillin, ciprofloxacin, and augmentin.[73] Ciprofloxacin resistance was also found in 4% of *Salmonella* spp. collected from children in a diarrheal study, while ampicillin resistance was present in 28% of *Salmonella* and 50% of *Shigella* strains.[74] Moreover, in a Ghanaian study of antibiotic resistance in enteric bacteria, *Salmonella* and *Shigella* were 100% susceptible to ciprofloxacin and less than 2% of *E. coli* isolates were resistant to ciprofloxacin. In another Nigerian study, 19% and 54% of *E. coli* isolated from diarrhea specimens was resistant to ciprofloxacin and nalidixic acid, respectively.[75] Furthermore, *E. coli* resistance to most beta-lactams ranged between 83%–94% in isolates collected from the stool of symptomatic children, whereas piperacillin/tazobactam susceptibility remained above 85%. Lastly, trimethoprim/sulfamethoxazole resistance was greater than 85% in symptomatic cases.[76]

Enteric fever has been a scourge upon military campaigns throughout history. A notorious outbreak of enteric fever occurred in the U.S. Army during the Spanish–American War of 1898 with an estimated 250 to 350 cases daily (approximately 24,000 total cases), resulting in 2,000 deaths.[77] West Africa is estimated to have a crude incidence of enteric fever of 38 cases per 100,000 persons per year.[78] Both *Salmonella paratyphi* A and *Salmonella typhi*, which are clinically indistinguishable, have been implicated as the causative agents.[78] Infections are most commonly acquired via ingestion of water or food contaminated by fecal matter. Patients with uncomplicated enteric fever typically present with nonspecific symptoms that include fever, headache, anorexia, myalgias, and malaise. It is also common for patients to have mild confusion, dry cough, and variable gastrointestinal symptoms (e.g., diarrhea, constipation, and abdominal pain). Mild, nonlocalizing, abdominal tenderness, and hepatosplenomegaly may be observed on physical examination.[79] In a Nigerian study that involved the collection of blood cultures from patients suspected to have enteric fever, *Salmonella typhi* isolates were resistant to ceftriaxone, cefuroxime, amoxicillin, ampicillin, ciprofloxacin, and augmentin.[73] Thus, there is the possibility of encountering ciprofloxacin-resistant *S. typhi* and/or *S. paratyphi* in West Africa, and if a patient is not clinically improving on ciprofloxacin, a change to azithromycin should be considered.[80]

Hepatitis A and E

Hepatitis E poses a potential threat to military personnel in the deployed setting because of its prevalence in areas of operation and epidemic potential in regions of conflict; however, there is no data from Liberia. In the past decade, serologic tests from the Western African country of Burkina Faso revealed the presence of anti-HAV IgG in 14.3% of blood donors and 23% of pregnant women, whereas hepatitis E antibodies were detected in 19.1% of blood donors and 11.6% of pregnant women.[81] Fortunately, vaccines against hepatitis A provide protection against this highly infectious and prevalent infection in West Africa. Nevertheless, the risk for acute hepatitis from hepatitis E virus remains a concern.

Brucella

Brucellosis is a bacterial infection acquired by consuming dairy products from infected animals and has been reported in deployed forces after eating unpasteurized cheese from the local economy or close contact with goats.[82,83] In a study of Togo West Africa, the prevalence of *Brucella* antibodies in humans ranged from 0.2 to 2.4% and in cattle from 7.3 to 9.2%, but no disease was detected in sheep or goats.[84] Numerous studies have noted the presence of *Brucella* spp. in the Cote d'Ivoire with a recent survey estimating that 10.3% of cattle had antibodies against *Brucella* spp.[85] A study of dogs in Nigeria also revealed 5.5% of 366 dogs had serology for *Brucella abortus* and 0.27% *Brucella canis*.[86] Prevention involves avoidance of unpasteurized dairy products.

Prevention

Command support of force health protection can help thwart the majority of enteric infections and maintain the health of the force. The areas of focus on prevention for any pathogens transmitted by the fecal–oral route have been on proper field sanitation, hand washing, obtaining food/water/ice only from approved sources, and proper food service sanitation. To prevent brucellosis, avoiding unpasteurized dairy products is typically adequate. In addition, there should be emphasis on the avoidance of eating and drinking on the local economy, although this is not always possible given operational goals. It is not always clear; however, if the food is the source of infecting pathogens versus how the food is prepared.[87] At this time, it is not recommended that people take prophylactic measures against deployment-related diarrhea, but to treat with loperamide and an antimicrobial such as a fluoroquinolone or azithromycin.[61,88] If soldiers are exposed to contaminated food or water, it is likely that they will be identified early and not progress to complicated enteric fever because of the twice daily temperature checks mandated during OUA.

The recommended predeployment vaccines targeting enteric infections include hepatitis A and intramuscular typhoid (VI polysaccharide) with reported efficacies of 94 to

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99% and 50 to 80%, respectively.[2,87,89] It should be recognized that the typhoid vaccine is only effective against strains *S. typhi* and not *S. paratyphi*.[89] Therefore, even if soldiers are vaccinated, enteric fever may still be acquired in West Africa, and the diagnosis should be considered in patients with a compatible exposure history and clinical syndrome. It is currently unclear what preventive strategy is available to avoid persistent and chronic diarrhea that has been seen with those deployed to Iraq and Afghanistan.[90]

Vector-Borne Diseases

Malaria

Malaria represents the highest vector-borne disease threat to deployers to Liberia. The nation is holoendemic for malaria with year-round transmission. Data on the malaria threat to military and civilian travelers have been extensively discussed in the Introduction section and will not be reiterated here. The risk does vary geographically, with the highest *P. falciparum* risk (entomologic inoculation rates approximately 50 infectious bites per year) in eastern counties, and lower risks (1–10 infectious bites per year) along the coast and near Monrovia.[91] The WHO reported that 100% of malaria cases were *P. falciparum* in 2013.[58] *Plasmodium ovale* is also likely transmitted throughout the country, albeit at extremely low rates.[92] *Plasmodium malariae* is rare, and *P. vivax* is rarely seen due to absence of Duffy antigen in the population.[93]

Dengue

Dengue virus (DENV) is transmitted globally in the tropics, predominantly in urban areas, by day-biting *Aedes* mosquitoes, in particular *Aedes aegypti* and in some circumstances *Aedes albopictus*, which have cosmopolitan distributions typically closely associated with human habitation. Dengue transmission has been confirmed sporadically in West Africa, often attributed to infection with sylvatic DENVs vectored by forest-dwelling zoophilic vectors such as *Aedes furcifer-taylori* and *Aedes aegypti formosa*. Sylvatic transmission has been thought to be limited, resulting in isolated cases or small outbreaks, in contrast to explosive epidemics that characterize urban transmission in Asia and the Americas.[94–97] An etiologic study of febrile illnesses in Sierra Leone identified dengue as a potential pathogen in 2% of cases.[98] Dengue infection typically causes an acutely disabling, but ultimately self-limited, febrile illness; a minority of cases are complicated by capillary leak, termed dengue hemorrhagic fever (DHF) or dengue shock syndrome. Very little DHF, if any, has been reported in Africa; however, it is suspected that this may be due to cases being mistakenly attributed to other etiologies, in particular malaria.[94] A case of DHF (grade II) because of infection with a sylvatic DENV-2 from Guinea Bissau was reported in a patient managed in Spain.[99] Recent modeling suggests substantial underreporting of dengue infections in Africa.[100] These authors concluded that there are likely as many clinical, but undiagnosed infections in Africa as in the dengue-endemic Americas, on the order of 16 million cases in 2010. The majority of these were in Nigeria (approximately 3 million), and similar in magnitude to Brazil where dengue is recognized to be highly endemic.

Chikungunya

Chikungunya virus is an alphavirus vectored by *A. aegypti* and, more recently, *A. albopictus* and originates from Central and East Africa. Infection typically causes a self-limited but often temporarily disabling febrile illness characterized by painful arthralgias, and in some cases prolonged convalescence. The Indian Ocean subpandemic in 2005–2006, resulting from transition event from East Africa to islands in the Indian Ocean, was associated with a mutation conferring fitness in the predominant vector, *A. albopictus*. Numerous chikungunya infections also have been reported from West Africa.[98,101,102] Serosurveys have demonstrated antibody prevalence between 30% and 50% in some populations, indicating common transmission and potentially suggesting mild or subclinical infections. Chikungunya virus is transmitted in rural Africa in a sylvatic cycle involving *A. furcifer-taylori*, which results in endemicity without explosive episodic outbreaks typical of urban transmission, similar to the experience with dengue. The closely related alphavirus, O'nyong-nyong, has also been demonstrated in West Africa.[102,103] Sindbis is also an alphavirus that can cause self-limited febrile illness characterized by malaise, myalgias, and arthralgias; often with a rash; clinical manifestations are similar to those of chikungunya and O'nyong-nyong, but generally milder and infection can be subclinical. The virus is widely distributed geographically.[104] The *Culex* mosquito vector has been reported across West Africa, but there is limited data from Liberia.[105]

Rift Valley Fever

Rift Valley fever is a zoonosis of economic importance because of its impact on livestock animals, and clinical significance because of occasional human infections that can manifest as life-threatening hemorrhagic fever or with acute neurological involvement. The virus is spread primarily by the *Aedes* mosquitoes in East Africa (the Rift Valley); however, other mosquitoes have shown vector competence and the virus has shown transmission capability in West Africa. Clinical cases have been observed in Senegal and serological studies from Sierra Leone and Liberia have reported IgM antibodies in 5 of 253 samples.[98,106]

West Nile Virus

West Nile virus is common in West Africa including reports from Senegal, Guinea, Sierra Leone, and Cote d'Ivoire.[98,107,108] There are data indicating that the regional *Culex* mosquito may be less competent at transmitting the virus than in other regions' mosquitoes, which might explain the relatively low rates in some areas of West Africa.[109]

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Crimean-Congo Hemorrhagic Fever

Traditionally, CCHF has been associated with tick exposures or slaughterhouses (as has been reported in Burkina Faso), but transmission may occur through human blood and body fluid exposures.[110] In a viral febrile study in Sierra Leone that overlapped with regions of Liberia, there were no cases of CCHF.[98]

Yellow Fever

Yellow fever virus circulates in urban and sylvatic cycles, the former being transmitted by *A. aegypti*, the vector of dengue and chikungunya. Yellow fever cases have been reported in Liberia throughout the 1990s and early 2000s.[111] Despite these reported outbreaks, substantial vaccine deployment efforts have been carried out with some success in Liberia.[112,113]

African trypanosomiasis

Rarely is this disease seen in nonendemic regions, with very few cases ever described in travelers to the United States and no reported cases in military personnel.[114,115] Although the tsetse fly is present in Liberia and the surrounding countries, there are no published reports of *Trypanosoma brucei gambiense*. However, Cote d'Ivoire has had less than 10 cases reported every year.[116]

Leishmaniasis

Leishmania spp. are endemic throughout much of West Africa; however, the overall disease prevalence appears to be under reported.[117] The animal reservoir is the *Arvicanthis niloticus* (African Grass Rat), which might influence protective measures for host and vector control. *Leishmania major* has been described in Senegal, Ghana, and Mali,[118–120] and Ghana has had evidence of *Leishmania tropica*.[121] Leishmaniasis also has been described in Burkina Faso with fewer cases from March to June and December, and greater numbers from August to October.[122] Visceral leishmaniasis because of *Leishmania infantum* was detected in dogs, and positive serology was reported in humans in Senegal and the Cote d'Ivoire.[123] The U.S. military experienced a considerable burden of cutaneous leishmaniasis during operations in Iraq and Afghanistan, showing the capability to aggressively identify the vector and host with implementing personal protective measures.[124–127]

Rickettsiae

A survey of ticks in Liberia revealed *Rickettsia africae* was present in the ticks *Amblyomma variegatum*, *Amblyomma compressum*, and *Rhipicephalus geigyi*, and *Rickettsia raoultii* was found in *Ixodes muniensis* ticks.[60,128] Ticks have also noted to have the rickettsia infections *Rickettsia conorii* subsp. *conorri*, *africae*, *sibirica* subsp. *mongolitimonae*, *aeschlimannii*, and *massiliae* in the region.[129,130] A spotted fever group study in Sierra Leone and Cote d'Ivoire revealed a prevalence of 5.3% and 6.2%, respectively, among the local populations.[131]

Murine typhus is spread from rats carrying *Rickettsia typhi* via the flea vector *Xenopsylla cheopis*. Although no assessment for this disease has been widely carried out in Liberia, it has been described in the coastal regions of other West Africa countries.[128] No cases were noted in the Cote d'Ivoire and the prevalence in Sierra Leone is 1.8%.[131]

Other Diseases

The WHO has noted that Liberia has endemic filariasis and onchocerciasis.[132] Onchocerciasis has areas of hyper- and hypoendemicity across the region from 95% in some regions to 25% in other regions, likely reflective of the prevalence of the vector, the black fly, and the breeding areas and feeding behavior.[133] A study looking at urban transmission of lymphatic filariasis was low despite movement of people from rural to urban locations for *Wuchereria bancrofti*.[134] The *Loa loa* vector (Chrysops fly) is also present, but there is a low burden of the disease.[135] In addition, Senegal has reported *Borrelia crocidurae* in *Senlocal egal* ticks.[136] Lastly, myiasis is associated with the infection caused by the African Tumbu fly (*Cordylobia anthropophaga*). This has been described in a British military member in Sierra Leone, as well as 248 cases of furuncular myiasis among Pakistani soldiers stationed in Sierra Leone.[137,138]

Prevention

The optimal method to prevent vector-borne disease remains avoidance of arthropod bites. Maximum compliance with 33% DEET can reduce bites on exposed skin by 56 to 95% for 2 to 12 hours; permethrin-treated uniforms can reduce bites through clothing by 84 to 99%; permethrin-treated bednets or effectively screened housing can reduce bites during sleep by up to 99%.[139–141] Bednet systems should contain at least 1,024 holes/square inch net mesh to ensure sandflies are unable to gain access. The appropriate uniform includes tucked pants into boots, long sleeves with the overblouse worn at all times, and only wearing physical training clothes (shorts and T-shirt) during exercise or sleeping.

Antimalarial chemoprophylaxis is required to augment prevention strategies among deployers to West Africa, and should be administered by direct-observed therapy when possible. The DoD recommends daily atovaquone/proguanil (Malarone or generics) as first line chemoprophylaxis in this region. This is based on evidence of partial liver schizonticidal activity of both proguanil and atovaquone[142] and the extended half-life of atovaquone, offering extended blood schizonticidal protection if a single dose is missed.[143] This drug should be taken with food or a glass of milk to optimize atovaquone absorption. Overall, it is well tolerated and highly effective (96–100% protection).[144] Major side effects have included diarrhea (29%), headache (16%), malaise (11%), abdominal pain (11%), nausea (11%), restlessness (10%), sore throat (10%), sweating (9%), and oral

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ulcers (9%) with infrequent reports of Stevens–Johnson syndrome.[145,146] It is given as a fixed dose and treatment failures have been reported among persons who weigh more than 100 kg.[147] Field effectiveness among Swedish military deployed to Liberia was 100%.[148] To prevent late prophylaxis failures, particularly during the 21 day Ebola incubation period, it is critical to complete the 7 day extension of chemoprophylaxis after leaving West Africa. Late *P. ovale* cases because of relapses appear to be reduced, but not eliminated by use of proguanil chemoprophylaxis among French troops deployed to neighboring Cote d'Ivoire.[149]

For those intolerant of atovaquone/proguanil, daily doxycycline chemoprophylaxis should be used. Doxycycline is active only against the blood stages of the parasite, exerting its action against the apicoplast.[150] It is 84 to 99% protective in clinical trials,[151] but field effectiveness has been poorer because of nonadherence. The French forces in Cote d'Ivoire have experienced a 7% chemoprophylaxis failure rate (mean 70 cases/1,000 person years between 2003 and 2012).[149,152] Doxycycline has little causal activity, so it must also be taken for 30 days upon leaving the country to suppress emerging blood stages. Mefloquine is effective as a third option, but less tolerated due to neuropsychiatric effects.

Due to the evidence that atovaquone/proguanil may reduce the development of hypnozoites[149,153] and side effects of primaquine, PART is not currently recommended for deployers to Liberia. Highest risk travelers for relapsing malaria, such as those previously diagnosed with *P. falciparum* malaria, indicating a high risk of exposure to mosquito bites in general, should be considered for PART.

Vaccines effective against the vector-borne diseases include the yellow fever vaccine with a near 99% efficacy; however, there is some toxicity related to the vaccine, especially in older patients.[154] During the current deployment, numerous deployers received the live attenuated influenza vaccine intranasal (Flumist) just before people receiving orders to Liberia. Because of the sudden deployment to Liberia, personnel were not able to wait the standard 4 weeks between receipt of live vaccines (except if they were provided at the same time) when they received the required yellow fever vaccine.[155] There are no data regarding yellow fever and live attenuated influenza vaccine administration impacting protective efficacy of either vaccine. The only data that are comparable include the administration of the measles vaccine before the yellow fever vaccine, which had no impact on yellow fever immunity (seroconversion averaged 76.4% during weekly serologic testing and at >28 weeks was 77.5%).[156]

Water Contact

Schistosomiasis

Schistosomiasis is caused by parasitic worms acquired through cercariae penetration of intact skin during exposure to contaminated fresh water (i.e., rivers, lakes, and irrigated fields). Schistosomiasis because of *Schistosoma haemotobium* and *Schistosoma mansoni* has been described throughout West Africa, including Liberia. A geostatistical model-based risk estimate of schistosomiasis in Liberia estimated very high endemicity across the majority of the region, particularly along the coast with rates of 60.2% in human studies.[157] The disease is also present in Ghana, Zambia, Burkina Faso, and Senegal.

Leptospirosis

This zoonotic disease is caused by infection with pathogenic members of the genus *Leptospira*. Leptospirosis in humans occurs due to contact with contaminated animal urine, standing water or moist soil, or with infected animal tissue. Leptospires enter the body through mucous membranes or conjunctivae, through small cuts or abrasions, and possibly through wet intact skin. There are no specific studies of the prevalence of leptospirosis from Liberia, but a recent epidemiologic survey suggested it is a widespread problem in West Africa.[158] Traditionally considered a rural or farming disease, it is often transmitted in urban areas because of rat exposure, overcrowding, and inadequate waste disposal. Seroprevalence surveys in asymptomatic humans have varied from 13 to 33% in series published from Nigeria and Ghana. Among febrile patients, low rates of leptospirosis infections (3.2%) are reported among inpatients with undifferentiated fever or jaundice.[159] Regarding travelers to Sub-Saharan Africa returning with acute and life-threatening fever, leptospirosis was the third most common cause.[55]

Prevention

The best prevention strategy for schistosomiasis and leptospirosis is avoidance of skin contact with fresh surface water. Vigorous towel drying after an accidental, very brief water exposure may help to reduce likelihood of the *Schistosoma* parasite from penetrating the skin. Doxycycline is effective in preventing leptospirosis in exposed military personnel during periods of high exposure.[160] Extension to other populations or scenarios has shown mixed results and may increase side effects.[161,162] The dose for doxycycline prophylaxis is 200 mg once per week and should be considered for high-risk individuals.

Sexually Transmitted Infections

Most deployed operations have general orders against sexual activity, to include no sexual activity with prostitutes. Regarding the Liberian operations, there is a policy prohibiting sexual contact for service members deployed in support of OUA.

Syphilis, Gonorrhea, and Chlamydia

Adolescents and young adults ages 10 to 24 years in Sub-Saharan Africa account for a large burden of the global HIV/STI crisis.[163] Contributing factors among this demographic include, for example, engaging in unprotected sexual intercourse; having multiple sexual partners; lacking the

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skills to correctly and consistently use condoms, including inadequate knowledge about condom use and the unavailability of condoms; and perceived invulnerability.[163] The overall prevalence of STIs (other than HIV-1) is largely unknown in West Africa and limited data are available for select countries in the region. In Burkina Faso, the seroprevalence of syphilis was reported to be 1.5% among first time blood donors.[163] A surveillance study of symptomatic patients with STIs in Ghana reported detection of gonorrhea and chlamydia in 18% and 9% of cases, respectively.[164] Among the small number of patients with gonorrhea culture and susceptibility results in this study (n = 7), all isolates were resistant to ciprofloxacin, penicillin and tetracycline, and susceptible to ceftriaxone and cefixime. These findings are consistent with the high rates of fluoroquinolone resistance in gonorrhea in the United States and worldwide. The U.S. treatment recommendations for STIs, including syphilis, gonorrhea, and chlamydia, are also applicable to West African populations.[165]

Hepatitis B and C

As part of the management of the Ebola outbreak, patients are receiving whole blood transfusions. Although the prevalence of hepatitis B and C (HBV, HCV) in Liberia is largely unknown, a small study of blood donors in Monrovia, Liberia in the mid-1990s showed a HBV surface antigen carrier rate of 12.4%, similar to the contemporary estimate of >8% for West Africa.[166,167] The greatest global burden of HCV is in Sub-Saharan Africa with a prevalence of 5.3%.[167,168] These and other infections are potential bloodborne pathogens that can be transmitted via transfusion of blood products. As an example, data from U.S. service members who received emergency transfusion products in Iraq and Afghanistan from military donors showed a single transfusion transmitted HCV infection case and one case of human T-lymphotropic virus type I.[21,22]

HIV-1 and HIV-2

The United Nations estimates the adult prevalence of HIV-1 in Liberia is 1.1% (0.9–1.3%), which is approximately twice the prevalence in the U.S. population (0.6%).[169] In addition, HIV-2 is also present throughout West Africa, with the highest prevalence reported in Guinea-Bissau, where 8% of adults and 20% of persons over 40 years of age were determined to be infected.[170] Nonetheless, the prevalence of HIV-2 in Liberia is unknown. Although clinical manifestations of persons with HIV-2 infection are the same as those with HIV-1 infection (i.e., compromised immune function and subsequent opportunistic infections and cancers), HIV-2 is associated with lower viral load levels and slower rates of CD4 decline and clinical progression compared with HIV-1.[171] Diagnostic tests can detect both HIV-1 and HIV-2; however, additional tests may be necessary to distinguish between these viruses.[171,172] Treatment of HIV-2 differs from HIV-1 in that nonnucleoside reverse transcriptase inhibitors are not active against HIV-2.[173] Although the integrase inhibitor raltegravir appears active against some HIV-2 isolates, there are insufficient clinical data for use of raltegravir in the setting of HIV-2.[174] The protease inhibitor (PI) combination of lopinavir/ritonavir is more active against HIV-2 than several other PIs and HIV-2 is susceptible to the nucleoside reverse transcriptase inhibitor class of antiretrovirals.[174,175] The differences in susceptibility for various antiretrovirals against HIV-2 have important implications for PEP after occupational exposures (e.g., needlesticks) or nonoccupational exposures (e.g., sexual contact). The U.S. guidelines for PEP have been published.[176,177] However, to account for the presence of both HIV-1 and HIV-2 in West African populations, medications prescribed for PEP should include a ritonavir-boosted PI (such as lopinavir/ritonavir) in combination with two non-nucleoside reverse transcriptase inhibitors (such as tenofovir/emtricitabine).[175] Antiretrovirals should not be stored at temperature extremes and package inserts for lopinavir/ritonavir, raltegravir, and tenofovir/emtricitabine state these agents should be stored at or near room temperature (77°F) and excursions up to 86°F are permitted.

Prevention

Education on reducing risk, including abstinence and proper use of condoms for those who elect to have sexual contact, has been provided. In addition, general order number one indicates no sexual activity will occur, to include with local personnel or commercial sex workers. PEP after percutaneous or sexual contact will be addressed with the medications listed above. In addition, all personnel previously received hepatitis B vaccine, which has a 90% efficacy.

Aerosolized Dust or Soil Contact and Animal Contact

Lassa Fever

The natural reservoir for Lassa is the multimammate rat *Mastomys natalensis* that lives in houses and surrounding fields. Lassa fever is typically acquired through aerosol exposure whereas cleaning up rodent-infested buildings during the dry season and has a substantial impact across West Africa with 5,000 to 10,000 deaths per year, and total cases at 300,000 to 500,000.[178,179] Liberia has had frequent cases of Lassa fever across the region with a 13.6% mortality rate.[180,181] A spatial map developed through evaluation of cases, animal reservoir, and environments reveals Liberia at high risk especially the northern regions of the country.[182] Further spatial analysis confirmed areas in Liberia at higher risk, with the counties of Lofa, Bong, and Nimbia being considered hyperendemic regions.[183,184] Furthermore, there were regional serological differences between Ebola and Lassa fever prevalence in Liberia with Ebola higher in central Liberia and Lassa fever more common in northwest Liberia.[185] The clinical presentation can be

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similar to Ebola with bleeding complications noted in approximately 10% of cases and an overall mortality rate of approximately 18%.[186]

Helminths and Other Neglected Tropical Diseases

Soil-transmitted helminthes are widely endemic throughout Liberia.[132] For control of these diseases, the country would need to dedicate preventive therapy to 3.3 million. There was also a 90% hookworm prevalence in Liberia in the late 1960s that included *Necater americanus* and *Americanus duodenale*, but no recent studies have been performed.[187] Other soil-transmitted helminth infections observed in the region included trichuriasis and ascariasis.[188] Surveillance studies have noted widely prevalent helminths across West Africa (particularly Sierra Leone and Cote d'Ivoire), including strongyloidiasis.[189,190] Although guinea worm has been reported in West Africa, it is primarily detected in Mali.[191]

Anthrax

Anthrax exposure to either biological warfare release or inoculation from the environment is a concern for the U.S. military. Military members often support the local economy although deployed through purchase of locally made gifts. The occurrence of inhalation anthrax from dried skins for drums has been described most notably where a drum was made from hard-dried goat hides from Cote d'Ivoire.[192–194]

Rabies

In 1982, in Zorzor District in Liberia, there were 31 people bitten by rabid dogs and another 6 exposed, of which 3 died, but no recent evaluations have been reported.[195] Risk is likely present; however, bites often go unreported. In 2011, a 25-year-old U.S. Army soldier died of rabies infection contracted in eastern Afghanistan. A prior study between 2001 and 2010 reported 643 animal bites of which 325 (50.5%) were from dogs. One hundred and seventeen received rabies vaccine in the first 0 to 7 days after injury and 25 were provided rabies immune globulin. An additional 17 received the rabies vaccine 8 to 30 days after injury and the only chart that listed "exposure to rabies," got the rabies vaccine between days 31 and 90.[196] After the soldier from Afghanistan died, a follow-on study in Afghanistan between September and December 2011 revealed the presence of 126 animal bites.[197] The 4-month period described 126 bites and implies that the 643 bites reported between 2001 and 2010 in the Army were grossly underreported.

Q-Fever

An Air Force survey of vector-borne and zoonotic disease from 2000–2011 revealed 33 cases of Q-fever in DoD beneficiaries. This included 18 with reported travel, of which 3 were within the U.S. Africa Command.[198] A serosurvey of humans and cattle in western Africa (i.e., Nigeria, Senegal, Ghana, Cote d'Ivoire, Burkina Faso, and Niger) revealed the presence of Q-fever in cattle, human, and goat serum. Clinical disease was also reported in goats in Niger and humans in Burkina Faso.[199] A survey of ticks from Senegal revealed the presence of competent vectors ranging from 0 to 38% by region of the country with a separate study of humans serum samples having a prevalence of 3.7 and 25% in two regions.[200] In Togo, Q-fever was widely prevalent among human, cattle, goat, and sheep sera.[84]

Prevention

The U.S. personnel are not expected to be cleaning out old buildings as part of any operation in Liberia. Living quarters for a limited number of people will be older buildings, but these were cleaned before personnel arriving. The vast majority of personnel will be living in modular tents with connected bathrooms built in the last month. There will be maximal attempts to avoid bare skin contact with moist soil, which may be contaminated with human or animal feces. There is no current plan for postdeployment empiric therapy for helminths or other neglected tropical diseases.[201] Ribavirin has been prepositioned in country for prophylaxis in the event of high risk Lassa fever exposures.[202] To prevent rabies, the primary goal is to avoid animal contact, including not keeping any animal pets, and to enhance reporting of all bites or scratches. The circumstances of the bite should always be considered in evaluating the need for PEP. The bites of bats or of wild carnivores should be assumed to be rabid unless proven otherwise. Pre-exposure rabies series is indicated for Special Operations personnel and those with occupational contact with animals. To avoid Q-fever, there should be no contact with livestock, or with areas heavily contaminated by livestock such as barnyards. Avoid contact with livestock or consumption of undercooked meat for anthrax prevention. Anthrax vaccine is not mandated for OUA.

Respiratory

Viral and Bacterial Respiratory Pathogens

Despite the reductions in DNBI seen in more recent experiences, together with diarrhea, respiratory infections continue to account for the bulk of DNBI morbidity. Respiratory pathogens affecting military members in the deployed setting reflect those familiar in garrison. These include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, *Staphylococcus aureus*, *Streptococcus pyogenes*, respiratory viruses (particularly influenza), and *Legionella pneumophila*. One evaluation of seroconversion during deployment reported that 14% seroconverted to one of six pathogens including parainfluenza virus, pertussis, *C. pneumoniae*, *M. pneumoniae*, respiratory syncytial virus, and adenovirus; this proportion increased to 30% when influenza was also included. The pertussis rate was 2- to 4-fold higher than seen in the contemporaneous general U.S. population.[203]

Lower respiratory infections are the leading cause of death in low income countries, including those in West Africa. The

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population at highest risk includes children, particularly those with malnutrition; preexisting illnesses such as HIV or measles; those in extreme poverty, with household overcrowding, and with lack of health care access; those exposed to indoor air pollution or parental smoking. The HIV-infected adults and the elderly are also at particular risk. Epidemiologic and pathogen-specific data from sub-Saharan Africa in general are sparse, despite the overwhelming impact on morbidity and mortality. The burden of lower respiratory illness has been evaluated in The Gambia and Ghana;[204,205] with an incidence of 45 per 100 child-years, and 35% radiographically confirmed as pneumonia. Etiologic agents include high proportions of respiratory syncytial virus (37%), as well as adenovirus, parainfluenza virus, rhinovirus, and influenza.[206,207] Bacteria have been identified in approximately 75% of pneumonia in older children in The Gambia, largely *S. pneumoniae* and *H. influenzae*.[207] In HIV-infected patients, the relative proportion of gram-negative bacteria, including nontyphoidal *Salmonella* spp., increases.[208]

Three pathogens with respiratory transmission deserve particular mention with regard to U.S. deployers in the region. The first of these is influenza, commonly regarded as the most frequent vaccine-preventable illness in travelers to subtropical and tropical countries.[209] Influenza is a year-round illness in the tropics with peaks during rainy seasons in many tropical climates, but surveillance data from much of sub-Saharan Africa are limited.[210] Data from 14 years of surveillance in Senegal indicate 13% of influenza-like illness is caused by influenza and contributes to respiratory disease in all age groups.[211] Similar rates have been seen in Nigeria, and among children in Ghana, 23% of influenza-like illness was caused by influenza during the 2009 H1N1 pandemic.[212,213] Avian influenza (H5N1) has also been reported in West Africa since it was first detected in Nigerian poultry in 2006, with one human case reported in West Africa (also Nigeria).[214,215] Although preventive measures and vaccine for seasonal influenza exist, this common illness is clearly endemic, has demonstrated potential to disrupt operational missions, and prevention may be overlooked because of the perception of higher risk from other much less common endemic diseases.

Neisseria meningitidis

Meningococcal infection, while not regarded as a predominantly respiratory infection, clearly spreads through this route, and is regarded as intermediate risk in the region by NCMI. Much of West Africa is encompassed within the "meningitis belt," where the incidence of meningococcal disease is approximately 5 to 10 cases/100,000 population-year, and up to 1,000 cases per 100,000 during epidemics. Epidemics take place largely during the dry season.[216] Successful national vaccine campaigns have been established in Mali, Niger, and Burkina Faso, with others, including Nigeria, pursuing campaigns. Liberia and Sierra Leone are considered to be outside the typical "meningitis belt," and have not reported many of the large outbreaks that have affected adjacent countries in the region, but the "belt" appears to be spreading, with The Gambia, Ghana, Nigeria, Mali, and others outside the traditional range reporting outbreaks since the 1980s.[217] Most outbreaks in the region have been with serogroup A, which is covered in the vaccine deploying troops receive. As initial presentation may mimic any number of hemorrhagic fever virus infections, a high index of suspicion will be required to detect and treat both early and appropriately. Diagnostic testing, to include routine clinical microbiology, may be unavailable, requiring providers to empirically treat.

Tuberculosis

Some of the highest rates of pulmonary tuberculosis in the world exist in West Africa. In Liberia, the tuberculosis rate was 422/100,000 population in 2013, and this has been gradually uptrending since the 1990s, with a high burden of HIV coinfection. Nigeria's tuberculosis mortality rate is the second highest in the world (after Djibouti), with an estimated rate of 94/100,000 population.[218] Only 3% of newly diagnosed and 25% of retreated tuberculosis cases are tested for drug resistance in Liberia; of those that are, 2% and 20%, respectively, are MDR. Within West Africa, Cote d'Ivoire and Senegal report absolute numbers of MDR tuberculosis cases of 313 and 674, respectively, for 2013, but rates of drug susceptibility testing for newly diagnosed cases remain at 2% for both.[219] Tuberculosis skin test conversions have approximated 2% cumulative incidence after deployments to Southwest Asia, with higher risks seen in humanitarian operations in high-prevalence countries (e.g., Haiti), presumably because of higher exposures to local populations.[220] Although active tuberculosis cases in U.S. troops are rare, deployments were associated with 24% of these between 1998 and 2012, and represent the major risk factor for development of active tuberculosis in those without a positive tuberculin skin test at accession.[221] Diligent attention to screening and treatment of asymptomatic infections of returning troops will be required.

Prevention

As with most other infectious diseases related to deployment, effective preventive measures exist for acute respiratory disease in general, as well as influenza, meningococcal disease, and tuberculosis specifically. The efficacy of these measures will be largely related to the emphasis given by leadership. In close quarters, hand hygiene, the use of cough/sneeze etiquette and masks for symptomatic individuals, cohorting and isolation of infectious cases, and environmental disinfection are effective horizontal measures to decrease transmission of respiratory illness from most pathogens. Attention to space requirements is warranted, with a recommended 72 square feet per person, head-to-toe sleeping arrangements, and preferably with barriers between beds.[222] Broad application of vaccines for influenza, pertussis, and

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meningococcal illness prevention are recommended. As previously discussed in the yellow fever section, the administration of live attenuated intranasal influenza vaccine to many troops as part of the annual vaccine campaign presented a complication for those tasked shortly thereafter to deploy, as 28 days had not elapsed before yellow fever vaccine administration. Theoretically, this could complicate immune response to one or both vaccines, although data to suggest that this has a clinical impact are limited. Tuberculin skin testing in the U.S. Army is focused on targeted testing and not required as part of pre- or postdeployment mandatory activities.[223] Ventilation will be of special consideration when troops are spending time indoors with populations from high-prevalence areas, and health care facilities must develop plans for airborne isolation of those suspected to have active tuberculosis.

Person-to-Person

Ebola Virus Disease

The clinical syndrome associated with Ebola is relatively nonspecific, which has substantial impact on the development of an appropriate differential diagnosis when seeing a febrile patient in an endemic region.[224,225] There are also limited data regarding initial presentation since most of these studies from West Africa are from patients who present on day 5. It is unclear what role or impact asymptomatic infection might play.[226] At this time, there are no patient care or burial services to be provided by U.S. military personnel deployed to West Africa and any interaction with locals will incorporate strategies to avoid persons becoming ill.

Monkeypox

Monkeypox was first reported in the early 1970s during the smallpox eradiation campaign (reported in the 1980s in Liberia), and was shipped to the United States when prairie dogs from Ghana were imported as pets.[227,228] Although the disease is primarily spread from animal-to-humans, human-to-human second generation, but not third generation transmission, has been demonstrated.[227] Potentially infected animals include nonhuman primates, terrestrial rodents, antelopes, and gazelles.

Prevention

Strict barrier precautions are required for health care personnel or others in direct contact with blood or body fluids of sick or recently deceased patients. For monkeypox, avoiding close contact with ground squirrel and monkey reservoirs in rainforest habitats is recommended, along with precautions to prevent contact with aerosolized virus if someone has an exposure risk and clinical course consistent with monkeypox. Although there are data that the smallpox vaccine has cross protection, and many deployers have received it during operations in Iraq and Afghanistan, the smallpox vaccine is not mandated for this deployment.[229]

EVALUATION OF THE FEBRILE PATIENT

All febrile patients should be immediately queried about recent travel. Those febrile travelers returning within the past 21 days from the West Africa nations experiencing ongoing Ebola transmission need to be isolated and undergo a formal epidemiologic risk assessment issued by the Office of the Secretary of Defense and U.S. Africa Command informed by CDC guidance.[230]

Those with NO IDENTIFIABLE RISK include

- Contact with an asymptomatic person who had contact with person with Ebola.
- Contact with a person with Ebola before the person developed symptoms.
- Having been more than 21 days previously in a country with widespread Ebola virus transmission.
- Having been in a country without widespread Ebola virus transmission and not having any other exposures as defined above.

These individuals should be evaluated for alternate causes of a fever, and an Ebola diagnostic test is not indicated.

Febrile patients with HIGH, SOME, or LOW (but not zero) EPIDEMIOLOGIC RISK within the potential 21 day incubation period for Ebola are considered persons under investigation and should be considered for admission, isolation, and evaluation for Ebola as well as other febrile illnesses. The risk factor of deployment to Liberia, per se, does not necessarily mandate automatic assessment for Ebola, provided a comprehensive exposure history can be obtained and validated. Given its frequency and lethality, it remains important to promptly test for *P. falciparum* malaria using a malaria rapid diagnostic test and serial microscopy of malaria smears concurrent with initial Ebola assessment.[231] For those who had intermittently or regularly taken malaria chemoprophylaxis, the clinician must consider that malaria can present with an atypical pattern, and the lower parasitemia/antigen burden may make the diagnosis of malaria more difficult.[232] There is concern that the malaria rapid diagnostic test available for U.S. personnel might not adequately detect *P. ovale*, necessitating thick and thin smears or molecular approaches for definitive diagnosis.[233,234] Diagnostic tests should be limited to rapid antigen tests and malaria smears until Ebola is excluded, and may require empiric antimicrobial management based on the clinical syndrome at presentation. If an alternate diagnosis to Ebola is found, risk and surveillance returns to premorbid Ebola epidemiologic risk until the day 21 incubating period.

After 72 hours of symptoms, Ebola can be excluded by a negative reverse transcriptase polymerase chain reaction. A routine methodologic approach to diagnostic testing for other febrile illnesses in return travelers can be further pursued thereafter focusing on incubation period, disease presentation, and specific risk factors.[235–237] Given that most deployed personnel will be monitored for 21 days with twice-a-day temperature checks and medical evaluation, as well

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as the incubation period of many of the at risk diseases in the region, the majority of deployment-related infections will occur while the deployed member is still in the observation period and the military health system.

Evaluation of a febrile or symptomatic patient in Liberia is challenged by lack of robust diagnostic procedures for non Ebola disease. In addition, the limited holding capability in theater is a challenge given the potential attack rates of the various diseases. Patients with malaria during the Vietnam War and Somalia were managed an average of 8 days in their military treatment facility. This will influence evacuation when Ebola is in the differential, and prompt empiric therapy to include malaria, rickettsia, influenza, and bacterial infections. One must also not overlook the fact that coinfections can occur if exposure to various vectors occurs.[238,239] Empiric therapy for malaria in Liberia should be limited to those with severe illness (or situation in which testing is not possible), or a serial testing paradigm should be used. Options include artemether–lumefantrine if the person was on atovaquone–proguanil prophylaxis, or atovaquone–proguanil if they were on doxycycline. Empiric doxycycline for potential rickettsial infection, and fluoroquinolone or ceftriaxone for broad antibacterial coverage must be considered. Although QT prolongation with lumefantrine has been described, the risk appears low, and concomitant use of fluoroquinolones especially ciprofloxacin is likely safe.[240,241] Evaluation in an Ebola isolation unit is likely to be limited to point-of-care testing only until the disease is ruled out, with appropriate testing based upon the incubation periods (Tables I–VI), exposure risks, and clinical presentations.

MILITARY IDENTIFIED INFECTIOUS DISEASE THREATS WITH THE U.S. MILITARY'S REBALANCE AND FUTURE STUDIES

The U.S. military is realigning their forces to focus on regional activity as there is a rebalance from the Iraq and Afghanistan operations to Asia and Africa. As this is the first recent major deployment to a high-risk infectious disease region of the world, ongoing assessments of diseases that need to be addressed with this rebalance must take priority. These will drive future research and development for the U.S. military. A weighted matrix utilizing disease incidence rates country-by-country and disease severity of key infectious diseases was published in 2008. The key diseases identified (from 1 to 10) were: malaria, diarrhea-bacteria, dengue fever, Rift Valley Fever, gonorrhea, chikungunya, leptospirosis, HIV/AIDS, meningococcal meningitis, and CCHF. Ebola or other viral hemorrhagic fevers were not included in the list.[242] A follow on evaluation in 2010 listed the top 10 as: malaria, dengue, diarrhea, bacterial, MDR wound pathogens, leishmaniasis, Q-fever, norovirus and other viral diarrheal diseases, influenza, adenovirus, and leptospirosis. Regarding the other infectious diseases, CCHF was 13th, Lassa fever and other arena viruses 22nd, and Ebola/Marburg hemorrhagic fever 33rd.[243] This threat assessment process should be repeated given the change in geographic focus for military operations.

In addition, a discussion of emerging infectious disease risk lessons learned from Iraq and Afghanistan identified four key issues. Infectious disease diagnostics approved by the U.S. Food and Drug Administration are needed, as well as better training of those going down range in regions with emerging infectious diseases. High-level leaders also identified a need for standardized medical records to collect more accurate clinical and epidemiological data, and improved understanding of medical surveillance data on deployed forces and veterans.[244,245]

At this time, ongoing plans for assessing pre- and post-deployment serology with linkages to clinical presentations are being developed through various research programs. In addition, focus of infectious disease studies is shifting from combat-related injury infections, which has dominated research over the last 13 years, to travel medicine studies assessing diseases developed by our deployed personnel. Furthermore, DoD overseas research laboratories, which are primarily located in tropical regions such as Kenya, have robust activities that include support of foreign technicians and epidemiologists. Ongoing Ebola prevention and treatment studies are being arranged in the unlikely event of U.S. military personnel having a high-risk exposure. In addition, vector assessment studies are underway in Liberia for improved pathogen recognition and threat assessment. Overall, continued support through expertise and funding are required in preparedness, surveillance and response within the United States and also in the overseas DoD research laboratories.[244] This requires a combination of numerous programs, including the Navy, Army, Air Force, Public Health Service, Defense Health Program Joint Program Committee, National Institute of Allergy and Infectious Diseases, and the Defense Threat Reduction Agency. It will also require a regionally aligned approach based upon endemic diseases along with linking to civilian programs.

CONCLUSION

Those deploying in support of OUA are at substantial risk of developing infectious complications in addition to potential exposure to Ebola. The most likely threats would be diarrheal diseases and respiratory infection, which place a high priority on hygiene measures. Vector-borne diseases are also of concern, placing a premium on PPM. Malaria presents the greatest risk given the high attack rate and potential for severe diseases necessitating command emphasis on PPM and malaria chemoprophylaxis adherence with clinicians required to provide early and accurate diagnosis and therapy for malaria.

ACKNOWLEDGMENT

We would like to thank M. Leigh Carson for her assistance in preparing the manuscript.

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