Review



Emerging outbreaks associated with conflict and failing healthcare systems in the Middle East

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Abstract

The escalating conflicts in the Middle East have been associated with the rapid collapse of the existing healthcare systems in affected countries. As millions of refugees flee their countries, they become vulnerable and exposed to communicable diseases that easily grow into epidemic crises. Here, we describe infectious disease epidemics that have been associated with conflicts in the Middle East, including cholera, poliomyelitis, measles, cutaneous leishmaniasis, and diphtheria, that call for appropriate preventive measures. Local ongoing wars and failing healthcare systems have resulted in regional and global health threats that warrant international medical interventions.

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The escalating conflicts in the Middle East, particularly in Syria and Iraq, have been associated with a rapid collapse of their existing healthcare systems, resulting in public health catastrophes.¹ The devastation resulting from intensifying civil and regional wars in these countries has introduced alarming and self-perpetuating epidemics that have disseminated rapidly within the regions and have the potential to spread globally, creating even greater health emergencies.

In places like Iraq, Syria, and Yemen, the fighting and destruction have created favorable environments for the spread of these epidemics through widespread contamination of the water, disruption in food supplies, poor sanitation conditions, and massive displacement of large segments of the population. These conditions have resulted in overcrowding of refugees, which has been compounded by the lack of concerted and systematic public health responses.^{1–3} More than 10 million Syrians have been displaced, including 6.1 million within Syria and 4.8 million in bordering countries.⁴ Furthermore, the concurrent collapse of the public health and healthcare system in Syria has not only perpetuated the regional dissemination of several epidemics, but it has also prevented the implementation of effective infection control measures.

Several factors have contributed to the collapse of the healthcare system in Syria. These include, but are not limited to economic sanctions; wide destruction of healthcare facilities; shortage of healthcare personnel associated with large-scale immigration of healthcare workers and, at times, their physical elimination or injury; lack of access to essential drugs and medical supplies; and lack of secure routes and transportation.^{1,5} Sanctions (among other things) leading to interruptions in the power supply have contributed to interruptions in vaccination programs.⁶ The World Health Organization (WHO) has estimated that 40% of the ambulances in Syria have been ruined; 57% of public hospitals are severely damaged; and 37% are out of service.¹ Another report has indicated that at least 160 physicians have been killed in Syria alone, while hundreds others have been jailed or kidnapped, resulting in the massive migration of >80,000 physicians.⁵ In addition, prior to the Syrian war, 90% of pharmaceutical needs were locally produced, and this has been reduced to only 10% presently. The problem has been compounded by an extreme shortage of pharmaceutical supplies from outside the country due to the lack of safe uninterrupted transportation as well as the sanctions imposed.^{2,5}

In the following sections, we briefly describe several infectious disease outbreaks that have occurred in the Middle East and that are perpetuated by deteriorating healthcare systems associated with local and regional conflicts. The resulting deficient hygiene, sanitation, and water supplies in the affected areas have major health implications and have imposed a massive disease burden. We also review the interventional efforts reported and outline the preventive measures implemented in the affected areas where possible.

Cholera

Cholera is unique among waterborne bacterial infectious diseases in its potential to cause pandemics. Over the last 200 years, the world has witnessed 7 pandemics of cholera. We are currently in the second and the third waves of the seventh cholera pandemic attributed to a *Vibrio cholerae* O1 el Tor strain.⁷ Notably, the second wave of the seventh pandemic was associated with the acquisition of additional antibiotic resistance, and the third (ie, current) wave has been associated with the acquisition of a

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Table 1. Cholera Outbreaks Associated with Conflict in the Middle	East
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Infectious Disease	Year	Geographic Area	Est. No. of Cases	Source of Outbreak	Exacerbating Factors	Proposed Interventions	Reference
Cholera	2015	Iraq	5,000	 Overpopulated communities and refugee settings Heavy rain/flood Destruction of infrastructure 	 Inadequate sanitation Contaminated sanitary and water supplies 	 Treatment of drinking water (boiling, water purification tablets) Hygiene promotion Vaccinations campaigns Introducing the 1-dose cholera vaccine to improve compliance Cook food and consume immediately Avoid raw food Boil unpasteurized milk 	12
	2016-ongoing	Yemen	1,051,789				15,19

cholera toxin variant; both of these are major concerns and could lead to a global public health disaster.⁸

Cholera outbreaks occur in the background of poor sanitation and inadequate access to clean drinking water.⁹ This setting has been the hallmark of the perpetuating civil wars in Iraq, Syria, and Yemen, whereby water and sanitation management as well as infrastructure have been damaged either intentionally or accidently. For example, the 2015 cholera outbreak in Iraq is thought to be related to the low water levels in the Euphrates¹⁰ as well as the winter flooding, which likely contaminated the Euphrates River and shallow wells with sewage water (Table 1). Two previous outbreaks in Iraq, noted to be of a lesser severity, were reported during 2007 and 2012 and had similar environmental commencements. They affected the northern governorates including Babel, Baghdad, and Kerbala.¹¹

Between September and November 2015, the WHO reported a severe cholera outbreak in Iraq, with >5,000 confirmed cases and several deaths.^{12,13} However, the WHO representatives in these areas admit to underreporting because of logistic surveillance difficulties, particularly in the active war zones.

Some reports indicate that this cholera outbreak has spread to neighboring Syria, Kuwait, and Bahrain, with a risk of turning this localized outbreak into a region-wide epidemic.¹⁴ The areas where the largest numbers of cholera cases have been detected include the Shiite cities of Najaf and Karbala, where millions of Shiite Muslims travel annually on religious pilgrimages to their holy shrines.

In response to the 2015 outbreak, the Iraqi Ministry of Help with the assistance of international governmental agencies (IGOs), initiated a vaccination campaign targeting at least 255,000 people, mobilizing the largest oral cholera vaccine (OCV) stockpile and providing supportive care and educational benefits to raise awareness.¹³ The outbreak seemed to have subsided by December 2015.¹³ However, among the people who received immunization, the proportion that received the 2 full vaccinations was estimated to range from 21% to 90%. This lack of vaccination coverage is thought to have been influenced by several critical factors including lack of compliance, the continuing displacement of individuals, and the shortage of the vaccination supplies.¹³

For the past 3 years, the ongoing civil war in Yemen has highly impacted the basic public health sanitation infrastructure of this country, manifesting a cholera outbreak. This outbreak was first reported in October 2016, and the number of suspected cases exceeded 1,051,789 individuals by January 2018. This phenomenal increase reported by the WHO and the Yemen Ministry of Public Health makes this cholera outbreak the largest epidemic in the world.¹⁵ Vital public health infrastructures in civilian areas have been totally destroyed or made inoperable, resulting in massive displacement of the affected population into crowded and unsanitary conditions.¹⁶ Currently, ~2,000 attributable deaths have been reported, and the outbreak has extended geographically, affecting nearly all the governorates in the country.^{15,17}

The WHO and Yemen partners in the Global Health and Global Water Sanitation and Hygiene Cluster (WASH) or Global WASH cluster (GWC) have responded by providing medical supplies such as diagnostic kits, rehydration solutions, and chlorination tablets, to hospitals handling cholera cases. Small interventions like these are not costly and are capable of decreasing fatality rates among infected patients by 50-fold.¹⁸ These organizations have also supported the opening, rehabilitation, and maintenance of more than 39 diarrheal treatment centers.¹⁹ As a result of these interventions, the incidence of cholera began declining and continued to decline until May 2017, when an upsurge in cases was noted. This reversal is believed to have occurred after a catastrophic failure of the sewer system in Sanaa was caused by continuous airstrikes on the city coincident with the beginning of the rainy season. These factors, in addition to severe malnutrition, contributed to the increased morbidity of the disease.^{16,20} The weekly surveillance cases had been decreasing for the preceding 20 weeks, as reported in late January 2018.¹⁵ This decreasing trend occurred despite the fact that the 1 million doses of the oral cholera vaccine that had been allocated from the global stockpile were cancelled in July 2017 due to fear of the vaccine's ineffectiveness and the realization that the large volume of people at risk dramatically exceeded the supply.²¹ This move could have been of benefit had it been done earlier in the course of the crisis. Apparently, vaccination plans with a more adequate amount of vaccine to be allocated are still being researched.²²

One potential solution to the previous vaccination issues is the newly approved single-dose oral cholera vaccine (Vaxchora), which could provide the needed efficacy²³ and improve compliance by providing a single dose of the vaccine rather than the conventional 2 separate dose vaccinations required. This solution has been hindered, however, because the effectiveness of Vaxchora has not been established in persons living in cholera-affected areas, and the vaccine's effectiveness has not been established in persons who have pre-existing immunity due to previous exposure to *V. cholerae* or who previously received a cholera vaccine.

The WHO, in collaboration with United Nations Office f or the Coordination of Humanitarian Affairs (UNOCHA), the European Commission's Humanitarian Aid Office (ECHO), and the Office of Foreign Disaster Assistance (OFDA), are working on optimizing their surveillance systems to be able to detect, investigate, and intervene adequately when an outbreak is suspected.²⁴ The WHO and partners recently directed a cholera risk assessment program to classify cholera into 4 risk categories based on (1) population density, (2) access to clean water and sanitation, (3) level of service in camps, and (4) direct exposure to conflicts. This effort aimed at predicting future outbreaks during these presumably high-risk periods.²⁵

Poliomyelitis

In 2014, the WHO estimated that more than 7,600 Syrians were infected with poliomyelitis, with subsequent spread of the infection to Iraq (Table 2).²⁶ This outbreak occurred after 15 years of eradication of poliomyelitis in Syria during the preconflict era.²⁷ Most of the polio reported in Syria occurred in the northeastern province of Deir El Zur, which was the epicenter of the outbreak.²⁶ However, several other cases were reported in the rural areas of Damascus, Aleppo, and other rural regions.

Poliomyelitis is a virus that lives in sewage-contaminated water and food. Hence, several war-related factors contributed to this poliomyelitis outbreak. First, particularly during the war, raw sewage was pumped directly into the Euphrates River, which provides drinking and wash water to many villages. This occurred simultaneously with the discontinuation of chlorination of previously potable water.²⁸ Second, poliomyelitis is a vaccine-preventable disease, and the vaccination coverage in Syria dropped from ~91% in 2010 before the conflict to as low as 45% by 2013.³ An estimated 58% of the polio cases reported in children during the outbreak in Syria and Iraq had never received the polio vaccine.²⁹ Third, several boosters of polio vaccines are required to confer protective immunity, which impedes the success of polio vaccination programs. Incomplete vaccination was reported in 37% of the children with polio in Syria and Iraq in October 2013.²⁹ In addition to the warrelated factors described above, overcrowding of tens of thousands of displaced and refugee populations inside and outside Syria has occurred. This population has limited healthcare access, unsanitary living conditions, and limited (or no) access to communicable disease vaccinations.¹

In addition, the strain of poliomyelitis in Syria has been linked to a wild-type strain found in Pakistan, which is suspected to have been introduced into Syria by a jihadist fighter from Pakistan.^{30,31} The dissemination of this virus within the region has also been reported; cases of polio have been described in Lebanon, Jordan, as well as Iraq.³² Polio in Syria has been declared a public health emergency that requires international efforts and solidarity to prevent a global epidemic. Fortunately, this outbreak was successfully contained and interrupted within 6 months through the implementation of proper surveillance measures. After multiple vaccination campaigns in Syria, monitoring coverage improved from 79% in December 2013 to 93% in March 2014.²⁹ The last case of polio in Syria was reported in January 2014. A similar positive response was also seen in Iraq. In addition to providing humanitarian aid, health hygiene, clean water and sanitation, as well as facilitating healthcare delivery and vaccination, a high level of systematic surveillance should be maintained to prevent further outbreaks.^{29,33}

No polio cases have been documented in Yemen since the beginning of the conflict. To maintain the polio-free status achieved in Yemen in 2006, and after the last immunization campaign in April 2016, a nationwide polio immunization campaign was launched in February 2017, targeting the general population and particularly children in high-risk groups.³⁴

Measles

Measles is a highly contagious viral illness that has a high efficiency of airborne transmission, but the disease is vaccine

Table 2. Viral Outbreaks (Polio/Measles) Associated with Conflict in the Middle East

Infectious Disease	Year	Geographic Area	Est. No. of Cases	Sources of Outbreak	Exacerbating Factors	Proposed Interventions	Reference
Poliomyelitis	2014	Syria	7,600	 Inadequate vaccination Overcrowded living quarters Poor sanitation and hygiene 	Collapse of healthcare system Sloppy surveillance	 Hygiene medicine and environmental health: decontaminating water, treating sewage, and restoring sanitation. Routine immunization (Sabin oral and Salk inactivated poliovirus vaccines) Surveillance for acute flaccid paralysis 	26
Measles	2013–2016	Syria	7,000	 Lack of or inadequate vaccination Crowded refugee camps 	 Collapse of healthcare system Restricted access to care 	 Vaccination campaigns and access to care Active surveillance 	35
		Jordan	373				37
		Lebanon	2,078				38
		Syrian refugees in Lebanon	369				
	2012-2017	Yemen	5,773				41
Hepatitis A	2015	Syria	49,300	 Poor sanitation and hygiene Crowded refugee camps Lack of or inadequate vaccination 	 Collapse of healthcare system Restricted access to care 	Proper hand hygieneHealth education sessionsEarly detection	35

preventable. A measles epidemic has been reported in Syria during the current period of unrest, particularly in the northern regions of the country such as Aleppo. An estimated 7,000 cases have been reported by the WHO and Médecins Sans Frontières (MSF) organizations: ~200 cases in 2013; 4,309 in 2014; 1,617 in 2015; only 85 cases in 2016; and an upsurge in 2017 with 733 laboratory-confirmed cases (Table 2).^{35,36} The measles epidemic disseminated to neighboring countries such as Jordan, where 24 cases were reported in 2012 and >4-fold more (>200 cases) were reported in 2013.³⁷ These estimates declined to 38 by 2015. In addition, only 9 cases were reported among the Lebanese population in 2012, but this number increased to 1,760 by 2013. Then, the reported numbers of measles cases went down to 205 in 2014, to 39 in 2015, and to 44 in 2016. Such trends have been similar among the Syrian refugees in Lebanon: 232 measles cases were reported in 2013, 107 in 2014, 12 in 2015, and 18 in 2016.³⁸

Moreover, a decline has been documented in the rates of measles vaccinations in Yemen, which has reached as low as 41%.³⁹ This vaccination decline resulted in increased numbers of cases, with >847 measles cases by December 2011; 2,143 cases in 2012; and 1,634 cases in 2017.^{40,41}

Measles vaccination rates dropped nationwide in Syria from a stable rate of 82% in 2010 to as low as 53% in 2015, dipping to 17% in some northern cities like Kobanî.^{42,43} Through December 2016, an estimated 4.56 million children had been immunized against measles in the accessible areas of the Syria, but despite all efforts, the national vaccination rates have remained low, reaching only 65% for 2016.³⁵ To address this void, the WHO held health education conferences in areas considered to be at high risk because the resistance of parents hindered the immunization campaigns.^{35,36} Unfortunately, a muscle relaxant (atracurium) was accidently mixed up with a diluent used with the measles vaccine and caused the deaths of 17 children, thus causing further anxiety for parents needing to vaccinate their children.⁴⁴

Vaccination campaigns are critically important to vulnerable populations in these areas of the world. However, the escalating conflicts in the northern areas of Iraq and Syria, as well as Yemen, are hampering these immunization campaigns significantly.

Leishmaniasis

Leishmaniasis is transmitted to humans by the bites of infected female phlebotomine sand flies, and it constitutes a major public health problem in the eastern Mediterranean region (EMR).⁴⁵ Four types of Leishmania spp cause most of these infections in humans; cutaneous leishmaniasis accounts for the largest number of cases. Globally, the estimated numbers of cases of leishmaniasis annually are 12 million for cutaneous leishmaniasis and 2.5 million for visceral leishmaniasis. Also, an estimated 1.5 million cases of cutaneous leishmaniasis and 500,000 cases of visceral leishmaniasis are reported annually among 88 countries.^{45,46} The EMR is an ill-defined geographical region in which most countries have experienced some form of hostilities or civil war over the past 20 years, whether major invasions, internal strife, or cross-border clashes. This unrest has led to massive movements of populations, including refugees and military personnel, which have contributed to several outbreaks of cutaneous leishmaniasis.

For decades, cutaneous leishmaniasis has been recognized as a skin-deforming infection transmitted by a sand fly. It is endemic in northern Syria, particularly Aleppo and Damascus.¹ However, with the recent conflict in Syria, increasing violence from civil war, and terrorist activity leading to vast population displacement, an epidemic in 2012 involved >52,000 confirmed cases (Table 3).^{47,48}

Despite leishmaniasis being endemic in Lebanon, a cutaneous leishmaniasis outbreak began among Syrian refugees in Lebanon in September 2012, and by 2013, 1,033 cases had been confirmed; 97% of them were among Syrian refugees. The average age of these patients was 17 years, with 80% being <18 years old.^{44,49,50} In this particular outbreak, 85% of the cases were caused by *L. tropica*, a species epidemic to Aleppo that causes aggressive large, disfiguring lesions and a prolonged disease course that necessitates intramuscular treatment.⁴⁹ The Lebanese Ministry of Public Health, in collaboration with the WHO, launched a coordinated campaign to contain the spread of this infection, which included spraying pesticides to kill the vector, providing free treatment and diagnosis for new cases, establishing a referral system with 12 treatment clinics

Table 3. Leishmaniasis Outbreaks Associated with Conflict in the Middle East

Infectious Disease	Year	Geographic Area	Est. No. of Cases	Sources of Outbreak	Exacerbating Factors	Proposed Interventions	Reference
Cutaneous leishmaniasis	2008	Iraq	1,250	 Mass population displacement, increasing numbers of Syrian refugees Sand fly, increasing rodents 	Collapse of healthcare infrastructure	 Spraying pesticides Using insect repellent Surveillance and vigilant monitoring of disease activity 	52
	2009		5,000				58
	2011		2,978				24
	2012		2,486				
	2012	Yemen	2,475				59
	2012	Syria	52,000				47
	2013		71,000				35
	2014		46,000				
	2013	Lebanon	1,033				50

across Lebanon, and producing public awareness and health education materials.¹ However, controlling the source of this infection in northern Syria, particularly in and around Aleppo, has not been possible because of the conflict in that area. Recently, due to different war-related factors, new outbreaks have been reported from different areas bordering Syria, including Turkey and Iraq.⁵¹

Cutaneous leishmaniasis is a neglected disease in Yemen due to the lack of awareness of the natural course of the disease and the possibility of medical treatment. Despite poor documentation and underestimation of its burden, this disease seems to be endemic in this country-it occurs nationwide.46 The interruption of healthcare services, the poor housing conditions, the current armed conflict in Yemen, the human migration from cities to villages, the arrival of refugees from other endemic countries such as Iraq and Syria, the absence of active detection and national reporting systems, and the lack of systematic national efforts to control the disease are all risk factors for enhanced transmission of cutaneous leishmaniasis in Yemen.⁴⁶ Effective treatment accompanied by measures for prevention of reinfection should reduce the incidence of anthroponotic cutaneous leishmaniasis. Control of cutaneous leishmaniasis in Yemen should be based on the best knowledge of the Leishmania parasite species and of different reservoir hosts and vector behaviors so that effective control measures can be undertaken. To address the problem of leishmaniasis in the EMR in the future, collaborative efforts with the WHO and supporting ministries of health of the regions should be undertaken through a strategic plan that includes the following measures: establishing a regional surveillance system, implementing training strategy, allocating appropriate resources for early detection, providing free medication, and facilitating subregional collaboration.52

Diphtheria

Diphtheria is a bacterial infection caused by Corynebacterium diphtheria that can result in respiratory and cutaneous diseases. It can be transmitted through respiratory secretions or skin lesions of affected patients or asymptomatic carriers. Since the introduction of the diphtheria vaccine, the disease has become rare in developed countries. However, diphtheria is resurging in developing countries as a result of poor socioeconomic status; compromised healthcare infrastructure; poor access to care; and shortages of vaccines, antitoxins, and antibiotics. In addition to the other disease outbreaks reported in Yemen, the WHO and Reuters have reported a large outbreak of diphtheria affecting close to 500 people since August 2017, with rapid spread in multiple governorates and a high fatality rate of 10%, particularly in children.53-55 The armed conflict and imposed blockade of Yemen's ports has resulted in shortages of food and medical supplies, poor access to care, the inability to perform the required diagnostic laboratory testing, and a decline in the rate of vaccination (>60% of the suspected cases had not received any vaccination). The MSF are working with the WHO to allow diagnostic laboratory testing on suspected cases to identify cases that require isolation, to provide treatment and antitoxins, and to provide prophylaxes to the patients' close contacts.

Other infectious diseases

Clusters of hepatitis A outbreaks have been reported during the Syrian conflict over the last 2 years, particularly among displaced Syrian populations. An outbreak of hepatitis A among Syrian refugees in northern Iraq in 2013 was halted by the efforts of the WHO, other international organizations, and local health authorities to improve conditions in the camps.⁵⁶ Across Syria, 49,300 cumulative cases of hepatitis A were reported in 2015.³⁵

In addition, other infectious diseases, such as multidrugresistant tuberculosis, have been reported, particularly in association with the Syrian crisis. Lebanon has reported a 27% increase in the incidence of TB attributable to the Syrian refugees.⁵⁷ The Al Noor Chest Disease Sanatorium in northern Jordan has reported high rates of tuberculosis, including multidrugresistant tuberculosis, among Syrian refugees who are seen in its outpatient clinics.⁵⁷ In Jordan and Turkey, this population does not have access to public health care at Ministry of Health facilities,⁴⁵ which puts refugees at higher risk of contracting and transmitting the disease.

In conclusion, given the catastrophic implications of these infectious disease epidemics in the Middle East, both at the regional and the global levels, a concerted collaborative effort needs to be initiated that joins the WHO and relief governmental agencies on one side with IGOs and NGOs on the other.

Numerous unanswered questions could be raised regarding Middle East countries amid civil conflicts, and several limitations to our data should be considered. Unfortunately, countries under the siege of conflicts face difficulty collecting data, particularly from combat zones, destroyed areas, and displaced people. Therefore, the proper analysis of the actual impact of the conflicts in the re-emergence and spread of the infectious diseases, the assessment of the postconflict needs, as well as the results of the targeted interventions, should be undertaken by IGOs in collaboration with NGOs to evaluate the capacity of the health system and its functionality in the postconflict era. Without a structured surveillance system and/or mandatory reporting mechanism, most, if not all, of the highly communicable diseases will continue to disseminate and be underreported, especially in the background of regional conflicts and displaced refugees. Although there could be a correlation between emerging infectious diseases and failing healthcare systems, identifying a direct association without good surveillance systems or hard measurable data is challenging.

Governments should take responsibility by acknowledging the early appearance of these emerging diseases, which plays a tremendous role in prevention and management. Denying and hiding the initial signs of disease dissemination have been reported throughout history in different settings all over the world.¹⁸ Regional cooperation should be enhanced, and communication among various agencies providing healthcare and relief through the establishment of large network should be facilitated to disseminate information and share expenses.

The opportunity certainly exists to provide public health resources and structured support for the civilian populations in these war-torn areas to address their needs. The international community, including medical professionals and infectious disease specialists, can have a positive impact by alleviating the suffering of millions in this region. Providing access to clean water, improving sanitation and hygiene, supplying medications, establishing mass vaccination campaigns, supporting medical staff, offering access to health care, and instituting surveillance programs are of paramount importance to the prevention, diagnosis, treatment, reporting, and control of infectious disease outbreaks. **Acknowledgments.** The authors wish to thank Health Outreach to the Middle East and the Worldwide Institute of Medical Education for their support of the efforts and investigations outlined in this publication.

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