



Pediatric Infectious Diseases Encountered During Wartime—Part 1: Experiences and Lessons Learned From Armed Conflict in the Modern Era

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Abstract

Purpose of Review Armed conflicts occur globally, with some regions experiencing heightened instability for many years. A better understanding of the infectious disease impact on children in armed conflict will allow aid organizations to anticipate and mitigate the most serious problems.

Recent Findings Armed conflicts are estimated to have caused approximately 30 million civilian deaths during the past 27 years, with two-thirds occurring in women and children. Children are extremely vulnerable to the mass population displacements, experiencing a combined loss of safety, nutrition, shelter, hygiene, and health care. Under these circumstances, the emergence and prevalence of multiple infectious diseases can result in heightened morbidity and mortality long after active conflict ceases.

Summary Factors leading to increased infectious diseases in populations in crisis due to armed conflict and lessons learned from recent outbreaks are discussed in detail. Acute respiratory infections, diphtheria, measles, varicella, and cholera are a few of the more common infectious diseases that take advantage of populations displaced or disrupted by conflict. Key issues include the ability of countries or non-governmental organizations (NGOs) to keep up with basic childhood immunizations, and how rapidly disease outbreaks are recognized and addressed with disease-specific interventions.

Keywords Conflict · Children · Infections · Displacement · Vaccine-preventable diseases (VPD)

Introduction

The overall burden of infectious diseases, resulting in morbidity and mortality for all children globally, has improved tremendously over the past 25 years [1]. This positive trend, however, has been largely offset in regions destabilized by armed conflict, which have grown in complexity and duration, despite many other advances in technology and global health. Armed conflict represents a clear and present threat to the daily lives of many people throughout the world. In 2019, a total of 358 conflicts were reported worldwide, with

over half of them being violent, and 15 being full-scale wars [2]. The trauma inflicted goes beyond just the immediate warring factions, and has profound impacts on the region's most vulnerable populations. Twenty-first century armed conflicts have been predominantly marked by asymmetric warfare, state vs non-state actors, and unconventional tactics and tools, which have brought combat activities into children's environments and increased their risk for injury and/or death. Several recent reviews, focusing on the multiple threats faced by this population, are highlighted below.

The American Academy of Pediatrics (AAP) published a technical report in 2018 on the "Effects of Armed Conflict on Children," indicating that over 10% of the world's children (an estimated 246 million individuals) are affected by armed conflict. This burden includes both direct physical injury and psychological trauma, plus a host of other impacts on their living conditions, impairing their ability to develop into healthy adults [3]. This report discusses the fluidity of defining "armed conflict," as well as affirms several international agreements that have promoted the need to protect

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children from conflict, and offers interventions to “mitigate the effects on children.” A recent systematic review of 155 conflicts from 1945 until the current era underscores the broad definition of the scope of “armed conflict,” ranging from low-intensity and state-sponsored conflict, to all-out war, with dramatic mortality and significant internal and external population displacement [4•]. Basic mortality statistics are well-described in an analysis of 1118 armed conflicts occurring from 1990 to 2017, in 193 countries, which included data from the Global Burden of Disease Study—2017, and the Uppsala Conflict Data Program [5•]. They reported additional mortality of nearly 30 million excess civilian deaths above the baseline levels for these countries over this time period, with a striking additional mortality in children under 5 years of age (263.7 per 100,000) associated with conflict. Most deaths were related to indirect impacts of conflict, with two-thirds due to communicable diseases (the number one cause of mortality), plus maternal, neonatal, and nutritional diseases secondary to conflict’s adverse impact.

The World Health Organization’s (WHO) “Health and Peace Initiative” is described simply on their website as: “Health and peace are interrelated. In the words of the Director-General of WHO, Dr. Tedros, ‘there cannot be health without peace, and there cannot be peace without health.’ Conflicts are a major obstacle to health, while a lack of access to health and basic social services can lead to feelings of exclusion, which are in themselves a major driver of conflict and violence.” [6]. Despite the wide recognition of these adverse impacts, conflicts continue. These two manuscripts will first review the types and patterns of infectious diseases at the regional population level, and identify factors associated with armed conflict that exacerbate infectious diseases. The second part will examine infectious disease risks for the individual pediatric patient, who may be a victim of trauma, and other specific types of injuries associated with modern armed conflict. This includes the direct effects of injuries caused by blunt force, blast, penetrating, and burn injuries, and how they create an opportunity for infections.

To date, there has been a regrettable lack of publications characterizing the specific infectious complications of direct injuries sustained by children during armed conflict. Recent literature is heavily influenced by the prolonged military conflicts in Iraq and Afghanistan, which have provided more clarity on the infectious complications associated with wartime trauma in military populations. Among the authors, Drs. Cirks, Ottolini, and Rajnik have extensive experience caring for the pediatric populations impacted by those conflicts. These reviews are an attempt to fill that knowledge gap, by initially discussing the impact of conflict on the types of infectious diseases seen in children in conflict regions, followed by an attempt to combine the existing pediatric combat trauma injury literature, which is mostly descriptive of injury location, type, and severity, with the recent

advances in adult combat causality infection management. By synthesizing the material, we will draw inferences for the infectious complications of individual pediatric patients directly injured during armed conflict, as well as provide general recommendations and resources to assist those managing them. One limitation, however, is that the body of literature cited in these manuscripts is influenced by the perspective of practitioners from well-resourced countries during their military experiences, during combat operations in the Middle East and Southwest Asia, or periodic humanitarian efforts. Local nation literature is either not as accessible due to English language publication criteria or not cataloged in PubMed.

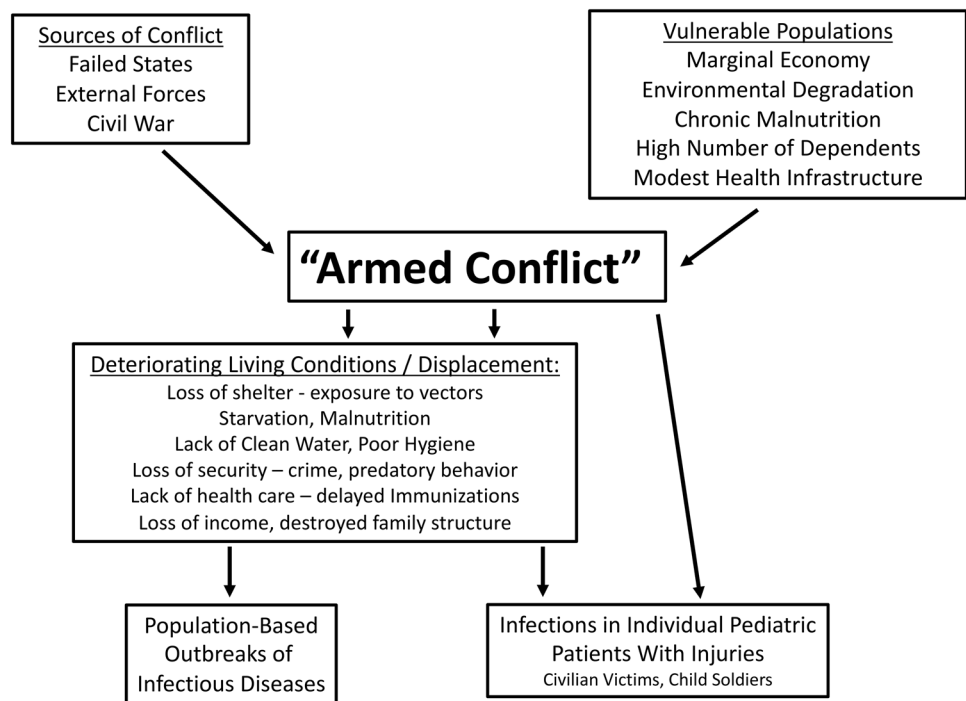
Armed Conflict Leads to Complex Humanitarian Emergencies

Figure 1 highlights the interrelatedness of the factors that lead to both outbreaks of infectious diseases impacting the children of the involved populations, as well as the unique types of infections that take advantage of injuries resulting from armed conflict. Economic, environmental, demographic, and other factors place populations at high vulnerability to any stress, which in turn suffer devastating results from the “failed governance” and resulting armed conflict [2, 3, 4•, 5•, 6]. The most vulnerable populations often suffer from long-standing issues that lead them to be less resilient to the impact of armed conflict, as noted [7]. Possibly, the most important factor is that in low-resource regions, conflict frequently leads to intra- or international displacement of large numbers of people, with resulting loss of livelihood, family structure, shelter, clean water, hygiene, adequate nutrition, access to immunizations and health care, and security. Taken together, these factors create an environment conducive to population-based outbreaks of infectious diseases that disproportionately impact children. These contribute to increased mortality that continues long after the active phase of a conflict is completed which, as noted above, commonly exceeds the initial mortality attributed to direct injury.

Lessons Learned From Recent Regional Conflicts

Several regions of the world have been focal points for combined internal and international conflicts during the 1990s and through the first portion of the twenty-first century. Table 1 summarizes some of the more dramatic examples that have occurred in the last 25 years. Table 1 begins with the initial observations from the entire global experience with armed conflict, followed by some of the

Fig. 1 The complex dynamics of armed conflict



detailed European data obtained from the recent wave of asylum seekers from multiple African, Eastern Mediterranean, and Asian countries. The remainder of Table 1 focuses more specifically on the geographic regions defined by the WHO, and includes many of the lessons learned about specific infectious diseases in entire populations and in specific pediatric age groups. Many of these lessons are referenced in the discussion below.

Impact of Common Infectious Diseases on Populations, Particularly Children

Recent experiences have shown that certain infectious diseases commonly, and almost predictably, emerge in regions of conflict, especially those of larger scale or prolonged duration [3, 25, 33, 34, 35]. For this discussion, it may be most convenient to categorize them by the factors that lead to outbreaks during conflict, summarized in Table 2.

Vaccine-Preventable Diseases

Possibly, the most dramatic category includes the vaccine-preventable diseases. The primary objective of the Global Vaccine Action Plan (GVAP) 2011–2020 was for all countries to reach $\geq 90\%$ national coverage with all vaccines included in the country’s national immunization schedule (tailored to WHO regions) by 2020 [36]. A recent Morbidity and Mortality Weekly Report (MMWR) of data through the end of 2018 indicated continued global success with the

administration of Bacille Calmette-Guerin (BCG); most of the diphtheria, pertussis, and tetanus (DTP) and polio vaccine series, and at least one dose of measles vaccine [37]. More sporadic coverage was noted with the administration of the second measles vaccine, hepatitis B in the newborn period, the third DTP, and use of the pneumococcal vaccine, particularly in the African and Eastern Mediterranean regions that have the highest concentrations of active conflict zones.

The report also noted that countries impacted by active conflict are less likely to possess the infrastructure to accurately track vaccine administration, and often lack external surveillance systems. In regions of prolonged conflict, unusual epidemiologic patterns of childhood diseases have been noted. For example, Iraq has been plagued by conflict for nearly 40 years: the Iran-Iraq war of the 1980s, followed by the 1990–1991 Gulf War, a decade-long course of sanctions, the USA’s invasion in mid-2003, followed by a protracted civil war. Conflict increased during the 2007–2008 “Surge” of military activity, and a subsequent reduction of conflict led to the removal of most US forces by 2011. Conflict returned, however, in 2014 through 2017, with the establishment and subsequent reduction of the Islamic State in the north and western regions. A recent report summarizes the reported incidence data for 32 communicable diseases, gathered by the Iraqi Ministry of Health, from 2004 through 2016 [26]. Despite nearly 30 years of conflict, rates of the most common vaccine-preventable diseases were relatively stable for measles, mumps, polio, and tetanus, while rates for neonatal tetanus, diphtheria, pertussis, and rubella

Table 1 Lessons learned from recent conflicts

Region	Conflict/years	Affected populations	Infectious disease outbreaks and lessons learned	References
Global	137 low/medium-intensity, conflicts 1990 to 2017	3.8 million mothers; 1.1 million children < 5 years in ecological survey	-Conflict countries have higher maternal/child mortality rates, despite all improvements within past 3 decades; poorer, less educated, and more rural families suffered much worse—lower DPT, MMR, and care for illness	Akseer et al. [8]
	193 country analysis from 1990 to 2017	Analysis—Uppsala Conflict Database and Global Burden of Disease Study, 2017	-1118 unique armed conflicts reviewed, “all cause” mortality strikingly increased in children < 5, #1 etiology was communicable diseases	Jawad et al. [5•]
	36 studies of ARI in crises from 1980 to 2009	Armed conflicts, forced displacement, nat. disasters, and nutritional emergencies	-30 million conflict-related deaths, 2/3 indirect and in women and children	Bellos et al. [9]
Europe (asylum seekers)	African and Eastern Mediterranean asylum seekers (peaked in 2015)	Records review from asylum seekers—Germany	-69% of crises reviewed were caused by armed conflict	
		Serum from young asylum seekers—Netherlands	-ARI/AURI #1 or 2 cause of morbidity and mortality	van den Heuvel and Stammitz [10]
		Antimicrobial resistance, 23 studies of recent migrants	-Deaths under age 5 nearly doubled in populations in crises	
Europe	Mostar, Bosnia—1993 to 2003	Bosnian Civil War, compared to 10 years later	-Only 67% children 1 to 4 years had documented measles immunizations	Freidl et al. [11]
			-High rate of “voluntary refusal,” reported by 21% of the non-vaccinated	
			-Specific gaps in immunity to diphtheria, hepatitis A, hepatitis B	
			-Measles seroprevalence lower in adults under 25 years of age	
			-Pooled prevalence of AMR carriage or infection of 25.4%, up to 33% in high migrant communities; predominantly MRSA and AMR GNRS	Nellums et al. [12]
			-Higher rates of tonsillitis and pharyngitis during conflict than afterwards	Jelicic et al. [13]
			-Higher rates of ARI in young infants during conflict than afterwards	
Africa	DRC 2018–2020	2nd prolonged Ebola outbreak, in Eastern Congo	-Ebola erupted in conflict regions in the DRC= 3481 cases (66% fatal)	Ebola virus disease - DRC [14]
			-Diminished after NGO’s immunized 303,000 with rVSV-ZEBOV-GP	
			-Est. 300,000 Excess deaths, 2.7 million displaced (most post-conflict)	Degomme 2010 Boutayeb 2019 NY Times 2021 [15, 16, 17]
			-Over 80% of excess deaths not due to violence	
			-Diarrhea related deaths <5yo significantly increased in 3 years post-conflict	
			-Infant mortality rates up to 3-fold higher in conflict regions(0 years later	
			-Measles vaccination dropped to 41% in 2004;	
			rebound to 80% by 2015	Tsai et al. [18]
			-Under 6 mortality 6th highest in 1999, improved to 28th post-conflict	
			-By 2013, #1 cause of death was malaria, #2 pneumonia	

Table 1 (continued)

Region	Conflict/years	Affected populations	Infectious disease outbreaks and lessons learned	References
Eastern Mediterranean region	Operation Pillar Israeli-Palestinian Nov 2012–Feb 13	7420 pediatric patients in a Moroccan military hospital (19.9% of all seen)	37% Respiratory issues with 67% ILI; plus a small mumps outbreak 23% GI with 19% diarrhea, 48% intestinal helminth complaints -High coliform counts in local well water used by displaced people	Elyajouri et al. [19]
	Yemeni Civil War 2014–current	Sept 2016 July 2018 > 1,000,000 cases of cholera	-Challenges to control include sanitation/hygiene, surveillance, case management, vaccination, and coordination of all resources	Spiegel et al. [20]
	Syrian Civil War 2011–present	Report on 2.7 million displaced Syrians in Turkey >200,000 Syrians killed, ½ of population displaced Experience of the Galilee Medical Center 2013–2016	-Re-emergence of measles, polio, leishmaniasis, MDR-TB, MDR-Gram-negative organisms, hepatitis A, malaria, and varicella -Rising measles, polio, leishmaniasis, diarrhea, hepatitis A, typhoid, TB -Cutaneous leishmaniasis rising in adjacent Turkey, Lebanon, & Jordan -83% MDR carriage from 128 children screened: 78% ESBL, 9% CRE, 7% MDR <i>A. baumannii</i> , 5% MRSA, 3% VRE; 19% eventually developed MDR UTI, osteomyelitis, or surgical infections; 58% correlated with screening	Doganay and Demiraslan [21] Ozars et al. [22] Kassem et al. [23]
		Impact of Syrian Civil War on its own population and on neighboring Jordan	-6.6 M internally displaced; 4.8 million Syrians fled to Lebanon, Turkey, Egypt, Iran, and Jordan; 57% Syrian public hospitals destroyed -rise in polio, measles, TB, 40% inc. of TB in Jordanians near Syria	Nimer [24]
	Iraq, Syria, South Sudan, Yemen	Continual conflict leading to regional instability and internal and external population displacement	-Measles outbreaks in every region, Iraq in 2007–2009, S. Sudan 2015–2017 -Cholera emerged to a moderate degree (close to 20,000 cases) in South Sudan 2014–16 leading to a large immunization campaign in 2014 -Massive outbreak of cholera in Yemen from 2016 through 2017 -Polio briefly seen in Iraq in 2013, possibly spillover from Syria -Wild-type polio in Syria emerged in 2013 (strains similar to Pakistan) resulting in extensive immunization of nearly 25 million region children, but difficulties reaching besieged/occupied regions	Raslan et al. [25]
	Iraq	32 comm. diseases reported to Iraq MOH, 2004 to 2014	-Rise of all communicable diseases during the surge in late 2007 to 2009 -Measles in 2009, mumps in 2004, 2016, rubella in 2004; cholera in 2008	Zhao et al. [26]

Table 2 Factors increasing infectious disease outbreaks in children

Category	Commonly identified outbreaks	Factors increasing occurrence in conflict regions
Vaccine-preventable diseases	Tetanus, diphtheria, polio, pertussis, measles, mumps, varicella, <i>Haemophilus influenzae</i> type B (Hib), meningococcus, pneumococcus, hepatitis B, rotavirus, TB	Missed/delayed pediatric immunizations Loss of maternal immunizations Difficulty tracking/recording immunization delivery
Environmental conditions	Acute respiratory illnesses (including COVID-19), diarrhea illnesses (cholera, others), skin conditions	Crowding, poor hygiene/sanitation, lack of clean food and water, inadequate nutrition
Underlying regional diseases	Vector-borne parasites (malaria, leishmaniasis), vector-borne viruses, other parasitic diseases	Inadequate shelter, degraded vector control, lack of clean food and water for consumption and hygiene
Diseases exacerbated by exploitation	HIV, STIs	Extreme poverty, loss of security/sexual violence, reversion to outdated practices, loss of women's rights

decreased slightly during this period. Overall, however, rates of all communicable diseases increased significantly during periods of increased conflict, especially during 2007–2008 intensification of combat activity during the “Surge.” Of interest, select outbreaks occurred, including mumps and rubella in 2004; a regional measles outbreak and a small cholera outbreak in mid-2008; and mumps again in 2016. All these outbreaks correlated with periods after intensification of conflict [26•]. In response to the lessons learned by emergence of vaccine-preventable diseases in recent conflicts, the WHO developed a strategic plan in 2013 entitled, “Vaccination in Acute Humanitarian Emergencies: A Framework for Decision Making.” In the WHO strategic plan, a three-step process is proposed: epidemiologic assessment of the risk of vaccine-preventable diseases (VPDs); followed by a consideration of the supply and feasibility of vaccine delivery; and finally a realistic review of impediments as well as facilitators of vaccine delivery programs, including security, staffing, funding, and formation of partnerships and consensus among stakeholders [35•].

Prominent VPDs Associated with Armed Conflicts

A brief discussion of some of the most important vaccine-preventable diseases that have emerged during recent conflicts follows. These are also referenced in Table 1, which highlights specific regional conflicts.

Measles

The emergence of measles (rubeola) often reflects the degree of disruption that occurs in a population during a large-scale or prolonged conflict. The combination of its high infectivity (R_0 of 12–18) with crowded conditions, delayed immunizations, and malnutrition in disrupted or displaced populations makes measles one of the perennial challenges for children caught in regions of armed conflict [38]. In regions with high birth rates, it only takes months for a population group

without routine immunizations to decrease the percentage of people with protective immunity below the threshold needed to ensure herd immunity. This is well-described by a recent review, which discusses the risks presented by the dangerously low rates of first vaccine coverage (well below the ideal high 80%) in many regions of conflict [34]. Afghanistan, the Central African Republic, South Sudan, Somalia, and portions of Syria and Yemen are well below 70%. As noted above, in a separate and more detailed study of the measles epidemiology from 2005 to 2010 in Iraq, a substantial regional outbreak occurred in the central and southern regions outside the major city, concomitant with and after the USA’s “Surge” in 2008 [27]. Additionally, the observed measles vaccine failure was high (66%), which the authors proposed it might be related to the well-known difficulties in vaccine handling, administration, and keeping the vaccine stable (cold chain), all of which are more challenging when public health infrastructure is under the duress of conflict. A recent update shows a rebound in coverage up to 83% for 2018, indicating that such problems, once identified, can be addressed quickly [34]. To further highlight this threat, on September 20, 2021, the USA confirmed 16 cases of measles and 4 cases of mumps in Afghan nationals and US citizens being resettled from Afghanistan. This displaced population was being housed in “Safe Haven” locations awaiting permanent relocation to the USA and other coalition countries. It is estimated that the vaccine rate for measles in Afghanistan is 60% [39].

Polio

Truly, heroic efforts in surveillance and resources for immunizations have been expended to eliminate wild-type polio worldwide, with five of six WHO regions being declared wild polio virus (WPV)–free by August of 2020 [40]. Unfortunately, both wild-type polio and vaccine-derived polio viral isolates continue to circulate in under-immunized regions of the world, especially in those areas with long-

standing low-to-medium-intensity conflicts. A recent WHO update [41] highlights the continuing difficulty in controlling wild polio (WPV1) spreading between Pakistan and Afghanistan. This problem has been compounded by local vaccination bans enforced by the Taliban and other militant groups, and recently hampered further by COVID-19 restrictions of personal movement. A significant concern is the continued spread of vaccine-derived polio virus (cVDPV2), even after the removal of poliovirus type 2 from the international oral vaccine in 2016. This vaccine-derived poliovirus has continued to spread in many regions of low-intensity conflict in Central and North Africa and the Middle East, including Afghanistan and Pakistan, and regions of Iran and Tajikistan [41]. The spread of this virus will be combatted by regional immunization with a novel oral polio vaccine strain against type 2 (nOPV2). COVID-19 travel restrictions may temporarily limit the spread of cVDPV2, due to decreased population movements, but also thwarts the implementation of immunization programs throughout the affected regions.

Diphtheria

While less common in nations with intact long-term immunization programs, prolonged conflict and loss of infrastructure facilitate the emergence of diphtheria in a population. After a surge of over 157,000 cases and 5000 deaths which occurred in former Soviet Republics in the early 1990s, cases abated, and disease was more sporadic [42]. A summary of the recent epidemiology of diphtheria (using WHO and UNICEF data) reports that from 2016 to 2019, diphtheria has re-emerged significantly in several countries. In 2017 alone, 8819 cases of diphtheria were reported worldwide, a near doubling from rates seen between 2006 and 2013 [42]. Countries with recent specific outbreaks include Bangladesh, which has absorbed nearly a million Rohingya refugees from Myanmar; Yemen, which has been engaged in a brutal civil war since 2014; and Venezuela, whose health system has been in a state of collapse for nearly a decade. In this study, countries with diphtheria sorted into two groups. The first included those with high numbers, where the majority of cases occur in unimmunized individuals who were largely under 15 years of age. In the second group, countries with only sporadic diphtheria usually had better immunization rates, and cases occurred more often in individuals with partial immunization, who were often over the age of 15 [42]. This observation indicates that waning immunity is a serious problem, which led the WHO in 2017 to recommend following the primary three-shot immunization series, with an additional three immunizations with a diphtheria toxin-containing vaccine, at 12–23 months, 4–7 years, and 9–15 years of age [43].

Tetanus/Pertussis

The WHO and UNICEF data indicate good progress in increasing the administration of the third dose of DPT, from 72 to 86% globally in 2016 [44]. In the Middle East and North Africa regions, however, current data estimates that 1.3 million young children miss at least DPT3, and that 88% of these under-immunized children reside in Syria, Yemen, Iraq, Egypt, and Sudan, all regions that have had prolonged internal conflicts. Syria's rate was estimated to be the lowest, at 42% in 2016 [44]. In addition, many of these war-torn nations face extreme inequity in vaccine distribution, with lower rates for internal marginalized populations, ranging from those unaccounted for in urban slums, to nomadic populations. The authors of one detailed review of this region propose combatting these trends by “(1) identifying and accounting for displaced, mobile and neglected populations; (2) assessing and addressing missed opportunities for vaccination, including by expanding immunization into the second year of life and beyond; and (3) engaging effectively with the private/non-governmental health providers in the coordination, provision, and reporting of immunization services.” [44].

Varicella

Varicella (VZV) is often considered a milder illness, with less morbidity and rarer mortality. Despite the 1998 WHO recommendation that vaccine programs be implemented in regions where VZV is “a significant public health burden,” other more serious infectious diseases such as wild-type polio, neonatal tetanus, and measles have received higher priority in regional vaccine action plans [45]. Frequently, populations are left to develop this disease as a “normal” childhood experience. The more severe systemic disease in adults, however, coupled with the wide variety in rates of protection, can result in VZV having a significant impact after conflict-related degradations in local systems. The clinical epidemiology of primary VZV (chickenpox) in Iraq was described using surveillance data from primary health care centers from 2007 to 2011 [46]. During this period, a dramatic increase in the incidence occurred, rising from 75 cases per 100,000 in 2007, to 187 cases in 2008, peaking at 222 cases in 2011. Although this increase paralleled other rises in VPDs as noted above, widespread immunization against VZV was not implemented at this time [26•]. Over 65% of cases occurred in children 5 to 14 years of age, with only a 1% occurring over age 45. Because these cases were documented during the expected March to June seasonal peaks, it appeared that the disease was following some of the natural patterns seen in non-immunized populations.

Diseases Due to Collapse of Clean Food, Water, Shelter, and Hygiene

Respiratory Disease Outbreaks

Other than for the COVID-19 pandemic, respiratory illnesses are generally monitored in a population by tracking the overall burden of acute upper and lower (AURI/ALRI) respiratory infections, due to the variety and difficulty in identifying specific pathogens in austere environments. In a systematic global review of the burden of ARI related to conflict, the results of 36 studies were gathered from the last nearly 40 years (with 69% performed in populations affected by armed conflict), to derive some broad conclusions about the impact of respiratory disease in “crisis-affected populations.” [9] As noted in Table 1, deaths under the age 5 can nearly double in populations in crises (though accurate comparison baseline rates can be hard to determine), and acute respiratory illnesses are the first or second most common cause of morbidity and mortality across all ages, though greatest in the first year of life.

COVID-19 (SARS-CoV-2)

At the time of this writing, the global pandemic due to the coronavirus commonly referred to as COVID-19 remains the world’s most challenging problem. Well-resourced nations are making substantial progress in immunizing their populations, to hopefully to reduce the burden of disease within their confines, though the emergence of variants may make that strategy more complex than initially anticipated. Plans to protect the globe’s most vulnerable populations are still evolving. In the early phase of the pandemic, serious disease was uncommon in children, except for the relatively rare multisystem inflammatory syndrome (MIS-C), though the later emergence of new variants resulted in higher rates of severe disease in children. The emergence of the delta variant in the USA in the summer of 2021 led to a significant increase in hospitalizations in children and adolescents, and may predict a greater impact as new circulating viruses emerge [47].

Since public health measures for the prior year have included avoiding close contact with non-familial members, heightened personal protection, and scrupulous hygiene, one can easily surmise the level of transmissibility of this virus that would exist in crowded camps of persons displaced by conflict. Effective pandemic control requires state-of-the-art viral diagnostic testing, as well as the ability to rapidly expand intensive care treatment with isolated intensive care unit beds, which need to be served by adequate numbers of well-protected

frontline professionals, a significant challenge in resource-constrained environments.

One of the most dramatic examples has been in the experience of the Rohingya people, who have been displaced in great numbers by the very active internal conflict in Myanmar since 2016. Nearly 900,000 Rohingya people have been displaced into neighboring Bangladesh in the region known as Cox’s Bazaar, creating one of the largest series of refugee camps in the world [30]. An outbreak of COVID-19, which began in April of 2020, initially resulted in nearly 400 documented cases among the refugees, while the host community had over 5500. Heroic efforts have established and maintained testing capabilities, and adequate advanced hospital care, resulting in encouragingly low mortality rates. The country of Bangladesh has partnered with the WHO to implement a vaccination plan for both host citizens and refugees, and large-scale vaccination of higher risk refugees began in earnest in August of 2021 [48].

Diarrheal Diseases

The control of food and waterborne illnesses, especially diarrheal pathogens, faces challenges similar to those reported for respiratory diseases. Traditionally, diarrhea is often only second to respiratory illness in morbidity and mortality in young children in crisis situations. Reasons include several factors such as water cleanliness, hygiene, and sewage handling in crowded displaced populations, as well as the nutritional status of young children [3]. One disease that is specifically identified and tracked, due to its huge impact on displaced populations, is cholera. The majority of the population of Yemen has been displaced due to its civil war, and a resulting massive outbreak of cholera occurred that may have infected over 1 million people between 2016 and 2018 [20]. An interesting analysis of national surveillance data from the Yemeni outbreak showed a significant correlation between regional rates of casualties (conflict-related injuries and death) and the number of cholera cases in that region, suggesting a direct relationship between intensity of armed conflict and local cholera activity [49]. During the prolonged conflict in the Darfur region of Sudan, diarrhea-related illness was a major contributor to excess mortality in children under 5 years of age, both during the initial conflict period and for years afterwards [15]. The prolonged disruptions in that country are reflected by a persisting inequity in infant mortality rates, which were three times higher in conflict regions than in more stable portions of that country, a full 10 years after reduction of the most intense armed conflict [16].

Vector-Borne/Regional Tropical Diseases

Many of the rapidly developing but low-resource countries that suffer from conflict are also located in regions where common “tropical” diseases are endemic. In these areas, due to a degradation of housing and the loss of regional vector control, such diseases have exploded. Several countries in the Eastern Mediterranean Region have seen higher rates of cutaneous leishmaniasis in children, particularly in Syria with the massive displacement of people and destruction of housing [21, 22]. Intestinal helminthic diseases were noted as a common pediatric complaint in a Moroccan hospital supporting families impacted by the brief 2012 Israeli-Palestinian conflict Operation Pillar [19]. It is estimated that over 400,000 cases of malaria occurred in Venezuela in 2017 alone [31]. The increased burden for these endemic tropical diseases highlights the indirect and long-term impact that conflict has on the general health of the local populations.

Diseases of Exploitation—Human Immunodeficiency Virus and Sexually Transmitted Infections

Armed conflict is frequently associated with sexual exploitation, with the combined loss of societal structure and security protection for civilian populations; unfortunately, children are not protected from these consequences. A recent example is presented in a review of 720 reports of child abuse obtained from one of the more active conflict regions during the immediate aftermath of the protracted civil war in Sri Lanka, from 1983–2009. Over 4000 incidents of abuse were reported between 2009 and 2014, with 83% of events sexual in nature, mostly committed against young females. Recorded abuses included high rates of attacks from known contacts, plus a large number children forced into marriage [29]. A significant number of unintended pregnancies were noted, but very little human immunodeficiency virus (HIV) or sexually transmitted infections (STIs) were reported.

The Eastern and Central Democratic Republic of Congo has seen nearly 30 years of warfare, with millions of deaths and great internal displacement. The ensuing extreme poverty and infrastructure breakdown has contributed to HIV rates that are among the highest in Africa. Multiple social studies reveal that young women are forced into transactional sex work to survive, with little access to health care to protect them from STIs in general, and HIV in particular [50, 51]. Although the association of HIV with combat has been studied in detail, a linear relationship with conflict may not be easily delineated. A review of 12 studies performed between 1990 and 2010 in diverse conflict regions tried to identify common factors placing women and children at risk for HIV acquisition [52]. These included population displacement, outbreaks of sexual violence as

both a weapon of conflict, and concomitant chaos, and the victimization of young women. The concurrent breakdown in public health systems leaves few resources to mitigate the risk of HIV, especially in regions of higher prevalence. More recent complex epidemiologic modeling suggests that assuming a direct relationship between armed conflict and HIV may be an oversimplification [53]. The conclusion of their findings is that it may be more appropriate to recognize that populations in conflict-affected states with pre-existing HIV burdens are particularly more vulnerable to other stressors, such as natural disasters that can greatly exacerbate the negative impact of HIV disability-adjusted life years (DALYs).

Conclusions

This first of two articles has reviewed how armed conflicts in the modern era adversely impact the health of many of the world’s children, largely through population displacement. Such disruption severely limits the availability of basic human necessities, including nutrition, shelter, hygiene, clean water, security, livelihoods, and family support. The loss of these essential needs facilitates outbreaks of common childhood respiratory infections and diarrheal illnesses such as cholera, as well as the resurgence of local endemic diseases, such as malaria and cutaneous leishmaniasis. Prolonged disruptions in immunization programs can eventually lead to outbreaks of measles, diphtheria, tetanus, and other vaccine-preventable diseases. The second article, entitled “Infectious Diseases Complications in the Individual Pediatric Patient” will focus on the types of personal injuries seen in children in areas undergoing armed conflict, the resulting infectious disease complications, and some of the recent evidence predicting mortality from modern complex injuries and their complications. There also will be a brief discussion of approaches to mitigating and managing the infectious complications of combat injuries in children.

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