Neglected Tropical Diseases

Mary Ann McDowell Sima Rafati *Editors*

Neglected Tropical Diseases — Middle East and North Africa



Neglected Tropical Diseases

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Neglected Tropical Diseases - Middle East and North Africa



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Human beings are members of a whole, In creation of one essence and soul. If one member is afflicted with pain, Other members uneasy will remain. If you've no sympathy for human pain, The name of human you cannot retain. Saadi Shirazi 1210–1291

بنی آدم اعضای یکدیگرند که در آفرینش زیک گوهرند چو عضوی به درد آورد روزگار دگر عضوها را نماند قرار تو کز محنت دیگران بی غمی نشاید که نامت نهند آدمی

Preface

The Neglected Tropical Diseases (NTDs) are a group of 17 viral, bacterial, protozoan, and helminth infections that disproportionately affect the most vulnerable populations. The concept of NTDs begun to take shape following the 2000 Millennium Development Goals put forth by the United Nations, specifically Goal # 6 to combat HIV/AIDs, malaria, and other diseases. Although the "other diseases" category spurred substantial debate, it is now accepted that the 17 diseases classified as NTDs by the World Health Organization (WHO) represent some of this "other" category. Compared to HIV/AIDs, malaria, and tuberculosis at 42.1 %, NTDs have generally been ignored (i.e., neglected), receiving only 0.6 % of official assistance for health (Liese and Schubert 2009). These diseases do not cause substantial global mortality; however, morbidity can rival HIV/AIDs and malaria (Murray et al. 2012; Vos et al. 2012). Importantly, NTDs are some of the most common diseases on the globe, thrive in impoverished regions, and perpetuate the cycle of poverty, causing mental impairment in children and hindering socioeconomic development.

The Middle East and North Africa (MENA) is highly endemic for several NTDs. This region is economically diverse, encompassing both oil-rich and resource-poor nations. 340 million people live in the region, of which 12 % (~50 million) live on less than \$2 per day (World Bank 2010). While global efforts to eliminate some NTDs have been successful in MENA countries, many have not received such attention. Soil-transmitted helminth infections are the most prevalent NTDs in the MENA; however, modifications in human behavior, recent environmental changes, and political turmoil have increased the risk for many others. The present volume, Neglected Tropical Diseases in the Middle East and North Africa, covers the most prevalent NTDs in the MENA region, including chapters on dengue virus, rabies, brucellosis, leprosy, trachoma, toxoplasmosis, cutaneous and visceral leishmaniasis, fascioliasis, schistosomiasis, and soil-transmitted helminth infections. The authors of individual chapters are experts in their respective fields, either MENAendemic scientists or non-endemic researchers with an intimate knowledge of these diseases in the MENA region. This book emphasizes disease burden, clinical manifestation, and current control approaches and outlines the major obstacles for viii Preface

reducing the burden of NTDs in the MENA. In most cases, social determinants, including human migration, political instability, urbanization, and agricultural practices, are all drivers in preventing control of these devastating diseases. In particular, the recent political landscape in the region has had devastating impacts on public health management leading to a breakdown in control efforts and an increase in outbreaks. Increased surveillance efforts, including advanced training, improved diagnosis methods, and mandatory reporting, are needed for most of the NTDs in the region. Successful strategies to combat the burden of NTDs will undoubtedly require strong political commitment and intimate international collaboration involving research, policy, and veterinary and human health implementation sectors.

The hope is that this volume will stimulate increased awareness and commitment from research institutions, funding agencies, and governments to eliminating the devastation caused by NTDs in the MENA region. Ultimately, we desire strengthened cooperative efforts of all the MENA nations for controlling the burden of NTDs and international commitment to stabilize the political situation in the region.

We express our deep appreciation to the editorial staff of SpringerVerlag, in particular Claudia Panuschka and Ursula Gramm, for their organization and editorial expertise. We also are thankful to Dr. Peter Hotez for the opportunity to contribute to such an important project. Finally, we are extremely grateful to all the contributing authors for their valuable contributions, cooperation, and patience to this project. We value their time and insight.

It is with our deepest regret that one author, Professor Rashida Barakat, passed from this world before this project came to fruition. Her contribution to this volume and her tireless efforts towards schistosomiasis control in Egypt will be forever remembered. It is to this distinguished scholar and mentor that we dedicate this book.

Notre Dame, IN, USA Tehran, Iran Mary Ann McDowell Sima Rafati

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Soil-Transmitted Helminth (STH) Infections in the MENA Region

Mohammad Bagher Rokni, Wael M. Lotfy, Peter J. Hotez, and Nilanthi R. de Silva

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Abstract Soil-transmitted helminths (STHs), or geohelminths, including Ascaris lumbricoides, Trichuris trichiura, Ancylostoma duodenale, Necator americanus, and Strongyloides stercoralis are a group of intestinal nematode parasites transmitted through contaminated soil, vegetables, and water. STH infections are leading neglected tropical diseases that affect the Middle East and North Africa (MENA) region. To conduct this review, publication databases related to STHs in the MENA countries were surveyed. Search engines utilized were PUBMED, SCIRUS, GOO-GLE SCHOLAR, IMEMR, The Global Atlas of Helminth Infections, and local sources. Overall the MENA region accounts for less than 10 % of the global number of cases of STH infection. Results show that ascariasis has the lowest rate of infection as 0.02 % in Oman and 56 % as the highest rate in the Palestinian Territories. More than 20 million infections with ascariasis are in the MENA region. As for trichuriasis, a range of 0 % infection in Lebanon to 45 % infection in Somalia was found; overall about seven infections are in the MENA region. For hookworm infection, five to ten million infections are in the MENA region with infection rates ranging between 0 % in Algeria and 50 % in Kuwait (50 %). Minimal data for strongyloidiasis were available, but the estimates range from 0.0 % in Algeria to 15.5 % in the Palestinian Territories. Overall, anthelminthic drug coverage through periodic deworming is extremely low in the MENA region. Here we describe various risk factors in transmission of STHs in the region and report the prevalence of contamination of vegetables with the parasites' eggs. Moreover, different aspects of clinical manifestations, control, prevention, and treatment will be discussed.

Keywords Soil-transmitted helminths • MENA region • Helminths • Prevalence

Background

Soil-transmitted helminths (STHs), also called geohelminths, are a group of intestinal nematode parasites transmitted primarily through contaminated soil, vegetable, and water. They exhibit direct life cycles that require no intermediate hosts or vectors. The soil provides conditions under which development of unembryonated eggs to the infective stage can take place, with human infection occurring through ingestion of eggs (Ascaris lumbricoides, Trichuris trichiura) or larvae (Ancylostoma duodenale) or through direct larval penetration (Necator americanus, Ancylostoma duodenale, Strongyloides stercoralis. The STHs together represent

Diseases	Population at risk (millions)	People infected (millions)	People with morbidity (millions)	Deaths (thousands)	DALYs (thousands)
Hookworm infection	3195	576–740	150	0 –65	3,231
Ascariasis	4211	807– 1,221	350	3–60	1,315
Trichuriasis	3212	604-795	220	0–10	638
Strongyloidiasis		30-100	Not determined	Not	Not
	determined			determined	determined

Table 1 Global disease burden of soil-transmitted helminths modified from Murray et al. (2013), Lozano et al. (2013), and Fürst et al. (2012)

the most common parasitic infections of humans worldwide. They have particular public health relevance because of significant child morbidities (WHO 2002, 2012). The extraordinary numbers of STH infections, which approach two billions, are a reflection of a remarkably successful adaptation to survival of the eggs or larval stages in the environment and parasitism in humans lasting years (de Silva et al. 2003). They present an enormous global disease burden, resulting in more than five million disability adjusted life years lost annually according to a new Global Burden of Disease 2010 Study (Murray et al. 2013), with ascariasis also causing a significant number of deaths in young children (Lozano et al. 2013). Moreover, STH infections are regarded as one of the world's leading causes of intellectual and physical growth deficits and disabilities (Bethony et al. 2006).

In the MENA region the STHs disproportionately affect the estimated 65 million people living on less than \$2 per day (Hotez et al. 2012). The basis by which poverty promotes endemicity of STH infections has not been well studied in the MENA region, although presumably this situation reflects high rates of inadequate sanitation and access to clean water especially in impoverished rural and some urban areas. In 2003, de Silva et al. estimated that the MENA area harbor about 23 million cases of ascariasis which constitute about 2 % of the global disease burden, 7 million cases of trichuriasis which equals about 1 % of the global burden, and 10 million cases of hookworm infections which equals about 1 % of the global burden (de Silva et al. 2003), numbers that were modified in Hotez et al. (Hotez et al. 2012). The World Health Organization (WHO) estimates that approximately 9 % of children at risk for STH infections live in its Eastern Mediterranean Region (WHO 2013). The most updated data in Table 1 depict various features of STHs.

The MENA Region

According to World Bank, the MENA region includes countries of the Middle East and North Africa: Middle East: Afghanistan, Bahrain, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Pakistan, Qatar, Saudi Arabia, Syria, United Arab

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Emirates, West Bank and Gaza; North Africa: Algeria, Djibouti, Egypt, Libya, Malta, Morocco, Somalia, Sudan, Tunisia, and Yemen. Almost 400 million people, approximately 5 % of the world's population, live in the MENA region, led by Egypt (80 million), Iran (75 million), Algeria (36 million), and Morocco and Iraq (31–32 million each) as the most populated countries (Hotez et al. 2012).

Methodology

For this review, publication databases related to STHS in the MENA countries were surveyed. Search engines utilized were PUBMED, SCIRUS, GOOGLE SCHOLAR, IMEMR, Global Atlas of Helminth Infections (GAHI), and local sources. Database searches were not restricted by date. In addition to full text papers, abstracts were also reviewed. The panel of key words utilized was "Ascaris lumbricoides," "Trichuris trichiura," "Strongyloides stercoralis," "Necator americanus," "Ancylostoma duodenale," "Hook worms," and related terminology of diseases, e.g., ascariasis. In addition to papers in English, papers published in other languages such as French, Persian, and Arabic were considered as well.

Ascaris lumbricoides Linnaeus, 1758

Etiology, Life Cycle, and Major Clinical Manifestations

Ascaris lumbricoides, is one of the leading infectious agents of humans affecting up to one billion or more (Holland 2009). The Egyptian medical papyri documented human infection of *As. lumbricoides* since the time of pharaohs (Grove 1990; Hoeppli 1959). This worm is possibly the earliest recorded human helminths; it is referred to in texts from Mesopotamia, Greece, Rome, and China.

Humans acquire *As. lumbricoides* via ingestion of embryonated eggs in both rural and some impoverished urban environments. The eggs are almost ubiquitous in the soil of poor environments and they tenaciously adhere to inert substances. After ingestion, the liberated larvae migrate from the intestine through the liver, heart, and lungs where they cause wheezing and Loeffler's pneumonitis, which clinically resembles asthma. Indeed in Saudi Arabia seasonal asthma has been linked to endemic *As. lumbricoides* infection (Gelpi and Mustafa 1967). After *As. lumbricoides* larvae return to the gut they develop into adult worms, typically in the jejunum and ileum where they can grow to 15–40 cm in length. The adult worms result in vitamin A malabsorption and other malnutrition syndromes that result in growth stunting and cognitive deficits. Adult worms in the ileum of small children can cause acute intestinal obstruction, which can result in an estimated 2,700 deaths annually (Lozano et al. 2013).

Prevalence of Ascariasis in the MENA Region

Table 2 illustrates the prevalences of STHs including ascariasis in different countries of the MENA region. Accordingly, the lowest rate of infection was shown in Oman as 0.02~% and the highest rate in Palestine with 56~% infection.

Studies conducted by (de Silva et al. 2003) estimated that the MENA region had about 23 million infections with ascariasis, accounting for approximately 2–3 % of the global estimates of disease burden. Ascariasis may represent the most common neglected tropical disease in the MENA region. Among the MENA countries, Egypt leads in the number of cases of ascariasis with about 8.3 million infections. Yemen is the country with the second highest number of infections (5.8 million infections), followed by Iran with 5.1 million infections, and Morocco with 1.3 million infections (Hotez et al. 2012). In Egypt, the prevalence of ascariasis in Lower Egypt was higher than in Upper Egypt (El-Gammal et al. 1995). Recent studies in either Upper or Lower Egypt showed discrepancies in prevalence rates in different samples and localities (Bakr et al. 2009; El-Masry et al. 2007; El-Nofely and Shaalan 1999; El-Sahn et al. 1997; Hamed et al. 2013; Ibrahium 2011; Mahfouz et al. 1997; Mohammad et al. 2012).

In Yemen *As. lumbricoides* has been reported as 0.42–15.9 % (Baswaid 2008; Nasher 1988). In Oman during 1994–1998 ascariasis has been reported from 0.02 to 1.1 % (Ibrahium 2011). A study in Lebanon during two periods of 1997–1998 and 2007–2008 shows that although the rate of infection has decreased, the risk of infection still persists (Table 2) (Araj et al. 2011). In Algeria, from 1,042 individuals examined, 0.4 % were infected with ascariasis (Benouis et al. 2013).

In Libya, in primary schoolchildren among 1,039 stool specimens, *As. lumbricoides* was detected in 0.1 % of cases (Sadaga and Kassem 2007). From 126 samples of fresh vegetables, 85 (86 %) cases were contaminated with *Ascaris* eggs (Abougrain et al. 2010).

Trichuris trichiura (Linnaeus, 1771) Stiles, 1901

Etiology, Life Cycle, and Major Clinical Manifestations

Tr. trichiura or **Trichocephalus** trichiura is commonly known as whipworm because of its characteristic morphology. The ecological and environmental requirements of Tr. trichiura eggs are similar to those of As. lumbricoides. After egg ingestion the Tr. trichiura larvae migrate to the cecum and ascending colon where they develop to adult worms approximately 3–5 cm in length. In cases of moderate and heavy infections, the host's inflammatory response to adult whipworms results in Trichuris colitis, which resembles inflammatory bowel disease. In very heavy infections (more than 500 worms), worms spread throughout the colon to the rectum, where they cause hemorrhages, mucopurulent stools, symptoms of dysentery (Trichuris dysentery syndrome) with rectal prolapse.

Table 2 Summary of published reports on prevalence of STHs in countries of the MENA region

			II				Year of	
Country	AL (%)	AL (%) SS (%)	(%)	HW (%)	HW (%) Kind of study	Subjects (No.)	study	Reference
Afghanistan	40.9	1	6.6	0.7	CBS	Schoolchildren (1,001)	2003	Gabrielli et al. (2005)
Algeria	0.4	1	1	ı	HBS	All (1,042)	1010-1011	Benouis et al. (2013)
Algeria	1.4	0.0	ı	0.0	CBS	All (11,601)	1984–1988	Bachta et al. (1990)
Iran	1.5	1	0.1	<0.1	CBS	All (53,995)	1999–2000	Sayyari et al. (2005)
Iran	0.57	0.5	ı	ı	CBS	Food handlers (62,007)	2000–2009	Saki et al. (2012)
Israel	20.3	4.5	19.2	54.2	CBS	Ethiopian immigrants (5,412)	1990	Nahmias et al. (1991)
Jordan	4.9	1	1.1	2.5	CBS	Food handlers (283)	1990	al-Lahham et al. (1990)
Kuwait	5.0	2.0	28	50	HBS	Housemaids (100)	ı	Grover et al. (2008)
Lebanon	2.0	0.1	0.2	0.05	HBS	(14771)	1997–1998	Araj et al. (2011)
Lebanon	1.0	0.5	0.0	0.1	HBS	(7,477)	2007–2008	Araj et al. (2011)
Morocco	13.3	ı	13.3	ı	CBS	Children (610)	ı	Amahmid and Bouhoum
								(2005)
Oman	0.02-	1	0.2	I	CBS	School children (2,213)	1994–1998	Idris et al. (2001)
Pakistan	22.8	1	(2.5)	ı	HBS	All (237)	2008	Ahmed et al. (2012)
Pakistan	1.9	ı	9.0	4.6	CBS	Farmers & Textile	2002–2003	Ensink et al. (2005)
						laborers (1,704)		
Palestine	99	15.5	2.7	ı	CBS	All (1,000)	2011–2002	Al-Zain and Al-Hindi (2005)
Palestine	0.0 - 1.3	0.02-	1	0.01-	HBS	All (123,290)	2000-2009	Bdir and Adwan (2010)
		0.24		0.12				
Qatar	0.3	ı	0.5	2.1	HBS	Immigrants (9,208)	2005–2008	Abu-Madi et al. (2010)
Qatar	2.1	ı	10.8	7.9	HBS	Immigrants (1,737)	2005–2006	Abu-Madi et al. (2008)
Qatar	2.5	0.5	3.5	8.3	HBS	Immigrants (1,538)	2008	Abu-Madi et al. (2011)
Saudi Arabia	25.9	6.0	26.7	27.4	HBS	Expatriate workers (1,019)	1994	Abahussain and Abahussain (2005)

2005–2007	2006–2008	1996–2003	2004-2009	- Peltola et al. (1988) from	517 cases	I	2007 Baswaid (2008)	
All (10,	(23,278)	(63,892)	(12,054)	(517)		(60,268)	(200)	
HBS	HBS (All)	HBS (All)	HBS (All)	CBS (Children and	mothers)	HBS (Immigrants)	HBS (Restaurant	workers)
0.036	15.4	13.2	0.02	ı		2.4	1.7	
0.36	12.5	13.1	0.03	45		6.2	ı	
0.07	ı	3.0	I	ı		1	I	
99.0	15.9	12.6	0.05	17		9.9	1.7	
Saudi Arabia	Saudi Arabia	Saudi Arabia	Saudi Arabia	Somalia		United Arab Emirate	Yemen	

AL, Ascaris lumbricoides; SS, Strongyloides stercoralis; TT, Trichuris trichiura; HW, Hook worms; CBS, Community-based study; HBS, Hospital-based study

Allergic manifestations such as urticaria, rhinitis, and eosinophilia are frequently seen (Chandrasekhara et al. 2007). A significant number of patients, especially children with longstanding massive infections, have dysenteric syndrome presenting with chronic mucous diarrhea, rectal prolapse, anemia from chronic blood loss and iron deficiency, clubbing of fingers, protein-energy malnutrition, and growth retardation. Deficits in cognitive function and stunting have been observed in infected children, hindering educational achievement and psychomotor development. In rare cases the parasite may cause intussusception that mimics acute appendicitis (Alkhulaiwi et al. 1996; To et al. 2006).

Prevalence of Trichuriasis in the MENA Region (Table 2)

According to Table 2, a range of 0.0–0.2 % infection in Lebanon to 45 % infection in Somalia with this parasite has been demonstrated. *Trichuris trichiura* is the second most common roundworm of humans. In 2003, it was estimated that 800 million people were infected worldwide (de Silva et al. 2003). Approximately 7–9 million infections are in the MENA region which equals about 1 % of the global estimates (de Silva et al. 2003; Hotez et al. 2012). In this region, trichuriasis infections are highest in Morocco with about 3.2 million infections, followed by Egypt with about 1.7 million infections, then Iran with 1.6 million infections, and Yemen with 1.5 million infections (Hotez et al. 2012).

It was reported that in a slum area of Alexandria (Egypt), dwellers experienced an increase in trichuriasis (Curtale et al. 1998). This species was reported among the parasites mechanically transmitted by cockroaches and flies in Egypt (El-Sherbini and El-Sherbini 2011; El-Sherbini and Gneidy 2012).

Hookworms

Different species of the family Ancylostomatidae are commonly known as hookworms. They colonize the intestinal tract of man and other mammal hosts. Among the different known hookworms, only two species, *Ancylostoma duodenale* and *Necator americanus*, are known to have a major public health importance (de Silva et al. 2003).

Hookworms are the third most common STH of humans. In 2003, de Silva et al. estimated that 740 million people were infected worldwide, and the greatest prevalence estimates of infection were in sub-Saharan Africa (29 %); East Asia and the Pacific Islands (26 %); China (16 %); and South Asia (16 %). Worldwide, *Ne. americanus* is the predominant hookworm species, while *An. duodenale* is more geographically restricted. In Egypt pure *An. duodenale* infections have been noted (el Shazly et al. 1998). More typically, mixed infections with both species may be common in the Middle East, although very few epidemiological studies have

attempted to differentiate hookworm species (Brooker et al. 2004; Eid et al. 2008). The eggs of the two species cannot be distinguished morphologically. To identify these hookworm species the larvae must be examined. Larvae cannot be found in stool specimens unless the specimen is left at ambient temperature for a day or more (de Silva et al. 2003).

Ancylostoma duodenale (Dubini, 1843) Creplin, 1845

Necator americanus (Stiles 1902) Stiles, 1906

Etiology, Life Cycle, and Major Clinical Manifestations

Fully developed adult *Ne. americanus* worms are smaller than *An. duodenale* worms (females are up to 11 and 13 mm long, respectively; males are slightly smaller), and consequently cause more blood loss from their hosts, 0.2 vs. 0.05 ml/worm/day (Loukas and Prociv 2001). However, *Ne. americanus* is more widespread worldwide and, therefore, more significant as a cause of disease burden (Hotez et al. 2005). *Ne americanus* tends to be much more tropical in distribution (Schad 1991), whereas *An. duodenale* is often better adapted to more northerly latitudes in the subtropics, including areas of the Middle East.

Humans acquire hookworm infection through larval skin penetration, although *An. duodenale* is also infective via the oral route (Bethony et al. 2006). Upon skin penetration the infective larvae migrate through the lungs and are coughed and swallowed. Acute upper gastrointestinal discomfort occurs as the larvae enter the gastrointestinal tract and resume their development to become adult worms. This period often coincides with the onset of eosinophilia. Adult hookworms in the small intestine produce blood loss leading to iron and protein losses. Iron deficiency anemia results when host iron reserves are depleted. In recent systematic reviews, moderate and heavy hookworm infections were linked to anemia in children (Smith and Brooker 2010), whereas even light infections could cause anemia in some populations of both pregnant and nonpregnant adults (Smith and Brooker 2010; Brooker et al. 2008). In heavy infections protein malnutrition can also occur.

Prevalence of Hookworms in the MENA Region (Table 2)

About five to ten million infections are in the MENA region which accounts for approximately 1 % of the global disease burden (de Silva et al. 2003; Hotez et al. 2012). In the MENA region, hookworm infections are highest in Egypt with about 3.6 million infections, followed by Iran with about 0.4 million infections, then Saudi Arabia with 0.4 million infections, and Oman with 0.2 million infections (Hotez et al. 2012).

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According to Table 2, the lowest and the highest rate of infection with hookworms belong to Algeria (0.0 %) and Kuwait (50 %). However, among immigrant populations, a prevalence of 54.2 % was reported in Ethiopian immigrants to Israel (Nahmias et al. 1991).

An. duodenale infection is reported from Morocco (Jiménez-Albarrán and Odda 1994), Algeria (Pampiglione and Hadjerès 1965), Tunisia (Al-Binali et al. 2006), Egypt (Kuntz et al. 1956; Mohamed et al. 1985; Mohamed et al. 1988; Wells and Blagg 1956), Palestine (Scott et al. 1934), Israel (Avins et al. 1971; Brauman et al. 1982), Jordan (Altaif 2011), Lebanon (Yenikomshian and Berberian 1932), Syria (Yenikomshian and Berberian 1932), Saudi Arabia (Zaglool et al. 2011; Al-Binali et al. 2006; Abdel-Hafez et al. 1986), Yemen (Farag 1985), Oman (Patel and Khandekar 2006), and Iraq (Farhan 2012; Kadir and Salman 1999; Niazi et al. 1975).

In Egypt, laborers in agriculture are significantly at risk of *An. duodenale* infection (Bakr et al. 2009). In contrast to ascariasis, ancylostomiasis is more prevalent in Upper Egypt than Lower Egypt (Augustine et al. 1930; Miller et al. 1980; Scott 1939). *An. duodenale* was reported among the parasites mechanically transmitted by cockroaches and flies in Egypt (El-Sherbini and El-Sherbini 2011; El-Sherbini and Gneidy 2012).

Strongyloides stercolaris (Bavay, 1876) Stiles et Hassall, 1902

Because of the difficulties in diagnosing *St. stercoralis* infections, we know the least about strongyloidiasis in terms of its prevalence and global disease burden. The GBD 2010 Study, for instance, did not provide an estimate in DALYs of human strongyloidiasis. Some estimates indicate, however, that this STH affects between 10 and 40 % of the population worldwide (Schär et al. 2013). Because of its ability to produce autoinfection and multiply in the body, the infection can persist for decades, even more than 75 years in some cases (Schär et al. 2013). Under selected conditions patients who receive corticosteroids (e.g., during solid organ transplantation or for treatment of autoimmune disease or malignancy) or in HTLV-1 coinfections, *St. stercoralis* can cause a hyperinfection syndrome associated with severe morbidity and mortality.

Etiology, Life Cycle, and Major Clinical Manifestations

The life cycle of St. stercoralis embraces two free-living and parasitic cycles.

Under the normal environmental conditions, the first-stage rhabditiform larvae (L1) after passing in the stool will transform to adult free-living worms and start a free-living cycle. Under the unfavorable conditions, the rhabditiform larvae become third-stage filariform larvae (L3) and switch to parasitic cycle to infect humans through penetrating the skin and after an internal migration reside in small

Country	Community-based surveys	Hospital-based surveys	Refugees and immigrants
Egypt	2.5	11.1	_
Iran	0.3	0.6	_
Iraq	_	24.2	_
Israel	94.9	_	_
Jordan	0.03	_	_
Kuwait	_	16.3	_
Oman	3	_	_
Palestine	_	4.2	_
Saudi Arabia	_	12.5	7.1
Sudan	3.7	_	_
Tunisia	_	0.5	_

Table 3 Country-wide prevalence rates for *Strongyloides stercoralis* for countries of MENA region (Schär et al. 2013)

intestine (Schär et al. 2013). The adult worms in the small intestine produce eggs which hatch and release L1 larvae in gut. Under conditions still not well defined the L1 can continue their developmental program while still in the intestine to become L3 leading to autoinfection. When autoinfection is dysregulated, both hyperinfection and disseminated infection can result.

Strongyloidiasis is a wide spectrum disease in the context of clinical manifestations including enteritis resulting from the adult worms in the small intestine to life-threatening hyperinfection syndrome and disseminated disease, which can occur in patients receiving exogenous corticosteroids or in patients with HTLV-1 coinfection. The basis by which steroids or HTLV-1 can trigger *St stercoralis*-induced hyperinfection is not known.

The most important feature is its role as a fatal disease in immunocompromised individuals and patients receiving corticosteroid therapy (Schär et al. 2013).

Prevalence of Strongyloides stercoralis in the MENA Region

In general, information on infection rates and prevalence of the parasite is scarce in the region. Table 3 provided by Schar et al. depicts the most updated and comprehensive information on the prevalence of the disease in some countries of the MENA region (Schär et al. 2013). Table 2 provided by the present authors shows the lowest and the highest rate of infection as 0.0 % in Algeria and 15.5 % in Palestinian.

The reality is that in comparison to other STHs, the diagnosis of this disease is more difficult. Many surveys conducted in the region were based on only one stool sample examination which is of low sensitivity. Normally more samples should be examined over consecutive days from one subject to reach a decisive conclusion (Marti and Koella 1993).

Environmental and Human Factors that Promote STH Infections in the MENA Region

Some of the major influences of STH infections in the MENA region include the following elements.

Animals

The major STH infections of humans are not generally thought as zoonotic diseases. Thus, *As. lumbricoides* is mainly a human (anthroponotic) parasite. However, the results of a study carried out in Egypt suggested that dogs could act as reservoir hosts of *As. lumbricoides* and environmental contaminators that increase risk of infection in humans (Shalaby et al. 2010). In Saudi Arabia, the Arabian sacred baboon, *Papio hamadryas arabicus*, may play a role in transmission of *Ascaris* spp. to neighboring human communities (Nasher 1988).

Foreign Workers

Several countries in the MENA region employ foreign workers as household servants and in the construction sector. Many from Asian and African countries are believed to be infected with different parasitic diseases because they are coming from countries of low socioeconomic levels and inadequate medical care and may serve as disease reservoirs (Table 2). Although in many nations in the MENA region the immigrant workers are required to pass selected clinical examinations it is not uncommon for them to become reinfected upon return to their native homeland (Abu-Madi et al. 2010).

Geophagia

Geophagia (Soil-eating habit), which is a kind of pica, has been reported from many countries of the region. Soil is an important source of infection which contains many parasites' eggs especially STHS (Geissler et al. 1998). In Pakistan, geophagia was reported as 24.8 % in participant children (Mehraj et al. 2008).

Wastewater

The role of wastewater in spreading STH infections has been confirmed in two surveys in Morocco. For example, the prevalence of ascariasis in the schoolchildren from an area contaminated with wastewater versus a control group was 32.8 vs. 1.45 %, respectively (Bouhoum and Amahmid 2000). Similarly, Habbari et al. in another part of the country reported the prevalence as 20.5 vs. versus 3.8 % (Habbari et al. 2000).

In Tunisia, the concentration of *Ascaris* sp. was 455 eggs per liter and 46 eggs per liter in raw wastewater and treated wastewater, respectively (Ayed et al. 2009), which indicates that even treated wastewater might still serve as a source of infection for ascariasis.

The role of sewage is especially critical in Afghanistan, where tens of millions of Ascaris eggs were recovered from sources of water that were simultaneously contaminated with sewage and also used for irrigation and wells holding drinking water (Safi and Buerkert 2012).

Vegetables

An important vehicle of ascariasis transmission is through the ingestion of eggs adhering to vegetables. Different studies in countries of MENA region show that eggs of STHs are present in vegetables. It is important to note that consuming raw vegetables is a traditional habit in several different nations of the region. Another issue is that vegetables are washed in water, which after treatment are still contaminated with parasites' eggs (Bolbol 1992; Amin 1988).

In Saudi Arabia, the presence of *As. lumbricoides* eggs in treated municipal wastewater of the Riyadh metropolitan area was reported (Bolbol 1992). In two different studies in Egypt and Saudi Arabia, it was found that *As. lumbricoides* eggs were common in leafy vegetables and the use of tap water does little to remove them (Al-Binali et al. 2006; Fawzi et al. 2004). Study of vegetables in Saudi Arabia showed the contamination with *Ascaris* eggs as 26.3 % and *Ancylostoma* 11.8 %. Altogether, 16.2 % of all samples were found contaminated with different parasites' eggs (Al-Megrm 2010).

In Bahrain, sludge produced in the central sewage treatment plant was found contaminated with *As. lumbricoides* eggs. It is used for agricultural purposes and poses a threat to public health (Amin 1988).

In Algeria, of 36 tomato, 36 cucumber, 27 lettuce, and 27 cress samples examined, eggs of *Ascaris* spp. were detected in 19 %, 75 %, 96 %, and 96 %, respectively (Abougrain et al. 2010).

In Iran, a prevalence of 2 % and 1 % infection with As. lumbricoides eggs in vegetables has been reported in two studies (Daryani et al. 2008; Garedaghi et al. 2011). From 44 farms and 20 markets, 40 farms and all 20 markets had

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parasitic contamination in Tehran (Gharavi et al. 2002). In addition, 5.4 % and 2.17 % of examined samples of vegetables had *Ascaris* and hookworm eggs, respectively (Nazemi et al. 2012).

Fertilizer

Primitive agricultural practices using human feces as fertilizer are responsible for the high prevalence of ascariasis in certain regions of the world. Raw wastewater reuse can lead to a high risk of ascariasis (El Kettani and Azzouzi 2006). In a field study in Marrakech, Morocco, where raw sewage is used to fertilize crop fields, *As. lumbricoides* eggs were detected at the rate of 0.18 eggs/kg in potatoes, 0.27 eggs/kg in turnip, 4.63 eggs/kg in mint, 0.7 eggs/kg in carrots, and 1.64 eggs/kg in radish (Habbari et al. 1999).

In addition to aforementioned cases, more risk factors of critical significance in the region are as follows: (1) Lower socioeconomic status; (2) Lack of access to clean water; (3) Poor hygienic environment; (4) Poor education; (5) Overcrowded conditions; (6) Poverty; (7) Not washing hands after defecation; (8) Immigrants

Polyparasitism

Although understudied, STH coinfection with other intestinal parasites is believed to be common in the MENA region. In Pakistan, in 13.9 % of patients are coinfected with ascariasis and *Giardia* (Mehraj et al. 2008). In addition, 1.68 % of mixed infestations of *As. lumbricoides* and *Tr. trichiura* as well as 0.84 % coinfection with *As. lumbricoides* and *Giardia lamblia* were reported in Pakistan (Ahmed et al. 2012). In Iran polyparasitism was reported in 2 % of schoolchildren from Tehran, 8.2 % of food sellers in Kashan, 5.8 % of students from Hormozgan, and 0.8 % of those attending day-care centers in Tehran (Rokni 2008). Another study reports 5.53 % and 0.6 % of coinfection for two and three parasites, respectively (Mowlavi et al. 2008).

Treatment, Control, and Preventive Measures

In Israel, the cure rate for necatoriasis by treatment with 400 mg of albendazole was 84.4 %; besides, albendazole, 400 mg for 3 days, cured 92 % of the cases with *St. stercoralis* infection (Nahmias et al. 1991).

In 2001 the World Health Assembly adopted a resolution for frequent and periodic deworming through mass drug administration (also known as "preventive chemotherapy") as a means to control STH infections. While the initial

recommendation was for school-aged children, the WHO has since recommended that coverage should be extended to preschool-aged children at risk for acquiring infection. Typically this is conducted by mass drug administration with single dose albendazole (400 mg) or mebendazole (500 mg). The WHO's major region that covers the MENA area is known as the Eastern Mediterranean Region. Unfortunately coverage of both preschool-aged and school-aged children in this area has been low. For 2011, WHO estimated that only 16–17 % of the more than 25 million preschool-aged children at risk for STH infection receive deworming treatments, while less than 1 % of the more than 55 million school-aged children have received deworming (WHO 2013). Overall of the roughly 80 million children in the region, only 5–6 % received either albendazole or mebendazole treatments in 2011 (WHO 2013).

Despite this overall poor coverage for STH infections there are some success stories. In Oman, a set of single annual dose of albendazole 400 mg, health education and promotion of environmental health, succeeded to reduce the prevalence of $Ne.\ americanus$ in two parts of the country from 40 to 1.3 % and from 6 to 0 %, respectively, among rural and urban school children (Idris et al. 2001). In the Sultanate of Oman the climate is in favor of hookworm transmission and in some parts of the country infection with hook worms varies from 13 to 60 % (Idris et al. 1995). Fallah et al. reported that parasites' eggs were detected in 32.6 % of unwashed, 1.3 % of traditionally washed, and not in any standard washed samples of vegetables (P < 0.001) (Fallah et al. 2012). Therefore it clearly shows the importance of washing vegetables with standard methods which is easily conveyable to the people of the region.

Iran stands out among the countries which have experienced a remarkable decrease on the prevalence and incidence of helminthic diseases. Recent estimates show the prevalences of ascariasis, strongyloidiasis, hookworm as $0.1\,\%$, $0.3\,\%$, and $<1\,\%$ of the population (Rokni 2008). Ascariasis has decreased significantly from $86.3\,\%$ in 1961 to merely $0.3\,\%$ in 1995 (Rokni 2008). In another study in Iran, among food handlers, the infection with ascariasis decreased from $1.55\,\%$ in 2000 to $0.48\,\%$ in 2009 (Saki et al. 2012). Moreover, out of 1494 examined subjects from nomad people in southwest of Iran, ascariasis and strongyloidiasis was detected in $0.13\,\%$ and $0.6\,\%$ of cases (Mowlavi et al. 2008). It is another reason that the rate of infection with STHs is decreased remarkably in Iran, because lots of risk factors are there among nomads in terms of infection with STHs.

In Libya, a significant difference was noted between parasitic infections and parent's education (P = 0.000), socioeconomic status of the family (P = 0.000), family size and number of rooms in houses (P = 0.000), and source of water for human consumption (P = 0.05) (Sadaga and Kassem 2007).

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Concluding Remarks and Future Priorities

Despite the facts that most of the MENA region is comprised of middle income rather than low-income countries, and most parts are environmentally unfavorable to transmission, STH infections are still widespread. Ascariasis in particular is pervasive in much of the region. Undoubtedly, a major reason for rampant STH infections is the near absence of deworming in the schools and for school-aged children and limited targeting of preschool aged children.

The basis for low anthelminthic drug coverage needs to be better understood. The MENA region is notable for its political turmoil in many of its countries. Unfortunately this phenomenon has imposed a vast negative impact on different aspects of the human affairs including public health and parasitic diseases. STHs, as shown in this article, have critical role on increasing the sorrows of the people there. International cooperation among the ministers of health to promote universal deworming of school-aged children is a high priority and there is urgency to establish a climate of political will in this area.

In addition, it is likely that the actual amount of infection in the region is underestimated. One reason is the number of stool examinations that are routinely conducted. Many researchers prefer to conduct single stool examination, which results to underestimate the true prevalence. One or two samples are often not enough to yield a trustful estimation (Marti and Koella 1993).

As for strongyloidiasis, it is necessary to recommend researchers to utilize higher sensitivity diagnostic methods, such as Koga Agar plate culture, the Baermann, ELISA, and advise them to examine at least three samples of stool to be sure of the output. Unfortunately for this reason in the MENA region, most studies conducted on STHs lack of any data on *St. stercoralis*.

Ultimately, the MENA region still needs time to overcome some serious political hardships and the looming and actual prospect of conflict. As political agitations increasingly become more common there is a risk that public health might become compromised, as we have recently seen in Syria with resultant emergence of cutaneous leishmaniasis (Aleppo ulcer). Increasingly it might be necessary to rely on international organizations such as the WHO and their Eastern Mediterranean Regional Office (EMRO) in order to intervene and assist in surveillance and mass drug administration.

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