The Need for Including Hepatitis a Vaccine in Routine Childhood Immunization Programs in Europe as a Response to the Influx of Refugees from the Middle East and North Africa (MENA) Regions

S. Ramia, N. Melhem, K. Kreidieh

Abstract—The world is facing an unprecedented displacement crisis. Recently, over 1.1 million asylum seekers have been granted protection status in the European Union (EU). The majority of these asylum seekers were from countries of the Middle East and North Africa (MENA) region. This influx carries with it a potential introduction of infectious diseases that have been eliminated in the EU, which poses a challenge for EU health authorities. Compared to MENA region countries where Hepatitis A Virus (HAV) endemicity is high to intermediate, member states of the EU show very low (Western Europe) to low (Eastern Europe) levels of HAV endemicity. Because of this situation, there is an ongoing public health concern in high-income countries, like members of the EU, that many adults remain susceptible to HAV outbreaks. The overwhelming majority of the EU members' states do not include HAV vaccine in their immunization calendars. Hence, this paper urgently calls for the implementation of new policies regarding HAV in EU members' states.

Keywords—European Union, Hepatitis A, MENA Region Refugees, Vaccine preventable diseases.

I. BACKGROUND

THE ongoing conflict in the Middle East (mainly Syria and Iraq), North Africa (mainly Sudan and Libya), and the Greater Horn of Africa (mainly Eritrea, Somalia, and South Sudan) has left hundreds of thousands killed or wounded in addition to the displacement of more than 10 million throughout the World [1]. According to the United Nations High Commission on Refugees (UNHCR), the bulk of those displaced from the Middle East came to neighboring countries: Turkey (about 1.9 million people), Lebanon (about 1.2 million people), Jordan (about 650,000 people), and Iraq (about 250,000 people) and slightly more than 10% of them are seeking safety in Europe [1]. The majority of the MENA refugees are concentrated in Serbia and Germany (57%), compared to 31% in Sweden, Hungary, Austria, Netherlands,

and Bulgaria, and 12% in the remaining members of the European Union [2]. These numbers are accelerating daily and so is the challenge for proper settlement of the refugees [3]. This influx of refugees to Europe presents the European health authorities with a serious challenge as it carries with it the potential of introducing infectious diseases that have been eradicated in the continent. These diseases include poliomyelitis, measles, to mention only few. The breakdown in the healthcare infrastructure in all these countries experiencing the conflict had led to the discontinuation of vaccination programs in these countries. Moreover, the lack of vaccination in addition to over crowdedness, the miserable living condition, and the lack of basic health care facilities culminated in outbreaks of serious vaccine-preventable diseases such as polio [4] and measles [5] in refugee camps in Syria and in neighboring countries [6]. Although most of the European populations are immunized against polio, measles, and other vaccine-preventable diseases, there are however certain infections (Ex: Hepatitis A Virus -HAV-) that might present a serious challenge to the European health authorities since these infections are not vaccinated against and could have a public health burden.

II. HEPATITIS A VIRUS

A. Morbidity and Mortality of HAV

HAV is a non-enveloped RNA picornavirus that causes clinical diseases and continues to cause significant morbidity in many parts of the world [7]. Recent estimates indicate a global incidence of 1.9% with 119 million cases have been infected with HAV in 2005 [8]. HAV is transmitted primarily via ingestion of contaminated food or water or via direct contact with an infected person. The severity of HAV infection increases with age [8]. The overwhelming majority of children <5 years of age show no sign of infection (asymptomatic) compared to the more than 70% of cases in older children and adults that show jaundice. Similarly the proportion of cases requiring hospitalization increases with age ranging from 21% in children <5 years, to 53% among adults aged ≥ 60 years [9]. There has been a reduction in the overall mortality rate of Hepatitis A, at least in the United States, during the years after implementation of recommendation for routine HA vaccination of children [10]. The incidence of infection is strongly correlated with access to

S. Ramia is with the Medical Laboratory Sciences Program, Faculty of Health Sciences, American University of Beirut, P.O Box 11-0236, Riad El Solh 1107 2020, Beirut, Lebanon. (phone: 009611350000 ext.: 4698; fax: 009611744470; e-mail: sramia@aub.edu.lb).

N. Melhem is with the Medical Laboratory Sciences Program, Faculty of Health Science, American University of Beirut, Beirut, Lebanon. (e-mail: melhemn@aub.edu.lb).

K. Kreidieh, was with the Medical Laboratory Sciences Program and Faculty of Health Sciences, is now with the Faculty of Medicine, American University of Beirut, Beirut, Lebanon. (e-mail: ka28@aub.edu.lb).

safe drinking water, to the levels of hygiene and sanitations, and to socioeconomic conditions [11], [12]; and hence major geographic differences exist in endemicity. In the past decade, HAV was responsible for several outbreaks in the United States and the costs of HAV sporadic have been reported to range up to \$36 million per outbreak [13].

B. Epidemiology of HAV: Middle East and North Africa (MENA) Region vs. Members of the European Union

Anti-HAV seroprevalence in MENA region countries have been recently reviewed [14]. In most of these countries there has been a gradual shift of HAV epidemiology from childhood to adulthood during the past 20 years. According to the World Health Organization (WHO), a seroprevalence of 60-74% among children aged 10-14 years translates into intermediate endemicity [15]. The epidemiological shift from endemic or highly endemic to intermediate endemicity has been noticed mainly in the Gulf countries (Saudi Arabia, Kuwait, Qatar, and Emirates) [16]-[19] and in several other MENA countries including Lebanon, Jordan, and Tunisia [20]-[22] due to improved water, sanitation, and socioeconomic conditions. It must be mentioned that with this epidemiological shift, the disease burden associated with Hepatitis A will increase as more susceptible adults might acquire symptomatic and severe forms of the disease. Western Europe has consistently shown a very low prevalence rate of HAV infection compared to only low prevalence rates in Central and East Europe. In many European Union countries, the incidence rates of HAV infection has declined since the mid-1990s to low levels. The decline in incidence rates put susceptible populations at risk of acquiring HAV infection and therefore a greater likelihood of outbreaks in countries with low and even intermediate endemicity. Recently, two relatively large outbreaks have been reported in Eastern Europe between 2000 and 2009: One in Prague, the Czech Republic [23] and the other one in Latvia [24]. More than 1,600 people were affected in the Prague outbreak compared to more than 3,200 cases in Latvia. In both outbreaks, affected individuals were mainly adults (20-45 years old) and with low socioeconomic status.

III. THE NEW CHALLENGE TO THE EUROPEAN HEALTH AUTHORITIES

WHO confirmed an outbreak of polio in the North East of Syria in 2013 – an area that has been poliomyelitis free since 1999- that left 10 children paralyzed [25]. Consequently, emergency vaccination campaigns against poliovirus in and around Syria have resulted in 650,000 children being vaccinated [26]. There is fear that polio could be introduced back into the European Union from the Syrian refugees [27], [28]. It was argued however, that European people, who had the oral polio vaccination, had a very low to no risk of contracting polio [29]. In contrast to the vaccine coverage against polio in Europe, the overwhelming majority of European countries do not include the HAV vaccine in their immunization calendars (Table I). There is a growing public health concern in high-income countries, like most European countries where the HAV infection rate is usually low, that

many adults remain susceptible to HAV infection and are at high risk of severe HAV symptoms and maybe death [7]-[9]. Moreover, HAV infection may cause a significant economic burden to individuals, families, and communities where a high proportion of susceptible older adults live [10], [29]. Refugees from Syria and Iraq for example pose no threat to Lebanon, Jordan, or Turkey since these countries are considered as having intermediate HAV endemicity [8]. The majority of the Gulf-countries already introduced HAV vaccination to their national immunization schedule due to the recent epidemiological shift in HAV from endemic to intermediate endemicity [14]. Paradoxically, Syrian refugees from the MENA region countries pose no threat to the health authorities in the Gulf-countries because the accommodations of refugees by these countries have been very minimal. On the other hand, refugees from the MENA region became the single largest group of persons granted protection status in the European Union. Hence, these refugees act as a vector for HAV transmission and put a wide range of the hosting population (e.g. health care providers, school children, and others) at highest risk of acquiring HAV infection.

IV. HAV VACCINE AND VACCINATION

Inactivated HAV vaccine has been shown to be safe and effective for the prevention of HAV disease [30]-[32]. Vaccine induced anti-HAV antibodies have been shown to persist for at least 15 years [33] with mathematical modeling predicting that detectable antibodies are likely to persist for at least 25 years [34]. In countries encountering transition of HAV endemicity from high to intermediate levels, the WHO recommends integration of vaccination against HAV into the national immunization schedule for children aged >1 year [23]. This large-scale immunization however, is not recommended for highly-endemic or endemic countries. The Advisory Committee on Immunization Practices (ACIP) in the USA in 2006 recommends targeting HAV immunizations to include all children at the age of 12-23 months [35]. Introduction of HAV vaccine to National Immunization Programs at the regional level is showing encouraging results. Large scale immunizations of children with HAV vaccine have been introduced in Saudi Arabia, Bahrain, Qatar, and Emirates (Table II) [36]. In Europe, few countries currently practice HAV vaccination and not in the whole country (Table I). The impact/spread of HAV outbreaks among refugees on/to the hosting European countries is expected as was the case in other hosting countries such as Lebanon, Jordan, and Iraq. We believe that due to the sudden and unfolding crisis of the influx of refugees to Europe, new policies regarding HAV vaccination should be implemented in European Union countries. As a starting point, it is believed that HAV vaccination should target groups who are dealing with refugees (e.g. health care workers and non-governmental organizations (NGOs)), as they might play a role in introducing HAV into the vulnerable populations.

Since Western Europe, where most of the refugees are concentrated, has consistently shown a very low seroprevalence rate of anti-HAV compared to low anti-HAV

seroprevalence rates in Central and Eastern Europe [8], perhaps vaccination campaigns targeting high-risk groups in West-European countries and introducing vaccination to the routine national childhood immunization programs in East European countries are practical and reasonable approaches at the present time. Such measures if considered by the European countries, will reduce the risk of morbidity and mortality among susceptible children and adolescents in these countries. Moreover, better reporting and completeness of information of HAV new cases through the European Surveillance System (TESSy) are needed, as this will increase the ability to monitor risk factors and evaluate the impact of interventions aiming to reduce virus circulation [37]. Finally, it must be mentioned that improving health care access for refugees in the hosting countries, including vaccination of preventable diseases like HAV, are urgently needed in order to prevent and control the introduction of different infectious diseases to different countries.

TABLE I
EUROPEAN COUNTRIES THAT RECOMMEND HEPATITIS A VACCINATION
ACCORDING TO WHO VACCINE-PREVENTABLE DISEASES MONITORING

SYSTEM 2015 GLOBAL SUMMARY					
Country*	Schedules	Entire Country	Comments		
Finland		Yes	Only for special risk groups		
Greece	>12 months (x2)	Yes			
Iceland		Yes	Risk groups		
Italy		Yes	Recommended for persons with clinical, behavioral, or occupational indications		
Russia	20-26 months	No			
Slovenia		Yes	In case of epidemiological indications, travelers		
Spain		Yes	Risk groups		

*All the rest 36 European countries do not recommend Hepatitis A vaccine.

TABLE II
MENA REGION COUNTRIES THAT RECOMMEND HEPATITIS A VACCINATION
ACCORDING TO THE WHO VACCINE-PREVENTABLE DISEASES MONITORING
SYSTEM 2015 GLOBAL SUMMARY

Country	Schedules	Entire Country	Comments
Bahrain	18-24 months	Yes	Catch up vaccination for 12 and 13 years
Israel	18-24 months	Yes	Given also to special risk groups
Qatar	18-24 months	Yes	
Saudi Arabia	18-24 months	Yes	
Turkey	18-24 months	Yes	

*All the rest 19 MENA countries do not recommend Hepatitis A vaccine.

REFERENCES

- [1] UNHCR. "UNHCR Mid-Year Trends 2015".2015.
- [2] UNHCR."UNHCR Global Appeal 2015 Update- Europe Regional Summary".2015.
- [3] "Adapting to migration as a planetary force", in Lancet, London, England, vol. 386, 2015, pp. 1013.
- [4] Tajaldin B, Almilaji K, Langton P, Sparrow A, "Defining Polio: Closing the Gap in Global Surveillance", Annals of Global Health, vol. 81, 2015, pp. 386-395.
- [5] Djebbi A, Bahri O, Mokhtariazad T, Alkhatib M, Ben Yehyia A, Rezig D, et al., "Identification of Measles virus genotypes from recent outbreaks in countries from the Eastern Mediterranean Region", Journal

- of Clinical Virology: the official publication of the Pan American Society for Clinical Virology, vol. 34, 2005, pp. 1-6.
- [6] Cousins S, "Syrian Crisis: health experts say more can be done", in Lancet, London, England, vol. 385, 2015, pp. 931-934.
- [7] Matheny SC, Kingery JE, "Hepatitis A", American family physician, vol. 86, 2012, pp. 1027-1034, quiz 10-2.
- [8] Jacobsen KH, Wiersma ST, "Hepatitis A virus seroprevalence by age and world region", Vaccine, vol. 28, 2010, pp. 6653-6657.
- [9] Ciocca M, "Clinical course and consequences of Hepatitis A infection", Vaccine, vol. 18, 2000, supplement 1, pp. 71-74.
- [10] Daniels D, Grytdal S, Wasley A, "Surveillance for acute viral hepatitis United States 2007", Morbidity and mortality weekly report Surveillance summaries, Washington, DC, vol. 58, 2009, pp. 1-27.
 [11] Jacobsen KH, Koopman JS, "Declining Hepatitis S seroprevalence: a
- [11] Jacobsen KH, Koopman JS, "Declining Hepatitis S seroprevalence: a global review and analysis", Epidemiology and Infection, vol. 132, 2004, pp. 1005-1022.
- [12] Jacobsen KH, Koopman JS, "The effects of socioeconomic development on worldwide hepatitis A virus seroprevalence patterns", International Journal of Epidemiology, vol. 34, 2005, pp. 600-609.
- [13] Luyten J, Beutels P, "Costing infectious disease outbreaks for economic evaluation: a review for hepatitis A", PharmacoEconomics, vol. 27, 2009, pp. 379-389.
- [14] Melhem NM, Talhouk R, Rachidi H, Ramia S, "Hepatitis A virus in the Middle East and North Africa region: a new challenge", Journal of viral hepatitis, vol. 21, 2014, pp. 605-615.
- [15] Mohd Hanafiah K, Jacobsen KH, Wiersma ST, "Challenges to mapping the health risk of hepatitis A infection", International journal of health geographics, vol. 10, 2011, pp. 57.
- [16] Alkhalidi J, Alenezi B, Al-Mutfi S, Hussain E, Askar H, Kemmer N, et al., "Seroepidimiology of hepatitis A virus in Kuwait", World journal of gastroenterology, vol. 15, 2009, pp. 102-105.
- [17] Almuneef MA, Memish ZA, Balkhy HH, Qahtani M, Alotaibi B, Hajeer A, et al., "Epidemiologic shift in the prevalence of Hepatitis A virus in Saudi Arabia: a case for routine Hepatitis A vaccination", Vaccine, vol. 24, 2006, pp. 5599-5603.
- [18] Bener A, Al-Kaabi S, Derbala M, Al-Marri A, Rikabi A, "The epidemiology of viral hepatitis in Qatar", Saudi journal of kidney diseases and transplantation: an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia, vol. 20, 2009, pp. 300-306.
- [19] Sharar ZA, Rajah J, Parsons H, "Childhood seoprevalence of hepatitis A in the United Arab Emirates", Tropical doctor, vol. 38, 2008, pp. 65-66.
- [20] Hayajneh WA, Balbeesi A, Faouri S, "Hepatitis A virus age-specific sero-prevalence and risk factors among Jordanian Children", Journal of medical virology, vol. 87, 2015, pp. 569-574.
- [21] Letaief A, Kaabia N, Gaha R, Bousaadia A, Lazrag F, Trabelsi H, et al., "Age-specific seroprevalence of hepatitis A among school children in central Tunisia", The American journal of tropical medicine and hygiene, vol. 73, 2005, pp. 40-43.
- [22] Melhem NM, Jaffa M, Zaatari M, Awada H, Salibi NE, Ramia S, "The changing pattern of hepatitis A in Lebanese adults", International Journal of infectious diseases: IJID: official publication of the International Society for Infectious Diseases, vol. 30, 2015, pp. 87-90.
- [23] Castkova J, Benes C, "Increase in hepatitis A cases in the Czech Republic in 2008- an update", Euro surveillance: bulletin European sur les maladies transmissibles = European communicable diseases bulletin, vol. 14, 2009.
- [24] Perevoscikovs J, Lucenko I, Magone S, Brila A, Curikova J, Vennema H, "Community-wide outbreak of hepatitis A in Latvia in 2008- an update", Euro surveillance: bulletin European sur les maladies transmissibles = European communicable diseases bulletin, vol. 14, 2009.
- [25] Arie S, "Polio outbreak leads to calls for a "vaccination ceasefire" in Syria", BMJ, Clinical Research edition, vol. 347, 2013, pp. 6682.
- [26] World Health Organization UCsF, "Over 20 million children to be vaccinated in Syria and neighboring countries against polio, say WHO and UNICEF", 2013.
- [27] Eichner M, Brockmann SO, "Polio emergence in Syria and Israel endangers Europe", in Lancet, London, England, vol. 382, 2013, pp. 1777
- [28] Hives-Wood S, "Syrian refugees could bring polio to Europe, experts warn", BMJ, Clinical Research Edition, vol. 347, 2013, pp. 6778.
- [29] Northdurft HD, "Hepatitis A vaccines", Expert review of vaccines, vol. 7, 2008, pp. 535-545.
- [30] Kohl I, Nemecek V, Summerova M, Chlibek R, Nad'ova K, Minarikova O, "Long-term protective effect of post-exposure Havrix administration

World Academy of Science, Engineering and Technology International Journal of Medical and Health Sciences Vol:11, No:8, 2017

- during viral hepatitis Type A outbreaks", European Journal of epidemiology, vol. 21, 2006, pp. 893-899.
- [31] Lopez EL, Contrini MM, Mistchenko A, Debbag R, "Long-term immunity after two doses of inactivated hepatitis A vaccine, in Argentinean Children", The Pediatric infectious disease journal, vol. 29, 2010, pp. 568-570.
- [32] Van Herck K, Van Damme P, "Prevention of hepatitis A by Harvix: a review", Expert review of vaccines, vol. 4, 2005, pp. 459-471.
- [33] Van Herck K, Jacquet JM, Van Damme P, "Antibody persistence and immune memory in healthy adults following vaccination with a twodose inactivated hepatitis A vaccine: long-term follow-up at 15 years", Journal of medical virology, vol. 83, 2011, pp. 1885-1891.
- [34] Bovier PA, Bock J, Loutan L, Farinelli T, Glueck R, Herzog C, "Long-term immunogenicity of an inactivated virosome hepatitis A vaccine", Journal of medical virology, vol. 68, 2002, pp. 489-493.
- Journal of medical virology, vol. 68, 2002, pp. 489-493.

 [35] Brundage SC, Fitzpatrick AN, "Hepatitis A", American family physician, vol. 73, 2006, pp. 2162-2168.
- [36] Organization WH, "WHO vaccine-preventable diseases: monitoring system", 2015 global summary, 2015.
- [37] Severi E, Tavoschi L, Carillo Santisteve P, Bonfigli S, Westrell T, Arnheim Dahlstrom L, et al., "Hepatitis A incidence in the EU: what can we learn from the available data?", Journal of viral hepatitis, vol. 22, 2015, pp. 1-18.