

The Syrian refugees crisis brings challenges to the health authorities in Europe: hepatitis A virus is a case in point

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The ongoing 3-year Syrian Civil war has left hundreds of thousands killed or wounded in addition to the displacement of more than 6.5 million Syrians throughout the world [1]. According to the United Nations High Commission on Refugees (UNHCR), the bulk of those displaced are hosted by neighboring countries: Lebanon (approximately 1.2 million people), Jordan (approximately 650,000), Iraq (approximately 250,000) and Turkey (approximately 1.9 million) [1]. It has been reported that slightly more than 10 % of the displaced Syrian refugees are seeking safety in Europe. The majority of the Syrian refugees in Europe are concentrated in Serbia and Germany (57 %) compared to 31 % in Sweden, Hungary, Austria, Netherlands and Bulgaria, and 12 % in the remaining 37 European Countries [2]. These numbers are increasing daily along with the associated challenge of their adequate settlement [3].

The influx of refugees to Europe presents the health authorities with the potential of introducing infectious diseases that have had low rates of morbidity and mortality in the hosting countries across time. These diseases include measles, polio, hepatitis A virus (HAV), hepatitis B virus (HBV), tuberculosis, human immunodeficiency virus (HIV), hepatitis C virus (HCV), cutaneous leishmaniasis, schistosomiasis, MERS-CoV, *Haemophilus influenzae type b* (Hib), as well as many vaccine-preventable diseases (DTap, meningococcal, varicella) that have been reported

to be on the rise among Syrian refugees in Lebanon, Turkey, Jordan and Iraq [4–7].

The breakdown in the Syrian health care infrastructure led to the discontinuation of vaccination programs in the country. The disruption of vaccination in addition to overcrowdedness, the miserable living condition and the lack of basic health care facilities culminated in severe outbreaks of vaccine-preventable diseases such as polio [8] and measles [9] in refugee camps in Syria and neighboring countries [10]. While most of the European populations are immunized against vaccine-preventable diseases, an imminent challenge is introduced due to the Syrian settlement in Europe especially due to the lack of implementation of vaccination against expected re-emerging infections; hepatitis A virus infection is a case in point.

HAV, a non-enveloped RNA virus belonging to the family *picornaviridae*, continues to cause significant morbidity in many parts of the world [11]. Recent estimates indicate a global incidence of 1.9 % with 119 million cases infected with HAV [12]. HAV virus is primarily transmitted via ingestion of contaminated food or water or through direct contact with an infected person. The severity of HAV infection increases with age [12]. The overwhelming majority of children <5 years of age show no sign of infection (asymptomatic) compared to more than 70 % of cases in older children and adults presenting with jaundice. Consequently, the proportion of cases requiring hospitalization increases with age ranging from 21 % in children <5 years to 53 % among adults aged ≥60 years [13].

The endemicity of HAV is ranked as high, intermediate or low in different geographic areas. The level of endemicity correlates with sanitary and hygienic conditions [14]. Consequently, the incidence of hepatitis A infection is strongly correlated with access to safe drinking water, to

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the levels of hygiene and sanitations and to socioeconomic conditions [15, 16]. While the latter is true for developing countries and countries with economic transition, and despite the fact that a reduction in the overall mortality rate of hepatitis A has been reported in the United States especially during and following the implementation of the routine vaccination of children [17], several outbreaks of HAV were reported in the in the United States. The costs of HAV sporadic have been reported to range up to \$36 million per outbreak [18, 19].

The World Health Organization (WHO) confirmed an outbreak of polio in the North East of Syria in 2013—an area that has been poliomyelitis free since 1999. The outbreak resulted in 10 cases of paralysis among children [20]. Consequently, emergency vaccination campaigns against poliovirus were implemented in and around Syria with 650,000 children receiving the vaccine [21]. There was fear that polio could be introduced back into the European Union from the Syrian refugees [22, 23]. It was argued however, that Europeans are at a very low to no risk of contracting polio due to exposure to vaccination [23]. In contrast to the vaccine coverage against polio in Europe, the overwhelming majority of European countries do not include HAV vaccine in their immunization programs [24].

Consequently, a growing public health concern of impact on high-income countries is advanced. The European countries, where HAV infection rates are usually low, many adults remain susceptible to the virus [11, 13]. Moreover, HAV infection may cause a significant economic burden to individuals, families and communities where a high proportion of susceptible older adults live [17, 25]. Syrian refugees pose no threat to Lebanon, Jordan, Iraq or Turkey since these countries are considered having intermediate HAV endemicity [12]. 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 [26]. Paradoxically Syrian refugees pose no threat to the health authorities in the Gulf countries because the accommodations of Syrian refugees by these countries have been very minimal. Consequently, Syrian refugees became the single largest group of persons granted protection status in the European Union.

The currently available hepatitis A vaccine has been shown to be safe and effective for the prevention/reduction acute cases [27–29]. Vaccine induced anti-HAV antibodies have been shown to persist for at least 15 years [30, 31]. In countries where endemicity is shifting from high to intermediate levels, the WHO recommends the integration of vaccination against HAV into the national immunization schedule for children >1 year old [32]. This large-scale immunization policy is not recommended for highly-endemic or endemic countries; instead targeted vaccination of

high-risk groups is recommended. These high risk groups include men having sex with men, injecting drug users, travelers to high or intermediate endemic countries, in addition to patients with chronic liver disease with increased risk of fulminant hepatitis A [32]. Several countries are implementing the above guidelines set by the WHO including the United States [33]. The introduction of hepatitis A vaccine to the National Immunization Programs at the regional level is showing encouraging results. To our knowledge, Bahrain, Israel, Qatar, Saudi Arabia and Turkey integrated hepatitis A vaccine in their national immunization policies and schedules [24, 26]. In Europe, Greece is the only European Union member that in 2008 introduced HAV vaccine in their routine national childhood immunization program [34]. Finland, Iceland, Italy, Russia, Slovenia and Spain are among the European countries administering hepatitis A vaccine to high risk groups [24].

The impact/spread of HAV outbreaks among refugees on/to the hosting European countries, classified as low endemic countries for HAV, is expected as was the case in other hosting countries such as Lebanon, Jordan and Iraq [35, 36]. Consequently, we believe that strategic policies, regarding HAV, are needed to be implemented in the European countries hosting Syrian refugees. In areas with low to very low endemicity for HAV, such as the Western and Northern countries of Europe [37], the following strategies are recommended:

- 1) HAV vaccination should target groups, such as health care workers and non-governmental organizations (NGOs), who are dealing with refugees as they might play a role in introducing HAV into the vulnerable populations.
- 2) Providing health education and health promotion to communities in direct contact with the refugees emphasizing HAV mode of transmission, risk behaviors and the benefits of screening, immunization and treatment; among other measures.
- 3) Better reporting and completeness of information on HAV new cases through the European Surveillance System (TESSy) as this will increase the ability to monitor risk factors and evaluate the impact of interventions aiming to reduce virus circulation [38].

In addition to the above mentioned strategies, it is recommended that European countries with low to intermediate endemicity, such as Southern and Eastern countries of Europe [37], introduce HAV vaccination to their routine national childhood immunization programs. This would be a cost-saving approach since it might lead to herd immunity among the Europeans as was the case in the United States in 2006 [39]. Nevertheless, such immunization programs should include careful cost-benefit analysis [40].

Needless to say that in order to minimize infection risks: providing adequate shelters to avoid crowding, ensuring good sanitation and hygiene and providing access to medical care for the Syrian refugees in Europe are also crucial [41].

We believe that a rapid action should be taken by the European authorities to implement the above mentioned strategies. This will help in the control of HAV infection and in the possibility to prevent any future epidemic in Europe. Moreover, a collaborative initiative between stakeholders and local organizations can facilitate the communication and the interaction with refugees affected by cultural and physical barriers in addition to the impact of conflict. Research funding is also desirable to assess the health problems affecting Syrian refugees and the hosting community and to improve access to health services.

References

1. UNHCR. UNHCR Mid-Year Trends 2015. 2015. <http://www.unhcr.org/56701b969.html>.
2. UNHCR. UNHCR Global Appeal 2015 Update - Europe Regional Summary. 2015. <http://www.unhcr.org/5461e5f80.html>.
3. The Lancet. Adapting to migration as a planetary force. *Lancet* (Lond, Engl). 2015;386(9998):1013.
4. Alawieh A, Musharrafieh U, Jaber A, Berry A, Ghosn N, Bizri AR. Revisiting leishmaniasis in the time of war: the Syrian conflict and the Lebanese outbreak. *Int J Infect Dis*. 2014;29:115–9.
5. Cookson ST, Abaza H, Clarke KR, Burton A, Sabrah NA, Rumman KA, et al. Impact of and response to increased tuberculosis prevalence among Syrian refugees compared with Jordanian tuberculosis prevalence: case study of a tuberculosis public health strategy. *Conflict Health*. 2015;9:18.
6. Ritz N, Brinkmann F, Garcia BS, Tebruegge M, Kampmann B. Tuberculosis in young refugees. *Lancet* (Lond, Engl). 2015;386(10012):2475–6.
7. Sharara SL, Kanj SS. War and infectious diseases: challenges of the Syrian civil war. *PLoS Pathog*. 2014;10(10):e1004438.
8. Tajaldin B, Almilaji K, Langton P, Sparrow A. Defining polio: closing the gap in global surveillance. *Ann Global Health*. 2015;81(3):386–95.
9. Djebbi A, Bahri O, Mokhtariazad T, Alkhatib M, Ben Yahia A, Rezig D, et al. Identification of measles virus genotypes from recent outbreaks in countries from the Eastern Mediterranean Region. *J Clin Virol*. 2005;34(1):1–6.
10. Cousins S. Syrian crisis: health experts say more can be done. *Lancet* (Lond, Engl). 2015;385(9972):931–4.
11. Matheny SC, Kingery JE. Hepatitis A. *Am Family Phys*. 2012;86(11):1027–34 **quiz 10–2**.
12. Jacobsen KH, Wiersma ST. Hepatitis A virus seroprevalence by age and world region, 1990 and 2005. *Vaccine*. 2010;28(41):6653–7.
13. Ciocca M. Clinical course and consequences of hepatitis A infection. *Vaccine*. 2000;18(Suppl 1):S71–4.
14. World Health Organization. Global alert and response (GAR): hepatitis a surveillance and control. <http://www.who.int/csr/disease/hepatitis/whodocs/recdc2007/en/index4.html>.
15. Jacobsen KH, Koopman JS. Declining hepatitis A seroprevalence: a global review and analysis. *Epidemiol Infect*. 2004;132(6):1005–22.
16. Jacobsen KH, Koopman JS. The effects of socioeconomic development on worldwide hepatitis A virus seroprevalence patterns. *Int J Epidemiol*. 2005;34(3):600–9.
17. Daniels D, Grytdal S, Wasley A. Surveillance for acute viral hepatitis—United States, 2007. *Morb Morta Wkly Rep*. 2009;58(3):1–27.
18. Luyten J, Beutels P. Costing infectious disease outbreaks for economic evaluation: a review for hepatitis A. *PharmacoEconomics*. 2009;27(5):379–89.
19. Centers for disease control and prevention. Surveillance for viral hepatitis—United States, 2013. 2013. <http://www.cdc.gov/hepatitis/statistics/2013surveillance/commentary.htm#hepatitisA>.
20. Arie S. Polio outbreak leads to calls for a “vaccination ceasefire” in Syria. *BMJ* (Clin res ed). 2013;347:f6682.
21. World Health Organization, UN Children’s Fund. Over 20 million children to be vaccinated in Syria and neighbouring countries against polio, say WHO and UNICEF. 2013. <http://reliefweb.int/report/syrian-arab-republic/over-20-million-children-be-vaccinate-d-syria-and-neighbouring-countries>.
22. Eichner M, Brockmann SO. Polio emergence in Syria and Israel endangers Europe. *Lancet* (Lond, Engl). 2013;382(9907):1777.
23. Hives-Wood S. Syrian refugees could bring polio to Europe, experts warn. *BMJ* (Clin res ed). 2013;347:f6778.
24. World Health Organization. WHO vaccine-preventable diseases: monitoring system. In: 2015 global summary. 2015. http://apps.who.int/immunization_monitoring/globalsummary/schedules.
25. Nothdurft HD. Hepatitis A vaccines. *Expert Rev Vaccines*. 2008;7(5):535–45.
26. Melhem NM, Talhouk R, Rachidi H, Ramia S. Hepatitis A virus in the Middle East and North Africa region: a new challenge. *J Viral Hepat*. 2014;21(9):605–15.
27. Kohl I, Nemecek V, Summerova M, Chlibek R, Nad’ova K, Minarikova O. Long-term protective effect of post-exposure Havrix administration during viral hepatitis Type A outbreaks. *Eur J Epidemiol*. 2006;21(12):893–9.
28. Lopez EL, Contrini MM, Mistchenko A, Debbag R. Long-term immunity after two doses of inactivated hepatitis A vaccine, in Argentinean children. *Pediatr Infect Dis J*. 2010;29(6):568–70.
29. Van Herck K, Van Damme P. Prevention of hepatitis A by Havrix: a review. *Expert Rev Vaccines*. 2005;4(4):459–71.
30. Ott JJ, Irving G, Wiersma ST. Long-term protective effects of hepatitis A vaccines. A systematic review. *Vaccine*. 2012;31(1):3–11.
31. Van Herck K, Jacquet JM, Van Damme P. Antibody persistence and immune memory in healthy adults following vaccination with a two-dose inactivated hepatitis A vaccine: long-term follow-up at 15 years. *J Med Virol*. 2011;83(11):1885–91.
32. World Health Organization. WHO position paper on hepatitis A vaccines: june 2012-recommendations. *Vaccine*. 2013;31(2):285–6.
33. Centers for disease control and prevention. Vaccine information statements (VIS): hepatitis A. 2011. <http://www.cdc.gov/vaccines/hcp/vis/vis-statements/hep-a.html>.
34. Mellou K, Sideroglou T, Papaevangelou V, Katsiaflaka A, Bitoulas N, Verykoui E, et al. Considerations on the current universal vaccination policy against hepatitis A in Greece after recent outbreaks. *PLoS ONE*. 2015;10(1):e0116939.
35. Lebanese ministry of public health WHO. Lebanese weekly epi-monitor. 2014. http://www.moph.gov.lb/Prevention/Surveillance/documents/epimonitor_20140215.pdf.
36. UNHCR. Syrian regional refugee response inter-agency information sharing portal. 2014. <http://data.unhcr.org/syrianrefugees/regional.php>.
37. Gossner CM, Severi E, Danielsson N, Hutin Y, Coulombier D. Changing hepatitis A epidemiology in the European Union: new challenges and opportunities. *Eur Surveill*. 2015;20(16):21101.

38. Severi E, Tamoschi L, Carrillo Santistevé P, Bonfigli S, Westrell T, Arnheim Dahlstrom L, et al. Hepatitis A incidence in the EU: what can we learn from the available data? *J Viral Hepat.* 2015;22(S2):1–18.
39. Rein DB, Hicks KA, Wirth KE, Billah K, Finelli L, Fiore AE, et al. Cost-effectiveness of routine childhood vaccination for hepatitis A in the United States. *Pediatrics.* 2007;119(1):e12–21.
40. World Health Organization. Hepatitis A vaccines. *Wkly Epidemiol Rec.* 2000;75(5):38–44.
41. Semenza JC, Carrillo-Santistevé P, Zeller H, Sandgren A, van der Werf MJ, Severi E, et al. Public health needs of migrants, refugees and asylum seekers in Europe, 2015: infectious disease aspects. *Eur J Public Health.* 2016;26:ckw023.