

Commentary

Zika virus: no cases in the Eastern Mediterranean Region but concerns remain

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لا توجد حالات فيروس زيكا في إقليم شرق المتوسط، ولكن المخاوف تظل قائمة

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الخلاصة: بعد إعلان منظمة الصحة العالمية في 1 فبراير/ شباط من عام 2016 "حالة طوارئ ذات أهمية دولية في مجال الصحة العامة" بخصوص مجموعة حالات صغر الرأس والاضطرابات العصبية التي يمتثل أن تكون مرتبطة بفيروس زيكا، أجرى مكتب منظمة الصحة العالمية الإقليمي لشرق المتوسط ثلاث جولات من الاجتماعات الطارئة لتناول تعزيز إجراءات التأهب في الإقليم. وقد قُدمت الاجتماعات أحدث المعلومات عن الوضع الراهن، وأتفق على مجموعة من الإجراءات كي تتخذها الدول لتعزيز قدراتها في مجال التأهب والتصدي للعدوى بفيروس زيكا ومضاعفاته. والإجراء الأكثر إلحاحاً هو تعزيز ترصد كل من الأوبئة والحشرات من الآن وحتى موسم الأمطار القادمة في البلدان التي يُعرف فيها وجود بعوضات (أييدس). إن فيروس زيكا - كغيره من الأمراض المنقولة بنواقل - تشكل تحدياً استثنائياً للبلدان بسبب طبيعتها المعقدة التي تتطلب كفاءات متعددة الاختصاصات وتفاعلاً سريعاً وقوياً بين القطاعات الملتزمة بذلك. وإن منظمة الصحة العالمية تعمل عن كثب مع شركاء وبلدان لضمان تقديم الدعم الأمثل للبلدان في سبيل الحد من مخاطر هذا التهديد الصحي الذي ظهر مؤخراً.

ABSTRACT Following the WHO declaration on 1 February 2016 of a Public Health Emergency of International Concern (PHEIC) with regard to clusters of microcephaly and neurological disorders potentially associated with Zika virus, the WHO Regional Office for the Eastern Mediterranean conducted three rounds of emergency meetings to address enhancing preparedness actions in the Region. The meetings provided up-to-date information on the current situation and agreed on a set of actions for the countries to undertake to enhance their preparedness and response capacities to Zika virus infection and its complications. The most urgent action is to enhance both epidemiological and entomological surveillance between now and the coming rainy seasons in countries with known presence of *Aedes* mosquitoes. Zika virus like other vector-borne diseases poses a particular challenge to the countries because of their complex nature which requires multidisciplinary competencies and strong rapid interaction among committed sectors. WHO is working closely with partners and countries to ensure the optimum support is provided to the countries to reduce the risk of this newly emerged health threat.

Maladie à virus Zika : malgré l'absence de cas dans la Région de Méditerranée orientale les craintes persistent

RÉSUMÉ À la suite de la déclaration de l'OMS le 1^{er} février 2016 faisant état d'une urgence de santé publique de portée internationale, eu égard à l'existence de groupes de cas de microcéphalie et de troubles neurologiques potentiellement associés à la maladie à virus Zika, le Bureau régional de l'OMS de la Méditerranée orientale a conduit trois cycles de réunions d'urgence en vue d'améliorer les mesures de préparation dans la Région. Les réunions ont fourni des informations actualisées de la situation actuelle et ont permis de convenir d'un ensemble d'actions à entreprendre par les pays afin d'améliorer leurs capacités de préparation et de réponse face à l'infection à virus Zika et ses complications. L'action la plus urgente consiste à améliorer la surveillance épidémiologique et entomologique à partir d'aujourd'hui et jusqu'à la prochaine saison des pluies dans les pays où la présence de moustiques *Aedes* est établie. La maladie à virus Zika, comme toutes les maladies à transmission vectorielle, constitue un défi pour les pays du fait de sa nature complexe qui nécessite des compétences multidisciplinaires et une interaction forte et rapide entre les secteurs impliqués. L'OMS travaille en étroite collaboration avec ses partenaires et les pays afin de garantir que le meilleur soutien soit apporté aux pays en vue de la réduction du risque de cette nouvelle menace sanitaire émergente.

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Introduction

Since the Zika virus (ZIKV) was first identified in 1947 in Uganda (1), few human cases were reported until 2007 when the first Zika outbreak was reported in Yap, Micronesia (2). These early reports described the disease as relatively mild: about 20% of people infected with ZIKV develop mild fever, skin rash, conjunctivitis, arthralgia and/or arthritis, while the rest are asymptomatic. However, the virus became the latest threat to global health security when the Director-General of WHO declared on 1 February 2016 that recently reported clusters of microcephaly and neurological disorders potentially associated with ZIKV constituted a Public Health Emergency of International Concern (PHEIC) (3).

The temporal and geographic association between ZIKV infection and an increase in neurological disorders was first observed in French Polynesia in 2014 (4). During the current outbreak of ZIKV in America region, Brazil witnessed an apparent 20-fold increase in incidence of microcephaly cases from April 2014 to 2015 (5). In April 2016, a seminal review by scientists from the US Centers for Disease Control and Prevention concluded that a causal relationship exists between prenatal ZIKV infection and microcephaly and other serious brain anomalies (6). Among several studies reviewed were cases of vertical transmissions of ZIKV in women infected at the end of the first trimester of pregnancy, along with evidence of ZIKV in brain of two fetuses with microcephaly (7,8). Based on these and other studies (9,10), there is now scientific consensus that ZIKV is a cause of microcephaly and Guillain-Barré syndrome.

Following the declaration of the PHEIC, the WHO Regional Office for the Eastern Mediterranean conducted three rounds of emergency meetings with a view to enhancing preparedness and response capacities for ZIKV infection and its complications. The first two rounds of meetings held on 22–23 and

28–29 February in Cairo and Casablanca respectively had a good representation of the health ministries of the 22 Member States of the Region. These two meetings provided up-to-date information on ZIKV infection and its complications drew up a set of priority actions to be implemented by the Member States and WHO to enhance preparedness and response capacities. The third round of the meeting took place on 20–21 April 2016 in Cairo and called in regional partners including UN agencies, international organizations, academia and technical institutions to discuss the scope of scaling up the preparedness actions for Zika in the Region. The outcomes of the first two meetings with the Member States were discussed in the third meeting and a joint action plan was developed with partners to implement the priority actions in countries; this included a region-wide advocacy campaign to be launched jointly to raise awareness on Zika and other arboviral infections.

This overview highlights the current situation in the Region, the current knowledge gaps on the circulation of ZIKV in the past in the Region as well as recommended actions that the countries should consider to enhance their preparedness and response capacities.

Situation in the EMR

Although no human infection from ZIKV has so far been reported from any country in the Eastern Mediterranean Region, serological evidence of the circulation of ZIKV has been reported in at least two countries: Pakistan (11) and Egypt (12). The current situation does not rule out that cases of ZIKV infection may appear in the Region as travel is likely to contribute to the risk of importation of the virus. While the risk of importation is equally high in all countries in the Region, the risk of local transmission following the introduction of the virus through a viraemic patient returning from a country with active ZIKV circulation remains high in countries where the mosquitoes that primarily transmit this virus

exist. According to this risk stratification, countries therefore need to enhance their preparedness measures.

Mosquitoes belonging to the *Aedes* genus, particularly *Aedes aegypti* and *Aedes albopictus*, which are the species most incriminated as vectors of ZIKV and other arboviral diseases, have been found in a number of countries in the Region including Djibouti, Egypt, Lebanon, Oman, Pakistan, Saudi Arabia, Somalia, Sudan and Yemen. Sporadic cases of dengue fever, either locally transmitted or imported, have been reported from Djibouti, Egypt and Oman while explosive outbreaks of dengue fever have been reported in the past from Pakistan (13), Sudan (14) and Yemen (15), chikungunya from Yemen (16) and yellow fever from Sudan (17). These outbreaks have been propagated by the high density of *Aedes* mosquitoes that usually peaks during the summer months and also during the rainy season when water for household use is temporarily stored in household containers, especially in urban areas. It has been observed that temperature plays a role in adult vector survival, viral replication and infective period (18). These climatic conditions will favour the geographic expansion of the *Aedes* mosquitoes distribution and the risk of spread of ZIKV and other arboviral infections such as dengue, chikungunya and yellow fever in the endemic belt.

Vector-borne diseases pose a particular challenge to national public health authorities because of their complex nature requiring multidisciplinary competencies and strong rapid interaction among committed sectors. *Aedes* mosquitoes have been found in at least 9 countries of the Region, while their presence or absence is still to be assessed in the rest of the area. Therefore a strong entomological surveillance system is needed in the Region.

Knowledge gaps on circulation of Zika virus in the Region

A number of key knowledge gaps have been identified regarding the circulation or transmission of ZIKV in the past in the Region, including: a) *Aedes*

vector distribution in the endemic belt; b) evidence of silent ZIKV circulation in the Region; c) evidence of increased incidence of microcephaly and Guillain-Barré syndrome in the *Aedes*-endemic belt in the past during an active circulation of arboviruses; and d) causal link between microcephaly, Guillain-Barré syndrome and/or other neurological disorders and other arboviral infections in the endemic belt of *Aedes* mosquitoes during an active circulation of dengue, chikungunya and/or yellow fever virus in the past.

Public health measures for preventing ZIKV infection

Mosquito surveillance remains as a key component of any local integrated vector management programme. Preventing or limiting the transmission of dengue, chikungunya and Zika viruses is completely dependent on the control of mosquito vectors and reduction of person–mosquito contact. A strong entomological surveillance system is crucial for obtaining data on the distribution of vector(s), the extent and types of breeding habitats, and the intensity and seasonal fluctuations of breeding of mosquitoes. Entomological sampling methods to assess *Aedes* population density and evaluate the control interventions have been largely implemented, especially in South-East Asian countries. There is a need to introduce and adapt those methods in countries through standardized protocols, including traditional Stegomyia indices to be used in outbreak prevention.

Lack of entomological capacity for arboviruses is one of the main contributing factors to poor entomological surveillance and control. An inventory of resources for medical entomology in the Region (i.e. experts, training institutes, research agencies and laboratories working for medical entomology) needs to be conducted. Furthermore, a network of medical entomologists needs to be established to support the work of entomological surveillance and vector control for arboviral diseases. A plan to build capacity for entomological surveillance and vector control through the use of

regional/international resources/centres of expertise needs to be developed. The key vector control measures targeting all stages of the *Aedes* mosquitoes include environmental, biological and chemical methods. Population movement, climate change and insecticide resistance remain key concerns.

There is a strong need to build/strengthen an early warning system to pre-empt/predict and detect early vector-borne diseases in the Region through integrating vector surveillance with syndromic based and event-based disease surveillance and using the surveillance data efficiently to predict and detect early the transmission risk. Operational research needs to be conducted to determine national thresholds for entomological indices that can be useful to pre-empt/predict the occurrence of an epidemic.

The signs and symptoms of ZIKV infection often overlap with those of other arboviral infections making clinical diagnosis uncertain. Diagnosis can be confirmed by laboratory testing for the presence of ZIKV RNA or specific anti-Zika antibodies in the blood. However, a conventional antibody test (ELISA) in the *Aedes*-endemic belt remains a particular challenge because of cross-reactivity with other flaviviruses (e.g. dengue, yellow fever, West Nile viruses). The plaque-reduction neutralization test (PRNT) for virus-specific neutralizing antibodies (IgG) in serum samples is considered a confirmatory test. ZIKV may also present a risk to blood safety. There are reports of confirmed positive ZIKV RNA among healthy blood donors during the outbreak in French Polynesia (2013/14) (19) and recently two probable cases of ZIKV transmission by blood transfusion have been reported from Campinas, Brazil (20).

Countries reporting sporadic ZIKV in travellers arriving from affected countries pose little, if any, risk of onward transmission. Nonetheless, all travellers need to stay informed about ZIKV and other mosquito-borne diseases. They should adhere closely to steps that can prevent mosquito bites while travelling and practice safe

sex, especially pregnant women and their partners, including through the correct and consistent use of condoms. Pregnant women need to be advised not to travel to areas of ongoing ZIKV transmission. Travellers to mass gatherings occurring in countries with active ZIKV transmission should follow the normal travel advice provided by their health authorities.

The International Health Regulations (IHR) 2005 requirements' at points of entry related to vector-borne diseases, as specified in Annex 5, call for establishing vector surveillance and control at points of entry and a minimum distance of 400 m from point of entry facilities (operations involving travellers, conveyances, containers, cargo and postal parcels). A vector surveillance and control programme should be appropriately designed for each point of entry using a risk assessment approach. Conveyances leaving a point of entry situated in an area where vector control is recommended should be disinfected. However, and in the context of ZIKV, the decision to implement WHO disinsection recommendations is dependent on individual country risk assessment for vector control. Currently, there is no WHO guiding document on disinsection of ships, however, the guidelines of the International Maritime Fumigation Organization on fumigating ships can be used as a reference (21).

Risk communication for ZIKV infection should take into consideration the varied context of countries in the Region, such as when a country is preparing for ZIKV, when a country has the first confirmed case of ZIKV with travel history to an affected country, when a country has the first confirmed case of ZIKV with no travel history, and when a country experiences a ZIKV outbreak. The public messages need to be timely, precise, applicable and relevant, i.e. tailored to the audience for which they are intended. Communication products should be tested (pre and post) to analyse the public impact of their messages and to ascertain whether behavioural changes to control the vector have in fact been achieved.

In view of the extensive actions that need to be taken forward in the countries in all the areas of work outlined above, the Member States acknowledged the importance of having strong public health leadership for effective coordination among all stakeholders, including the community, to reduce the risk of ZIKV infection in countries.

Conclusion

During the current ongoing outbreak, WHO estimates that there could be 3-4 million cases of ZIKV infection in the Americas in the next 12 months (22). The risk of international spread of ZIKV to other regions is a real concern, as demonstrated by the recent finding that the Zika strain responsible for the outbreak in Cape Verde, Africa was most likely imported from Brazil (23). In the EMR, the risk of local transmission poses further concern. Owing to a lack of laboratory diagnostic capacities for ZIKV in countries where the *Aedes* mosquitoes exist, many of which are affected by protracted conflict and have

fragile health systems, any silent introduction of the virus may go undetected and trigger sustained local transmission. As populations living in the countries in the *Aedes* mosquito belt would supposedly be immunologically naïve to ZIKV, the ubiquitous presence of the vectors might contribute to rapid transmission of ZIKV amongst the at-risk population if not detected and contained early.

The current situation where no cases of ZIKV have been reported in the Region, either locally acquired or travel-associated, presents an opportunity to improve surveillance and fill other gaps in preparedness and response capacities as required under the IHR 2005. Boxes 1 and 2 shows a number of recommendations that countries may consider to implement; these came out of the two rounds of meetings in February 2016. The most urgent is to enhance both epidemiological and entomological surveillance between now and the coming rainy seasons in countries with a known presence of *Aedes* mosquitoes. Such efforts should be directed to both early identification and recognition of ZIKV transmission as well as identification

of any abnormal or sudden increase in congenital birth defects for which there is no plausible reason. As the density of *Aedes* mosquitoes is expected to peak during the summer months and during the rainy seasons in these high-risk countries, necessary vector control efforts need to be directed at reducing the potential breeding sites of mosquito populations and/or their interactions with humans to below levels that can sustain an epidemic.

Such actions certainly warrant heightened support from all concerned. WHO is working closely with partners from the countries and other regions, as well as other UN agencies, in order to ensure optimum support to countries to reduce the risk of ZIKV infection and its complications.

The countries of the EMR demonstrated outstanding solidarity, public health vigilance and shared responsibilities during the threat of introduction of Ebola virus disease. The time has again come to show the same level of collective understanding, purpose and effort in order to mitigate this newly emerging health threat.

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Box 1 Recommended actions to enhance preparedness and response capacities for prevention and control of Zika virus infection in EMR countries with evidence of transmission of dengue, chikungunya and yellow fever viruses in the past

1. Identify hot spots (risk mapping) through uniform and standardized risk assessment and stratify areas by spatial and geographic distribution of *Aedes* mosquitoes and past arbovirus epidemics.
2. Develop/update a geo-referenced atlas of *Aedes* and their current susceptibility status, which should be used as the basis for developing an insecticide resistance management strategy; use this information to update the categorization of high risk, low risk and receptive countries.
3. Establish a sentinel surveillance system for *Aedes* mosquitoes in areas with high density including at designated points of entry, and collect data regularly to pre-empt and detect the occurrence of high densities of *Aedes* mosquitoes and target these areas for vector control.
4. Develop/update an integrated vector management strategy with strong focus on entomological surveillance and control measures, supported by a clear operational plan defining the role of each sector.
5. Establish an early warning system for detection of clusters of ZIKV infection and other vector-borne diseases by:
 - using a uniform case definition for syndromic surveillance of acute febrile syndrome;
 - using a sentinel-based syndromic surveillance system for clusters of acute febrile syndromes in high risk areas (hot spots) as complementary to the routine disease surveillance system;
 - integrating the syndromic disease surveillance system with the sentinel based entomological surveillance system for *Aedes* mosquitoes and periodically share disease and entomological surveillance data and other information;
 - establishing an event-based surveillance system (including a community-based surveillance system where possible)
 - utilizing existing surveillance (e.g. measles, birth defects and acute flaccid paralysis) to detect ZIKV infection and its complications;
 - enhancing timely reporting and information sharing between the epidemiology, laboratory and entomology surveillance units.
6. Improve appropriate laboratory diagnosis and testing capacities for ZIKV infection, including establishing appropriate links with external reference laboratories for sample testing.
7. Keep blood transfusion services updated about measures to ensure a safe supply of blood.
8. Consider disinfecting conveyances arriving from a country with active ZIKV transmission using risk assessment approach and using WHO standard recommendations for disinsection.
9. Establish a sentinel based surveillance system for congenital birth defects using consistent case definitions and harmonized data collection tools, and follow-up clinical outcomes of pregnant women suspected to be infected with an arboviral disease.
10. Collect retrospective data on birth registrations, trace them back and try to establish any baseline/comparator data to assess the trend of congenital birth defects (especially microcephaly).
11. Conduct regular public awareness campaigns to proactively inform the public of the ZIKV situation, urge communities to keep areas in and around the home free from mosquito breeding sites through applying appropriate risk communication messages and strategies in accordance with local culture and behavioural practice, and provide communities with the appropriate knowledge, information and tools to protect themselves from mosquito bites.
12. Develop/update epidemic and pandemic contingency plans for ZIKV infection as well as standard operating procedures for an incident command system and for strengthening coordination.

Box 2 Recommended actions to enhance preparedness and response capacities for prevention and control of Zika virus infection in EMR countries with no presence of *Aedes* mosquitoes or with presence of *Aedes* mosquitoes but no evidence of transmission of dengue, chikungunya and yellow fever viruses in the past

1. Raise awareness of travellers going to areas with active transmission, including those participating in mass gathering activities, through issuance of appropriate advisories to reduce the possibility of exposure to mosquito bites.
2. Enhance coordination and collaboration between travel, trade and health sectors to ensure implementation of related WHO recommendations.
3. Increase knowledge and awareness of all aspects of ZIKV infection among clinicians, health care workers and other stakeholders.
4. Improve appropriate laboratory diagnosis and testing capacities for ZIKV infection, including establishing appropriate links with external reference laboratories for sample processing.
5. Keep blood transfusion services updated about measures to ensure a safe supply of blood.
6. Establish sentinel surveillance of *Aedes* mosquitoes in areas with past information of *Aedes* distribution and take prompt action targeting breeding sites in a radius of 400 m in the event of any increase in *Aedes* density.
7. Conduct surveys to collect data on *Aedes* mosquitoes in countries with no known vectors and enhance surveillance of mosquitoes in areas bordering countries with known vectors.
8. Monitor imported goods (e.g. used tyres, bamboo) by quarantine measures to avoid entry of invasive species of mosquitoes and implement vector surveillance and control at designated points of entry as per IHR (2005).

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