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ANNUAL EPIDEMIOLOGICAL SURVEILLANCE REPORT

Malaria in Greece, 2016

Introduction

Malaria is a parasitic infection, transmitted through the bite of the infected female *Anopheles* mosquito. Five species of Plasmodium cause disease to humans: *Plasmodium falciparum, P. vivax, P. ovale, P. malariae* and *P. knowlesi*. *P. falciparum* and *P. vivax* are the most common.

The most common symptoms of malaria (chills, high fever, sweating, malaise, headache and muscle aches) manifest usually 1-4 weeks after infection with the parasite, while relapses of the disease are usually observed in short intervals but up to five -and in extreme cases even up to eight- years after *P. vivax* infections. A number of effective anti-malarial drugs are available to treat the infection; starting the treatment promptly is essential in avoiding complications and interrupting the transmission of the disease in the community.

Malaria is currently endemic -with ongoing transmission- in 91 countries around the world (WHO, World Malaria Report, 2016), mainly in sub-Saharan Africa, Asia and Latin America. Until the mid-twentieth century, several countries in Europe and North America were malaria endemic, but after an intense malaria control program it was eradicated.

Malaria surveillance in Greece

Data are derived from the reports of laboratory-confirmed malaria cases and the enhanced surveillance systems of the Hellenic Center for Disease Control & Prevention (HCDCP). The Department of Epidemiological Surveillance and Intervention undertakes a verification procedure through communication with the treating physicians, the hospital and the reference laboratory for malaria. Case, focus and environmental investigation are undertaken by the staff of the Department of Epidemiological Surveillance and Intervention of local public health authorities, for every locally acquired malaria case throughout Greece. In addition, in specific areas with recorded clusters of locally acquired malaria cases over the last years, active searching of malaria cases, door-to-door is implemented (see below).

Malaria surveillance data in Greece, 2009 – 2015

Greece was declared free from malaria in 1974, following an intense control program (1946-1960). Since then and up until 2016, several (20-110 cases) imported cases were reported annually to the HCDCP referring to patients infected abroad (returning travelers or migrants from malaria endemic countries). Increasing numbers of imported malaria cases is expected due to the increase of travels and population $Page \mid 2$ movements worldwide, and is observed in all developed countries. According to the European Centre for Disease Control and Prevention (ECDC), in 2014 more than 6,000 malaria cases were recorded in EU/EEA countries.

Additionally, since 2009 a number of locally acquired P. vivax malaria cases have been recorded in various areas of the country (i.e., among patients without travel history to a malaria endemic country), mainly as sporadic introduced cases but also in clusters (in 2011- 2012). Most areas where locally acquired cases were recorded over the last years were rural close to wetlands with high number of persons from endemic countries.

The number of malaria cases in Greece reported to the HCDCP by year of symptom onset (for imported cases) or infection (for locally-acquired cases) and by epidemiological classification (imported/ locallyacquired) is presented in Table 1. Table 2 presents locally acquired *P. vivax* malaria cases by probable Region and Regional Unit of exposure, years 2009-2015.

Year of symptom onset/	Case classification						
infection	Imported cases	Locally-acquired cases ²					
2009	44	7					
2010	40	4					
2011	54	42					
2012	73	20					
2013	22	3					
2014	38	0					
2015	79	8 ³					

Table 1: Reported malaria cases by year of symptom onset¹ (for imported cases) or infection (for locallyacquired cases) and by epidemiological classification (imported/ locally-acquired), Greece, 2009 - 2015.

1. Cases with no information regarding symptom onset were classified according to the year of hospitalization or notification to the HCDCP.

2. Recorded P. vivax relapses and locally-acquired P.malariae cases attributed to previous transmission periods (two cases in 2012) are not included in the Table.

3. Two cases, with symptom onset in 2016 that were attributed to the 2015 transmission period are included.

Design	Designal Unit	Year of infection							$\boxed{\frac{1}{1}}$
Region	Regional Unit	2009	2010	2011	2012	2013	2014	2015	
Peloponnese	Lakonia	6	1	36	10	0	0	1	
Attica	East Attica		1	2	4	0	0	2	
Sterea Ellada (Central Greece)	Viotia	0	2	1	2	0	0	1	
	Evoia	0	0	2	0	0	0	0	
	Karditsa	0	0	0	2	1	0	0	
Thessaly	Larisa	0	0	1	0	0	0	3*	
	Trikala	0	0	0	0	0	0	1	
East Macedonia	Xanthi	0	0	0	2	0	0	0	
& Thrace	Evros	0	0	0	0	2	0	0	
Total		7	4	42	20	3	0	8*	

Table 2: Locally acquired *P. vivax* malaria cases by probable Region and Regional Unit of exposure and year of infection, Greece, 2009-2015

*Two cases, with symptom onset in 2016 that were attributed to the 2015 transmission period are included.

This case classification is based on epidemiological criteria (e.g. history of travel within the last 3 years to a malaria endemic country). However, recent *Plasmodium* genotyping results suggest that a number of cases previously classified as "imported" are actually locally acquired (e.g. some of the malaria cases in immigrants from malaria endemic countries residing in the Municipalities of Evrotas, Lakonia and Sofades, Karditsa, in transmission periods 2011-2012). These cases concerned migrants from endemic countries in 2011 (n=9) and 2012 (n=11), who were residing in the municipalities of Evrotas Lakonia and Sofades Karditsa (data to be published).

Malaria surveillance data, Greece, 2016

In 2016, a total of 121 laboratory diagnosed malaria cases were reported to the HCDCP;

- 111 cases were classified as imported: 91 (82%) cases among immigrants from malaria endemic countries and 20 cases among travelers (returning from Africa). Of the 91 cases in immigrants from malaria endemic countries:
 - 80 were in immigrants from the Indian Subcontinent/ South Asia and 11 from Africa,
 - 14 cases concerned immigrants visiting friends and relatives at their country of origin,
 - 18 cases were recorded among immigrants/refugees residing in camps/ reception centers in Aegean islands (and three more in other hosting facilities).

- Six (6) *P. vivax* malaria cases were classified as introduced locally acquired, with the following probable places of exposure:
- one case from the Municipality of West Ahaia, Regional Unit (RU) of Ahaia ("Achaea"), Region of West Greece (with onset of symptoms in the week 26/2016 (27/06-03/07/2016)),
- one case from the Municipality of Andravida-Kyllini, RU of Ileia ("Heleia"), Region of West Greece (with Page | 4 onset of symptoms in the week 29/2016 (18-24/07/2016)),
- two cases from the Municipality of Lagadas, RU of Thessaloniki, Region of Central Macedonia (with onset of symptoms in the week 29/2016 (18-24/07/2016)),
- one case from the Municipality of Skiathos, RU of Magnesia and Sporades ("Magnisia"), Region of Thessaly (with onset of symptoms in the week 31/2016 (01-07/08/2016)), and
- one case from the Municipality of Tempi, RU of Larissa, Region of Thessaly (with onset of symptoms in the week 44/2016 (31/10-06/11/2016)).
- Two (2) *P. vivax* locally acquired cases from the Municipality of Tempi, RU of Larisa, Region of Thessaly, with symptom onset in 2016, were attributed to the previous transmission period in 2015, according to the laboratory and epidemiological investigation. It was considered that they were probably infected in the same village where one locally acquired case was recorded in 2015 (and where one more locally acquired case was recorded in 2015).
- The case classification for two (2) *P. vivax* malaria cases was undetermined, since the area and time of their exposure could not be defined, either due to inadequate information or to complex travel history.

No locally acquired malaria case was directly linked to the presence of refugee/migrant camps in the area.

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Figure 1. Probable Regional Unit (RU) of exposure of introduced locally acquired malaria cases, Greece, 2016 (n=6)



<u>Table 3</u> presents the reported malaria cases in Greece by epidemiological classification (imported/ locally acquired), status (immigrants/ returning travelers) and place of residence (for the imported cases) or probable exposure (for the locally acquired cases).

Table 3.	Malaria	cases	by	epidemiological	case	classification,	status	and	Plasmodium	species,	Greece,
2016 (n=	119*).										

Epidemiological case classification and status		Plasmodium species								
		P. vivax	P. falciparum	P. falciparum P. falciparum P. falciparum Unspecified + P.ovale + P.malariae						
Imported	Immigrants	81	9	0	1	0	91			
cases	Travelers	1	17	1	0	1	20			
Locally acquired cases (all introduced)		6	6 0 0		0	0	6			
Unknown		2	0	0 0 0		0	2			
Total		90	26	1	1	1	119			

*Two locally acquired *P. vivax* cases, with symptom onset in 2016, attributed to 2015 transmission period are not included.

HCDCP activities for the management of malaria, 2011-2016

Since 2012, HCDCP has developed and continuously implements an Action Plan for the Management of Malaria. In addition, during summer 2015 the "National Action Plan for the Management of Malaria" of the Ministry of Health was published. According to these, a series of activities are implemented nationwide for the prevention and management of malaria, with the collaboration of national, regional and local $Page \mid 6$ authorities. These activities for the management of malaria include:

Ι. Risk assessment for the re-emergence of malaria: All areas (Regions, Municipalities) are assigned a Risk Level from 0-3, taking into consideration the malaria cases reported since 2009, and other local risk factors (entomological, environmental and demographic data). The Risk Level defines the activities implemented in each area.

Enhanced malaria surveillance and intervention activities: 11.

- Case finding: In order to promptly detect all malaria cases, raise awareness among local health professionals and active case detection activities in high risk areas are implemented and support is provided for the laboratory diagnosis of malaria.
- Case investigation: HCDCP investigates all notified malaria. For locally-acquired cases, an in-depth interview with the patient is conducted, in order to identify the estimated place of exposure and the risk for further local transmission.
- Immediate communication to stakeholders and health professionals at national and local level, after the reporting of each locally-acquired malaria case to the HCDCP:
 - Hierarchy of the Ministry of Health (MoH), i.
 - Regional public health authorities, ii.
 - iii. Municipalities,
 - iv. MoH Committee for the Prevention and Management of Tropical Diseases,
 - Working Group for the designation of vector-borne disease (VBD) affected areas, v.
 - vi. National Centre for Blood Donation, responsible for the relevant blood safety measures,
 - vii. Physicians practicing in the affected area, to raise their awareness for investigating suspect cases.
- Focus investigation reactive case detection: HCDCP investigation teams are deployed after the notification of each locally acquired case to perform a "focus investigation", in an area indicated by the epidemiological, entomological and environmental investigation. In this activity, all immigrants from malaria endemic countries in the focus were tested for malaria (RDT, microscopy and PCR), while individuals from non-endemic countries were screened for malaria compatible symptoms and tested for malaria accordingly. Fever screening was repeated on a regular basis for a month after the initial investigation.
- **Environmental and vector investigation** is performed in the area after the detection of each locally acquired malaria case (or imported case in a receptive area), in order to identify Anopheles breeding sites and other risk factors for local transmission.

- Proactive malaria case detection (PACD) in Evrotas Municipality, Lakonia: The HCDCP, in collaboration with the Region of Peloponnese, the Municipality of Evrotas, the University of Thessaly –MALWEST project (www.malwest.gr) and Doctors Without Borders (2012), supported from 2011-2014 a field team in the area for the active detection of malaria cases. Since 2015, the field team -with staff from the University of Thessaly and coordination from the HCDCP- is $Page \mid 7$ supported by the Region of Peloponnese to continue the PACD programme, undertaking also the radical treatment and focus investigation of all recorded malaria cases. A significant number of immigrants from malaria endemic countries (mainly Pakistan) live and seasonally work in Evrotas. During the field visits, health promotion information is provided for protection against mosquitoes and fever screening and/or testing for malaria is performed regularly. In May-November 2016, fever screening visits were performed every 7-15 days in immigrant and Roma residences. A total of 800-1,000 migrants were screened (600-700 migrants systematically in 7 villages and 200-300 migrants in 5 other villages depending on the need).
- III. Enhancing laboratory diagnosis of malaria: Since 2012, HCDCP has distributed Rapid Diagnostic Tests (RDTs) for malaria to Hospitals and Health Centers in areas with recently recorded local malaria transmission, and in areas with large populations of immigrants from endemic countries (i.e., large urban centers, in refugee/migrant camps, reception centers and the nearby Health Units), aiming at prompt diagnosis and treatment of malaria cases. RDTs have contributed significantly to the early detection of malaria cases in our experience and have been proven a valuable field tool.

In addition, HCDCP recommends and supports the transportation of samples from any laboratory in Greece to the reference laboratory (Department of Parasitology, Entomology and Tropical Diseases of National School of Public Health) for verification of diagnosis and further identification (and genotyping) of *Plasmodium* species.

- IV. Administration of antimalarial prophylactic therapy to immigrants from malaria endemic countries: In 2013 -2015, following the proposal of the HCDCP Working Group on Vector-borne Diseases and the approval of the Committee for the Prevention and Management of Tropical Diseases of the Ministry of Health, the field team in Lakonia delivered one course of antimalarials for P.vivax infection (Chloroquine + Primaguine) to all immigrants from malaria endemic countries who lived in the Municipality of Evrotas. The antimalarials were administered using directly observed treatment (DOT) protocol with the informed consent of the participating immigrants and following testing of G6PD levels. The antimalarial course targeted P.vivax hypnozoites in order to reduce the reservoir and interrupt transmission of the disease in the particular area. The purposefulness to implement this action is evaluated according to the epidemiological data and the risk assessment of each period.
- V. Case management Standardization of the malaria treatment in Greece, according to treatment guidelines developed by the HCDCP with the input of experts in infectious diseases. HCDCP also maintains a small stockpile of specific anti-malarial medicines for timely distribution to Health Units in cases of emergency.
- VI. Increase awareness amongst health professionals for the diagnosis and management of malaria. HCDCP staff delivers presentations and organizes seminars for health professionals in Health

Centers/Hospitals in areas with recently recorded locally acquired cases. Informative letters are also sent to all hospitals and Medical Associations on an annual basis.

- VII. Communication to the public on malaria and personal protection measures against mosquitoes:
- Educational material on malaria and protective measures against mosquitoes is available on the Page | 8 HCDCP website (<u>www.keelpno.gr</u>). Information material (leaflets, posters) is distributed according to the needs.
- In areas with locally acquired cases recorded, the HCDCP field team informs the local population, and raises awareness about malaria and the necessary protective measures against mosquitoes during the focus investigations.
- VIII. Designation of affected areas Blood safety and haemovigilance measures: An inter-sectoral Working Group (WG) on the designation of VBD affected areas (under the MoH Committee for the Prevention and Management of Tropical Diseases) considers all available epidemiological and laboratory data for each locally-acquired case and decides on the characterization of malaria affected areas in Greece. This designation is then used by the National Centre for Blood Donation to issue guidance on blood safety. The list of affected municipalities is published on our website (www.keelpno.gr) and updated regularly according to reported locally acquired cases. Post donation and post transfusion information to donors and other haemovigilance measures are in place following relevant guidance from the Coordinating Haemovigilance Centre/ H.C.D.C.P..

IX. Vector control activities - Entomological surveillance:

- Raising awareness and guidance to Regional Authorities: HCDCP communicates regularly with all Regional Authorities in Greece recommending the timely planning, organization and implementation of integrated vector control programmes, identifying the high risk areas. Detailed technical guidance is timely communicated by the HCDCP to the Regional administrations all over the country, in order to assist them to implement on time the calls for tender for integrated vector control programs. In 2016, further awareness was raised regarding risk assessment and intensifying mosquito control programs accordingly around camps hosting refugees/migrants.
- Monitoring of the vector control programme implementation across the country.
- Distribution and placement of Long Lasting Insecticide-treated Nets (LLINs): According to WHO and ECDC guidance, HCDCP distributes (since 2013, in each transmission period) LLINs to immigrants, in the Municipality of Evrotas, Lakonia, after obtaining a special license from the Ministry of Rural Development and Agriculture. The distribution, placement and monitoring of the proper use of the nets is implemented by the PACD field team, which conducts the active case detection in the area. In 2016, 112 nets were distributed to migrant residences.
- **Participation in the implementation of indoor residual spraying (IRS):** The Region of Peloponnese implements every summer indoor residual spraying (IRS) in migrant residences in the area of Evrotas. The PACD field team participates in the activity by indicating migrant residencies in the area. HCDCP continues to recommend this vector control method in this area.

- Entomological surveillance: The HCDCP, in collaboration with the Department of Parasitology, Entomology and Tropical Diseases of the National School of Public Health (NSPH), the Benaki Phytopathological Institute, the MALWEST project (2012-2014), Universities, Regions, local authorities and subcontractors of the local mosquito control programmes has implemented, participated or coordinated -from 2010 to 2015- active vector surveillance programme. For the 2016 transmission period, vector surveillance was conducted in limited areas, from NSPH, with the voluntary participation of Regions, local authorities and their subcontractors. HCDCP recommends that local authorities should perform vector surveillance annually, especially in areas with risk factors for local malaria transmission (e.g. rural areas with large populations from malaria endemic countries) and collects any available vector surveillance data from these areas, as well as from areas with recent local transmission.
- Communication with international public health stakeholders: The HCDCP communicates frequently
 for exchange of knowhow and information on malaria cases and activities with the ECDC and WHO, as
 well as with a number of European and international agencies and networks.
- X. Due to the increased migrant/ refugee population residing in the country in reception and accommodation camps, a series of targeted activities have been organized in these camps, including: strengthening malaria surveillance and diagnosis, distribution of rapid diagnostic tests to the camp clinics and nearby Health Units, recommendation for systematic entomological surveillance in the area, risk assessment (collection of available entomological, environmental and demographic data) and, if necessary, intensification of mosquito control measures, personal protection measures against mosquitoes for the hosted migrants. The Ministry of Health issued a circular in 2016 regarding the placement of the camps hosting refugees/ migrants from malaria-endemic countries at least 6km away from large *Anopheles* mosquito breeding sites and villages with recently recorded local malaria transmission. In July 2016, HCDCP staff from Athens and Thessaloniki, in cooperation with the regional public health authorities of Central Macedonia region, performed field visits in camps in the Region, in order to collect more data and further asses the risk.

Conclusions

As indicated by the malaria surveillance data, the risk of re-appearance of the disease in specific - vulnerable and receptive- areas of the country exists, especially where the presence of adequate numbers of *Anopheles* mosquitoes (the competent vector of the disease) is combined with the presence of malaria patients coming from endemic countries.

Following a peak of locally acquired malaria cases between 2011- 2012 their number declined steadily in the following years. This coincided with a number of intense and costly public health interventions implemented since 2011, with the collaboration of various stakeholders at the national, regional and local level, which have contributed to the successful prevention of the re-establishment of malaria in Greece.

However, sporadic introduced locally acquired malaria cases were still recorded up to 2016, in vulnerable and receptive areas around the country, indicating the need to sustain the activities for the prevention of the disease a priority for the public health authorities.

Early detection and eradication treatment of malaria cases, together with mosquito protection and effective vector control measures represent the main components of the public health strategy to prevent

P.vivax reintroduction in high risk areas of the country. In this context, all the above need the maintenance of high level of preparedness and awareness of health and public health services, at local, regional and national level. In addition, important determinants for the prevention of local malaria transmission in Greece include the continued offer of free access to health services for migrants for the timely diagnosis and treatment of malaria, the open communication with the migrant population and achieving a minimum ${
m Page\,|\,10}$ standard for their living conditions and well-being.

Advice for travelers in Greece:

The HCDCP, based on the surveillance data available until now and the implemented prevention measures in the areas where locally-acquired P.vivax malaria cases have been reported, maintains that the risk to travelers for malaria infection in Greece is very low. Chemoprophylaxis for malaria is not recommended for visitors to areas where locally acquired malaria cases have occurred until today. Personal protective measures against mosquitoes are strongly encouraged.