



RAPID RISK ASSESSMENT

Autochthonous *Plasmodium vivax* malaria in Greece

23 August 2011

Main conclusions and recommendations

Greece reports six cases of *Plasmodium vivax* infection in Evrotas, Lakonia, Peloponnese region, and Chalkida in Evoia since June 2011. The main risk related to the current event is to persons living in, visiting and working in the particular area of Evrotas in the district of Lakonia (and potentially Chalkida in Evoia, though more information is needed) in Greece. The local transmission of *P. vivax* malaria to humans is believed to have occurred here over the last three years and is likely to continue producing annual clusters of human cases. However, the risk for further extension of malaria transmission into the EU related to this event is considered low at present.

Public health issue

Cases of autochthonous malaria due to *Plasmodium vivax* reported in Greece.

Source of assessment request and consulted experts

This rapid risk assessment was undertaken following an internal decision at ECDC.

ECDC would like to thank the following external organisations and experts who were consulted for this assessment: Department of Surveillance and Intervention of the Hellenic Centre for Disease Control and Prevention and National School of Public Health, Greece; João Pinto (Instituto de Higiene e Medicina Tropical, Portugal), Christophe Lagneau (EID Méditerranée, France) and the World Health Organization.

Disease background information

Plasmodium vivax is one of the main five *Plasmodium* species that cause human malaria (*P. vivax*, *P. falciparum*, *P. malariae*, *P. ovale* and *P. knowlesi*); all are transmitted through the bite of female *Anopheles* mosquitoes.

The main symptoms of malaria, in general, are cyclical fever and chills, headache, weakness, vomiting and diarrhoea. The most common complication is enlargement of the spleen. The incubation period for *P. vivax* usually ranges from 10 to 21 days, but might reach up to a year. Unlike *P. falciparum* malaria, *P. vivax* malaria is rarely fatal. However, *P. vivax* relapses often occur months to years after treatment due to the fact that the parasites can develop dormant forms (hypnozoites) in the liver. Relapses are not prevented by current chemo-prophylactic regimens, with the exception of primaquine, which should always be added to treatment regimens to eradicate dormant liver forms.

Among the five *Plasmodium* species, *P. vivax* has the widest distribution in the world; nevertheless this parasite is not endemic in EU and EEA/EFTA countries. Between 2006 and 2009, the confirmed rate of malaria cases in EU and EEA/EFTA countries remained stable around one per 100 000 population. Of those cases for whom the relevant information was available, 99.5% were imported [1]. Within the WHO European Region, autochthonous *P. vivax* infections are regularly reported from Eastern Turkey, even though this trend is decreasing. In Spain, in 2010, a case of autochthonous malaria (*P. vivax*) was also reported from the Aragon region [2].

Autochthonous cases of malaria in Greece have previously been reported in 1999 and 2000 [3][4]. After several years of zero reports, six cases of autochthonous malaria were reported in 2009 (through the European Surveillance System – TESSy 2009) and one again in 2010, all residing in the same area of Evrotas [5]. The cases from 2009 were associated with two imported cases of *P. vivax* from Pakistan and Afghanistan, occurring in the summer in the Peloponnese region in southern Greece. In addition to these two imported cases, six autochthonous cases with *P. vivax* infection were identified from the same region in September and October 2009. All reported cases fully recovered.

It is known that insect vectors for malaria are present in Greece. Specifically in the Peloponnese region, the following species have been identified: *A. maculipennis s.s.*, *A. sacharovi*, *A. hyrcanus* and *A. superpictus* [6]. *A. sacharovi* is commonly found from May to September in wetlands and rice paddies, with the highest numbers of adult mosquitoes being observed from July onwards.

Event background information

Since June 2011, a total of six cases of malaria with no reported travel history to a malaria-endemic country were notified to the Hellenic Centre for Disease Control and Prevention through the mandatory notification system. All six cases were diagnosed with *P. vivax* malaria.

Four of these malaria cases were notified in the small agricultural and wetland area of Evrotas (aprox. 5 820 hectares) in the district of Lakonia, Peloponnese region, southern Greece. One case is a young Roma child, and three cases are adult Greek citizens not belonging to a minority group. This is the same small geographical area where the eight laboratory-confirmed cases of *P. vivax* malaria occurred between August and October 2009 (two imported cases and six autochthonous cases) and the one case in 2010. The two remaining cases are in adult Greek citizens that reside close to the town of Chalkida, in the district of Evoia, where no previous autochthonous malaria cases had been reported. These were notified in late July 2011. The median time between onset of fever and diagnosis for all cases was six days (range: 4–9 days). Figure 1 indicates the place of residence of the confirmed six cases from Greece.

Both the Lakonia and Evoia districts have a large population of non-documented migrant farm workers from malaria-endemic countries (e.g. Indian subcontinent).

The Hellenic CDC has established an enhanced surveillance system to identify other potential cases in both geographic areas. Local health professionals (primary care, private practitioners and hospital physicians) were contacted to raise awareness among the medical community regarding early malaria diagnosis and treatment. Despite enhanced surveillance, no additional malaria cases have been reported from adjacent areas in Lakonia or Evoia or other nearby districts.

Blood safety measures were also implemented for the donations coming from both areas. All blood donations tested by blood smear to date have been negative for *Plasmodium*. At the same time, random blood samples (n=120) collected from residents in the area of Evrotas, were also negative.

Entomological investigations in 2009 revealed the presence of *A. sacharovi* in the area of Evrotas. In June 2011, adult *Anopheles* spp. mosquitoes were not identified in CO₂ and light traps, although a limited number of *Anopheles* larvae were found in the wetlands.

Figure 1 Geographic distribution of confirmed cases of *P. vivax* infection in Greece, June–August 2011



Source: Hellenic CDC

Intensified measures to control the mosquito population including larviciding (Bti) and adulticiding with pyrethroids (conventional and ULV spraying) have been implemented by the local authorities to prevent local malaria transmission. Health promotion activities with communicational material (brochures, posters, TV spot) produced by the Hellenic Centre for Disease Control and Prevention were also carried out during the summer 2011.

In Romania, a case of *P. vivax* infection was reported this week in a man with disease onset (fever and malaise) in July 2011 [7]. In the two months prior to his return to Romania he had been working in the same area of Evrota, Lakonia. Apart from Greece, this man only reports travelling to Sicily, Italy, in 2010. He does not live near to an airport and no other malaria cases have been reported from the area in which he lives [8].

ECDC threat assessment for the EU

This is the third consecutive year in which autochthonous cases have been reported from Greece. The cases reported in 2009 (eight cases) and four of the cases reported in 2011 are from the same geographic area.

Based on the available information it is not possible to ascertain whether the local transmission is due to an imported case of malaria with subsequent onwards transmission to nearby residents by local mosquito vectors, or whether there is an established human reservoir of *P. vivax* in this region that contributes to annual malaria clusters and hence established transmission of the parasite. Further investigations into the likelihood of these two scenarios would be warranted to ensure an appropriate assessment of the related risk and the relevant public health response. The exposure history for the two recent cases from Chalkida, Evrota, is also insufficient to draw any conclusions on where they might have been infected.

Given the simultaneous presence of competent malaria vectors and infected/parasitaemic humans in the area of Evrotas, Lakonia, Peloponnese, in Greece, we cannot exclude that similar cases will continue to occur in this area in the future. Such cases may occur among residents, but also among people visiting or working in this area, including from other EU countries. Increased awareness among local health practitioners to ensure a rapid diagnosis and treatment has been ensured by the Greek authorities. In addition, information to residents and visitors on preventing mosquito bites is an important element of the implemented public health response.

The malaria situation in Greece is probably of limited risk to the rest of the European Union. However, health practitioners in other Member States should be reminded to include malaria infection in the differential diagnosis in symptomatic persons returning from these areas in Greece. The new reported case from Romania highlights the importance of this.

The risk of re-establishment of autochthonous transmission of malaria in wider continental Europe continues to be unlikely, as it is dependent upon mosquito distribution and abundance, vectorial capacity and vector competence of the mosquitoes, as well as introduction of parasite through travel of patients carrying gametocytes of *Plasmodium* spp. Some of these factors depend on climate and environment; no changes in species distribution of anopheline mosquitoes related to climate change have been observed yet in the EU but cannot be excluded in the future. For this reason, continued close monitoring of the situation in areas of the European Union where *Anopheles* mosquito populations are present is important, including increased awareness among clinicians, to rapidly identify and report suspected malaria cases to respective authorities, and ensure an appropriate public health response.

Conclusions

The main risk related to the current event is to persons living in, visiting and working in the particular area of Evrotas in the district of Lakonia (and potentially Chalkida in Evoia, though more information is needed), in Greece. The local transmission of *P. vivax* malaria to humans has occurred effectively in that area in three consecutive years and is likely to continue producing annual clusters of human cases. However, the risk for further extension of malaria transmission into the EU related to this event is considered low at present.

ECDC continues to closely monitor this event with the Hellenic CDC and WHO and will update this rapid risk assessment when needed.

Contact

support@ecdc.europa.eu

References

- [1] European Centre for Disease Prevention and Control (ECDC). Annual Epidemiological Report 2011 (2009 data) (in press).
- [2] Santa-Olalla Peralta P, Vazquez-Torres MC, Latorre-Fandos E, Mairal-Claver P, Cortina-Solano P, Puy-Azon A, et al. First autochthonous malaria case due to *Plasmodium vivax* since eradication, Spain, October 2010. Euro Surveill. 2010 Oct 14;15(41):19684.
- [3] Kampen H, Maltezos E, Pagonaki M, Hunfeld KP, Maier WA, Seitz HM. Individual cases of autochthonous malaria in Evros Province, northern Greece: serological aspects. Parasitol Res. 2002 Mar;88(3):261-6.
- [4] Kampen H, Proft J, Etti S, Maltezos E, Pagonaki M, Maier WA, et al. Individual cases of autochthonous malaria in Evros Province, northern Greece: entomological aspects. Parasitol Res. 2003 Mar;89(4):252-8.
- [5] Bezirtzoglou C, Dekas K, Charvalos E. Climate changes, environment and infection: Facts, scenarios and growing awareness from the public health community within Europe. Anaerobe. 2011 Jun 2.
- [6] Ramsdale C, Snow K. Distribution of the genus *Anopheles* in Europe. European Mosquito Bulletin. 2000;7:1-26.
- [7] Personal communication. Philippe Parola and Corneliu Popescu, EuroTravNet. 19 August 2011, email communication.
- [8] Personal communication. Adriana Pistol, Romanian National Institute. 19 August 2011, email communication.