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Perspective

Malaria in Laconia, Greece, then and now: a 2500-year-old pattern

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SUMMARY

Background: Malaria is still an active threat in many areas of the world. In Greece, in an area of the Laconia region, malaria epidemics have been recorded since as early as the 5th century BC. A local outbreak of malaria was reported in the summer/autumn of 2011.
Method: A comparative research study of historical and modern sources was carried out in order to explore the malaria outbreaks occurring in the area of Laconia, Greece.
Results: The study revealed that the central area (Elos and Skala), the peak season (early autumn), the *Plasmodium* species (*P. vivax*), the mosquito vector (*Anopheles sacharovi*), and the risk factors (wetlands and population movements) have, more or less, remained unchanged throughout the 2500-year span in Laconia.
Conclusions: Unique regional features preserve a seemingly recurring pattern of malaria outbreaks in this area of Greece. This study, based on low-cost effective research, offers a clear public health message. The Greek authorities responsible for health policy could build upon these findings in order to achieve the desired eradication.

"Exhalations from marshes and mud give birth to diseases", Hippocrates

1. Introduction

Although the history of malaria predates humanity, our understanding of its causative agents begins in 1880, when Charles Louis Alphonse Laveran was the first to discover protozoan parasites in the blood of affected patients.[1] The *Plasmodium* genus currently comprises at least 172 named species, infecting a wide range of mammals, birds, reptiles, and amphibians. *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, and *P. knowlesi* are implicated in human malaria, with female *Anopheles* mosquitoes being their exclusive transmission vectors.[2] *P. falciparum*, associated with acute, highly complicated and often fatal disease, is the predominant species, accounting for 92% of malaria cases globally.[3] On the other hand, *P. vivax*, extending well beyond the tropics, accounts for almost half of the malaria cases outside of Africa, with up to 390 million clinical infections per year. The species is traditionally thought to cause benign, possibly relapsing disease, although recent observations are beginning to challenge the notion of vivax malaria as a rare and fastidious killer.[4] *P. malariae*, *P. ovale*, and *P. knowlesi* have a limited distribution worldwide.[5,6]

Despite the ongoing application of extensive control measures on a global scale, malaria remains the most significant parasitic infection in humans, claiming over a million lives annually.[3] Factors contributing to the resurgence of the disease in modern times include population movements within or through endemic countries, the spread of chloroquine resistance among malaria parasites, and the emergence of insecticide-resistant mosquitoes.[7] In this context, Greece reported 36 cases of *P. vivax* malaria infection in 2011 (as of September 27), the vast majority of which (30 cases) were associated with the Evrotas area of Laconia district (mostly localized in the plain of Elos, Skala village, Figure 1), located in the Peloponnese region of southern Greece. *Anopheles sacharovi* has been recognized as the dominant vector in this region. Among those 30 cases, 14 were in Greek citizens who had no history of travel to an endemic country, and 16 were in migrant workers mainly from Pakistan, with an undetermined importation status. Anti-malaria therapy was successful in all patients, with the exception of one fatality in an elderly male who had significant comorbidities.[8]

It is well known that Laconia is an area where epidemics, or occasionally high incidences, of malaria have been systematically recorded in the past, and it would be interesting to explore

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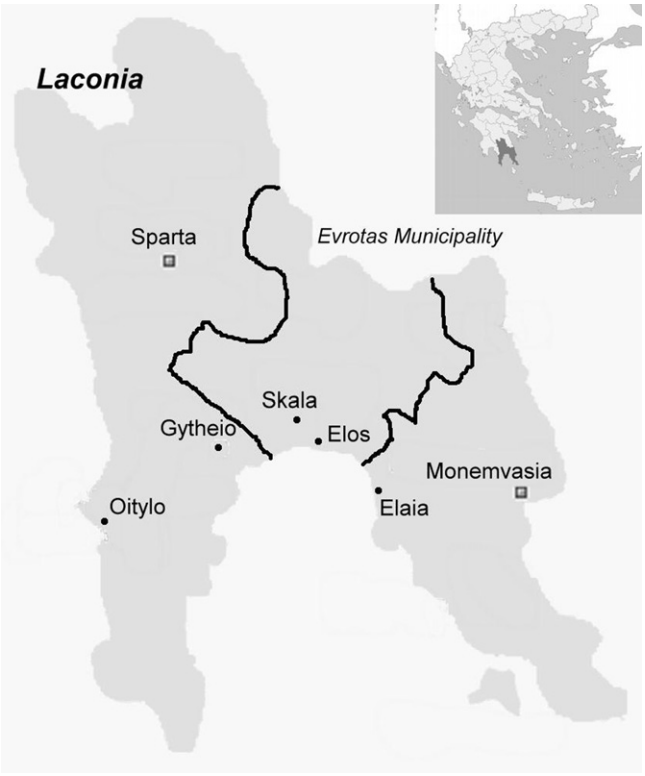

Figure 1. Map of Laconia and the Evrotas municipality, indicating the position of the most important sites for malaria.

whether specific area characteristics are preserving common features throughout the centuries. Thus, the objective of the current study was to elucidate the patterns of malaria outbreaks in this province in order to suggest policy interventions to effectively eradicate the disease.

2. Methods

A comparative research of historical and modern sources was undertaken in order to explore the malaria outbreaks in the area of Laconia, Greece. The authors put extra effort into uncovering relevant primary sources. We suggest this model of research as quite effective in resource-limited settings, like modern Greece, since it constitutes a low-cost way to trace significant evidence in order to aid health policy measures.

3. Results

3.1. 5th Century BC

Hippocrates frequently referred to a burning disease. This is the fever he mentioned more than any other in his writings, thus we can reasonably assume that the disease was unusually prevalent during his times.[9] He also recorded a feverish disease epidemic attributed to factors emanating from marshes.[10] It has been suggested that these infections (which occurred acutely, had remissions, and were occasionally fatal)[11] are to be identified with remittent or sub-continuous malarial fever.[10,12,13] The confusing part of this assumption is that while malaria in the Mediterranean is a summer disease, Hippocrates clearly asserted that this fever occasionally occurred in the autumn and winter.[10,11] The true explanation for this lies most probably in the fact that the malaria season (when malaria was endemic) differed across Greece; it has been recorded that in the area of Sparta, epidemics occurred from mid-September to November.[14]

Figure 2. The plain of Elos in Laconia, Greece. Wetlands and marshes are clearly visible (photo courtesy of Antonis A. Kousoulis; May 15, 2011).

According to historical sources it seems probable that malaria spread severely in Greece around the 5th century BC. Torrents and gorges were common enough and, by partially drying up in the summer, would form little pools. Many lowlands became marshes after heavy rain. Notably, in Laconia, there is a plain named Elos, meaning swamp, exactly because the surrounding area (remarkably close to the 2011 epidemic) has many swamps and marshes (Figure 2). Interestingly, the Greek word for malaria, elonosia, stems from the very same word (*elos + nosos*, thus the disease of the marsh). Therefore, when the number of malaria patients coming in from abroad increased, as they certainly did during the frequent warfare of the time, malaria epidemics were a certainty. And after these epidemics, the country offered the perfect preconditions for the disease to become endemic.[10,15]

P. vivax may well have been the cause of early malaria epidemics in Greece, since paleopathological evidence shows that it diverged approximately two million years ago from a group of parasites endemic in apes,[16] and coevolved with humankind in the Mediterranean countries.[17,18] From Hippocrates' descriptions of the clinical features of the probable malaria epidemics, it appears that either *P. vivax* or *P. malariae* must have been the predominant pathogen.[13]

3.2. Early 20th century

The Greek Anti-Malaria League, following the model of similar institutions in Italy, was founded in 1905. Its first work was to estimate the prevalence of the disease throughout the country. Shortly after the forming of this association, a severe malaria epidemic, peaking in late August–September, occurred in Greece.[19] Data from areas around Laconia in 1905 reveal the severity: about 20% of the inhabitants of today's Evrotas municipality had the disease, 3–5% in the highlands and 100% in the plain of Elos. In nearby areas 2–10% of the inhabitants were patients in Gythion, 5–15% in Oitylo, 10–50% around the village of Elaia, a small number in Kythira, but 40–60% in one of its districts. All in all, it was calculated that out of a total population of 2 433 806 studied, no fewer than 960 048 were attacked by malaria and 5916 died.[14]

The pathogen and the vector causing that epidemic, which was more severe in the plain of Elos in Laconia, are uncertain. However, the low mortality may imply infection with *P. vivax*. Historically, we cannot be sure of the *Anopheles* species responsible for previous malaria epidemics in Greece. However, it is notable that *A. sacharovi* has been systematically observed in Laconia since the 1940s, thus we could reasonably assume that it is a species residing in Laconia, perhaps responsible for historical epidemics.[20]

Table 1
Common characteristics of historical and current major malaria outbreaks in Laconia, Greece

	Significant malaria outbreaks in Laconia, Greece			
	5th century BC	Early 20th century	Mid 20th century	2011
Main areas	Plain of Elos	Plain of Elos	Plain of Elos	Plain of Elos
Season	Mid-September–November	August–September	August–September	August–October
Recorded risk factors	Marshes, population movement due to warfare	Marshes, wetlands	Wetlands, resistance to DDT of *Anopheles sacharovi*, intra-country migration	Wetlands, possibly migrant movements
Species	*Plasmodium vivax*, or *Plasmodium malariae*	Uncertain (low mortality may imply *Plasmodium vivax*)	*Plasmodium vivax*	*Plasmodium vivax*
Dominant vector	Mosquitoes described, hard to identify (Historically *Anopheles sacharovi* seemingly dominant in the plain of Elos)	Uncertain	*Anopheles sacharovi*	*Anopheles sacharovi*

The Greek Anti-Malaria League, benefiting from the personal aid of the Nobel laureate Sir Ronald Ross,[21] took many measures to fight malaria in the early 20th century. It ranked as its foremost action the education, through lectures, circulars, and public notices, of both the public and physicians on malaria and new discoveries concerning this disease. In order to successfully fight malaria, a combination of two measures was suggested: (1) the draining of the marshes or the extermination of the Anopheles mosquitoes, and (2) the killing, by quinine, of the parasites in the blood of the infected.[14] However, drying up the marshes around the large Greek lakes was subject to engineering difficulties, and there were problems with the distribution of pure quinine, which could not reach the poor safely. Moreover, it is now well known that only primaquine eradicates the hypnozoite form of the parasite from the liver, from where relapses of the disease can occur.

3.3. Mid 20th century

A new project against malaria was initiated in the mid 20th century, in particular during the 1940s and 1950s, following the introduction of the insecticide DDT (dichlorodiphenyltrichloroethane). Supported by valuable data from geographical and entomological surveys, the abundance of DDT for air-spraying, and the work of Gregory Livadas at the School of Hygiene, the project had many advantages. Centralized control, research on the common vectors, members of the Royal Hellenic Air Force piloting air-spraying airplanes, and extended house spraying were the first steps.[22]

Regarding the local outbreaks occurring in Laconia around these years (a period of huge intra-country migration), Elos and Skala were the center, resistant *A. sacharovi* was the usual vector, and the malarial species involved was *P. vivax*.[20,22,23]

4. Discussion

The study and comparison of historical data bring to light a potentially recurring pattern in the malaria outbreaks occurring in the district of Laconia. As vividly revealed in Table 1, all the epidemics in this district were mainly localized to the plain of Elos, tending to peak in the early autumn. To a great extent they can be attributed to some population movement and to the area wetlands, which preserve the potentiality for new outbreaks. Moreover, taking into account clinical features and historical studies, we can reasonably assume (in some cases with less certainty) that these epidemics are normally associated with the pathogen species *P. vivax* and the mosquito vector *A. sacharovi*.

All these features were seen in the most recent epidemic in 2011. Particular characteristics of the area of interest include a large influx of migrants from malaria endemic countries occurring in recent years. Furthermore, this area is nowadays characterized by freshwater springs, a complex network of 130 km of irrigation and drainage channels, the Evrotas river delta, the brackish Vivari lake, which seasonally dries out, and the coastal wetlands that form part of a nature reserve within the Nature 2000 Network.[8] Over and above this, studies from Greece have shown some correlation between DDT and Dieldrin resistance, but a clear double-resistance has been found only in Skala, thus indicating an excessive use of insecticides.[24]

There appears to be a lack of significant references on malaria epidemics in Laconia in the time window between the 5th century BC and the 20th century AD. However, in the 1st century AD, it is certain that Greeks were familiar at least with the features of a disease resembling malaria. Through the writings of eminent physician Aretaeus of Cappadocia, it is plain enough that he lived when malaria was universal and, in some places, severe. He convincingly cited the unhealthiness of autumn and the evening time, undoubtedly referring to the season of the year and the time of the day when mosquitoes are most dangerous.[25] In another passage he wrote that marshy districts are always unhealthy and in summer pestilential. Interestingly enough, physician Agathinus from Laconia wrote a special treatise on semi-tertian fevers, proving the continuing endemicity of the disease in the area.[26]

In conclusion, our comparison offers a clear public health message, since the lessons of the past, implemented in the present, point to specific directions regarding the responsible factors for the repeating malaria epidemics, also indicating how low-cost research (much needed in the current resource-limited Greek environment) may aid policy interventions. For example, active case finding and residual indoor spraying has been proposed among the main measures to control this local outbreak, and since April 2012 an integrated mosquito control program has been conducted by the municipality of Evrotas.[27]

Unique regional features seem to have preserved a recurring pattern of malaria outbreaks in Laconia, Greece, for 2500 years. In order to support its claims of eradication, even in areas where malaria is traditionally highly prevalent, the Greek public health authorities could build upon these findings.

Conflict of interest: No competing interest declared.

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