Malaria in North Africa: A Review of the Status of Vectors and Parasites[1]

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J. Entomol. Sci. 55(1): 25–37 (January 2020)

Abstract This article presents the status of *Anopheles* mosquito species and malaria parasite occurrences in North Africa. Because information is dispersed among numerous sources, we assimilated the information into a synthesis of the current status and potential of the disease in the region. Malaria transmission has been interrupted in North Africa, but the risk of re-emergence remains high. Indeed, competent vectors are present across the region, and the number of imported cases is increasing. The dominant parasite among imported cases is *Plasmodium falciparum* Welch in Tunisia, Algeria, and Morocco and *Plasmodium vivax* Grassi & Feletti in Libya and Egypt. In northwestern Africa (Tunisia, Algeria, Morocco), vectors formerly responsible for malaria transmission are *Anopheles labranchiae* Falleroni and *Anopheles sergenti* Theobald, whereas *Anopheles pharoensis* Theobald and *Anopheles sergenti* are the main malaria vectors in Egypt. *Anopheles multicolor* Cambouliu and *An. sergenti* are the major potential vectors of malaria transmission in Libya. In 2014, malaria caused by *P. falciparum* (1 case) and *P. vivax* (23 cases) were documented in Aswan Governorate, Egypt, indicating probable re-emergence of transmission, although these cases are considered as imported. In Algeria, local cases caused by *P. falciparum* in 2013 suggested probable re-emergence of malaria transmission. Four cases of airport malaria were noted for the first time in Tunisia during summer 2013 and were caused by *P. falciparum*. The presence of competent malaria vector species, together with high numbers of imported malaria cases each year, underscores the risk of re-emergence of autochthonous transmission in all countries of North Africa.

Key Words *Plasmodium falciparum*, *Plasmodium vivax*, *Anopheles*, re-emergence, malaria

Malaria constitutes a major public health problem, causing significant mortality and morbidity worldwide (World Health Organization 2017). *Plasmodium* spp. are the causative agents of malaria; their dispersal is generally via humans as reservoirs and *Anopheles* mosquitoes as vectors (World Health Organization 2006). Five species of parasites are involved: *Plasmodium falciparum* Welch, *Plasmodium vivax* Grassi & Feletti, *Plasmodium malariae* Laveran, *Plasmodium*

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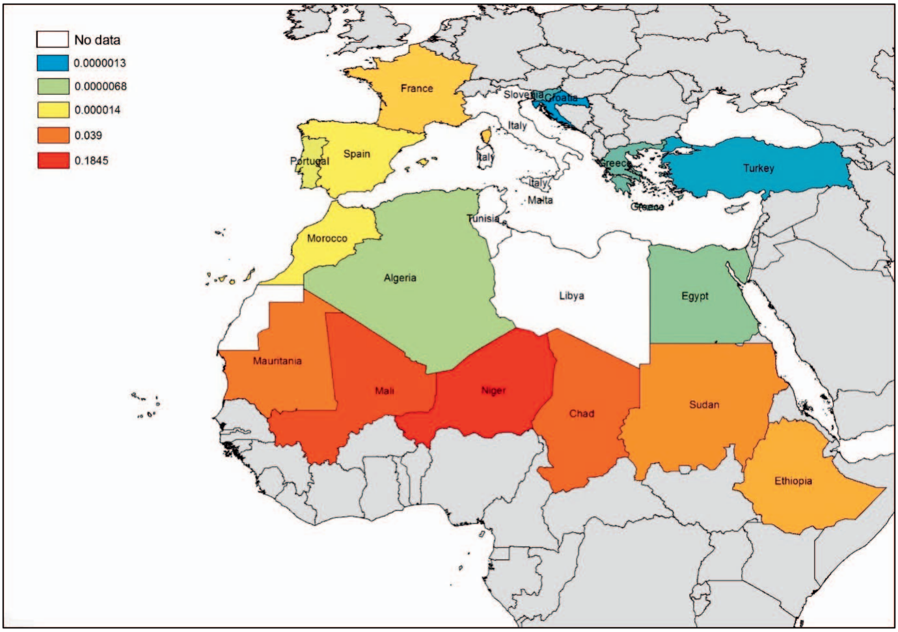

Fig. 1. Estimates of malaria incidence per capita in 2014 by using data from the U.S. Centers for Disease Control and Prevention for countries across North Africa and in neighboring countries of Africa and southern Europe countries (http://www.who.int/malaria/publications/world-malaria-report-2015/en/).

ovale Stephens, and the monkey malaria *Plasmodium knowlesi* Knowles. Among these species, *P. falciparum* is the most virulent and dangerous, frequently causing cerebral malaria. Malaria is a serious disease that threatens the lives of humans in tropical and subtropical areas worldwide (World Health Organization 2010). It is endemic in $>$100 countries inhabited by 3.2 billion people and visited by 125 million travelers annually. Travelers may be infected when they visit countries where malaria is endemic and then return to their home countries (Fig. 1), creating opportunities for successful establishment of the disease in new regions.

In all, 512 species of *Anopheles* mosquitoes are known worldwide, of which at least 70 are capable of transmitting malaria to humans (Gilles and Warrell 2002). Of these species, 41 are classified as dominant vector species (World Health Organization 2007). Vector competence differs significantly among species of *Anopheles*: some species are more zoophilic than anthropophilic, whereas others have life spans that are too short to ensure development of parasites into the infective sporozoite stage (Gilles and Warrell 2002).

The state of knowledge of *Anopheles* mosquitoes and malaria parasites in North Africa is dispersed and disorganized, which led to the development of this review article. Our aim herein was to update information available for malaria circulation in regard to vector mosquitoes and malaria cases in North Africa. We have

Table 1. Summary of dominant *Anopheles* vectors of human malaria in countries of North Africa.

Country	*An. labranchiae*	*An. sergentii*	*An. pharoensis*	*An. multicolor*
Tunisia	+++	+++	−	+
Algeria	+++	+++	−	+
Morocco	+++	+++	−	+
Egypt	−	+++	+++	+
Libya	+	+++	−	+++

+++, presence in high density; +, presence in low density without any proven vectorial role; −, absence.

assimilated scientific literature and reports to summarize the current status and history of malaria occurrence and the potential for elimination and eradication of malarial vectors in the region. However, for some countries, reliable information and data may be lacking.

Our approach was to collect and review all published and unpublished reports on malaria and *Anopheles* mosquitoes in North Africa. We conducted exhaustive reviews of information via Google Scholar (http://scholar.google.com). All historical documents were used in the present report, and several web pages were accessed. We present our findings by country.

Morocco

The Kingdom of Morocco lies at the western end of North Africa. It has Atlantic and Mediterranean coastlines and is bordered to the east by Algeria (Fig. 1). Morocco has an area of 710,850 km^2, with a population of 33 million people.

Transmission. Malaria was endemic to Morocco until 1973 (Adlaoui et al. 2011). *Plasmodium falciparum*, *P. vivax*, and *P. malariae* were reported among the recorded cases (World Health Organization 2007). *Anopheles labranchiae* Falleroni was the major vector in the north, whereas *Anopheles sergenti* Theobald was the major vector in the south (Table 1; Fig. 2; Gaud 1948, Senevet and Andarelli 1956, Guy 1963). Morocco joined with the global malaria elimination strategy in 1997 (Anonymous 2001), resulting in the number of indigenous cases of *P. vivax* progressively reducing to 19 cases, 4 cases, and 1 case in 2002, 2003, and 2004, respectively. No transmitted cases were reported in 2005 and thereafter. Morocco has recently been ranked among countries from which malaria has been eliminated. However, malaria risks remain in the country due to the widespread geographic distribution of the vector *An. labranchiae* in Morocco (Trari et al. 2004), along with a resurgence in the number of imported malaria cases (Anonymous 2004), decreased vigilance by health services, increased mobility of human populations, and current urbanization.

Routes of infection. A malaria control program was launched in Morocco in 1965, led by the Ministry of Health. Morocco received technical and financial support from the World Health Organization and other health organizations,

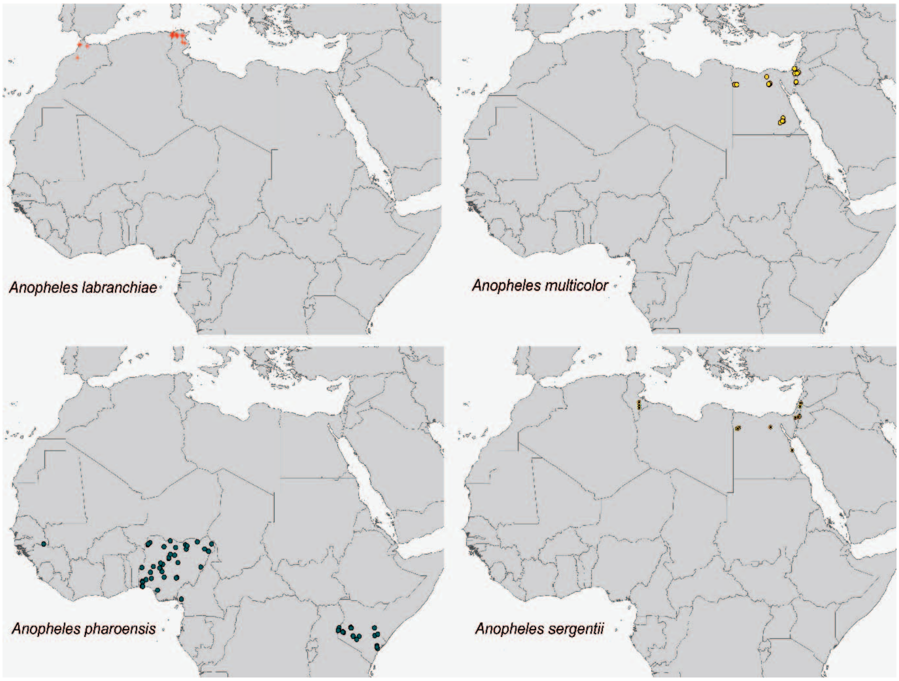

Fig. 2. Digital accessible knowledge regarding known occurrences of known malaria vector species in North Africa and neighboring regions, using data from GBIF (https://www.gbif.org/) and VectorMap (http://vectormap.si.edu/). Note in particular the major gaps and near-complete absence of information from across North Africa.

although most of the funding came from local governmental resources (World Health Organization 2007). Finally, the World Health Organization announced Morocco as malaria free in 2005; however, the country receives >100 imported cases annually. Most imported cases come from sub-Saharan Africa and are concentrated in Casablanca and Rabat, with a few cases in Fes and Agadir (Soraa et al. 2006; Faraj et al. 2008; Lalami et al. 2009). Risk of re-emergence of malaria in Morocco, thus, remains high, given the presence of proven vectors and regular importation of malaria cases.

Since 2005, no indigenous cases of malaria have been detected in Morocco. However, numbers of cases of imported malaria (75 in 2007) have increased steadily, owing to increased international travel and migratory flow from countries where the disease is endemic and most common. The Ministry of Health announced on World Malaria Day in 2014 that 322 malaria cases of importation were recorded in Morocco. Although Morocco was declared in 2005 as free from indigenous malaria, increasing trans-Saharan travel, development of transport facilities, and flow of populations from the south for study and employment all act to increase vulnerability and risk (Lalami et al. 2009).

History of control programs. Since the launch of the malaria control program in Morocco in 1965, numbers of indigenous cases decreased steadily from 30,893 in 1963 to 1,000 in the late 1980s, down to 4 cases in 2003 and 1 case in 2004. Efforts aimed at elimination of *P. falciparum*, the species responsible for severe malaria, via a structured and well-adapted control strategy focused on detection and control of the mosquito vectors. This positive evolution of the epidemiological situation made it possible, as of 1999, to put in place a strategy aimed at elimination of indigenous malaria in Morocco, focused on intensifying control measures and training health professionals in at-risk provinces. Imported cases are treated with great rigor through a prevention strategy implemented as of January 2011, based on epidemiological surveillance and vector control programs.

Algeria

Algeria has 41.2 million inhabitants and is the largest geographic country in Africa, with an area of 2,381,741 km^2. Algeria is bordered to the northeast by Tunisia, to the east by Libya, to the west and southeast by Morocco, to the south by Western Sahara, Mauritania, Mali, and Niger, and to the north by the Mediterranean Sea (Fig. 1).

Transmission. The World Health Organization announced that Algeria had recorded 189 local malaria cases and 12 malaria-related deaths since 2000 (World Health Organization 2010). The country had an average of 10,000 cases annually in the 1990s and had a constant risk of importation from neighboring countries to the south (Snow et al. 2012, World Health Organization 2014). The numbers of cases decreased by 73% for autochthonous cases and 29% for imported cases between 2012 and 2013 (World Health Organization 2014). *Plasmodium falciparum* was the dominant species among all imported cases in 2013 (World Health Organization 2014). The potential vectors responsible for spread of malaria in Algeria are *An. labranchiae* and *An. sergenti* (Fig. 2, Table 1). Secondary vectors have been recognized along the border with Mali: *Anopheles multicolor* Cambouliu, *Anopheles hispaniola* Theobald, and *Anopheles gambiae* Giles (Boubidi et al. 2010, Sinka et al. 2010).

Routes of infection. No local malaria transmission is occurring presently in Algeria despite the numbers of local ($n = 16$) and imported ($n = 600$) cases in 2013 (World Health Organization 2014). Most imported cases were in the southern parts of the country, in the provinces of Tamanrasset and Adrar, along the border with Mali and Niger (Hamadi et al 2009, Ministry of Health 2009) where malaria is endemic and at high rates of incidence. Active case detection, quality assurance of diagnostic tools, and effective treatment with Primaquine® (Artesan Pharma) are now the rule in the country (World Health Organization 2010). The country planned to be malaria free by 2015, although that the goal has not been reached fully (World Health Organization 2015).

Most malaria cases in Algeria in the past two decades have been imported from Niger or Mali (World Health Organization 2014). The trans-Sahara Highway crosses the Sahara from northern Algeria to southern Nigeria and constitutes a major artery for trade. Algeria's southern borders with Niger and Mali are relatively porous, although each country is connected to Algeria by a single partially paved road only. The main cause of increased risk of malaria resurgence is the increased movement of populations into Algeria from the south (Bruce-Chwatt 1986). In view of intermittent political instability, the Algerian government recently announced the closure and militarization of its borders with all countries except Tunisia (Ahmad 2014, Deutsche 2013). Another risk would be the possible invasion of *Anopheles arabiensis* Patton into southern Algeria. Stafford-Smith (1981) reported this species in Agades, northern Niger, and stressed the danger of introducing this vector species to the oases of the Algerian Sahara.

History of control programs. During the Algerian War of Independence from France (1954–1962), malaria control activities stagnated and numbers of cases increased to 100,000 cases per year (African Union Conference of Ministers of Health 2007). In 1962, when Algeria won independence, a central office for malaria elimination was created that launched a phased elimination strategy that was immediately effective in reducing the malaria burden (Snow et al. 2012). Algerians were protected via dichlorodiphenyltrichloroethane control of mosquitoes and antimalarial drug administration on a mass-scale, except for the southern region which was largely undeveloped at the time (Manguin et al. 2008). In 1989, the Algerian government changed the structure of the health system, and malaria reached 200 cases per year by 1991 (Gazette de la Presse du Maghreb 2003). Between 2000 and 2013, however, Algeria reported just 189 local cases (World Health Organization 2014).

In 2009, Algeria increased surveillance of its borders through regional cooperation with Mauritania, Tunisia, Niger, Mali, and Libya to prevent illegal and unregulated immigration. Algeria uses geographic information system mapping and entomological surveillance to document movements of mosquito vectors in the southern region and border areas (Mokdad 2009). The national malaria program is now working to maintain epidemiological surveillance, strengthen capacity for testing and diagnosis, standardize treatment, increase training for health personnel involved in malaria control, and develop measures to prevent malaria importation from other neighboring countries.

Tunisia

Tunisia is the northernmost country in Africa. It is bordered to the west by Algeria, to the southeast by Libya, and to the north and east by the Mediterranean Sea (Fig. 1). Tunisia has an estimated population of $>$10.4 million people and an area of almost 165,000 km^2.

Transmission. *Anopheles labranchiae* and *An. sergenti* were involved in transmission of the disease in northern and southern Tunisia, respectively (Table 1; Fig. 2; Tabbabi et al. 2015). Other species, such as *An. hispaniola* in the north and *An. multicolor* in the south, are also suspected of transmitting the disease in the country (Tabbabi et al. 2015). Since 1980, however, only imported cases have been reported (Anonymous 1980–2013, Gmara 2006). Indeed, 98 imported cases were reported during 1999–2006 (Aoun et al. 2010). Most of the imported cases were in immigrants or travelers (75.5%) rather than Tunisians who travelled outside the country and returned home with the disease (24.5%; Aoun et al. 2010). Most cases (96.5%) were imported from sub-Saharan Africa. The dominant parasite species was *P. falciparum* (71.4%), followed by *P. ovale* (19.4%), with only 9.2% cases caused by other *Plasmodium* species. Re-emergence of malaria in Tunisia is possible, given the simultaneous occurrence of competent vectors and the number of imported malaria cases in the country (Chahed et al. 2001, Tabbabi et al. 2015).

With most imported infections caused by *P. falciparum* from tropical Africa (Bouratbine et al. 1998, Ayadi et al. 2000), genetic compatibility with the anopheline species of Tunisia is in question. All members of the *Anopheles maculipennis* group of European origin were tested (*An. maculipennis* sensu stricto, *Anopheles atroparvus* Van Thiel, *An. labranchiae*, *Anopheles* sp.) and were refractory to tropical *P. falciparum* (De Zulueta et al. 1975, Marchant et al. 1998). It is thus not clear that *An. labranchiae* of Tunisia would be refractory and able to transmit *P. falciparum*.

Both *An. sergenti*, vector of the disease in the southern parts of the country, and the *An. gambiae* group, belong to the subgenus *Cellia* (Mouchet and Danis 1991), suggesting possible competence of *An. sergenti* to transmit tropical *P. falciparum*. In Egypt, *An. sergenti* has been found infected with *P. falciparum* in natural conditions (Kenawy et al. 1990). The most worrisome situation in Tunisia would be exposure of local anophelines to strains of *P. vivax* from Morocco or *P. falciparum* from countries to the south or east, which are probably related to the old Tunisian strains and therefore potentially capable of infecting local *Anopheles* and providing a source of indigenous transmission. However, studies of the geographic origin of imported malaria cases over the past 20 yr showed that introductions of malaria cases from these two countries are rare (Bouratbine et al. 1998, Ayadi et al. 2000).

Routes of infection. Until its elimination, malaria was endemic in Tunisia, with an average of 10,000 cases per year (Chedli et al. 1985). No active transmission has been detected in Tunisia since 1979, when the last autochthonous malaria case was identified. In 1994, the World Health Organization classified the world into four major zones according to their malaria situation (Farid 1998) and included Tunisia in the group of countries that have successfully eradicated malaria. To date, the country has been able to maintain this success. However, the imported malaria cases, the persistence of local *Anopheles* populations, and possible importation or adaptation of an efficient vector species could facilitate restoration of endemic malaria transmission (Ben Zarroug 1987, Chadli et al. 1986). Recent trends in importation of cases from 5 to 8 cases between 1999 and 2001 and from 10 to 25 cases between 2002 and 2005 (Aoun et al. 2010) confirm these possibilities. Tunisia currently reports between 40 and 50 new cases of imported malaria each year (Tabbabi et al. 2015). Most (60%) come in the form of foreign students or other foreign nationals (Bouratbine et al. 1998), who generally live in or travel to large cities where anophelines are present.

Between 1969 and 1995, 63 cases of malaria infection at European airports were documented (Mouchet 2000, Raeber and Schussele 1997). Development of international tourism in endemic areas has favored such cases. However, low numbers of planes departing from Tunisia to such destinations make such possibilities unlikely. Four cases of airport malaria were reported for the first time in Tunisia during summer 2013; these cases were caused by *P. falciparum* (Siala et al. 2015). Finally, it is questionable whether climate change could promote a return of malaria beyond the Sahara in North Africa (Reiter 2000).

History of control programs. Since 1903, various efforts, including physical, chemical, and biological control measures against vectors, succeeded in interrupting transmission in Tunisia (Tabbabi et al. 2015). The fight against malaria in Tunisia started early, in 1907, with creation of the first malaria control program at the Pasteur Institute in Tunisia (Chadli et al. 1986). Since then, when malaria reached epidemic levels, efforts were intermittent. At least three attempts were made to launch control activities (i.e., 1935, 1944, 1959) before initiating the eradication program that proved successful in 1979 (Tabbabi et al. 2015). In light of this long experience, two conditions associated with upsurges of malaria morbidity were interruption of control efforts, with residual transmission remaining in certain foci, and the disruption caused by World War II.

Early diagnosis and treatment of imported cases are among the pillars of the present national control program (Chadli et al. 1986). Regular assessment of the epidemiological profile of imported cases makes it possible to adapt and optimize control strategies. Routine microscopic diagnosis is done in a central laboratory and 13 regional laboratories employing 50 microbiologists in total, with external quality control of the Institut Pasteur de Tunis Laboratory, which reviews all positive slides and 10% of negative slides.

Libya

Libya is bordered by the Mediterranean Sea to the north, Egypt to the east, Chad and Niger to the southwest, Sudan to the southeast, and Algeria and Tunisia to the west (Fig. 1). Libya has a population of $>$6 million people and is the fourth largest country in Africa, with an area of almost 1.8 million km^2.

Transmission. Malaria has a long history in Libya, with *P. falciparum* transmitted by local vector species *An. multicolor* and *An. sergenti* (Ramsdale and de Zulueta 1983). *Plasmodium vivax* has been the dominant parasite in the country. Malaria caused by *P. falciparum* infections is now rare and limited to a few southern regions only.

Several potential vectors are present in Libya, but only *An. multicolor* and *An. sergenti* have been reported as proven vectors of malaria (MacDonald 1982; Table 1; Fig. 2). The epidemiological role of *An. multicolor* has been demonstrated in several situations in which the species is capable of sustaining the parasite for long periods, albeit at low levels of transmission (Ramsdale and de Zulueta 1983). As elsewhere in North Africa, *An. sergenti* is a proven vector in Libya (Zahar 1974). *Anopheles labranchiae* is the major vector of *P. vivax* but in limited areas near the coast (Ramsdale and de Zulueta 1983).

Routes of infection. Few data are available, but importation of malaria cases from other African countries remains a concern. Risk of introduction of the Afrotropical vectors, *An. arabiensis* and *An. gambiae*, especially into the Fezzan in southwestern Libya, remains a serious concern. A more direct route by which these Afrotropical vectors might reach the country is from the Tibesti region (Chad). Indeed, only 400 km separate the Gatrun oases of the southern Fezzan from Kayougue, in Chad, where developing larvae of *An. gambiae* have been found.

In Libya, a continuing influx of foreign workers, many from highly endemic regions to the south, ensures presence of a parasite reservoir probably larger than at any time in the past. Improved air and road transportation increasingly facilitate population movements within, as well as into, the country. The high risk of introduction of *An. arabiensis* and *An. gambiae* was already highlighted by Ramsdale and de Zulueta (1983) and remains a serious concern. Unfortunately, no data are available on the history of control programs in the country.

Egypt

Egypt is a transcontinental country, spanning the northeastern corner of Africa and southwestern extreme of Asia. Egypt is bordered to the northeast by Palestine, to the east by the Gulf of Aqaba, to the east and south by the Red Sea, to the south by Sudan, and to the west by Libya (Fig. 1). Egypt is the most populous country in North Africa, with >92 million inhabitants. It covers an area of 1,002,000 km^2.

Transmission. Twelve species of *Anopheles* are known to be present in Egypt, of which two are proven vectors: *Anopheles pharoensis* Theobald and *An. sergenti* (Table 1; Fig. 2). *Plasmoduim vivax* is transmitted by *An. pharoensis*; however, *P. falciparum* is transmitted by *An. sergenti* (Kenawy 1988). Previous studies have identified *An. multicolor* as a potential vector, because of its activity in transmission areas (Gad et al. 1964, Kenawy et al. 1986, Zahar 1974). Given the tendency toward zoophilia, low infection rates, and short lifetimes of the two proven vector species, malaria transmission is inconsistent in Egypt (Kenawy 2015).

Routes of infection. The disease was endemic in most of the country until 1998, but prevalence declined in the 1990s (Kenway 2015). Only cases imported from Sudan were detected in 1998, although some locally acquired cases occurred in El Faiyoum and Cairo (Kenawy 2015). An outbreak of *P. falciparum* (1 case) and *P. vivax* (23 cases) in 2014 in Aswan Governorate indicates probable re-emergence of transmission in Egypt, although published data identified them as imported cases (Kenawy 2015).

History of control programs. As detailed by Halawani and Shawarby (1957), malaria was endemic in almost all parts of the country and human infection rates reached 20% in some localities in 1960. However, malaria prevalence has shown a steady decrease in most of the governorates by 1990. Only 198 and 132 cases were reported in 1983 and 1990–1993, respectively, with transmission localized in El Faiyoum district. A rapid increase was observed in numbers of cases identified in 1994 ($n = 495$) and 1995 ($n = 808$). These changes led to an intensified multidisciplinary control program in the country that caused a steady decrease in the numbers of cases to 313 in 1997 and only 13 in 1998. From the end of 1998 until 2013, no local cases were reported (Kenawy 2015). In 2014, however, Egypt experienced an outbreak of *P. vivax*: 21 confirmed cases between May and June 2014. In response, the Egyptian Ministry of Health and Population considered a local emergency plan including early detection and rapid treatment of cases, vector control, public awareness, and intersectoral collaboration (World Health Organization 2017). A previous invasion of Egypt in 1942 by *An. gambiae*, which caused epidemics of malaria caused by *P. falciparum* reminds us of this potential risk (Theunissen et al. 2009) of the Afrotropical vector species reached 25 km north of Asyut, ~700 km north of the Sudanese border. More than 10,000 deaths were related to this epidemic in 1942 and 1943 (Shousha 1948). By 1945, *An. gambiae* was eradicated from Egypt and the epidemic waned.

It is difficult to explain how the 2014 outbreak started, but it was probably triggered by illegal cross-border movement of people between Egypt and Sudan. No malaria-infected individuals had recently traveled to Sudan, and all Sudanese examined for malaria ($n = 25$) were free of infection (Kenawy 2015). However, data regarding malaria and illegal migrants are scarce. Increases in immigration flow from Sudan to Egypt may thus allow establishment of the parasite within the country.

Conclusions

Countries of North Africa have demonstrated their ability to successfully control malaria transmission. However, risk factors including availability of vectors, open and porous borders, movements of people, political instability, and climate change have the potential to trigger rapid increases in malaria cases and modify the disease's eco-epidemiology in the region. Continuing influxes of foreign workers, many from highly endemic parts of Africa, via Libya, ensure maintenance of a parasite reservoir probably larger than at any time in the past. With favorable climatic conditions for development of the *Anopheles* vector and the malaria parasites in the vectors host, risk of malaria re-emergence in the region may become a problem of major interest.

We recommend that an agenda of research and surveillance be prioritized to prepare the region for future public health threats. Understanding vector ecology and biology, vector interactions with the pathogens, and future range shifts under changing climate can allow researchers and public health specialists to assess and anticipate vector transmission risks. Such detailed information can also promote development and evaluation of new and improved integrated vector control methods for prevention of malaria. These activities must consider international dimensions and should emphasize collaboration among countries to prevent vector and parasite spread events across borders.

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