# ELIMINATING MALARIA Case-study 10

# Successful elimination and prevention of re-establishment of malaria in Tunisia



UCSF GLOBAL HEALTH SCIENCES THE GLOBAL HEALTH GROUP From evidence to action





# ELIMINATING MALARIA Case-study 10

# Successful elimination and prevention of re-establishment of malaria in Tunisia







WHO Library Cataloguing-in-Publication Data

Successful elimination and prevention of re-establishment of malaria in Tunisia.

(Eliminating malaria case-study, 10)

1.Malaria - prevention and control. 2.Malaria - epidemiology. 3.National Health Programs. 4.Tunisia. I.World Health Organization. II.University of California, San Francisco.

ISBN 978 92 4 150913 8 (NLM classification: WC 765)

#### © World Health Organization 2015

All rights reserved. Publications of the World Health Organization are available on the WHO website (www.who.int) or can be purchased from WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel.: +41 22 791 3264; fax: +41 22 791 4857; e-mail: bookorders@who.int).

Requests for permission to reproduce or translate WHO publications –whether for sale or for non-commercial distribution– should be addressed to WHO Press through the WHO website (www.who.int/about/licensing/copyright\_form/en/index.html).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

Photo credit cover: National Malaria Control Programme, Tunisia

Design by Paprika, Annecy (France)

#### Printed in France

Please consult the WHO Global Malaria Programme web site for the most up-to-date version of all documents (http://www.who.int/malaria).

Publications of the University of California, San Francisco are available on the UCSF website (http://globalhealthsciences.ucsf.edu/global-health-group), Global Health Group, the University of California, San Francisco.

## **CONTENTS**

Acknowledgements
Acronyms and abbreviations
Glossary ix
Summaryxv
Malaria control period (up to 1966) xv
Malaria elimination through implementation of the Global Malaria Eradication Programme strategies and policies (1967–1979)xvi
Long-term successful prevention of reintroduction of malaria (1980 onwards) xvi
Conclusionsxvii
Introduction
The malaria elimination case-study series
Malaria in the WHO Eastern Mediterranean Region
Malaria in Tunisia
Country background
Geography
Climate and vegetation
Political organization and administrative divisions
Population
Economy
Health care policies and system
General health profile
Epidemiology and programme interventions over time
Parasites and vectors
Early control period, 1903 onwards
First malaria control campaign, 1934–1954
Efforts during the Global Malaria Eradication Programme (1955–1965)12
Malaria eradication–elimination programme (1966–1996)13
Prevention of reintroduction since 1996 15
Factors contributing to elimination and maintenance of malaria-free status in tunisia
How was malaria eliminated?
What are the main strategies and policies of the current programme for the prevention of re-establishment? 26
Challenges for the programme for the prevention of malaria re-establishment

Lessons learned and conclusions
Keeping malaria burden at a low level in the 1950s and 1960s
Malaria elimination through implementation of the Global Malaria Eradication Programme strategies and policies
Long-term successful prevention of re-establishment of malaria 40
Conclusions
References
Annex 1: Data sources and methods used
Annex 2: Estimated population per governorate, 2011
Annex 3: Tunisian health and development indicators
Annex 4: Malaria parasites and vectors, past and present
Annex 5: Standard reporting forms

## ACKNOWLEDGEMENTS

This case-study is part of a series of malaria elimination case-studies conducted by the WHO Global Malaria Programme and the Global Health Group at the University of California, San Francisco (UCSF/GHG).

The two groups wish to acknowledge the financial support of the Bill & Melinda Gates Foundation in developing the elimination case-study series.

The following institutions and individuals collected the data for this case-study: Dr Dhikrayet Gamara (coordinator of the Tunisia National Malaria Control Programme), Professor Karim Aoun (Pasteur Institute, Tunis), Professor Hamouda Babba (Faculty of Pharmacy, Monastir, and Laboratory of Maternity and Neonatology Centre of Monastir), Professor Mounir Ben Djemaa (Hedi Chaker University Hospital of Sfax), Mohamed Bel Kahla (Surveillance Officer at the Tunisia National Malaria Control Programme), Dr Ali Bouattour (Pasteur Institute, Tunis), Professor Aïda Bouratbine (Pasteur Institute, Tunis), Professor Emna Chaker (Laboratory of Parasitology and Mycology, La Rabta, Tunis), Professor Ahmed Ghoubantini (Faculty of Medicine, Tunis) and Dr Faiçal Zouiten (Infectious Diseases, La Rabta, Tunis).

Dr Jean-Olivier Guintran, formerly WHO/AFRO/Inter-Country Support Team and currently WHO/Vanuatu, was the lead author of the case-study. He compiled and analysed the information and drafted the text of this case-study, which was subsequently finalized in collaboration with Dr Hoda Atta and her team of the WHO Eastern Mediterranean Regional Office and Drs Rossitza Kurdova-Mintcheva and Aafje Rietveld of the WHO Global Malaria Programme.

The author would like to thank everyone who contributed to the development of this case-study, particularly Dr Dhikrayet Gamara (coordinator of the Tunisia National Malaria Control Programme), who facilitated the work of Dr Guintran in Tunis, and the reference librarians and other WHO staff who extracted a large amount of information from the WHO archives in Geneva and Cairo. The case-study was reviewed by Mr Laurent Bergeron, Dr Richard Cibulskis, Dr Michael Lynch, Ms Cara Smith Gueye and Dr Ghasem Zamani, who all provided valuable assistance and comments.

The author remains responsible for any errors and omissions.

## **ACRONYMS AND ABBREVIATIONS**

ABER	annual blood examination rate
ACD	active case detection
ACT	artemisinin-based combination therapy
AL	artemether-lumefantrine
API	annual parasite index
DBHC	Department of Basic Health Care
DDT	dichlorodiphenyltrichloroethane
DEHP	Department of Environmental Health and Protection
EMRO	WHO Regional Office for the Eastern Mediterranean
GDP	gross domestic product
GMEP	Global Malaria Eradication Programme
IRS	indoor residual spraying
MoH	Ministry of Health
NMCP	National Malaria Control Programme
NMEP	National Malaria Eradication Programme
WHO	World Health Organization

## GLOSSARY

The terms listed in this glossary are defined according to their use in this publication. They may have different meanings in other contexts.

#### active case detection

The detection by health workers of malaria infections at community and household level in population groups that are considered to be at high risk. Active case detection can be conducted as fever screening followed by parasitological examination of all febrile patients or as parasitological examination of the target population without prior fever screening.

#### annual blood examination rate

The number of examinations of blood slides for malaria by microscopy per 100 population per year.

#### attack phase

In malaria eradication terminology, the phase during which antimalarial measures applicable on a large scale and aiming at the interruption of transmission are applied on a total coverage basis in an operational area. The phase is sometimes called the period of total-coverage spraying.<sup>1</sup>

#### case definition (control programmes)

**confirmed malaria** – Suspected malaria case in which malaria parasites have been demonstrated in a patient's blood by microscopy or a rapid diagnostic test.

**presumed malaria** – Suspected malaria case with no diagnostic test to confirm malaria but nevertheless treated presumptively as malaria.

**suspected malaria** – Patient illness suspected by a health worker to be due to malaria. Fever is usually one of the criteria.

#### case definition (elimination programmes)

**autochthonous** – A case locally acquired by mosquito-borne transmission, i.e. an indigenous or introduced case (also called "locally transmitted").

**imported** – A case whose origin can be traced to a known malarious area outside the country in which it was diagnosed.

**indigenous** – Any case contracted locally (i.e. within national boundaries), without strong evidence of a direct link to an imported case. Indigenous cases include delayed first attacks of *Plasmodium vivax* malaria due to locally acquired parasites with a long incubation period.

**induced** – A case whose origin can be traced to a blood transfusion or other form of parenteral inoculation but not to normal transmission by a mosquito.

**introduced** – A case contracted locally, with strong epidemiological evidence linking it directly to a known imported case (first generation from an imported case, i.e. the mosquito was infected from a case classified as imported).

<sup>&</sup>lt;sup>1</sup> Terminology of malaria and of malaria eradication: report of a drafting committee. Geneva: World Health Organization; 1963.

**locally transmitted** – A case locally acquired by mosquito-borne transmission, i.e. an indigenous or introduced case (also called "autochthonous").

**malaria** – Any case in which, regardless of the presence or absence of clinical symptoms, malaria parasites have been confirmed by quality-controlled laboratory diagnosis.

#### case investigation

Collection of information to allow classification of a malaria case by origin of infection, i.e. imported, introduced, indigenous or induced. Case investigation includes administration of a standardized questionnaire to a person in whom a malaria infection is diagnosed.

#### case management

Diagnosis, treatment, clinical care and follow-up of malaria cases.

#### case notification

Compulsory reporting of detected cases of malaria by all medical units and medical practitioners, to either the health department or the malaria elimination service (as laid down by law or regulation).

#### case-based surveillance

Immediate reporting and investigation (and inclusion in the weekly reporting system) of every case.

#### certification of malaria-free status

Certification granted by WHO after it has been proved beyond reasonable doubt that the chain of local human malaria transmission by *Anopheles* mosquitoes has been fully interrupted in an entire country for at least 3 consecutive years.

#### consolidation phase

In malaria eradication terminology, the phase that follows the attack phase; it is characterized by active, intense and complete surveillance with the object of eliminating any remaining infections and proving the eradication of malaria. It ends when the criteria for eradication have been met.<sup>1</sup>

#### elimination

Reduction to zero of the incidence of infection by human malaria parasites in a defined geographical area as a result of deliberate efforts. Continued measures to prevent re-establishment of transmission are required.

#### endemic

Applied to malaria when there is an ongoing, measurable incidence of cases and mosquito-borne transmission in an area over a succession of years.

#### epidemic

Occurrence of cases in excess of the number expected in a given place and time.

#### eradication

Permanent reduction to zero of the worldwide incidence of infection caused by human malaria parasites as a result of deliberate efforts. Intervention measures are no longer needed once eradication has been achieved.

<sup>&</sup>lt;sup>1</sup> Terminology of malaria and of malaria eradication: report of a drafting committee. Geneva: World Health Organization; 1963.

#### evaluation

Attempts to determine as systematically and objectively as possible the relevance, effectiveness and impact of activities in relation to their objectives.

#### focus

A defined and circumscribed locality situated in a currently or formerly malarious area and containing the continuous or intermittent epidemiological factors necessary for malaria transmission: a human community, at least one source of infection, a vector population and the appropriate environmental conditions.

#### hypnozoite

The dormant stage of the malaria parasite present in the host's liver cells (limited to infection with *Plasmodium vivax* and *P. ovale*).

#### incubation period

The time between infection (by inoculation or otherwise) and the first appearance of clinical signs.

#### intervention (public health)

Activity undertaken to prevent or reduce the occurrence of a health condition in a population. Examples of interventions for malaria control include the distribution of insecticide-treated mosquito nets, indoor residual spraying with insecticides, and the provision of effective antimalarial therapy for prevention or curative treatment of clinical malaria.

#### local mosquito-borne malaria transmission

Occurrence of human malaria cases acquired in a given area through the bite of infected Anopheles mosquitoes.

#### maintenance phase

In malaria eradication terminology, period which begins when the criteria of malaria eradication have been met in an operational area and which will continue until world-wide eradication has been achieved. During this period vigilance is exercised by the public health services to prevent the spread of malaria imported from across the borders of the area concerned.<sup>1</sup>

#### malaria incidence

The number of newly diagnosed malaria cases during a specified time in a specified population.

#### malaria prevalence

The number of malaria cases at any given time in a specified population, measured as positive laboratory test results.

#### malaria-free

An area in which there is no continuing local mosquito-borne malaria transmission and the risk for acquiring malaria is limited to introduced cases only.

#### monitoring (of programmes)

Periodic review of the implementation of an activity, seeking to ensure that inputs, deliveries, work schedules, targeted outputs and other required actions are proceeding according to plan.

<sup>1</sup> Terminology of malaria and of malaria eradication: report of a drafting committee. Geneva: World Health Organization; 1963.

#### national focus register

Centralized database of all malaria foci in a country.

#### national malaria case register

Centralized database of all malaria cases registered in a country, irrespective of where and how they were diagnosed and treated.

#### outpatient register

List of patients seen in consultation in a health facility; the register may include the date of consultation; patient's age, place of residence and presenting health complaint; tests performed; and diagnosis.

#### parasite prevalence

Proportion of the population in whom *Plasmodium* infection is detected at a particular time by means of a diagnostic test (usually microscopy or a rapid diagnostic test).

#### passive case detection

Detection of malaria cases among patients who, on their own initiative, go to a health post for treatment, usually for febrile disease.

#### population at risk

Population living in a geographical area in which locally acquired malaria cases occurred in the current year and/ or previous years.

#### radical treatment

Treatment adequate to achieve radical cure. In *Plasmodium vivax* and *P. ovale* infections, this implies the use of drugs that destroy the hypnozoites (usually a combination of chloroquine for 3 days and primaquine for 14 days).

#### rapid diagnostic test

An antigen-based stick, cassette or card test for malaria in which a coloured line indicates that plasmodial antigens have been detected.

#### rapid diagnostic test positivity rate

Proportion of positive results among all the rapid diagnostic tests performed.

#### receptivity

Relative abundance of anopheline vectors and existence of other ecological and climatic factors favouring malaria transmission.

#### re-establishment of transmission

Renewed presence of a constant measurable incidence of cases and mosquito-borne transmission in an area over a succession of years. An indication of the possible re-establishment of transmission would be the occurrence of three or more introduced and/or indigenous malaria infections in the same geographical focus, for two consecutive years for *P. falciparum* and for three consecutive years for *P. vivax*.

#### relapse (clinical)

Renewed manifestation of an infection after temporary latency, arising from activation of hypnozoites (and therefore limited to infections with *Plasmodium vivax* and *P. ovale*).

#### relapsing case

A case contracted locally some time ago (maximum admissible period is equal to the natural life-span of *Plasmodium vivax* or *P. ovale* in the human host) or a recrudescence of *P. falciparum* or *P. malariae* after a period of unrecognized latency.<sup>1</sup>

#### slide positivity rate

Proportion of microscopy slides found to be positive for Plasmodium among the slides examined.

#### surveillance (control programmes)

Ongoing, systematic collection, analysis and interpretation of disease-specific data for use in planning, implementing and evaluating public health practice.

#### surveillance (elimination programmes)

That part of the programme designed for identification, investigation and elimination of continuing transmission, the prevention and cure of infections, and the final substantiation of malaria elimination.

#### transmission intensity

Rate at which people in a given area are inoculated with malaria parasites by mosquitoes. This is often expressed as the "annual entomological inoculation rate", which is the number of inoculations with malaria parasites received by one person in one year.

#### transmission season

Period of the year during which mosquito-borne transmission of malaria infection usually takes place.

#### vector control

Measures of any kind against malaria-transmitting mosquitoes intended to limit their ability to transmit the disease.

#### vector efficiency

Ability of a mosquito species, in comparison with another species in a similar climatic environment, to transmit malaria in nature.

#### vectorial capacity

Number of new infections that the population of a given vector would induce per case per day at a given place and time, assuming conditions of non-immunity. Factors affecting vectorial capacity include: the density of female anophelines relative to humans; their longevity, frequency of feeding and propensity to bite humans; and the length of the extrinsic cycle of the parasite.

#### vigilance

A function of the public health service during a programme for prevention of reintroduction of transmission, consisting of watchfulness for any occurrence of malaria in an area in which it had not existed, or from which it had been eliminated, and application of the necessary measures against it.

#### vulnerability

Either proximity to a malarious area or the frequency of influx of infected individuals or groups and/or infective anophelines.

<sup>&</sup>lt;sup>1</sup> Guidelines on the elimination of residual foci of malaria transmission. Cairo: WHO Regional Office for the Eastern Mediterranean, 2007 (EMRO Technical Publications Series, No. 33).

## **SUMMARY**

This case-study describes and evaluates malaria control activities in Tunisia, which aimed for a stable reduction in the disease burden during the 20th century, and the subsequent strategies to eliminate malaria. Tunisia's success in preventing the re-establishment of malaria and keeping the country free of the disease over the past 35 years is explained. Lessons for countries that are embarking on malaria elimination or are in the prevention of reintroduction phase are distilled.

### Malaria control period (up to 1966)

Malaria in Tunisia was widely distributed and holoendemic with a number of epidemics recorded early in the 20th century. Compulsory notification of cases was introduced in 1922. Both *Plasmodium falciparum* and *P. vivax* were widespread in the country and there were also some reports of *P. malariae*. The epidemic of 1932–1935 was especially severe, reaching a peak of nearly 16 000 cases in 1934. The monthly mortality rate exceeded 5 per 1000 inhabitants in the most severely affected areas, spleen rates were 70–90%, and the national annual parasite index (API) was over 7 per 1000 people. In response, a complex of control measures were introduced, including:

- active case detection and treatment by visiting health workers;
- establishment of quarantine stations to treat cases in remote rural areas and mobile laboratories to measure prevalence and map the zones of intense transmission;

- seasonal chemoprophylaxis with quinine;
- larval control (use of larvivorous fish in the main flood-prone areas);
- sanitation and drainage.

Following these measures, the API fell to approximately 2 per 1000 people by 1938.

Disruption of services during the Second World War resulted in a sharp rebound in the incidence of malaria, with more than 16 000 cases again reported in 1948 (API approximately 5 per 1000). The subsequent reintroduction of control activities cut the number of *P. vivax* and *P. falciparum* cases dramatically, from 14 563 in 1949 to 3884 in 1950; incidence thereafter was maintained at a low level.

In the late 1950s, after the launch of the Global Malaria Eradication Programme (GMEP), a national eradication strategy was developed with the assistance of the World Health Organization (WHO). However, the planned launch of this strategy in 1959 failed owing to a lack of funding. Instead, the country continued its malaria control activities with an emphasis on case detection by visiting health workers, chemoprophylaxis campaigns using amodiaquine, and larviciding - spraying of major water bodies with insecticides (dieldrin) and distribution of larvivorous fish in small bodies of water created by dams. The interventions, which still required substantial funding (about US\$ 100 000 per year for larval control and chemoprophylaxis), failed both to prevent the occurrence of further malaria epidemics and to effect interruption of transmission in the country.

## Malaria elimination through implementation of the Global Malaria Eradication Programme strategies and policies (1967–1979)

After a new epidemic in 1964, WHO helped to draw up a new six-year eradication programme; implementation began in 1967. However, elimination of malaria was eventually to be a much longer-term campaign and included the following phases: attack (1967–1972), consolidation (1973–1977) and maintenance (1978–1995), with prevention of reintroduction since 1996.

Tunisia obtained external funding for its malaria eradication programme only during the last few years of the GMEP (from 1967 onwards). As a result of intensive surveillance and control activities, *P. falciparum* disappeared from the north in 1971 and was totally eliminated from the country in 1979. The last *P. vivax* focus, spread across 15 communities, gave rise to 16 cases in 1975 and 6 in 1976. The last two cases of autochthonous relapse were recorded in Jendouba region in 1979: since that time, no local malaria transmission has been reported in Tunisia.

The approaches that succeeded in eliminating malaria in Tunisia country can be summarized as follows:

- Vector control. Indoor residual spraying (IRS) three times a year with dichlorodiphenyltrichloroethane (DDT) was one of the principal interventions during the attack phase and achieved a dramatic reduction in both the mosquito population and the level of transmission. Spraying was limited to the few remaining foci during the consolidation phase and then suspended in the late 1970s when transmission was interrupted. Throughout, vector control was guided by regular entomological surveillance of vectors and breeding sites and by recording and mapping of foci.
- *Efficient case detection*. Intensive active case detection (ACD) was carried out during monthly visits by health workers. The high annual blood

examination rate (ABER) during the campaign is an indicator of good coverage of the population with malaria examinations.

- *External quality control* of malaria laboratory diagnosis aimed at ensuring that the work of diagnostic laboratories throughout the country was of high quality.
- *Regular information* for decision-makers came from epidemiological investigation of malaria cases, reporting, notification and registration, data collection and analysis.
- Drastic reduction of the sources of infection was achieved by radical treatment with chloroquine and primaquine for *P. vivax* patients, and seasonal chemoprophylaxis with amodiaquine.

## Long-term successful prevention of reintroduction of malaria (1980 onwards)

Although Tunisia officially changed its policy to the prevention of reintroduction only in 1996, the country has successfully prevented the re-establishment of autochthonous malaria transmission since 1980. As an enabling factor during these past 30 years, the environment has undergone significant changes that have led to reduced receptivity to malaria. The efforts of the Government are directed principally at controlling the risk of *Plasmodium* species importation and preventing its consequences, through:

 Intense vigilance, early detection and prompt radical treatment of each imported malaria case. Special attention is paid to risk groups such as foreign students (active case detection through compulsory screening), travellers to countries with high malaria risk, and individuals with unexplained persistent fever. Efficient case management and quality of treatment are supported by use of a standard protocol for treatment and monitoring of cases and by the centralized system for procurement and dispensing of antimalarial drugs.

- Risk management for travellers. Recommendations for travellers are available at the Border Health Inspection unit at Tunis Airport and through the Department of Basic Health Care (DBHC) education leaflets distributed to travel agencies. Travellers to malaria-endemic countries can access antimalarial drugs for chemoprophylaxis free of charge and are monitored after return.
- Maintenance of a surveillance system based on compulsory case notification backed up by routine epidemiological investigation and classification of cases, plus reporting and analysis.
- Continued vector surveillance activities.
- Maintenance of epidemic preparedness in the country, keeping appropriate supplies and stocks of insecticides, antimalarial drugs, and laboratory reagents and consumables for malaria diagnosis in case of outbreaks.
- Maintenance of malaria expertise.

Financial support for these preventive activities is provided by the Government. The annual budget of the National Malaria Control Programme (NMCP) in 2012 was US\$ 145 500, used mainly for the purchase of laboratory consumables and of drugs for treatment and chemoprophylaxis. There is also regular support from WHO for drugs – necessary small quantities of artemisinin-based combination therapies (ACTs), primaquine, injectable quinine – and for microscopy training every two years. Tunisia is part of the malaria network of the WHO Regional Office for the Eastern Mediterranean (EMRO).

### Conclusions

Tunisia's experience should benefit other countries in North Africa and the Middle East that are situated in the same Palaearctic ecozone and that have recently eliminated malaria or are in the process of doing so. In addition to describing the efforts that led to elimination of the disease in Tunisia, this case-study outlines some of the tools that can be used to curb importation of the parasite and ensure early detection of the re-establishment of autochthonous transmission. Its contents are applicable to the many regions that have been declared free of malaria but that are visited each year by growing numbers of parasite carriers as the pace and volume of international travel inexorably increase.

## **INTRODUCTION**

# The malaria elimination case-study series

If countries are to make well-informed decisions on whether or how to pursue malaria elimination, an understanding of historical and current experiences of malaria elimination and prevention of reintroduction in other countries - particularly those in similar ecoepidemiological settings - is critical. The Global Malaria Programme of the World Health Organization (WHO/GMP) and the Global Health Group of the University of California, San Francisco - in close collaboration with national malaria programmes and other partners and stakeholders - are jointly conducting a series of case-studies on elimination of malaria and prevention of re-establishment. The objective of this series is to build an evidence base to support intensification of malaria elimination as an important step in achieving international malaria targets.

Ten case-studies are being prepared that, together, will provide insights into and lessons to be learned from a wide range of elimination approaches and geographical settings.

Tunisia was selected for a malaria elimination case-study because of its elimination success and because details of the country's achievements in maintaining its malariafree status over the past 35 years have not yet been made available in the public domain.

For this case-study, a desk review of malaria control history in Tunisia was conducted, followed by a country visit for collaborative work and interviews with representatives from the Ministry of Health, National Malaria Control Programme and other malaria control and elimination stakeholders. Face-to-face interactions with NMCP staff proved particularly helpful for the development of maps/graphs and for data consolidation and analysis. This case-study was drafted in conjunction with the Global Malaria Programme at WHO headquarters in Geneva and the WHO Regional Office for the Eastern Mediterranean in Cairo. It describes the efforts made by Tunisia in the course of the 20th century to control and gradually eliminate malaria. It also examines the strategies adopted to avoid reestablishment of the disease and discusses the challenges involved in safeguarding this achievement in the future.

Data collection and analysis methods for the case-study are elaborated in Annex 1.

## Malaria in the WHO Eastern Mediterranean Region

Current malaria endemicity in the WHO Eastern Mediterranean Region varies considerably. In 2012, seven countries (Afghanistan, Djibouti, Pakistan, Somalia, South Sudan, Sudan and Yemen) had areas of high malaria transmission. Transmission was limited in the two countries in elimination phase – the Islamic Republic of Iran and Saudi Arabia; here, the burden of malaria has diminished in recent years, except during 2010–2012 in Saudi Arabia when there was a slight increase in the number of local malaria cases as a result of rising malaria importation.

Four countries in the Region – Egypt, Iraq, Oman and the Syrian Arab Republic – are classified by WHO as being in the prevention of malaria reintroduction phase. No locally acquired cases have been reported in Egypt since 1998 (other than a localized *P. vivax* outbreak occurring in 2014) or in Iraq since 2010. The Syrian Arab Republic has reported no cases since 2005 (but the reporting system has been disrupted since 2010). Local malaria transmission was interrupted in Oman in 2004– 2006; since 2007, however, the country has been battling regular malaria outbreaks involving both *P. falciparum* and *P. vivax*.

Two countries have been recently certified as malariafree (United Arab Emirates in 2007 and Morocco in 2010) and several have been added as malaria-free to the WHO supplementary list (Kuwait in 1963 and Bahrain, Jordan, Lebanon, Libya, Qatar and Tunisia in 2012) (WHO *World malaria report*, 2012 and 2013).

## Malaria in Tunisia

Malaria has been known to exist on the coasts of North Africa since antiquity. Historians believe that it is from there that it progressively colonized southern Europe. The disease is thought to have spread from what is now Tunisia to Sicily and Sardinia in 700 BC. It is then thought to have entered central Italy at the time of the Roman Empire (1) and to have persisted for more than 20 centuries around the Mediterranean basin before being eliminated from European coastlines in the 1960s.

Tunisia eliminated malaria in 1979. It was the second Maghreb country after Libya (last local case in 1973) to accomplish this, despite having long experienced a high transmission rate in the north of the country and regular devastating epidemics. At a meeting in Tunis in 1997, the experiences of Tunisia and Libya encouraged the remaining endemic countries in North Africa (Algeria, Egypt, Morocco) to embark upon malaria elimination campaigns (2). Tunisia established mechanisms that enabled it to safeguard the elimination achievement for more than 30 years and gave rise to a number of technical documents on the elimination of residual foci and the prevention of reintroduction (3).

## **COUNTRY BACKGROUND**

## Geography

Tunisia is bordered by Algeria to the west and Libya to the south-east; it has two Mediterranean seaboards, to the north and east, and extends into the Sahara desert to the south. It covers an area of 163 620 km2 and lies between longitudes 8 and 18°E and latitudes 28 and 32°N. The topography (Figure 1) is varied, with a mountainous region in the north and west – an extension of the Atlas Mountains – and the Sahel plain to the east. The south of the country, which is mainly desert, is made up of a series of salt lakes (*chotts*), rocky plateaus and the dunes of the Great Eastern Sand Sea.

## **Climate and vegetation**

Tunisia's climate (Figure 2) can be divided into seven bioclimatic zones, ranging from a humid Mediterranean climate in the north-west to semi-arid or arid, becoming increasingly desert-like, towards the Sahara. Temperatures vary by latitude, altitude and proximity to the Mediterranean. Annual rainfall varies from more than 1000 mm in the north-west to around 380 mm in the centre and 20-50 mm in the south. The Medjerda in the north is the country's only permanent river. The centre of the country is characterized by steppe vegetation, while one-third of the territory to the south is desert (4).

# Political organization and administrative divisions

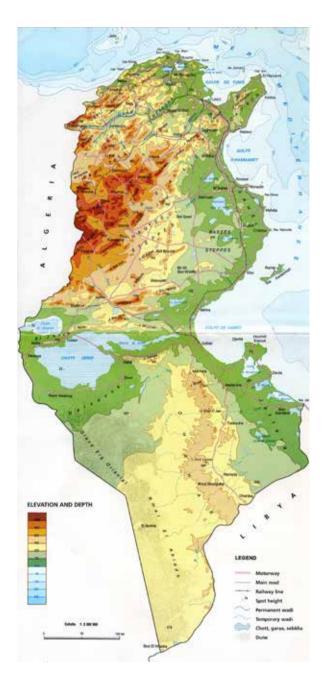
Tunisia gained independence from France in 1956, became a republic in 1959 and was a one-party state for many years. Following extensive civil unrest, parliament was dissolved in 2011. Power was then held by a constituent assembly before a president was elected by universal suffrage in 2014.

The country is divided into 24 governorates (Figure 3) named after their respective capitals and administered by governors appointed by the President of the Republic. The governorates are subdivided into 264 districts and a further 2073 sectors.

### **Population**

An improvement in living standards resulted in a demographic transition in the 1990s. The fertility rate decreased from nearly 6 in the 1960s to 1.8 in 2008. The total population was estimated at just under 10.7 million in 2011 (Annex 2). More than 67% of the population lives in cities; the population is relatively young, with 24% under 15 years of age and only 10% aged 60 years or over. The main urban centres, situated along the east coast, are Tunis, Sfax and Sousse (5).

### Figure 1. Relief map of Tunisia<sup>a</sup>



<sup>a</sup> Relief map of Tunisia. Tunisi: Tunisia Office of Topography and Cartography; 1999 (http://mappi.net/img/tunisie/carte\_Tunisie\_relief\_altitude\_profondeur.jpg, accessed 20 February 2015).

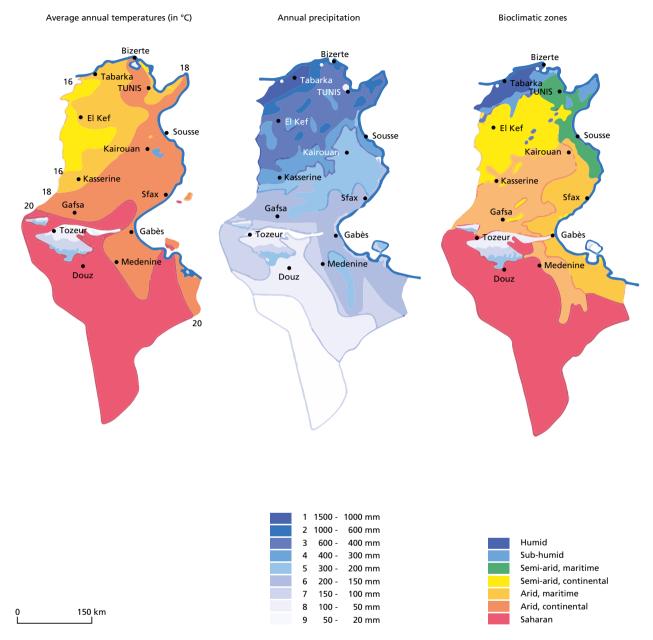
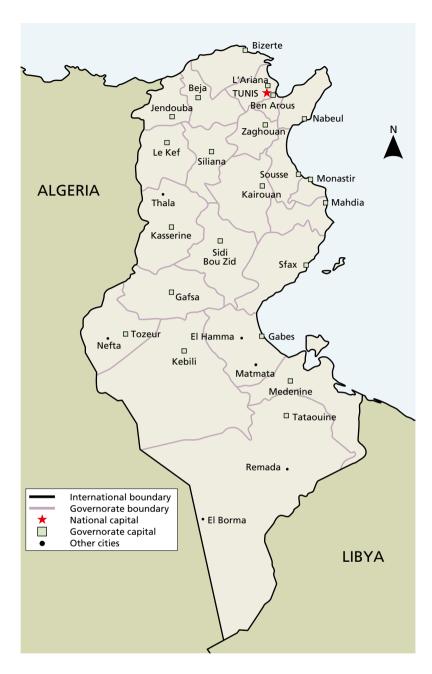


Figure 2. Average annual temperatures, annual average precipitation and the seven bioclimatic zones of Tunisia, 1967<sup>a</sup>

<sup>a</sup> Reproduced from reference (6) by kind permission of the Tunisia National Institute of Meteorology.





<sup>a</sup> Source: Tunisia National Malaria Control Programme.

### Economy

Over the past 20 years, Tunisia has undergone remarkable economic development. Its 5% annual growth rate over the period 1997–2007 placed it among the leading countries in the region. It is a middle-income country with a per capita gross domestic product (GDP) of US\$ 7810 in 2009. The economy has been transformed from one characterized by agriculture (wine, wheat and olive oil) and mining (phosphates) to one characterized by a more diversified and industrialized output. Despite the development of other sectors of the economy, agriculture has kept its social and economic importance and accounts for approximately 12.3% of GDP. The textile and agri-food sectors together account for 50% of production. The development of tourism began in the 1960s and now represents 6.5% of GDP. Despite the country's dynamic growth, the coastal regions continue to be more developed: there are significant disparities between these regions and the south and west, and also between urban and rural areas. The unemployment rate for the population as a whole was estimated at 13% in 2010, but was 30.7% among young people (15–24 years) and 44% among recent university graduates (5).

### Health care policies and system

Tunisia's health system is still largely dominated by the public sector. In 2008, health expenditure was US\$ 500 per inhabitant per year. The Government covered 54% of costs and allocated 10% of its budget to health. With 11.9 physicians per 100 000 inhabitants (7), the public sector handles 85% of hospital admissions and employs 60% of medical staff. In 2010, there were 2088 basic health-care centres and 123 local hospitals providing basic health care, resulting in an average of one basic health-care centre per 4750 inhabitants.

The secondary level comprises 34 regional hospitals located in the administrative centres of the governorates and in the main cities. At the tertiary level, there are 23 university hospitals. The national health insurance fund manages six polyclinics. Private health-care clinics have developed significantly in the past 10 years: there are now 116 such clinics, with a capacity of more than 2700 beds. The system of compulsory basic health insurance, administered by the national health insurance fund and financed by the contributions of employees and employers, was overhauled in 2007 and now covers 92% of employees (8). Within the Ministry of Health (MoH), health-care policy is implemented by the General Directorate for Public Health, which includes the Department of Basic Health Care (DBHC), the Department of Environmental Health and Protection (DEHP), the Department of School and University Medicine and the Department for Medical Research.

## General health profile

Sanitation and access to drinking water have improved greatly in recent decades, leading to a decline in transmissible diseases. Life expectancy at birth now exceeds 75 years. Measles, neonatal tetanus and poliomyelitis have been eliminated. The prevalence of HIV/AIDS remains stable at under 0.1% and the tuberculosis treatment success rate is 86%. Some health and development indicators are presented in Annex 3.

Remarkable progress has been achieved in tackling poverty, achieving universal primary education for boys and girls and reducing infant mortality. Infant mortality fell from 39 per 1000 live births in 1990 to 14 in 2010; over the same period, under-five mortality fell from 49 per 1000 live births to 16. Considerable progress is also being made in reducing maternal mortality: in 2010, the rate was 60 deaths per 100 000 births, down from 130 in 1990 (9).

Tunisia is poised to reach most of the Millennium Development Goals by 2015. However, regional differences still exist: high rates of maternal and perinatal mortality, and of diarrhoea and acute respiratory infections in children under 5 persist in poor rural and periurban areas and in the western and southern regions. Non-transmissible diseases are on the increase and cardiovascular diseases are the primary cause of death among adults, followed by cancer and accidental injuries. Risk factors such as obesity, diabetes and smoking are relatively common (5).

## EPIDEMIOLOGY AND PROGRAMME INTERVENTIONS OVER TIME

This section provides a chronological account of malaria epidemiology in Tunisia since the beginning of the 20th century and the main interventions during the successive phases of malaria control that led to elimination of the disease in 1979.

### Parasites and vectors

Both *P. falciparum* and *P. vivax* were widely distributed in Tunisia in the past, with some rare reports of *P. malariae* in the north. *Anopheles labranchiae* in the north and *An. sergentii* in the south are considered to be the two main vectors of malaria in Tunisia, although other species – such as *An. hispaniola* in the north and *An. multicolor* in the south – are also suspected of having a role in malaria transmission (Annex 4).

## Early control period, 1903 onwards

Malaria was widely distributed and caused severe health problems in Tunisia in the past. Early malaria control activities included larval control measures starting in 1903 along the railway line from Tunis to Bône in Algeria. In 1907, the malaria control section at the Tunis Pasteur Institute was created.<sup>1</sup>

The first malaria surveys were carried out between 1906 and 1909 on children aged 2–10 years in five areas in the humid north-west. These revealed spleen rates of between 86% and 100%, indicative of holoendemic malaria transmission. Public information campaigns were carried out and quinine was made available for febrile cases, also in remote areas. A number of epidemics were recorded between 1911 and 1928 and case notification was made compulsory in 1922. Malaria was present in all regions, with a parasite prevalence rate of 20-80%, depending on the location (10).

# First malaria control campaign, 1934–1954

In the summer of 1932 an epidemic began that was of sufficient severity to prompt a thoroughly planned response, coordinated by a reinforced malaria control service. The epidemic, which occurred after the torrential rains of the preceding winter, started in the Kairouan region, spread to Sousse, and ultimately affected the entire north-west. It lasted until 1935, reaching a peak of nearly 16 000 cases in 1934. Incidence rates quadrupled in some regions (11). Monthly mortality exceeded 5 per 1000 inhabitants in the most severely affected areas, where spleen rates were between 70% and 90% (10). The national API exceeded 7 per 1000 (Figure 4). In response, the country was divided into three operational sectors, and visiting health workers were trained and deployed in each health-care sector to detect and treat cases and establish larval control measures. Quarantine stations were set up to treat cases in remote rural areas and mobile laboratories measured prevalence and mapped the zones of intense transmission (Figure 5). Quinine was also administered preventively every 2 weeks through an extensive distribution network reaching into all communities. Other measures included larval control, by means of sanitation, drainage and the use of larvivorous fish in the main flood-prone areas. On an experimental basis, spraying activities were also conducted in some public areas. Following these measures, the API decreased to approximately 2 per 1000 in 1938.

<sup>&</sup>lt;sup>1</sup> Established in 1893, the Tunis Pasteur Institute is a public institution working in the area of health and scientific research under the authority of the Ministry of Health. Its purpose is to carry out surveys, missions, tests and scientific research in the fields of human and animal health. More information is available at: http://www.pasteur.tn.

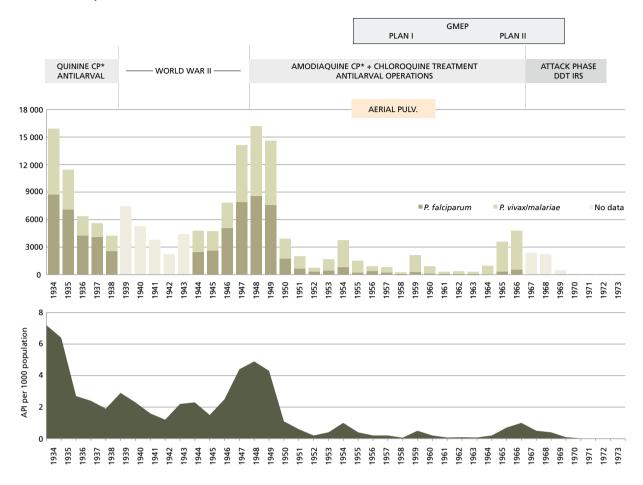


Figure 4. Annual number of reported malaria cases in Tunisia (by species), and main programme interventions, 1934–1973<sup>a</sup>

<sup>a</sup> Source: J.O. Guintran, based on desk review (10, 12, 13).



<sup>a</sup> Source: reference 11.

Services were completely disrupted during the Second World War, resulting in a sharp increase in malaria incidence: at its peak in 1948, more than 16 000 cases were reported (API approximately 5 per 1000). In response, larval control measures were reintroduced, chemoprophylaxis with 4-aminoquinoline compounds (premaline and amodiaquine) was extended to people living in all foci, and chloroquine was used for curative treatment. These measures brought the incidence down considerably. The number of *P. vivax* and *P. falciparum* cases dropped dramatically from 1950 onwards and was maintained at a much lower level than in the previous post-epidemic period 1936–1938 (Figure 4). Nevertheless, another small epidemic occurred in 1954.

## Efforts during the Global Malaria Eradication Programme (1955–1965)

Following the launch of the Global Malaria Eradication Programme (GMEP) in 1955 and Tunisia's national independence in 1956, WHO provided considerable technical assistance; a number of experts visited the country between 1956 and 1966 to assess the situation and develop a national malaria eradication plan (which was unfortunately never implemented owing to lack of funding).

An epidemiological analysis of the officially reported data showed a mild malaria burden in the country, with an API well below 1 per 1000. A survey carried out in 1958 among 16 000 children in 32 municipalities throughout the country indicated spleen rates generally below 10% (10). The highest risk was clearly in the northern areas of the country, and chemoprophylaxis was used there. However, meso- and hyperendemic foci survived in the north-west and in central Tunisia. While transmission was mainly low or non-existent on the east coast and in the south, isolated small foci also persisted there, and some highly active foci were discovered in small oases in desert areas in the south. Although the malaria control programme was by 1956 no longer an independent section of the MoH, control activities could be adjusted to the level of endemicity of geographical areas and foci. Chemoprophylaxis campaigns using amodiaquine focused on 11 risk sectors in northern Tunisia. Case detection in these risk sectors was facilitated by monthly home visits by specially trained health workers; in 1957, 279 such health workers were involved in this scheme nationwide. Vector control activities concentrated on larviciding: major water bodies were sprayed with insecticides (dieldrin) twice a vear, and small bodies of water created by dams were stocked with larvivorous fish. In 1956, the annual cost of larval control and chemoprophylaxis operations was estimated at about US\$ 100 0001 (14). As a result of these activities, malaria endemicity was maintained at a low level in the years that followed, with some minor outbreaks and epidemics.

Under the national malaria eradication plan, developed with WHO support, an independent National Malaria Eradication Service was to be set up with five staff members at national level and four regional centres (Tunis, Béjà, Sousse and Gabès), each with a laboratory covering the region. WHO planned to second four international staff to provide technical support. Annual spraying campaigns were envisaged, each lasting 3 months, to protect 2.5 million people; these campaigns would involve 75 team leaders, 675 operators and 150 workers, and would be overseen by 24 monitors and nine inspectors. The corresponding staff expenditure was estimated at US\$ 11 965 a year. The budget for the first year included the purchase of 85 vehicles, 1360 sprayers and 265 tonnes of DDT (10). The eradication plan was due to be launched in 1959 but did not receive adequate funding allocation: malaria no longer seemed to be a priority threat to public health.

<sup>&</sup>lt;sup>1</sup> Adjusted for consumer price index inflation: equivalent to US\$ 870 000 in 2015.

An epidemic began in 1964 that eventually resulted in nearly 5000 cases (mostly *P. vivax*) in 1966. This seemed to give new impetus to the idea of malaria elimination and another review of the situation was undertaken. Table 1 and Figure 6 show the geographical location of cases in 1963 and 1965 (*12, 15*). The 1963 and 1965 data give a good idea of the distribution of the persistent malaria foci in the country before the launch of eradication operations. The 1964–1966 epidemic did not affect just the north of the country: Kairouan and Sousse governorates, which had previously been virtually malaria-free, were also severely affected.

# Malaria eradication–elimination programme (1966–1996)

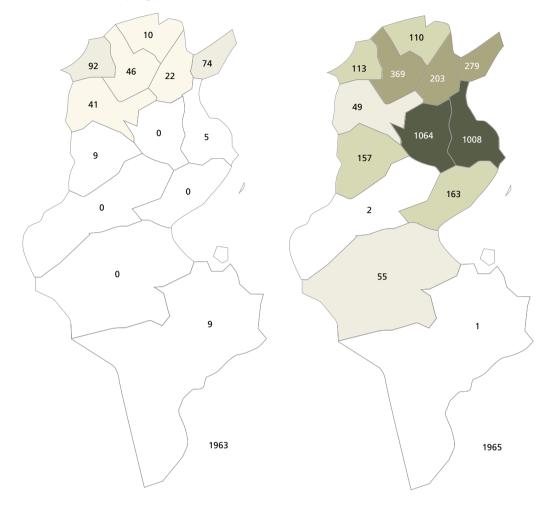
In 1966, WHO helped to draw up a new six-year eradication programme (*15*), and implementation began the following year. In the end, however, malaria elimination took much longer than the planned six years. It included the following phases: attack (1967– 1972), consolidation (1973–1977), maintenance phase (1978–1995) and prevention of reintroduction since 1996.

C	Annual number of cases				Total	
Governorates	1961	1962	1963	1964	1965	1961–1965
Sousse	8	4	5	264	1008	1289
Kairouan	9	0	0	209	1064	1282
Grombalia	113	45	74	114	279	625
Béjà	32	63	46	113	369	623
Tunis	52	25	22	50	203	352
Kasserine	0	1	9	149	157	316
Souk El Arba	11	11	92	55	113	282
Le Kef	12	141	41	2	49	245
Sfax	0	0	0	0	163	163
Bizerte	17	19	10	4	110	160
Gabès	5	0	0	3	55	63
Médenine	1	17	9	4	1	32
Gafsa	0	0	0	0	2	2

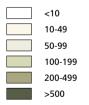
Table 1. Distribution of detected cases per governorate in the period 1961–1965 before the start of the attack phase of the national eradication programme<sup>a</sup>

<sup>a</sup> Source: references 12 and 15.

As a result of intensive surveillance and control activities, the disease burden was dramatically reduced and malaria foci gradually eliminated. *P. falciparum* disappeared in the north in 1971 and was totally eliminated in the country in 1979. The last foci of *P. vivax* in the Jendouba, Béjà and Aïn Draham regions, close to the Algerian border in the north-west, were carefully delimited and subjected to targeted spraying with insecticide and to systematic ACD. The last focus, spread across 15 communities, yielded 16 cases in 1975 and 6 in 1976. The last two cases of autochthonous *P. vivax* relapse were recorded in Jendouba region in 1979 *(11, 16)*. Figure 6. Distribution of annual number of cases per governorate in 1963 and 1965, before the attack phase of the national eradication programme<sup>a</sup>



Annual number of cases



<sup>a</sup> Source: J.O. Guintran, based on literature (15).

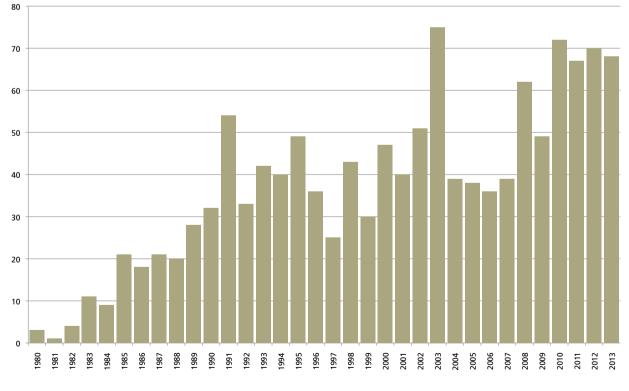
# Prevention of reintroduction since 1996

Although Tunisia's elimination plan called for the prevention of reintroduction phase to begin in 1996, the first measures to prevent reintroduction were applied as soon as elimination appeared to have been achieved. Free malaria diagnosis and treatment were provided from 1978 onwards (17) and screening of foreign students was introduced in 1984 (18). The year 1996 marked a strategic turning point: the National Malaria Eradication Programme (NMEP) was renamed the National Malaria Control Programme (NMCP); the consolidation and maintenance phases, as such, were discontinued; and surveillance was considerably reduced, with active case detection being abandoned and a new, more selective passive case detection strategy adopted. The strategy focused exclusively on preventing reintroduction of the disease, based on prevention and early detection of imported cases.

The cases notified since the interruption of transmission in 1979 have, with very few exceptions, been classified as imported; the exceptions are one late *P. malariae* recrudescence (19) and 11 cases of infection through blood transfusions, some of which have been described in detail elsewhere (11, 20). The origin of a case of *P. vivax* malaria in a French tourist after a trip to Tunisia, notified in 1988 (21), has never been confirmed.

Following the interruption of autochthonous transmission in 1980 and up to 2011, a total of 1273 imported malaria cases have been recorded. The number of reported imported cases is gradually increasing, with an annual average of 50 cases from 2004 to 2013. Since 2003, the annual number of imported cases has surpassed 60 six times, including from 2010 to 2013 (Figure 7). In 2013, *P. falciparum* malaria was detected in four neighbours in a residential area near Tunis Airport. After thorough investigation these were classified as "airport malaria", i.e. cases caused by a stowaway infected *Anopheles* mosquito that originated abroad.





<sup>a</sup> Source: reference 8 and NMCP data for 2012-2013.

## FACTORS CONTRIBUTING TO ELIMINATION AND MAINTENANCE OF MALARIA-FREE STATUS IN TUNISIA

### How was malaria eliminated?

The serious *P. vivax* epidemic that started in 1964 against the background of low malaria endemicity prompted the Government to renew its efforts for malaria elimination nationwide.

A national malaria elimination programme (designated at that time as an *eradication* programme) was developed with WHO assistance in 1966 and started activities in 1967. It was 12 years later – in 1979 – that the last autochthonous *P. vivax* cases were registered in Tunisia. Over the years, the country implemented all the malaria eradication phases recommended by WHO at the time, applying the relevant WHO strategies and policies. A summary of the strategic approaches to malaria elimination in Tunisia is presented in Table 2, with vector control and epidemiological surveillance forming the backbone of the programme throughout. The attack, consolidation and maintenance phases of the programme are described later in this chapter.

entomological monitoring the • Lar	S with DDT as leading intervention in the attack phase; limited to few foci in consolidation phase; suspended in the late 1970s
• Ent	rviciding tomological surveillance of vectors and breeding sites
• Ma • Ext • Cas • Epi • Rep • Da • Rac	tive and passive case detection (monthly rounds) intaining a high level of ABER ternal quality control of malaria laboratory diagnosis ses and foci recording and mapping idemiological investigation and classification of malaria cases and foci porting, notification and registration ta collection and analysis dical treatment of malaria patients and parasite carriers emoprophylaxis for risk groups

#### Table 2. Strategic directions for elimination of malaria in Tunisia (1967–1995)

Training of health personnel on malaria diagnosis, treatment, epidemiology, entomology and prevention

Public health education and community mobilization

Monitoring and evaluation of the effectiveness of the interventions undertaken

#### ATTACK PHASE, 1967–1972

# National Malaria Eradication Programme structure and financing

The NMEP, operational in 1967, was incorporated into the existing Department for Preventive Medicine and therefore was not autonomous. It was staffed by 35 senior professional personnel and 104 multidisciplinary unit chiefs at regional level, as well as 557 health workers, 50 microscopists and 23 entomologists working full time. In addition, it had a fleet of 100 cars and 500 motorcycles (13).

Using loans from the United States Agency for International Development, the Tunisian Government financed the programme to the amount of US\$ 900 000 a year. WHO contributed US\$ 500 000 over the six years of the attack phase and seconded two international technical officers.

#### Vector control

Vector control was the principal intervention, focusing on IRS. It is noteworthy that, for budgetary reasons, the attack phase never included the three southern governorates. The programme began in 1967 with geographical reconnaissance and an initial round of IRS in a pilot zone around Sousse; IRS was then carried out in April and May for three years in the 10 governorates of the northern and central regions. Around 280 tonnes of DDT were used every year to protect 2.5 million people. Only the northern part of Sfax governorate was ever sprayed, just one year before the start of the consolidation phase in 1969. In 1971, IRS was restricted to the whole of El Kef and Jendouba governorates; to parts of Kasserine, Bizerte, Nabeul and Tunis governorates (Figure 8); to areas along the Algerian border; and to persistent foci in Sfax and Kairouan governorates. In 1972 the north was practically malariafree (four cases), but some 15 cases were detected in the south and the three southern governorates were at last included in the pre-consolidation zone through spraying of identified foci in parallel with ACD. Larviciding was also carried out.

#### Surveillance

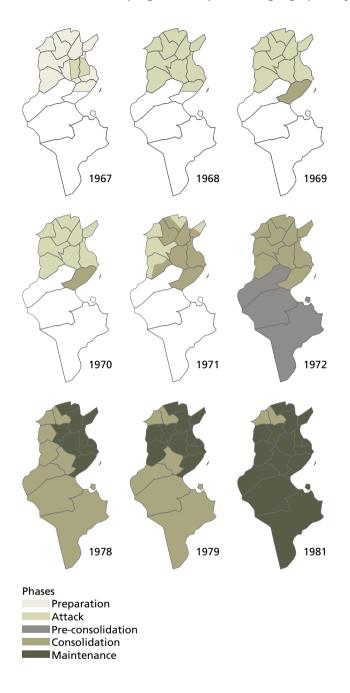
Both passive and active case detection were conducted. Active case detection of febrile patients was carried out during the health workers' monthly rounds in affected areas.

Microscopic diagnosis of malaria was carried out by one central and 13 regional laboratories employing 50 microscopists. Even in these early years, there was external quality control of malaria microscopy. The Tunis Pasteur Institute laboratory was considered the reference laboratory for quality-control purposes and re-examined all positive slides, as well as 10% of negative slides.

Among the population of Tunisia, ABER exceeded 10% in 1969 (22). The detection of a case triggered an investigation of the patient's circle of contacts.

Malaria patients were treated with chloroquine, and a 14-day primaquine treatment was added in cases of *P. vivax.* This radical treatment of *P. vivax* malaria eliminated the sources of infection. Identified cases were monitored once a month for a period of one year.

Figure 8. The various phases of the eradication programme represented geographically, 1967–1981<sup>a</sup>

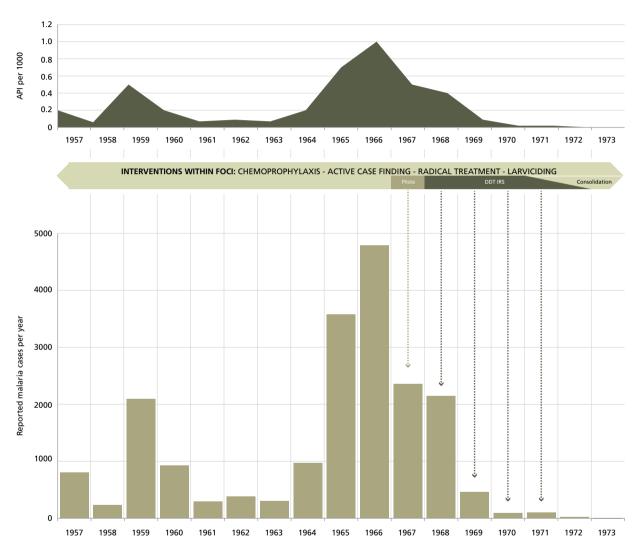


<sup>a</sup> Source: J.O. Guintran.

#### Results achieved

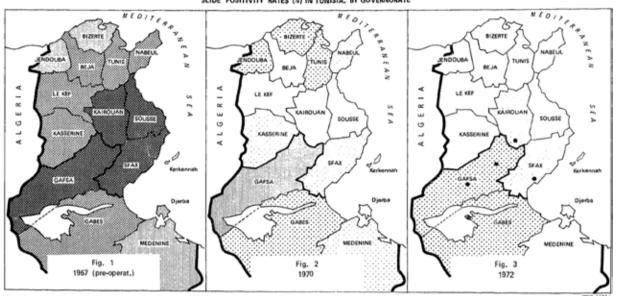
The complex of activities employed had a dramatic impact on the epidemiological indicators (Figure 9). In 1968, early in the attack phase, the national API was 0.4 per 1000; in Jendouba and Le Kef governorates, API values were 2.6 and 1.2 per 1000, respectively *(13)*. The following year, after just two rounds of IRS, the API was already below 0.1 per 1000 in the sprayed area. Moreover, the slide positivity rate - previously well over 1% - fell below 0.1% (Figure 10). In the 10 governorates of the attack zone, only 28 cases were detected in 1970 and 11 in 1971 (*13*).

A study directed by WHO was undertaken to ensure that elimination had been achieved. Every six months for three years between 1970 and 1972, serological surveys using immunofluorescence assays were carried out on 13 000 children in 18 communities scattered throughout the country. Results suggested that transmission had indeed been interrupted as of 1969 in all but one community, and no trace of recent transmission was found in 1972 (22).





<sup>a</sup> Source: J.O. Guintran, based on literature (13, 16).

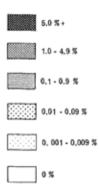


#### SLIDE POSITIVITY RATES (%) IN TUNISIA, BY GOVERNORATE

Note to Fig. 1 : the pre-operational rates of Sousse and Kairouan refer to 1966 as attack operations in these Governorates have started in 1967

Limit between Northern and Southern Governorates

Malaria foci in 1972



<sup>a</sup> Source: reference 22.

#### **CONSOLIDATION PHASE, 1973–1977**

Following the encouraging results obtained in the attack phase, the NMEP was reorganized in 1973 and incorporated into a new Department of Preventive and Social Medicine. By 1977, only two staff members and 39 microscopists continued to work full-time on malaria elimination, and the technical assistance provided by WHO was reduced to one person.

IRS was discontinued in the south in 1975 and subsequently limited to some 10 small foci in the northwest. Chemical larvicide was sprayed in recent foci and on water bodies created by northern dams every week during the summer (16). The strategy now relied chiefly on surveillance activities – active and passive case detection, carefully assessed in each intervention sector (Table 3 and Figure 11). The aim, as defined by national experts, was to maintain ABER at 9% (3.4% active detection and 5.6% passive detection) (16). Positive cases were carefully recorded and classified after the field investigation (Table 4), and foci, cases and spraying were mapped (Figure 12).

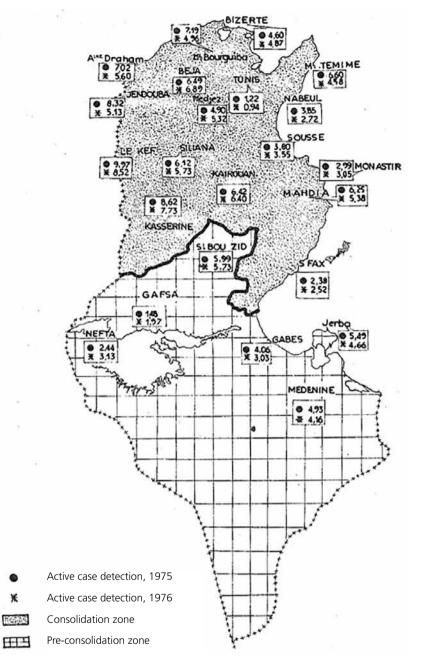
The disease was eliminated throughout the country 12 years after the start of the eradication programme activities: the last local *P. vivax* cases were registered in 1979.

				Slides e	<b>D</b>	Positive ABER				
Tunisia health districts	Population	Total	A.D.	P.D.	A.D. + P.D.	E.E.	E.E. Other		ABER (%)	API
Tunis, N. and S.	1 195 935	14 672	11 255	3417	14 672				1.23	
Bizerte	177 265	15 284	8642	6642	15 284				8.62	
Menzel Bourguiba	173 441	10 371	8603	1768	10 371				5.98	
Nabeul	267 045	16 085	7268	8817	16 085				6.02	
Menzel Témime	112 578	9853	5157	4696	9853				8.75	
Sousse	268 340	25 932	9535	16 397	25 932				9.66	
Monastir	228 204	21 787	6967	14 820	21 787				9.55	
Mahdia	217 447	20 543	11 698	8845	20 543				9.45	
Béja	178 971	25 049	12 329	12 277	24 606	443		2	13.75	0.0112
Medjez El Bab	67 259	12 099	3576	7749	11 325	774			16.84	
Jendouba	204 969	18 680	10 519	6250	16 769	1911		2	8.18	0.0097
Aïn Draham	86 997	12 793	4873	6095	10 968	1825		3	12.61	0.0345
Le Kef	229 232	32 562	19 535	12 878	32 413	149		2	14.14	0.0087
Siliana	186 039	21 856	10 670	11 186	21 856				11.75	
Kairouan	337 673	33 514	21 619	11 833	33 452	62			9.91	
Kasserine	239 981	29 024	18 541	10 483	29 024				12.09	
Sfax	479 486	34 661	12 087	22 574	34 661				7.23	
Total consolidation zone	4 650 862	354 765	182 874	166 727	349 601	5164		9	7.52	0.0019

#### Table 3. Example of screening test results table during 1976 consolidation phase<sup>a</sup>

<sup>a</sup> Source: reference 16.

Figure 11. Example of map showing results (ABER) of active case detection in each governorate during consolidation phase in 1975 and 1976<sup>a</sup>



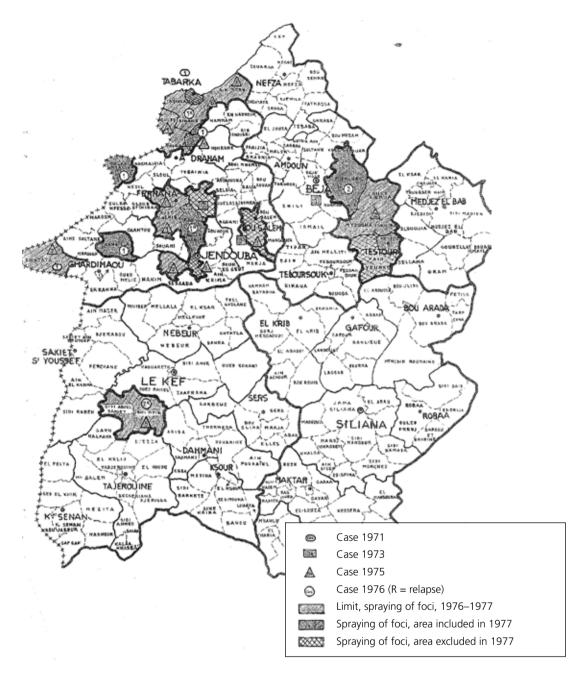
<sup>a</sup> Source: reference 16.

# Table 4. Example of classification of malaria cases notified during the 1976 consolidation phase (1 January – 31 December 1976)<sup>a</sup>

Regions	Date of blood collection	Age (yr)	Sex	Species	Epidemiological classification	Localities
Le Kef	03/04/1976	10	М	P. vivax	Autochthonous - relapse	Sidi M'tir
Aïn Draham	30/04/1976	60	М	P. vivax	Autochthonous - relapse	Ouled Ben Saïd
Jendouba	04/05/1976	22	F	P. vivax	Autochthonous - relapse	Bulla Regia
Le Kef	18/05/1976	16	М	P. vivax	Autochthonous - relapse	Sidi M'tir
Ain Draham	23/06/1976	41	М	P. vivax	Autochthonous (- relapse?)	Ouled M'Sallem
Aïn Draham	21/08/1976	17	М	P. vivax	Autochthonous	Ouled Cedra
Béjà	30/08/1976	15	М	P. vivax	Autochthonous	Munchar
Béjà	02/09/1976	3 1/2	М	P. vivax	Autochthonous	Munchar
Jendouba	16/10/1976	58	М	P. vivax	Autochthonous	Dkahaïlia-Sud

<sup>a</sup> Source: reference 16.

Figure 12. Reported malaria cases and focal spraying activities in the north-west, 1973–1976<sup>a</sup>



<sup>a</sup> Source: reference 16.

#### **MAINTENANCE PHASE, 1978–1995**

In 1978, nine governorates in the north-eastern part of the country entered the maintenance phase; these were followed by El Kef and Kasserine in 1979 and by Sidi Bou Zid, Gafsa, Gabès and Médenine in 1980. By 1981, only Jendouba and Béjà in the north-west remained in the consolidation phase.

#### Malaria programme network

By 1978, the NMEP was fully integrated into the preventive medical services. The two remaining health workers were expected to perform new tasks and adopt a multidisciplinary approach; many of their colleagues had already been seconded from their postings for training in other areas of public health or assigned to vaccination campaigns. The number of microscopists was reduced further from 39 in 1977 to 25 in 1981, leading to a sharp drop in blood screening capacity.

#### Malaria activities

In the governorates that entered the maintenance phase in 1978, IRS activities were discontinued. Thereafter, IRS was restricted to the remaining consolidation zones, where it was used in 16 000 households in the lastknown foci.

Active case detection was similarly discontinued in the governorates that had entered the maintenance phase; passive case detection, however, was strengthened. Blood testing was carried out on patients suspected of malaria on clinical grounds and on all febrile patients from the consolidation zones or who had recently received a blood transfusion. Imported cases were systematically recorded and measures to control and monitor importation began to be introduced.

For the areas in the south and north-west that were still in the consolidation phase, the reduced number of malaria microscopists resulted in blood screening targets being missed. In 1980, the active case detection rate in the consolidation zone was just 1.9% compared with the target of 3.4% and the passive case detection rate was 3.5% instead of 5.6%. In the maintenance zone, the passive detection rate did not reach 1.2% (17).

By 1991, case detection (passive and active) continued with a national ABER of 1.8% (23). In 1993, 76 174 slides were collected across the country and an ABER of approximately 3.6% was maintained in Jendouba and Béjà governorates, which were still officially in the consolidation phase (24). Thousands of slides continued to be sent to the Tunis Pasteur Institute every year for quality control purposes (25).

#### Validation of the interruption of transmission

Active case detection in 3365 communities in 1978 and a parasitological survey among more than 3000 people in the last two foci already supported the view that transmission had been interrupted (26). In 1991, a serological survey using indirect immunofluorescence assays was carried out among 6-year-old schoolchildren during two visits 6 months apart. The survey covered primary schools in 528 rural communities and the last-known foci in 20 governorates, excluding Tunis and other urban centres, giving a sample group of 26% of schoolchildren (19 000 out of the 78 000 enrolled). The specimens were analysed by the laboratories of the Tunis Pasteur Institute and the university hospitals in Tunis, Sousse and Sfax. No seropositive cases or seroconversions were detected, which strongly suggested that there had been no recent malaria transmission in Tunisia (27).

### What are the main strategies and policies of the current programme for the prevention of re-establishment?

The main components of the programme to prevent re-establishment of malaria transmission in Tunisia are epidemiological and entomological surveillance, early management of imported cases and prevention of onward transmission. An overview of the strategic directions of the programme, including sample activities, is provided in Table 5.

The sections below describe the organizational context and range of activities of the current programme for the prevention of re-establishment of malaria transmission in Tunisia. An example of programme activities during a recent occurrence of "airport malaria" in the country is provided in the section "Small outbreak of local cases in 2013".

#### INTERNAL ORGANIZATION AND SUPPORT

At the central level, the NMCP is part of the Parasitic Diseases Unit of the DBHC. The programme has no dedicated full-time staff; it is overseen by a physician who is also in charge of the tuberculosis control programme, and there is a senior health technician who is responsible for managing the surveillance system and also works on other parasitic diseases, for example leishmaniasis. To coordinate and implement its activities, the NMCP works with other units in the DBHC: Epidemiological Surveillance, Pharmaceuticals and Medicines, Laboratories, Blood Transfusion, and Health Workforce Training. Entomological surveillance activities are the responsibility of the Entomology Unit of the DEHP.

#### **LEGISLATION**

In accordance with a law of 1992, supplemented and amended in 2007, malaria is one of 28 diseases subject to compulsory notification. The other relevant legal provision is the DBHC monopoly on the procurement and distribution of antimalarials. These drugs have received marketing authorization but do not appear on Tunisia's official list of medicines *(28)* and are not sold in retail pharmacies.

#### EPIDEMIOLOGICAL SURVEILLANCE

Tunisia continues to operate the surveillance system established during the elimination phase. This system has been considerably scaled back since the interruption of active case detection and the change in the passive case detection strategy in 1996. It now focuses exclusively on the detection and monitoring of imported cases in order to limit the risk of malaria reestablishment (29).

#### Table 5. Strategic directions of the national programme for prevention of malaria re-establishment<sup>a</sup>

Strategic approach	Sample activities <sup>b</sup>
Malaria surveillance and prevention	<ul> <li>Early detection of each local and imported case, including through selective case detection among risk groups: <ul> <li>all foreign students (ACD)</li> <li>travellers to high-malaria risk countries: monitoring upon return from abroad</li> <li>individuals with unexplained persistent fever</li> </ul> </li> <li>Registration and timely mandatory notification to NMCP</li> <li>Epidemiological investigation of each malaria case</li> <li>Reporting and analysis</li> <li>Monitoring of imported cases</li> <li>Reducing the risk of possible transmission via blood banks by excluding donors who have travelled to a malarious area in the past 5 years</li> <li>Free malaria prevention services, including malaria chemoprophylaxis, for all individuals leaving the country for endemic areas</li> </ul>
Efficient case management	<ul> <li>Maintenance of diagnostic capacities</li> <li>Free examination and treatment services for malaria patients regardless of citizenship and residency status</li> <li>Standard protocol for treatment and monitoring of cases</li> <li>Centralized procurement and distribution of antimalarial medicines</li> </ul>
Continuing vector surveillance activities	Mapping and monitoring of breeding sites
Vector control activities	Biological control by larvivorous fish
Maintaining epidemic preparedness	<ul> <li>Ensuring appropriate supply and stock of insecticides in case of an outbreak</li> <li>Ensuring appropriate supply of antimalarial drugs</li> <li>Ensuring appropriate supply of laboratory reagents and consumables for malaria diagnosis</li> </ul>
Enhancing health education	<ul><li>Recommendations for travellers at Border Health Inspection at Tunis Airport</li><li>DBHC health education leaflets distributed to travel agencies</li></ul>
Maintaining malaria expertise	• Upgrading training for specialists involved in malaria prevention

<sup>a</sup> Source: reference 30.

 $^{\rm b}$  Interventions indicated in italics are initiatives that have been taken specifically by Tunisia.

#### **CASE DETECTION**

# Active case detection and screening of foreign students

The routine screening of foreign students was introduced in 1984. It is overseen in every university by branches of the Department of School and University Medicine at the MoH. Every year, before enrolment, all foreign students, regardless of nationality, are sent to the hygiene laboratory or relevant university hospital to undergo blood tests for malaria, lymphatic filariasis, HIV and schistosomiasis (18). In 1998, there were some 2500 foreign students in Tunisian universities, 28% of whom were from sub-Saharan Africa (25). It is therefore possible to estimate that approximately 700 students arrived from sub-Saharan Africa in September for the beginning of the university year. Between 2000 and 2011, around 1% of students tested were found to be carrying parasites; one-third of all imported cases (207/615) were detected in this way. Since 2011, the number of foreign students has increased slightly, stabilizing at around 3000 spread between the universities of Tunis, Sousse, Monastir and Sfax. More than 80% of these students are tested, but recently a growing proportion seem to avoid screening for various reasons (8).

#### Passive case detection

At one time, passive case detection focused on febrile patients attending health facilities. The target ABER was set at 5.4% for areas in the consolidation phase and 2.5% for areas in the maintenance phase. Since 1996, referral for malaria testing has been limited to the following febrile patients:

- travellers who have spent time in a country at risk in the past two years;
- patients with persistent unexplained fevers resistant to antibiotics;
- patients with persistent fever who have received a blood transfusion;
- persons who have recently been in contact with an imported case.

Between 20 000 and 32 000 slides were examined each year between 2000 and 2005 *(31)*, or approximately 0.2–0.3% of the population.

#### LABORATORY NETWORK AND QUALITY CONTROL

The recommended parasitological examination technique is the standard May–Grünwald Giemsastained thick and thin blood film combination. Rapid diagnostic tests are briefly outlined in the most recent technical guide but are not used (*30*). Parasitological diagnosis is free of charge and available in some 30 regional public health laboratories throughout the country (at least one in each governorate) and in an increasing number of private laboratories in the main cities. The network of public laboratories is centrally supervised by the Laboratories Unit and supplied with laboratory consumables by the DBHC.

A training session for public laboratory technicians is organized every two years in Monastir and funded by WHO. The systematic quality-control mechanism (i.e. the review of all positive slides and 20% of negative slides) that was used by the Tunis Pasteur Institute as the national reference laboratory during the elimination phase has not been operational for the past decade, but some hospitals and regional laboratories continue to send slides for re-examination from time to time.

#### **CASE MANAGEMENT**

Tunisia has chosen to apply a fairly strict set of measures to facilitate access to malaria case management of the best possible quality, as detailed below.

#### Free case management

In 1978, public-sector facilities instituted completely free malaria case management – diagnosis, treatment and hospitalization – regardless of the patient's nationality and place of residence (17).

# *Restricted and centralized distribution of medicines*

The DBHC pharmacy is the only body authorized to stock and dispense antimalarials in Tunisia. Only three medicines are available as first-line treatment of malaria in the country: quinine, artemether—lumefantrine and primaquine. Communicable disease units and private practitioners are allowed to keep stocks, which are replenished upon request by the DBHC pharmacy through an ordinary prescription. The same system is used to supply facilities that dispense mefloquine for prophylaxis.

#### Standard protocol for treatment and monitoring

Until recently, mefloquine was used to treat malaria caused by *P. falciparum*. In 2005, the ACT artemether– lumefantrine (AL) was adopted following a decision by a DBHC committee. Quinine, mefloquine and the combination atovaquone–proguanil are possible alternatives. In the event of serious symptoms or vomiting, patients must be admitted to hospital where injectable quinine is administered before treatment with AL. Malaria caused by other *Plasmodium* species is also treated with AL, in addition to radical treatment with primaquine for 14 days. A weekly treatment over eight weeks is recommended in cases of moderate glucose-6-phosphate dehydrogenase (G6PD) deficiency. Even if not routinely admitted to hospital, patients should be referred to the communicable disease unit of a university hospital; they should be monitored for one month, with parasitaemia tests on days 3, 7 and 28 (30).

Most patients are hospitalized in one of the country's five communicable disease units in Tunis, Bizerte, Sousse, Sfax and Monastir, or in clinics of the few recognized private-sector specialist facilities in Tunis and Sfax. Screened foreign students who are asymptomatic parasite carriers are generally referred to outpatient clinics (*32*). Of the 231 imported cases notified between 2002 and 2007, 73% were admitted to hospital; the median time between entry into the country and appearance of symptoms was 13 days, and the median time before treatment was a further 5 days (*32*). These times are comparable to those observed between 1980 and 1995 in cases detected by the Tunis Pasteur Institute (*25*).

# CASE INVESTIGATION, NOTIFICATION AND REPORTING

All malaria cases are epidemiologically investigated, and a standard form is completed. The compulsory notification of a confirmed case is carried out using a standard carbon copy form (Figure A5.1, Annex 5) from a counterfoil book. The completed forms must be sent to the DBHC and the regional health department that made the diagnosis. The DBHC Epidemiological Surveillance Unit is responsible for filing the case and entering it into a database on Epi-Info. The notified malaria cases are then communicated to NMCP, which requests the appropriate regional basic healthcare department to carry out an epidemiological investigation among the patient's circle of contacts. The DBHC's 1997 procedural manual indicates the steps that must be taken for the following three procedures relating to malaria (33):

- monitoring of the epidemiological situation of malaria

- epidemiological survey of the context of a malaria case
- monitoring and follow-up of international travellers

The procedures for epidemiological investigation following case notification (Figure A5.2, Annex 5) are particularly detailed. The surveillance focal point must seek out the necessary information to complete the standard seven-page form (Figure A5.3, Annex 5), the most recent version of which dates from 1993.

The National Observatory for New and Emerging Diseases, reporting to the MoH, was established in 2005 to strengthen health surveillance capacity and could soon become involved in malaria surveillance.

#### ANALYSIS AND DISSEMINATION OF DATA

The NMCP is responsible for filing the epidemiological investigation forms submitted by the regional departments and maintains a spreadsheet of all imported cases recorded throughout the year. A yearly report is then published, with a series of tables on the six principal case characteristics of the reported cases (age, sex, nationality, occupation, parasite species and origin of infection).

#### PREVENTION OF MALARIA IMPORTATION AND ITS CONSEQUENCES

#### Risk of importation

The breakdown of arrivals by nationality gives an idea of the movements of foreigners arriving from malarious areas. Of more than 6.9 million foreigners arriving in Tunisia in 2010, nearly 3.9 million were from malariafree countries. More than 2.9 million came from the Maghreb or Arab countries in the Middle East, where a risk exists only in a small number of foci (Tables 6, 7).

Passenger air traffic to and from Turkey and countries in the Caucasus region, where cases of *P. vivax* occurred until recently, is negligible. There is also very little traffic between Tunisia and Asian countries where *P. falciparum* persists, including Afghanistan, India, Islamic Republic of Iran and Pakistan. At present, therefore, Tunisia appears to be reasonably isolated from current areas of malaria transmission in Asia (Figure 13).

The main risk of parasite importation into the country is from the 45 000 travellers arriving from sub-Saharan Africa and Mauritania every year. Currently these travellers arrive on one of 10 direct weekly flights (four from Dakar, three from Nouakchott, one from Bamako and one from Abidjan) operated by Tunisair. The transfer of the headquarters of the African Development Bank (ADB) to Tunis in 2003, and the arrival of 300 employees and their families, may also have been a factor in the increased flow of cases of infection from these regions.

## Table 6. Distribution of imported cases in 2011, by country of origin of the infection<sup>a</sup>

Country of origin of the infection	No. of imported cases
Côte d'Ivoire	8
Guinea	7
Burkina Faso	6
Mali	4
Mauritania	7
Other West African country	7
Total West Africa	39
Chad	6
Cameroon	6
Other Central African country	4
Total Central Africa	16
South Asia	2
Not specified	10
Total	67

<sup>a</sup> Source: reference 8.

#### Table 7. Number of arrivals in 2010, by nationality<sup>a</sup>

Nationality	Number
Europeans	3 814 402
North Americans	36 203
Japanese, Chinese, Australian	23 989
Middle East	38 280
Libya	1 825 542
Algeria	1 060 043
Morocco	29 104
Mauritania	13 279
Sub-Saharan Africa	32 448
Other	32 348
Total	6 905 638
a Sauraa noformaa 24	

<sup>a</sup> Source: reference 34.

#### Characteristics of imported cases

Data on the principal characteristics of all imported cases between 1979 and 1999 (e.g. nationality, occupation, place of contamination) have been partially reported in the literature. Of the 245 cases handled by the Tunis Pasteur Institute between 1980 and 1995, 58% were foreign students and 38% were Tunisians; 93% were infected in Africa; and 75% were *P. falciparum* infections. Note should be taken of the 17% of infections by *P. vivax*, imported mainly from Mauritania (22 cases), followed by Asia or America (12 cases) and east Africa (seven cases). *P. ovale* and *P. malariae* each account for 4% of cases, and more than 60% of cases were detected in the months of October, November and December (25).

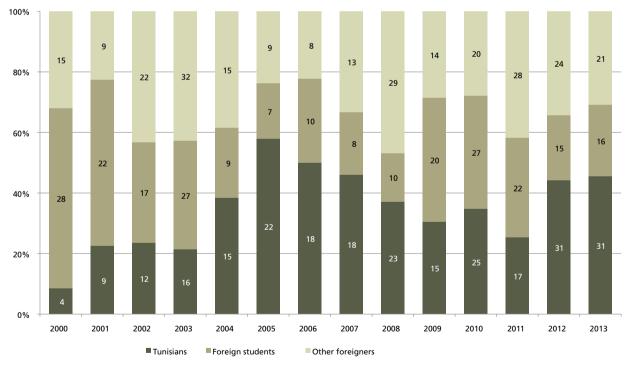
Similar characteristics are found in the 61 cases detected in the university city of Sfax between 1978 and 1998 (*35*): 78% were foreign students, 98% had been infected in Africa, and 85% were carrying *P. falciparum*. It should be noted, however, that 8% entered Tunisia by road and that three cases were infected in neighbouring Maghreb countries (Algeria, Libya and Morocco – the latter two no longer being endemic). The overwhelming majority (94%) of the 291 cases diagnosed at La Rabta hospital in Tunis between 1991 and 2006 had also been infected in Africa and 75% were carrying *P. falciparum (36*). Likewise, of the 98 cases detected at the Tunis Pasteur Institute between 1999 and 2006, 71% had been infected by *P. falciparum* and 96% had spent time in Africa (*37*).

More detailed annual national data are available from 2000 onwards (8). Of the 753 cases recorded from 2000 to 2013, one third were Tunisian nationals and half of the foreigners were students. The proportion of foreign students among reported cases declined slightly by 2005, whereas the proportion of Tunisians peaked that year at nearly 60%. Since then, this trend has reversed, and the proportion of foreigners among imported malaria cases has increased considerably (Figure 13), except in 2012–2013. By 2011, nearly 90% (555) of cases had been infected by *P. falciparum*, 6% (40) by *P. vivax*, 3% (19) by *P. ovale* and 1% (10) by *P. malariae* (8). These proportions have remained constant over the past decade. Only two deaths have been recorded in the past 11 years – a fatality rate of 0.3%.

Of the 67 notified cases in 2011, 57 (85%) were living in Tunis governorate. Half of the cases were notified by a university hospital (33/67), 20% (14 cases) by a clinic or a physician in private practice, and just 10% (7 cases) by peripheral health units. Thirty-nine cases (58%) had been infected in west Africa, 16 cases (24%) in central Africa and only two cases in Asia (Table 6). For 10 people (15%), four of whom were Tunisian and four Libyan, the notification form did not indicate the country where infection occurred.

In total, more than 95% of all imported cases recorded in the past 30 years were contracted in sub-Saharan Africa or Mauritania. Of these, some 20 asymptomatic cases are detected each year among approximately 700 students from sub-Saharan Africa, and 20 additional cases are notified, representing an incidence of around 10 cases per 100 000 travellers per year.





<sup>a</sup> Source: reference 8 and NMCP data for 2012–2013.

#### Free chemoprophylaxis for Tunisian travellers

Every year, approximately 20 Tunisians return from abroad infected and subsequently develop malaria. A distinction should be drawn between those travelling in an official capacity and those travelling independently. The first group are usually well informed, are monitored and are often provided with preventive measures by their employers. This group generally includes aid workers, diplomats, sports delegations, Tunisair flight staff and soldiers involved in peacekeeping operations. The risk is harder to control in the second group, which includes missionaries, tourists, commercial travellers and independent businessmen.

As yet, there is no official network of travel advice centres in Tunisia, and the Border Health Inspection Service at Tunis Airport is the only body providing advice and chemoprophylaxis for travellers. The DBHC publishes a leaflet, which it distributes to travel agencies and to Tunisair, to inform travellers of the risks in malarious countries and to encourage them to use chemoprophylaxis. Travel medicine has recently been officially recognized as a medical speciality and a dedicated Master of Science course is now offered at the Faculty of Medicine in Tunis.

The technical guide published by the DBHC in 2010 (30) includes recommendations for travellers and a classification of countries into three groups, as developed by the French National Institute for Health Surveillance on the basis of resistance to chloroquine (38). For the sake of simplicity, weekly mefloquine treatment was chosen for all countries regardless of their level of resistance to chloroquine. The WHOrecommended alternatives atovaquone–proguanil and doxycycline are not available for chemoprophylaxis (39). The DBHC supplies the Border Health Inspection Service at Tunis Airport with mefloquine and all residents in Tunisia can receive it for free on request. This service was used by 4980 travellers in 2011 (8).

#### Monitoring Tunisian travellers on return

When Tunisian travellers pass through the Border Health Inspection Service at Tunis Airport, they are required to complete a form indicating their home address and date of return. The form is sent to the NMCP and then to the relevant regional health-care department, which is responsible for monitoring travellers after their return. About 20 cases of malaria are reported every year in returning travellers.

#### PREVENTION OF INDUCED MALARIA THROUGH INFECTED BLOOD TRANSFUSIONS

A total of 11 cases of malaria transmitted through blood transfusion have been recorded since 1980 (30), including five cases since 2000 (32). Case detection for at-risk blood donors is based on screening questions that exclude individuals who have travelled to a malarious area in the previous five years. No parasitological or serological tests are carried out on the blood bags collected.

#### ENTOMOLOGICAL SURVEILLANCE

Entomological surveillance, which guided operations on foci throughout the elimination campaign, has gradually been abandoned. At the end of the 1980s, a single team continued to operate at a regional level in the north-west (40) and only four medical entomologists remained in service a few years later (23). The last entomological observations on *Anopheles* were made by the research programme carried out by the Tunis Pasteur Institute in the 1990s.

#### **VECTOR CONTROL ACTIVITIES**

Vector control activities are carried out by teams within the governorates, administered by the DEHP. These target mainly nuisance mosquitoes and vectors of arboviruses. Specific systematic actions targeting the adult forms of *Anopheles* have not been used since the last IRS, which concentrated on the remaining foci at the end of the 1970s.

#### Larval control

Larval control, based on careful surveillance of larval habitats, has been carried out since the first largescale monitoring operations in the 1930s. It remained part of the routine field activities of health workers nationwide in the 1950s, and it was still widely practised during the attack and consolidation phases in the most active foci, in combination with IRS during the elimination campaign in the 1970s. Relying at first on mechanical elimination of larvae and on the drainage of wetlands, techniques subsequently evolved with the use of insecticides (41) and finally the introduction of biological control methods. The extensive programme to build dams for agricultural purposes, which began in the 1990s, included the systematic introduction of larvivorous fish (*Gambusia affinis*) which had previously proved effective in Tunisia (42). Biological pesticides, such as *Bacillus thuringiensis* and *Bacillus sphaericus*, have been used more recently against *Culex pipiens* larvae.

#### THE COSTS OF PREVENTING RE-ESTABLISHMENT

The annual budget of the NMCP under the MoH was US\$ 145 500 in 2012. Almost all of this – US\$ 140 000 – was spent on the purchase of mefloquine for prophylaxis. The remaining US\$ 5500 was spent on microscopy staining products and laboratory consumables. Every year, WHO supplies the medicines required for AL treatment of 120 cases, radical primaquine treatment for 100 cases and injectable quinine. WHO also provides US\$ 3000 for a training session every two years for 20 microscopists.

#### SMALL OUTBREAK OF LOCAL CASES IN 2013

In July 2013, four cases of *P. falciparum* were detected among residents of the shores of the Lake of Tunis near Tunis-Carthage Airport (43). Epidemiological and entomological investigations indicated that these were cases of "airport malaria", probably caused by an infected imported vector.<sup>1</sup> Investigation and examination of other residents related to the malaria patients did not detect other malaria cases. The entomological investigation, which involved trapping mosquito larvae in the Lake of Tunis and drains from the airport, showed the presence only of *Culex* mosquitoes; no *Anopheles* were found. The lake is stocked with *Gambusia*  larvivorous fish. The timely response by the MoH and measures taken for the investigation of cases and focus, elimination of sources of transmission (prompt radical treatment) and prevention of resurgence – including scaled-up vigilance, entomological surveillance, staff retraining, health education – were impressive.

This example indicates the necessity of strict observance of current international regulations on the disinsectization of aircraft and ships (44) and of the measures prescribed for international aircraft arriving from endemic countries by the border health services in collaboration with the relevant departments of civil aviation.

### Challenges for the programme for the prevention of malaria re-establishment

#### RECEPTIVITY

The rapid success of IRS campaigns and the relative ease with which P. falciparum was eliminated using only two or three spraying cycles suggests that the vectorial capacity of the vectors present in Tunisia at the beginning of the elimination campaign was not very high (45). However, the mosquitoes re-established themselves after the discontinuation of the intensive vector control operations of the late 1970s. During the past 30 years, the environment has undergone significant changes that have affected receptivity. Rapid urbanization and changing patterns of vegetation as a result of the proliferation of agricultural schemes have tended to reduce receptivity. It has been observed that pollution of larval habitats has led to the virtual disappearance of anopheline mosquitoes and their replacement by Culex pipiens (46).

Conversely, large-scale water resource improvement works in the 1990s, designed to recover surface water run-off, and construction of hundreds of small dams in hilly areas could have resulted in increased numbers of potential habitats for the development of anophelines in unpolluted water. Thus, more than the persistence of *An. labranchiae* on the coast, the increased receptivity

<sup>&</sup>lt;sup>1</sup> "Airport malaria" is infection resulting from accidental importation of infected *Anopheles* by aircraft. It has also been reported in the vicinity of European airports.

related to *An. sergentii* and *An. multicolor* in the oases of Fezzan following a major irrigation project was considered potentially conducive to the re-establishment of autochthonous transmission (47).

Studies carried out in the 1990s in the last active foci confirmed the presence of anthropophilic vectors and the persistence of potential residual vectorial capacity. In the north-western region of the country, the most favourable from an environmental point of view, the vectorial capacity of *An. labranchiae* for *P. vivax* appeared high in August and September (48). In the central region, the probability of survival of *An. labranchiae* and *An. sergentii* and the summer temperatures appeared to be perfectly compatible with the life-cycles of *P. vivax* and *P. falciparum* (49).

The historical vectors of malaria in Tunisia are thus still present and potentially active during the summer months, but receptivity to malaria may nevertheless be considered low owing to a combination of environmental, climatic and socioeconomic factors that currently inhibit permanent re-establishment of transmission.

#### VULNERABILITY

Between 50 and 70 new cases of malaria are currently imported every year. Almost 60% of these cases are recorded among foreign students and travellers from malaria-endemic areas.

#### Importation of P. falciparum

More than 95% of imported infections are due to *P. falciparum* from tropical Africa, to which Tunisian vectors are perhaps refractory. In addition, the establishment within the flight perimeter of *Anopheles* of a reservoir of *P. falciparum* capable of infecting a local vector that would survive for the duration necessary for the development of *P. falciparum* seems highly improbable in the north of the country, given that settlement or transit centres are generally in the big cities where *Anopheles* is either very rare or non-existent. Tunisian vectors are more likely to be susceptible to *P. falciparum* from the Palaearctic ecozone, but the last focus in northern Africa, present in Egypt in 1990 (50), has been inactive since 1997, and contacts with those Asian countries where the species persists (for example Afghanistan) remain minimal (51). The *P. falciparum* strains in Yemen are Afrotropical as in sub-Saharan Africa, except on Socotra Island where they were Oriental and transmission has been interrupted. Although Palaearctic vectors are considered refractory to parasites of Afrotropical and Oriental origin, there is some speculation that *An. sergentii* may be more susceptible to the Afrotropical *P. falciparum*.

#### Importation of P. vivax

The small number of imported cases of malaria due to P. vivax should not disguise the fact that the risk of reestablishment of this species is certainly higher than for P. falciparum, given that it has a shorter life-cycle and is better adapted to local vectors. Recent examples abound of the re-establishment of this species in a number of Mediterranean countries (52-55). The vectorial capacity of An. labranchiae to transmit P. vivax in this ecozone is well documented (56, 57). Tunisia has probably been spared thus far, but the risk certainly exists. The principal flow of travellers, as mentioned previously, is from the Maghreb and Arab countries in the Middle East where malaria is gradually being eliminated. Morocco reported 781 autochthonous cases in 1990, although the most recent case occurred in 2004 and the country was certified malaria-free in 2010. The last recorded case in Egypt dates from 1997, and in the United Arab Emirates elimination of the disease was certified in 2007. Today, P. vivax survives in only a very few foci in Algeria (58). In the early 1980s, a small-scale serological survey of 106 schoolchildren found no positive cases despite a significant influx of immigrant workers from the Indian subcontinent who are frequent carriers of P. vivax (59). At present, Tunisia no longer sees significant inflows of travellers from countries further afield such as India and Pakistan, where P. vivax transmission is still frequent.

Although neighbouring Libya has significant trade and population exchanges with Tunisia – more than 1.8 million people entered Tunisia from Libya in 2010 (*34*) – the risk of importation of parasites should be zero because Libya has been considered malaria-free since 1973 (*50*) and has reported no autochthonous cases since that date. However, there is some concern, as malaria is regularly detected in Tunisia in individuals who have otherwise never travelled outside Libya (*25, 35, 37*).

#### **CLASSIFYING THE RISKS**

Effective control of the risk of reintroduction requires that risk to be sufficiently well defined. Among researchers who have studied the situation in Tunisia there is apparent consensus that the risk of malaria re-establishment is low. It is unlikely that the remaining vectors (which survive in rural areas) will come into contact with imported parasites (which are hosted mainly in the cities). Vectors in the north of the country are hardly, if at all, capable of transmitting *P. falciparum*. In any event, they survive only just long enough – 2 or 3 months in the course of the summer – to accommodate the life-cycle of *P. vivax*, and few people travel from countries where *P. vivax* is frequent.

Nevertheless, the possibility of transmission of *P. vivax* in rural areas to a handful of people over the course of one summer cannot be ruled out. Nor can the risk of *P. falciparum* transmission be totally excluded at oases in the south of the country, where high temperatures persist for longer periods and *An. sergentii* is found in abundance.

The occasional appearance of airport malaria (including infection due to *P. falciparum*) during the summer months is difficult to exclude, as was shown in 2013. Those events, however, demonstrated both the adequacy of the MoH response capacity and the lack of local vectors capable of transmitting the disease.

#### CONTROLLING THE RISK OF MALARIA IMPORTATION

Most of the imported parasites arrive in Tunisia on a small number of flights (10 weekly flights from sub-Saharan Africa operated by Tunisair). Among 45 000 arrivals from sub-Saharan Africa in 2011, only about 700 students were tested on enrolment at university; the remaining passengers are not subject to any special measures to limit the risk of re-establishment. The number of foreign travellers arriving from sub-Saharan Africa every year is relatively small and the incidence of imported cases (approximately 10 per 100 000 travellers) seems modest. By way of comparison, the rate was 34 cases per 100 000 in the Netherlands in 2007 (60) and 48 cases per 100 000 in France in 2008 (61).

Tunisians who travel to malarious areas are notified of the risk by travel agencies and the national airline and urged to visit the Border Health Inspection Service at Tunis Airport on departure. In 2011, approximately 5000 passengers benefited from free chemoprophylaxis (mefloquine) and were monitored upon their return. About 20 cases of malaria are reported every year in returning travellers.

#### **SURVEILLANCE**

Despite obligatory notification, a significant proportion of malaria cases detected in Tunisia are not picked up by the surveillance system administered by the DBHC. A retrospective survey by the National Observatory for New and Emerging Diseases covering the period 2002–2007 and focusing on the principal sources of case notifications revealed that only an estimated 73% of cases diagnosed by hospitals or laboratories (231/317) had been recorded by the DBHC surveillance system (32).

It is possible that a number of infections go entirely undetected, particularly among recent arrivals from endemic areas in Africa who have retained a degree of immunity and remain asymptomatic for some time. If and when they fall ill, some may resort to self-medication without parasitological investigation. The availability of high-quality medical services leads others to believe that the risk of failure to detect an acute episode due to *P. falciparum* must be negligible. Cases caused by other species and episodes of recrudescence of *P. vivax*, however, may go unheeded or be identified at a later stage.

#### **MANAGEMENT OF IMPORTED CASES**

With two deaths out of a total of 615 notified cases between 2000 and 2011 (555 of which were due to *P. falciparum*), the case-fatality rate is 0.3%, suggesting that the management of malaria is generally sufficiently prompt and efficacious. The median time elapsing before the start of appropriate care (5 days) reported for some case series indicates that there is still room for improvement in terms of encouraging patients to seek early medical advice. The fact that antimalarials are dispensed only by the DBHC is a guarantee of the quality of those drugs and facilitates monitoring of their rational use in a small number of clearly identified specialist health facilities. Rigorous parasitological evaluation of all cases and radical treatment of *P. vivax* and *P. ovale* cases are important steps in reducing the risk of onward transmission.

#### RESPONSE CAPACITY IN THE EVENT OF RE-ESTABLISHMENT

Small clusters of introduced cases have recently been observed in most Mediterranean countries, including Tunisia (see section "Small outbreak of local cases in 2013"). This scenario necessitates the rapid mobilization of a team to carry out epidemiological and entomological surveys. Targeted antivectorial interventions and epidemiological monitoring are also required. The capacity for detecting and investigating cases and foci should therefore be maintained, as should stocks of antimalarial drugs and insecticides.

### **LESSONS LEARNED AND CONCLUSIONS**

The history of malaria elimination in Tunisia shows that this is a long process requiring the application of comprehensive strategies and policies nationwide and substantial stable financial resources. Once malaria-free status has been achieved, additional long-term efforts and financing are needed to safeguard this achievement.

For 35 years, Tunisia has successfully avoided the reestablishment of autochthonous transmission through the implementation of strategies based on prevention, surveillance and early management of imported cases.

A number of lessons can be learned from the campaign to control, and later eliminate, malaria in Tunisia, and from the strategies that have effectively prevented the re-establishment of renewed local transmission over the past 35 years.

# Keeping malaria burden at a low level in the 1950s and 1960s

The malaria programme kept incidence low in the 1950s and 1960s by means of decentralized mass chemoprophylaxis campaigns and larval habitat control measures that were implemented extensively in the most receptive areas in northern Tunisia. However, the interventions applied and the substantial funding (around US\$ 100 000 annually for larval control and chemoprophylaxis) did not prevent the occurrence of a number of malaria epidemics, nor did they bring about the interruption of transmission in the country.

### Malaria elimination through implementation of the Global Malaria Eradication Programme strategies and policies

The malaria elimination programme was initially rolled out in the northern and central regions of the country only. A combination of widespread IRS using DDT and active surveillance led to the elimination of *P. falciparum* in less than five years. Seven more years of IRS and targeted active case detection were required to eliminate the last cases of *P. vivax*. More precisely targeted but equally thorough operations were carried out in semidesert ecozones and the oases in the south of Tunisia.

Tunisia was able to obtain funding for its malaria elimination programme only in the last few years of the GMEP. Nevertheless, it was able to pursue its efforts following discontinuation of the GMEP and to guide the consolidation and maintenance phases to completion. Thus, in 1979, Tunisia became the second country in North Africa, after Libya in 1973, to eliminate malaria.

Several aspects of the Tunisia malaria elimination approaches should be highlighted:

Three annual rounds of spraying with DDT were
a leading vector control intervention in the attack
phase and brought about a dramatic decrease in the
mosquito population and the level of transmission.
It was correctly limited to the few remaining foci in
the consolidation phase, then suspended in the late
1970s when transmission was interrupted.

- Vector control was guided by regular entomological surveillance of vectors and breeding sites, as well as by foci recording and mapping.
  - Intensive active case detection during the monthly visits of health workers in affected areas resulted in efficient case detection. The high level of ABER during the campaigns is indicative of good coverage of the population with malaria examinations.
  - External quality control of malaria laboratory diagnosis aimed at ensuring consistently high quality in the work of the diagnostic laboratories nationwide.
  - Epidemiological investigation of malaria cases, reporting, notification and registration, data collection and analysis provided decision-makers with regular information.
  - A dramatic reduction in the sources of malaria infection was achieved by conducting radical treatment of *P. vivax* patients with chloroquine and primaquine and through implementation of seasonal chemoprophylaxis.

# Long-term successful prevention of re-establishment of malaria

For more than 35 years, Tunisia has successfully prevented the re-establishment of autochthonous transmission. Although the malaria potential in the country is not high, malaria vectors are still present and the climatic conditions in the potential malaria season are favourable for re-establishment of local transmission if there are undetected and/or untreated sources of infection, i.e. infected individuals, especially with *P. vivax*. Government efforts therefore focus primarily on controlling the risk of *Plasmodium* species importation and preventing its consequences.

 Continued high levels of vigilance and early detection and treatment of each imported malaria case remain priority activities and require diagnostic capacities to be maintained. Selective case detection through free laboratory examinations among risk groups such as foreign students (ACD through compulsory screening), travellers to countries with a high malaria risk and individuals with unexplained persistent fever allows early identification of the potential sources of infection. Elimination of these sources is ensured by timely and free radical treatment for all malaria cases, provided by the MoH. Efficient case management and highquality treatment are underpinned by use of a standard protocol for treatment and monitoring of cases and by the existing system of centralized procurement and supply of antimalarial medicines (including their restricted distribution) according to MoH regulations.

The most plausible scenario for reintroduction would be a limited re-establishment of *P. vivax* transmission in the course of one summer, as recently observed in a number of countries in southern Europe. However, the flow of travellers and the number of imported cases from regions where *P. vivax* still predominates is negligible, and more than 90% of the 50–70 imported cases detected each year are infected by *P. falciparum* in sub-Saharan Africa countries. In this group, only about half of the affected travellers are Tunisian residents. The compulsory screening of 3000 foreign students improves detection and results in the treatment of approximately 20 often asymptomatic parasite carriers every year.

- Risk prevention for travellers is a key intervention in Tunisia. Tunisian residents travelling to malariaendemic countries are informed about the risk of contracting infection by the Border Health Inspection Service at Tunis Airport and through DBHC health education leaflets distributed to travel agencies. They are also provided, free of charge, with antimalarial drugs for chemoprophylaxis in line with WHO recommendations. On their return from malarious areas, Tunisian residents are monitored and, if febrile, are examined for malaria.
- Tunisia maintains a surveillance system based on compulsory case notification backed up by routine epidemiological investigation and classification of

cases. Regular reporting and analysis of the situation greatly assist planning of the appropriate antiepidemic measures.

• Routine larval control operations and IRS were suspended in the late 1970s and vectors are still present despite large-scale sanitation works and rapid urbanization. Studies in the 1990s indicated that their vectorial capacity remained intact during the summer months, although *An. labranchiae* could be refractory to African strains of *P. falciparum*.

Continued vector surveillance activities through monitoring and mapping of breeding sites provides important information to the MoH. Biological control by larvivorous fish is likely to contribute to the decline in mosquito density.

 Given the risk of re-introduction of malaria transmission in Tunisia and the lessons learned in other areas that experienced a re-establishment of malaria – such as in Central Asia, the Caucasus and Greece – the Government recognizes the importance of maintaining epidemic preparedness in the country. For this purpose, appropriate stocks of insecticides, antimalarial drugs and laboratory reagents and consumables for malaria diagnosis are maintained in case of outbreaks. Malaria expertise is maintained by regular training and retraining of specialists involved in malaria prevention. This study does not answer the question asked by many countries that eliminated malaria several decades ago: "When can we cease our measures for preventing re-establishment of malaria?" The extent to which relatively costly antimalarial measures can be phased out is difficult to assess in a context where a poorly understood risk of re-establishment of transmission continues, vectors persist, and there is a steady influx of infected travellers.

### Conclusions

Tunisia's experience should benefit other countries of North Africa and the Middle East that are situated in the Palaearctic ecozone, and have recently eliminated malaria or are in the process of doing so. In addition to the account of the efforts that led to elimination of the disease in Tunisia, this case-study outlines some of the tools that can be used to try to curb parasite importation and to ensure that the re-establishment of autochthonous transmission is detected sufficiently early. It provides material for reflection applicable to other previously-endemic countries and regions that have been freed of malaria but are visited each year by growing numbers of parasite carriers as the pace and volume of international exchange inexorably increase.

### REFERENCES

- Sallares R, Bouwman A, Anderung C. The spread of malaria to southern Europe in antiquity: new approaches to old problems. Med Hist. 2004;48(3):311–28.
- Report on the Malaria Coordination Meeting in North Africa. Cairo: WHO Regional Office for the Eastern Mediterranean; 1997 (unpublished report).
- Guidelines on prevention of the reintroduction of malaria. Cairo: WHO Regional Office for the Eastern Mediterranean; 2007.
- Climate atlas of Tunisia. Tunis: National Institute of Meteorology; 1999.
- National Institute of Statistics (NIS) Tunisia. Statistics, Demographic and social data, Population indicators, Population distribution by governorate, 2012 data (http://www.ins.nat.tn/indexen.php, accessed 23 March 2015).
- Climate atlas of Tunisia. Tunis: National Institute of Meteorology; 1967.
- World Health Statistics 2011. Geneva: World Health Organization; 2011 (http://www.who.int/whosis/whostat/2011/en/, accessed 23 March 2015).
- Rapport annuel du programme national de lutte contre le paludisme [Annual report of the National Malaria Control Programme]. Tunis: Department of Basic Health Care, Ministry of Public Health; 2011 (in French).
- The Millennium Development Goals Report 2011. New York: United Nations; 2011 (country-specific data available at http://mdgs.un.org/ unsd/mdg/data.aspx, accessed 23 March 2015).
- Farinaud ME. Rapport sur les conditions d'organisation d'une campagne d'éradication en Tunisie [Report on the organization of an eradication campaign in Tunisia]. Geneva: World Health Organization; 1958 (unpublished report; in French).
- Chadli A, Kennou MF, Kooli J. Les campagnes d'éradication du paludisme en Tunisie : historique et situation actuelle [Campaigns for the eradication of malaria in Tunisia: history and current situation]. Arch Inst Pasteur Tunis. 1986;63:35–50 (in French).
- Richter B. Rapport sur une enquête relative au paludisme en Tunisie [Report on malaria survey in Tunisia]. Geneva: World Health Organization; 1964 (unpublished report; in French).
- Wernsdorfer WH. Final report of 1970–1972 mission in Tunisia. Geneva: World Health Organization; 1973 (unpublished report).
- 14. Informations sur le programme de lutte contre le paludisme en Tunisie pour la Conférence inter-régionale sur le paludisme pour les régions de la Méditerranée orientale et de l'Europe [Information on malaria control programme in Tunisia for the inter-regional conference on malaria for Eastern Mediterranean and European regions]. Geneva: World Health Organization; 1956 (unpublished report; in French).
- Richter B. Rapport sur les conditions d'organisation d'une campagne d'éradication en Tunisie [Report on the organization of an eradication campaign in Tunisia]. Geneva: World Health Organization; 1966 (unpublished report; in French).

- Smolinschi M. Rapport de fin de mission 1972–1977 en Tunisie [Final report of 1972–1977 mission in Tunisia]. Geneva: World Health Organization; 1978 (unpublished report; in French).
- Smolinschi M. Rapport d'une mission d'évaluation du programme d'éradication du paludisme en Tunisie [Report of an evaluation mission of the malaria eradication programme in Tunisia]. Geneva: World Health Organization; 1981 (unpublished report; in French).
- Sghaier L, Yaacoub A, Bel Hadj S, Anene S, Kaouech A, Kallel K et al. Les parasitoses sanguines et urinaires chez les étudiants non résidents permanents en Tunisie [Blood and urinary parasitosis among nonresident students in Tunisia]. Rev Tun Infectiol. 2008;2(Suppl. 1):32–6 (in French).
- Siala E, Khalfaoui M, Bouratbine A, Harndi S, Hili K, Aoun K. Paludisme à *Plasmodium malariae*, une rechute 20 ans après un séjour en zone impaludée [Relapse of *Plasmodium malariae* malaria 20 years after living in an endemic area]. Presse Méd. 2005;34(5):371–2 (in French).
- Ben Ammar B, Kallel H, Kallel R, Barsaoui S, Bousnina S, Ben Ammar R. Le paludisme post-transfusionnel. A propos d'un cas chez l'enfant [Post-transfusion malaria. Apropos of a case in a child]. Tunis Med. 1989;67(2):101–5 (in French).
- Fisch A, Breuil J, Malkin JE, Lafaix C. Paludisme à *Plasmodium vivax* sur la côte tunisienne [*Plasmodium vivax* malaria on the Tunisian coast]. Presse Méd. 1988;17(26):1364 (in French).
- Ambroise-Thomas P, Wernsdorfer WH, Grab B, Cullen J, Bertagna P. Etude séro-épidémiologique longitudinale sur le paludisme en Tunisie [Longitudinal sero-epidemiologic study of malaria in Tunisia]. Bull World Health Org. 1976;54(4):355–67 (in French).
- Carnavale P. Rapport d'une mission OMS pour le Ministère de la Santé de Tunisie [Report of a WHO mission for the Ministry of Health of Tunisia]. Geneva: World Health Organization; 1991 (unpublished report; in French).
- 24. Molineaux P. Rapport d'une mission d'évaluation du programme d'éradication du paludisme en Tunisie [Report of an evaluation mission of the malaria eradication programme in Tunisia]. Geneva: World Health Organization; 1995 (unpublished report; in French).
- Bouratbine A, Chahed MK, Aoun K, Krida G, Ayari S, Ben Ismail R. Le paludisme d'importation en Tunisie [Imported malaria in Tunisia]. Bull Soc Pathol Exot. 1998;91(3):203–7 (in French).
- Oddo F. Rapport d'une mission pour le Ministère de la Santé de Tunisie [Report of a mission for the Ministry of Health of Tunisia]. Geneva: World Health Organization; 1995 (unpublished report; in French).
- Étude séroépidémiologique de la transmission du paludisme en Tunisie [Sero-epidemiological study of transmission of malaria in Tunisia]. Tunis: Department of Basic Health Care, Ministry of Health; 1993 (in French).
- Formulaire thérapeutique tunisien [Tunisian treatment form]. Tunis: Department of Pharmaceuticals and Medicines, Ministry of Health, 2008.

- Malaria elimination: a field manual for low and moderate endemic countries. Geneva: World Health Organization; 2007 (http://whqlibdoc.who.int/publications/2007/9789241596084\_eng. pdf, accessed 24 March 2015).
- Le paludisme en Tunisie. Guide technique de la prise en charge et de la lutte [Malaria in Tunisia. Technical guidelines for management and control]. Tunis: Department of Basic Health Care, Ministry of Health; 2010 (in French).
- Beljaev AE. Report of a WHO mission to the Ministry of Health of Tunisia. Geneva: World Health Organization, 2006 (unpublished report).
- Ben Alaya-Bouafif N, Chahed MK, El Bez H, Bellali H, Ayari L, Achoui A. Completeness of malaria notification in Tunisia assessed by capture recapture method. Asian Pac J Trop Dis. 2011;1(3):187–91.
- 33. Manuel de procédures de gestion des affaires des soins de santé de base [Manual of procedures for administration of basic health-care services]. Tunis: Department of Basic Health Care, Ministry of Public Health; 1997 (in French).
- Le tourisme tunisien en chiffres 2010 [Tunisian tourism in figures 2010]. Tunis: Tunisia National Tourism Office, Ministry of Trade and Tourism; 2011.
- Ayadi A. Le paludisme d'importation à Sfax (Tunisie) [Imported malaria in Sfax (Tunisia)]. Med Trop (Mars). 2000;60(1):99 (in French).
- 36. Belhadj S, Menif O, Kaouech E, Anane S, Jeguirim H, Ben Chaabane T et al.. Le paludisme d'importation en Tunisie: bilan de 291 cas diagnostiqués à l'hôpital La Rabta de Tunis (1991–2006) [Imported malaria in Tunisia: 291 cases diagnosed at Rabta hospital in Tunis (1991–2006)]. Rev Franc Laboratoires. 2008;399:95–8 (in French).
- 37. Aoun K, Siala E, Tchibkere D, Ben Abdallah R, Zallagua N, Chahed MK et al. Paludisme d'importation en Tunisie : conséquences sur le risque de réintroduction de la maladie [Imported malaria in Tunisia: consequences on the risk of resurgence of the disease]. Med Trop (Mars). 2010;70(1):33–7 (in French).
- Recommandations sanitaires pour les voyageurs 2007 [Health recommendations for travellers 2007]. Bull Epidemiol Hebd (Paris). 2007;(24):207–15 (in French).
- International travel and health. Geneva: World Health Organization; 2012 (http://www.who.int/ith/en/index.htm, accessed 25 March 2015).
- 40. Smolinschi M. Rapport d'une mission d'évaluation du programme d'éradication du paludisme en Tunisie [Report of an evaluation mission of the malaria eradication programme in Tunisia]. Geneva: World Health Organization; 1987 (unpublished report; in French).
- 41. Krida G, Bouattour A, Rhaim A, el Kebir A, Jlidi R. Investigation préliminaire de la sensibilité au chlorpyrifos de quatre échantillons larvaires d'anophèles de Tunisie [Preliminary investigation of four anopheles larvae samples susceptibility to chlorpyrifos in Tunisia]. Arch Inst Pasteur Tunis. 1998;75(3-4):199–203 (in French).
- Ghrab J, Bouattour A. Etude expérimentale de l'efficacité larvivore de Gambusia affinis holbrooki (GIRARD, 1859) (poisson-Poecilidae) [Experimental study of larval efficiency of Gambusia affinis holbrooki (GIRARD, 1859) (fish-Poecilidae)]. Arch Inst Pasteur Tunis. 1999;76(1-4):33–8 (in French).
- Siala E, Gamara D, Kallel K, Daahoub J, Zoulten F, Houzé S et al. Airport malaria: report of four cases in Tunisia. Malar J. 2015;14:42.
- International Health Regulations (2005), second edition. Geneva: World Health Organization; 2008. (http://whqlibdoc.who.int/ publications/2008/9789241580410\_eng.pdf, accessed 25 March 2015.

- 45. Chahed MK, Bouratbine A, Krida G, Ben Hamida A. Réceptivité de la Tunisie au paludisme après son éradication : analyse de la situation pour une adéquation de la surveillance [Receptivity of Tunisia to malaria after its eradication: analysis of the situation for adequacy of the surveillance]. Bull Soc Pathol Exot. 2001;94(3):271–6 (in French).
- 46. Krida G, Rhaiem A, Bouattour A. Effet de la qualité des eaux sur l'expression du potentiel biotique du moustique *Culex pipiens* L. dans la région de Ben Arous (sud de Tunis) [Effect of water quality on the expression of the biotic potential of *Culex pipiens* L. in the area of Ben Arous (south of Tunis)]. Bull Soc Entomol France. 1997;102(2):143–50 (in French).
- 47. Ramsdale CD. *Anopheles* mosquitoes and imported malaria in Libya. Mosquito Systematics. 1990;22(1):34–40.
- Bouattour A, Rhaim A, Bach-Hamba D. *Étude* de la capacité vectorielle d'Anopheles labranchiae dans la région de Nefza [Study of vectorial capacity of Anopheles labranchiae in Nefza region]. Tunis: Tunis Pasteur Institute; 1993 (in French).
- Bouchité B, Kennou MF, Chauvet G. Ethologie et capacité vectorielle des anophèles de Tunisie dans deux régions réceptives – Journine (Région du Nord) et Sidi Bouzid-Maknassy (Région du Centre) [Etiology and vectorial capacity of anopheles in Tunisia in two receptive regions – Journine (Northern Tunisia) and Sidi Bouzid-Maknassy (Central Tunisia)]. Tunis: Tunis Pasteur Institute; 1991 (unpublished report; in French).
- 50. World malaria situation in 1990. Bulletin World Health Org. 1992;70(6):801-4, 809-13.
- Eliminating malaria: learning from the past, looking ahead. Geneva: World Health Organization on behalf of the Roll Back Malaria Partnership Secretariat; 2011 (Progress & Impact Series, No 8).
- 52. Baldari M, Tamburro A, Sabatinelli G, Romi R, Severini C, Cuccagna G et al. Malaria in Maremma, Italy. Lancet. 1998;351:1246–7.
- Armengaud A, Legros F, Quatresous I, Barre H, Valayer P, Fanton Y et al. A case of autochthonous *Plasmodium vivax* malaria, Corsica, August 2006. Euro Surveill. 2008;11(11):E061116.3.
- Santa-Olalla Peralta P, Vazquez-Torres MC, Latorre-Fandos E, Mairal-Claver P, Cortina-Solano P, Puy-Azón A et al. First autochthonous malaria case due to *Plasmodium vivax* since eradication, Spain, October 2010. Euro Surveill. 2010;15(41): 19684.
- Danis K, Baka A, Lenglet A, Van Bortel W, Terzaki I, Tseroni M et al. Autochthonous *Plasmodium vivax* malaria in Greece, 2011. Euro Surveill. 2011;16(42): 19993.
- Toty C, Barré H, Le Goff G, Larget-Thiéry I, Rahola N, Couret D et al. Malaria risk in Corsica, former hot spot of malaria in France. Malar J. 2010;9:231.
- Romi R, Boccolini D, Vallorani R, Severini F, Toma L, Cocchi M et al. Assessment of the risk of malaria re-introduction in the Maremma plain (Central Italy) using a multi-factorial approach. Malar J. 2012;11:98.
- 58. World malaria report, 2013. Geneva: World Health Organization; 2013.
- Gebreel AO, Gilles HM, Prescott JE. Studies on the seroepidemiology of endemic diseases in Libya, IV. Malaria. Ann Trop Med Parasitol. 1985;79(4):341–7.
- van Rijckevorsel GC, Sonder GJ, Geskus RB, Wetsteyn JC, Ligthelm RJ, Visser LG et al. Declining incidence of imported malaria in the Netherlands, 2000–2007. Malar J. 2010;9:300.
- 61. Report of the activities of the National Malaria Referral Centre, 2009. Paris: National Institute of Health Surveillance; 2010.

### **ANNEX 1: DATA SOURCES AND METHODS USED**

Data for this case-study were collected from the following sources:

- WHO. Malaria-related materials at WHO headquarters in Geneva and EMRO in Cairo were consulted, as were registry and archives collections of reports of technical missions, reports of EMRO meetings, WHO publications, country data reported to WHO and other information on Tunisia.
- Country data, including national publications and manuals, MoH data, reports, regulations, orders, guidelines, and a number of documents and reports on the websites of various bodies based in Tunisia were consulted.
- Scientific publications concerning malaria in Tunisia were identified using PubMed (United States National Library of Medicine) using the

keywords "malaria", "Tunisia", "elimination" and/ or "eradication" and by screening scientific journals and other sources.

• Senior officials of relevant institutions (Ministry of Health, universities, research centres and health-care facilities) were interviewed in Tunisia.

The author collected, reviewed and epidemiologically analysed the data with the aim of characterizing the malaria situation in different periods and the effect of interventions. Analysis used the main epidemiological parameters and indicators such as: annual number of cases (autochthonous and imported); malaria morbidity and mortality; distribution of cases by various parameters including age and sex; geographical distribution of malaria; number, category and transition of malaria foci; parasites and vectors. The epidemiological data found in various documents were assembled in a spreadsheet and presented together with various key indicators in tables or maps.

### **ANNEX 2: ESTIMATED POPULATION PER GOVERNORATE, 2011**

Governorate	Population 2011 ('000s)
Tunis	1002
Sfax	944
Nabeul	763
Sousse	622
Ben Arous	589
Kairouan	565
Bizerte	551
Monastir	525
Ariana	510
Médenine	460
Kasserine	437
Jendouba	426
Sidi Bouzid	416
Mahdia	400
Manouba	375
Gabès	366
Gafsa	342
Béja	307
Le Kef	258
Siliana	235
Zaghouan	172
Kébili	152
Tataouine	148
Tozeur	105
Total	10 674

Source: National Institute of Statistics (NIS) - Tunisia. 2012 data (http://www.ins.nat.tn/indexen.php, accessed 23 March 2015).

# **ANNEX 3: TUNISIAN HEALTH AND DEVELOPMENT INDICATORS**

Indicators	Value	Year
Gross national income per capita	7810 <sup>a</sup>	2009
Per capita total expenditure on health	500 <sup>a</sup>	2008
General government expenditure on health as % of total expenditure on health	54	2008
General government expenditure on health as % of total government expenditure	10	2008
External resources for health as % of total expenditure on health	<1	2008
Human Development Index (rank)	81/169	2010
Life expectancy at birth (both sexes)	75 years	2009
Density of physicians	11.9/10 000 population	2010
Hospital beds	21/10 000 population	2010
Millennium Development Goals	Value	Year
Under-five mortality rate	21/1000 live births	2009
DTP3 immunization coverage among 1-year-olds	99%	2009
Measles immunization coverage among 1-year-olds	98%	2009
Infant mortality rate	18/1000 live births	2009
Maternal mortality ratio	60/100 000 live births	2008
Antenatal care coverage: at least 1 visit	96%	2010
Births attended by skilled health personnel	95%	2010
Fertility rate	1,8 per woman	2009
Net primary school enrolment rate	96%	2008
Adult literacy rate	78%	2008
Population using improved drinking-water sources	94%	2008
Population using improved sanitation	85%	2008
Estimated prevalence of tuberculosis	30/100 000 population	2009
Reported treatment success rate	86%	2009
HIV mortality rate	0.7/100 000 population	2009
Prevalence of HIV among adults aged 15-49 years	<0.1%	2009

<sup>a</sup> Purchasing Power Parity at international dollar rate.

Source: World Health Statistics 2011. Geneva: World Health Organization; 2011 (report and country data available at: http://www.who.int/whosis/whostat/2011/en/, accessed 23 March 2015).

### ANNEX 4: MALARIA PARASITES AND VECTORS, PAST AND PRESENT

### **Parasites**

In the first half of the 20th century, *Plasmodium falciparum* was the most frequently encountered species of malaria parasite in Tunisia. From the 1950s onwards, however, the frequency of *P. falciparum* declined progressively and *P. vivax* became the predominant species. The monthly distribution of cases in the 1960s shows the traditional transmission season of July to October, and a springtime peak caused by *P. vivax* contracted the previous year and reflected in relapses or cases with long incubation (1).

A malariometric survey carried out in 1957 confirmed that *P. vivax* generally predominated over *P. falciparum* in northern Tunisia, with some rare infections by *P. malariae* (*2*). The spraying campaign launched in 1968 eradicated *P. falciparum* from the north of the country by 1971; in southern and central regions, however, half of all the cases detected between 1970 and 1972 were caused by this species (*3*).

Since achieving elimination, the distribution of species reflects the distribution by country of infection. Thus, more than 90% of imported cases are caused by *P. falciparum*.

### Vectors

The variety and distribution of vector species have been investigated in a number of studies since the beginning of the 20th century; a total of 12 *Anopheles* species were identified in Tunisia over time (4). *An. hispaniola* is suspected of having been a secondary vector in the north and *An. multicolor*, which is thought capable of sustaining the transmission of malaria in the absence of the principal vector, probably contributed to transmission in certain foci in the south between 1970 and 1972 (3). However, *An. labranchiae* in the north and *An. sergentii* in the south are considered to be the two main vectors of malaria in Tunisia. *An. labranchiae* is found along the entire western Mediterranean coastline (Figure A4.1). It is known to be a predominantly endophilic and endophagic species with a preference for biting humans and for the clean water of lakes or large slow-moving rivers (5).

*An. sergentii*, which tolerates high temperatures and low humidity, is particularly well adapted to semi-desert areas and to the oases of North Africa and the Middle East (Figure A4.1). It is zoophilic by predilection and bites and settles inside and outside dwellings. It breeds in springs and small irrigation channels (*5*).

Studies show that, in Tunisia, *An. labranchiae* (predominantly in the north) and *An. sergentii* (predominantly in the south), are anthropophilic and endophilic by predilection (6). Temperatures in the country are conducive to transmission from June to October in the north and from May to November in the south; outside these periods the parasite's life-cycle cannot be sustained because temperatures are too low (7).

Tunisia is part of the Palaearctic biogeographical region which includes the Mediterranean, Europe and the Middle East, and stretches as far as Central Asia and parts of China (8). The vectors *An. labranchiae* and *An. sergentii* are not found in tropical Africa. The species *An. atroparvus* and *An. labranchiae* from Europe have often proved resistant to infection by *P. falciparum* from tropical Africa (9) and this may also be the case for *An. labranchiae* in Tunisia. It has been possible to obtain *P. falciparum* sporozoites from a strain of *An. labranchiae* found on the island of Corsica (10). However, *An. sergentii*, found in southern Tunisia, belongs to the subgenus *Cellia* and has a higher probability of being infected by tropical *P. falciparum* (11).

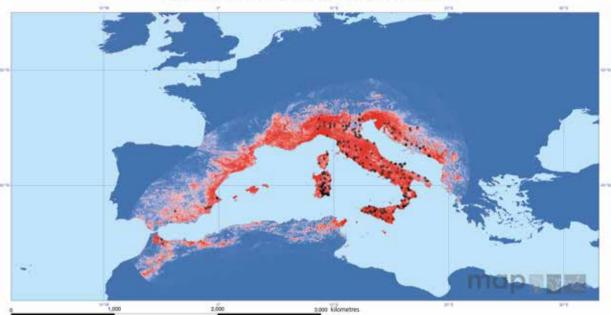
The hypothesis that Tunisia is being colonized from the south by new vector species adapted to tropical plasmodial strains, such as *An. arabiensis* has also been mentioned in

reference to the invasion of Egypt by *An. gambiae*, which caused devastating epidemics of *P. falciparum* in 1942 (*12*). The presence of *An. arabiensis* in the north of Niger raised fears of the possibility of its implantation around the oases

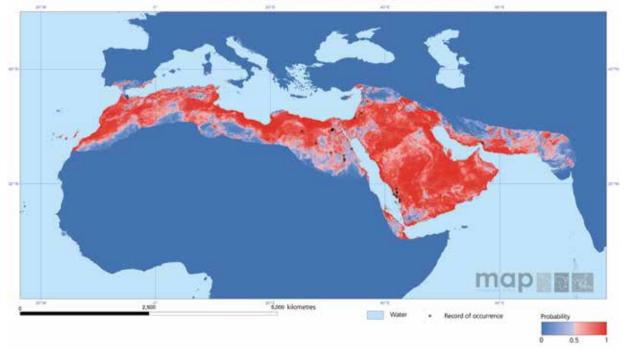
of the Algerian Sahara, along trans-Saharan routes (13). This has not been observed in Tunisia, where such an occurrence would appear improbable in the absence of an irrigated corridor similar to the Nile Valley.

Figure A4.1. Geographical extent of the two principal malaria vectors in Tunisia, An. labranchiae and An. sergentii<sup>a</sup>

The predicted distribution of Anopheles (Anopheles) labranchiae Falleroni, 1926



The predicted distribution of Anopheles (Cellia) sergentil species complex



<sup>a</sup> Source: reference 5.

### References

- Richter B. Rapport sur une enquête relative au paludisme en Tunisie [Report on malaria survey in Tunisia]. Geneva: World Health Organization; 1964 (unpublished report; in French).
- Farinaud ME. Rapport sur les conditions d'organisation d'une campagne d'éradication en Tunisie [Report on the organization of an eradication campaign in Tunisia]. Geneva: World Health Organization; 1958 (unpublished report; in French).
- Wernsdorfer WH. Final report of 1970-1972 mission in Tunisia. Geneva: World Health Organization; 1973 (unpublished report).
- Villain G, Dupoux A, Marini C. Contribution à l'étude de l'anophélisme tunisien et aperçu de la lutte antilarvaire [Contribution to the study of Tunisian anophelism and overview of larval control efforts]. Arch Inst Pasteur Tunis. 1935;24:309–42 (in French).
- Sinka ME et al. The dominant *Anopheles* vectors of human malaria in Africa, Europe and the Middle East: occurrence data, distribution maps and bionomic précis. Parasit Vectors. 2010;3:117.
- Ben Rachid MS, Ben Ammar R, Redissi T, Ben Said M, Hellal H, Bach-Hamba D et al. Géographie des parasitoses majeures en Tunisie [Geography of major parasitoses in Tunisia]. Arch Inst Pasteur Tunis. 1984;61(1):17–41 (in French).
- Bach-Hamba D, Bouchité B, Rhaiem A. Etude chorologique et morphotaxonomique des anophèles de Tunisie [Chronological and morphotaxonomic study of anopheles in Tunisia]. Tunis: Tunis Pasteur Institute; 1990 (in French).

- Mouchet J, Carnevale P, Coosemans M, Julvez J, Manguin S, Richard-Lenoble D et al. Biodiversité du paludisme dans le monde [Malaria biodiversity around the world]. Paris: John Libbey Eurotext, 2004 (in French).
- Marchant P, Eling W, van Gemert GJ, Leake CJ, Curtis CF. Could British mosquitoes transmit *falciparum* malaria? Parasitol Today. 1998;14(9):344–5.
- Toty C, Barré H, Le Goff G, Larget-Thiéry I, Rahola N, Couret D et al. Malaria risk in Corsica, former hot spot of malaria in France. Malar J. 2010;9:231.
- 11. Chahed MK, Bouratbine A, Krida G, Ben Hamida A. Réceptivité de la Tunisie au paludisme après éradication : analyse de la situation pour une adéquation de la surveillance [Receptivity of Tunisia to malaria after its eradication: analysis of the situation for adequacy of the surveillance]. Bull Soc Pathol Exot. 2001;94(3):271–6 (in French).
- Shousha AT. Species-eradication: the eradication of *Anopheles gambiae* from Upper Egypt, 1942–1945. Bull World Health Org. 1948;1(2):309–34.
- Smith DM. Mosquito records from the Republic of Niger, with reference to the construction of the new 'Trans-Sahara Highway'. J Trop Med Hyg. 1981;84(3):95–100.

## **ANNEX 5: STANDARD REPORTING FORMS**

#### Figure A5.1. Current reporting form for diseases subject to compulsory notification

#### **NOTIFICATION OF A COMMUNICABLE DISEASE OR DEATH RESULTING THEREFROM**

	First	name			Surnan	ne		D	ate of bi	rth	Se		Professio	on	$\Box$
								Day	Month	Yea	m M r F				
								-							
PATIENT DETAILS															
PATIENT DETAILS							PERMA	NENT	<b>FRES</b>	IDEI	NCE	C			
PA DI	Gove	rnorate			Distric	t 🗆	]	Comm	unity		A	ddress			
			niasis (1	20)			Urogenita		ons			Teta			
		ucellosi	· /				- gonococ		1	(099)				thematicus and others	
		nolera (( rtussis (	/				- <i>Chlamya</i> - Mycopla		5	(099)				s (080-083) oodborne intoxication (00	3-005)
D		phtheria					Cutaneous		aniasis .					uberculosis (011)	5-005)
Ι			hinococ	cosis	2		Visceral le			608 (08	(5)			ary tuberculosis (010, 012	2,016)
S			y echino		s 🖌 (	(122)	Leprosy ((	030)				(spe	cify)		
E			cosis (o	/	J		Meningoc		eningitis	(320	.5)		llpox (0		
A			/er (060)	·			Malaria (0	/						TION STATUS OF PATI	
S E			nd parat	yphoid	fever (0	02)	Plague (020) Acute poliomyelitis (045)				If disease targeted by national immunization programme, indicate status of patient:				
S		ral hepa ral hepa			l.	(070)	Rabies (07		IS (045)			pro	ogramme	e, indicate status of patter	Ш.
5		ral hepa			5	070)	Arthritis (	,				Corr	nletelv	immunized	
			ed viral l	nepatitis	5		$\square$ Measles (055)				Partially immunized				
			due to H			.19)	Syphilis (s	Syphilis (symptomatic, serological)				□ Not immunized			
								091)	(09	2)				unknown immunization s	tatus
	ate of on			ilt confi			RI	ESULTS	3			Name a	ind addr	ess of laboratory	
0	of diseas	e		laborate	5	• Mi	croorganism is	olated							
Day	Month	Year	YES		NO		ology + (test a								
						• Oth	ner (specify)								
								01		<u> </u>		1			
Was	s patient hosp		ed to	Dece	eased	Name	e and address o	t hospit	al	Servi	ce or	departm	ent	Medical file no.	
Y	ES 105p		0	YES	NO										
E		Γ													
Name	and addi	ress of r	otifying	officer								e of notifi		Signature and stam	p
									L		Day	Month	Year		

(Act No. 92-71 of 27 July 1992: Decree No. 93-2451 of 13 December 1993)

Source: Étude séroépidémiologique de la transmission du paludisme en Tunisie [Sero-epidemiological study of transmission of malaria in Tunisia]. Tunis: Department of Basic Health Care, Ministry of Health; 1993.

Figure A5.2 Procedural checklist for an "epidemiological survey in connection	with a case of malaria"
---	-------------------------

MINISTRY:	МОН	STANDARD OPERATING PROCEDURE	DATI	E: 25/04/1997 U	JPDATED:	
DEPARTMI	ARTIMENT, DDITC NATIONAL MALAKIA ERADICATION			or: Mr Abdelwaheb Kebir		
		PROGRAMME	Code	de PAGE 1/ 2		
DESCRIPT	FION OF PROCEDUR	E: EPIDEMIOLOGICAL INVESTIGATION	IN CC	ONNECTION WIT	TH A CASE OF MALARIA	
STEPS	DETAIL	ED DESCRIPTION OF PROCEDURE		RESPONSIBLE AGENCY	COMMENTS	
1.	RECEIPT OF INFOR	MATION		NMEP +		
1.	- Compulsory notific		epidemiological			
	- Notification by tele			service		
	- Other	F				
2.	CASE HISTORY			NMEP		
	- Request travel auth	orization and transport				
	- Appointment with	health facility that originated notification				
	~ ~	ity that originated notification				
	- Contact with attend	ling physician and patient				
	- Completion of surv	rey form			Use the form	
	_				« Epidemiological survey	
					in connection with a case o	
					malaria »	
3.	PARASITOLOGICAI	CONFIRMATION OF CASE		NMEP		
	- Retrieve the collect				If there is no slide, collect	
	- Collect other speci				other blood samples prior t	
		slides to reference laboratories			medication, if possible	
4.		EMIOLOGICAL INVESTIGATION DATA		NMEP	Record the case	
	- Origin of case				Proximity to a high-risk are	
	- Study of possible l				Existence of anophelism	
~		approaches and corrective action, if applicable			T0.1 1 1 1 1	
5.	ENTOMOLOGICAL			NMEP	If the case is a potential	
		th regional and local representatives			transmission risk (residence	
	<ul> <li>Preparation of nece</li> <li>Travel to area conc</li> </ul>	5			in a high-risk area)	
	- Identification of an	opheles breeding sites close to patient's dwelling	5			
6.	SCREENING OF CO	NTACTS		NMEP	If the case is a potential	
	- Establish contact w	ith regional and local representatives			transmission risk	
	- Identification of tar	get population				
	- Preparation of nece	essary material and equipment				
	- Collection of thick	blood film in area where patient resides				
7.	COMPREHENSIVE	OVERVIEW OF SITUATION FOLLOWING		NMEP		
	INVESTIGATION					
	- Confirmation and c	lassification of case				
		entomological situation and implementation of			Depending on case:	
	surveillance inter	vention measures			- Imported case	
					- Introduced case	
					- Paradoxical case	
					- Post-transfusion case	
8.	ARCHIVING OF ALL	L DATA COLLECTED		NMEP		

*Source:* Manuel de procédures pour l'administration des soins de santé de base [Manual of procedures for administration of basic health-care services]. Tunis: Department of Basic Health Care, Ministry of Health; 1997.

Figure A5.3 Cover page of the form for the survey to be carried out following notification of a case of malaria

MINISTRY OF HEALTH DBHC/S/D PROG/ORG./SMT National Malaria Eradication Programme

#### EPIDEMIOLOGICAL INVESTIGATION IN CONNECTION WITH A CASE OF MALARIA\*

#### I. IDENTIFICATION OF THE PATIENT

Surname:	First name:
Age: Sex:	Profession:
Nationality:	Family situation:
Current address in Tunisia:	
Permanent address abroad:	
Fermalient audress abroad.	
Date of most recent return to Tunisia:	
Places of residence (date and duration) sin	
Date of departure (for Tunisians)**	
Origin of travel ticket (travel agency)	
······	

#### II. CASE HISTORY

- Date of first symptoms in Tunisia: .. / .. / ..

-	Principal clinical signs reported:
-	Has the patient consulted a physician or visited a health facility?
	•••••••••••••••••••••••••••••••••••••••
-	If yes, name the physician(s) or facility (facilities)?
	When?
	•••••••••••••••••••••••••••••••••••••••

\* Document revised in March 1993.

\*\* Pertaining travel departure to malaria risk areas.

Source: Étude séroépidémiologique de la transmission du paludisme en Tunisie [Sero-epidemiological study of transmission of malaria in Tunisia]. Tunis: Department of Basic Health Care, Ministry of Health; 1993.



This case-study is part of a series of malaria elimination case-studies conducted by the World Health Organization (WHO) Global Malaria Programme and the University of California, San Francisco (UCSF), Global Health Group. The case-studies series documents the experience gained in eliminating malaria in a range of geographical and transmission settings with the aim of drawing lessons for countries that are embarking upon elimination.

## For further information please contact: **Global Malaria Programme**

World Health Organization 20, avenue Appia CH-1211 Geneva 27 Web: www.who.int/malaria Email: infogmp@who.int

