UNIVERSITÀ DEGLI STUDI DI MILANO
FACOLTÀ DI MEDICINA E CHIRURGIA

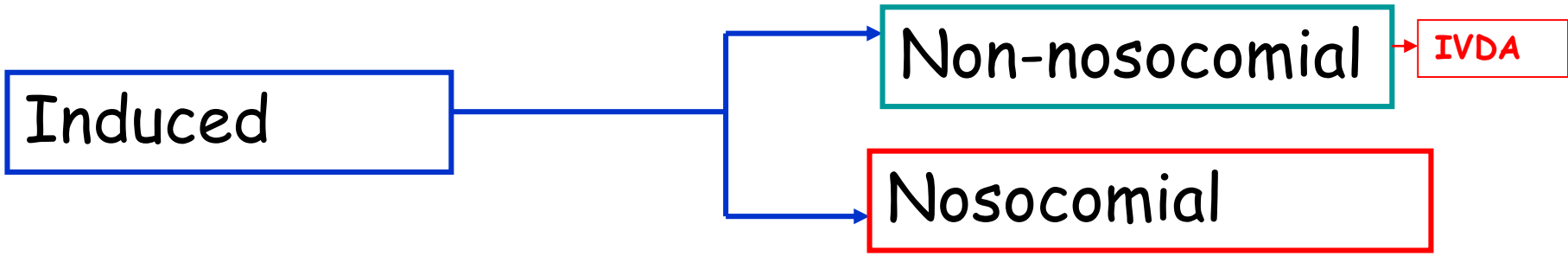
Malaria criptica, malaria nosocomiale e malaria da valigia :evidenze in Italia e nel Mondo

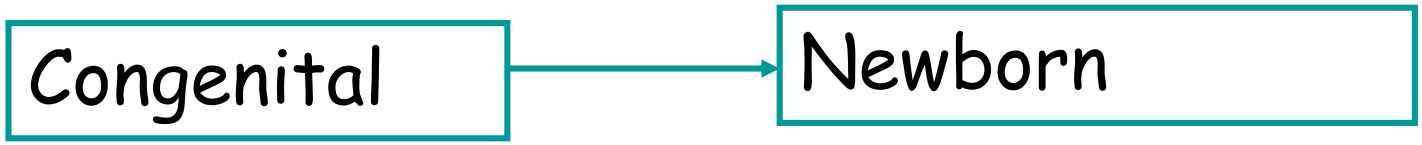
Spinello Antinori

Dipartimento di Scienze Biomediche e Cliniche "Luigi Sacco"

Milano, 28 maggio 2019

Non-mosquito transmitted malaria





Observed either in endemic and non-endemic countries

Challenging diagnosis of congenital malaria in non-endemic areas

Lorenza Romani[1†], Stefania Pane[2†], Carlo Severini[3], Michela Menegon[3], Gianluca Foglietta[2], Stefania Bernardi[1], Hyppolite K. Tchidjou[1], Andrea Onetti Muda[4], Paolo Palma[1*‡] and Lorenza Putignani[2,5*‡]

Abstract

Background: Congenital malaria is usually defined as the detection of asexual forms of *Plasmodium* spp. in a blood sample of a neonate during perinatal age if there is no possibility of postpartum infection by a mosquito bite. The incidence of congenital malaria is highly variable and seems related to several factors, such as different diagnostic methods for *Plasmodium* spp. detection, and area in which the epidemiologic analyses are performed. In non-endemic countries, cases of congenital malaria are rare. Hereby, a case of a congenital malaria in an HIV exposed child is reported.

Case presentation: A 2-month-old male child was admitted to Bambino Gesù Children's Hospital due to anaemia and exposure to HIV. He was born prematurely in Italy by cesarean section at 34 weeks' gestation after a bicorial, biamniotic pregnancy by a migrant woman from Nigeria. He was the first of non-identical twins. Combined with anaemia, spleen and liver enlargement was noted, malaria was hypothesized. Malaria laboratory panel was performed on the newborn, mother and other twin blood samples, as follows: (i) malaria rapid diagnostic test (RDT); (ii) Giemsa-stained thick and thin blood smears for *Plasmodium* spp. identification and parasitaemia titration; (iii) molecular screening and typing of *Plasmodium* spp. by multiplex qualitative PCR assay based on 18S rRNA gene. Genotyping of *Plasmodium falciparum* isolates from mother and child was performed by neutral microsatellite and highly polymorphic marker amplification.

Malaria J 2018;17:740

PUBLIC HEALTH REPORTS

VOL. 49 MARCH, 30, 1934 No. 13

Malaria Among Drug Addicts in New York City

An epidemic of aestivo-autumnal and quartan malaria among drug addicts in New York City transmitted by the use of contaminated hypodermic syringes

by Milton Helpern, M.D.

Sixteen fatal cases of aestivo-autumnal malaria of the cerebral type and one fatal case of quartan malaria complicated by broncho-pneumonia were autopsied by the office of the chief medical examiner during a recent 4-month period. The first case was autopsied September 29, 1933, and the most recent case was autopsied January 30, 1934. An additional fatal case of aestivo-autumnal malaria occurred and was autopsied at the United States Marine Hospital at Ellis Island and was called to our attention by Dr. E. A. Sweet, medical director, United States Public Health Service, thus bringing the total fatalities to 18. In every instance the deceased was a drug addict who injected heroin intravenously—the so-called "main-line shooter."

An investigation carried on with the assistance of Detective Jocker of the narcotic squad and Detective Oswald of the homicide squad of the police department revealed that almost all of the deceased addicts had frequented the same lodging houses, that many had never been out of New York City, and

Falciparum Malaria among Drug Addicts*

Epidemiologic Studies

HARRY MOST, M.D., D.T.M. & H. (ENG.)

Department of Medicine and Clinical Pathology, New York University College of Medicine, and The Third Medical and Psychiatric Medical Divisions of Bellevue Hospital, New York, N. Y.

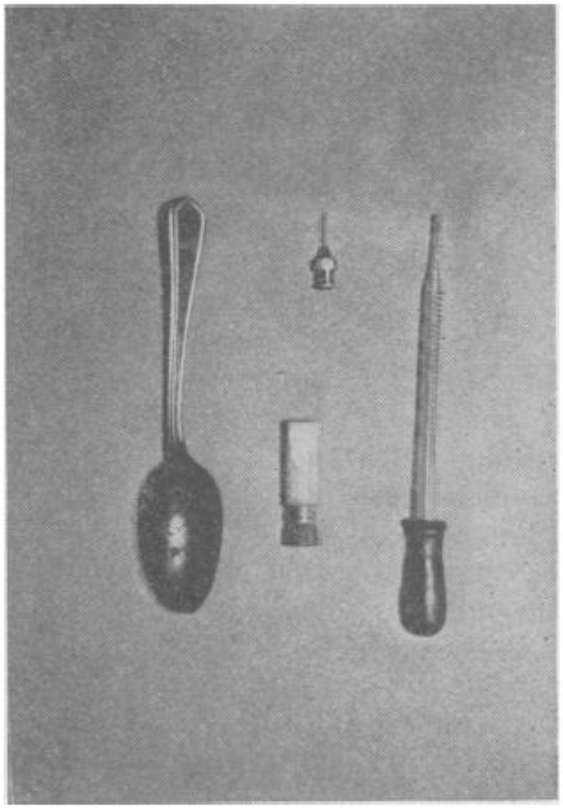


FIGURE 1.—IMPROVISED HYPODERMIC APPARATUS

Improvised hypodermic apparatus for self administration of heroin. The drug shown in the vial is dissolved in the spoon and drawn up into the medicine dropper, which acts as a syringe.

D. Types of Malaria, Bellevue Hospital, 1938

	Non-addicts	Addicts
P. vivax	7	1
P. falciparum	1	45
Total	8	46
Fatalities	0	9

E. Psychiatric Division, Bellevue Hospital, 1938

Number of admissions	26,210
Drug addicts	71
Drug addicts with malaria	27
Malaria fatalities	4

AMERICAN JOURNAL OF PUBLIC HEALTH April, 1940

Malaria Among Heroin Users

DONALD O. LYMAN, M.D., ROBERT J. BOESE, M.D., and LOIS ANN SHEARER, M.P.H.

The Ventura investigation indicated that the cluster of malaria cases originated from one or both of the two veterans because both shared their equipment and had documented parasitemia. One became symptomatic and sought treatment 2 to 3 weeks after onset of clinical illness in the other patients. The other had a number of clinical recurrences in the 5-month period between his return from Vietnam and the onset of illness in the group.

The reported incidence of malaria in the United States is higher than at any time since the

Use of heroin intravenously among U.S. troops in Vietnam is said to be great. In the United States there are an estimated 200,000 or more heroin users, mostly males under the age of 30 (*16*). In addition, the number of heroin users is believed to be growing. Thus, the potential is great for more cases of induced malaria through the use of narcotics in this country. This potential was realized again several months after the outbreak in Ventura, when a much larger outbreak of needle-associated malaria was observed in Bakersfield, Calif. (C. Friedmann and asso-

JAMA 1972;87:545-49

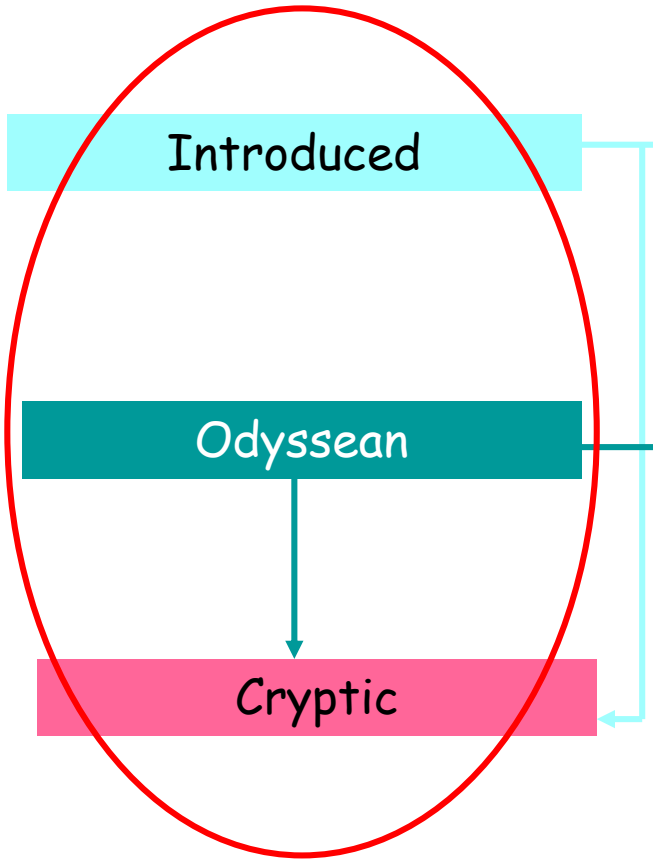
Nosocomial malaria

- Health-care acquired : needle-stick injury
- Laboratory acquired : vector-borne; needle-stick injury

Occupational malaria

- Transfusion-transmitted (unintentional)
- Organ transplant transmission (unintentional)
- Malariotherapy (intentional)
- Hospital transmission : through inoculation with blood or cells that contain parasite-infected erythrocytes

Mosquito-transmitted, locally acquired (autochthonous)



Natural to the area or country where it occurs

Acquired in a nonmalarious area, from local mosquitoes infected by having fed on individual with imported malaria

Acquired in a nonmalarious area, from the bite of an imported mosquito

Airport malaria

Baggage (luggage, suitcase) malaria

Container malaria

Port malaria

Taxi rank malaria

Minibus malaria

Tarantola AP et al. Emerg Infect Dis 2004;10:1878-9

Occupational Malaria Following Needlestick Injury

To the Editor: A 24-year-old female nurse was admitted to the emergency room at Bichat University Hospital in Paris, France, on July 4, 2001, with fever, nausea, and general malaise. She had no notable medical

On June 21, 2001, she sustained an accidental needlestick injury while taking a blood sample with an 18-gauge, peripheral venous catheter that had no safety feature. She

ed. The mother insisted that a blood smear be performed at a private laboratory in Paris. The smear was qualitatively determined positive for *P. vivax*. Subsequently, the patient was admitted to Bichat-Claude Bernard University Hospital with suspected malaria. A repeat blood smear conducted there identified *P. falciparum*.

The source patient was a 28-weeks' pregnant, 30-year-old woman of Kenyan origin who resided in France; she had visited Kenya and returned to France on June 1, 2001. On

Lancet 1995;346:1361

Needlestick malaria

SIR—A 27-year-old health care assistant came to our hospital with a 3-day history of fever, sweats, rigors, and frontal headache. His past medical history was unremarkable. He had never had clinical malaria. There had been no recent foreign travel (he left Sri Lanka 7½ years ago, and had visited France 3 years ago), but 10 days before admission he had been involved in the resuscitation of a 6-year-old Ghanaian boy. The child had *Plasmodium falciparum* infection with a parasitaemia of 1·7%, and a febrile convulsion. During resuscitation the health care assistant sustained a needlestick injury with a non-sterile needle.

Fiona L M Haworth, G C Cook

Occupational *Plasmodium falciparum* malaria following accidental blood exposure

22 documented cases

16 Europe (8 France; 3 UK; 2 Italy; 1 Germany, Portugal, Poland); 4 USA; 1 Kuwait, South Africa

Median incubation time to fever onset: 12 days (range 4-17 d)

Type of injury: 20 vascular access; 1 autopsy; 1 blood smear

13 Nurses; 6 physicians; 1 biologist; 1 researcher; 1 medical student

Clinical presentation: severe in 45%

1 death (Italian physician)

Tarantola A et al. Scand J Infect Dis 2005;37:131-40

Laboratory-acquired (vector-borne)

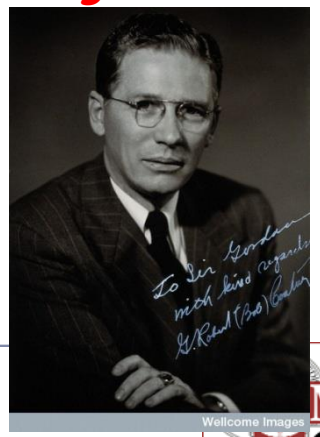
Don E. Eyles

I received a telephone call from Memphis, Tennessee, and heard the late Dr. Don Eyles say " Bob, I have monkey malaria" I was incredulous. Could it be true? I told him not to take chloroquine until we were sure. He replied that he expected I would say that so he had taken the drug before he called. Prior to taking the drug , he had drawn a 20 cc of his own blood and injected a portion of it into an uninfected monkey. I asked him to send the remainder to the Atlanta prison for transfer to volunteers.

It was, for Eyles's preliminary diagnosis was confirmed quickly, *Plasmodium cynomolgi* was the offending parasite.

May 5, 1960

Coatney GR. Reminescences:My forty-year romance with malaria. 1985 Transactions of the Nebraska Academy of Sciences and affiliated Societies.Paper 222



Vivax-Type Malaria Parasite of Macaques Transmissible to Man

Abstract. Transmission of *Plasmodium cynomolgi bastianellii* from rhesus monkeys to two human subjects by *Anopheles freeborni* and the occurrence of attacks of malaria in two other laboratory workers not exposed to human malaria suggests the existence of an animal reservoir of infection complicating malaria control and eradication.

During a period in which very large scale inoculations of monkeys with sporozoites were being carried out, two of our staff members (D.E.E. and N.C.O.) developed illness with fever which, after a remittent period, proved to have a tertian periodicity. *Vivax*-type parasites with enlarged erythrocytes and Schüffner's stippling were found in both individuals. Smears were made on new slides, stained in clean dishes with new stain. Presumably the source of the malaria was mosquitoes infected with monkey malaria, as neither individual had had any recent contact with human malarias.

Five milliliters of blood from D.E.E. were injected intravenously into an uninfected rhesus monkey (W633). Eight days later parasites were present, and a typical *cynomolgi*-type infection ensued in which parasite densities of several hundred thousand per cubic millimeter were attained. Five milli-

The mode of infection of the patients accidentally infected must certainly have been by mosquito bite. Both persons were dealing closely with heavily infected mosquitoes, and it must be acknowledged that the mosquitoes were not being handled with the care and respect accorded mosquitoes infected with known human malarias. The devel-

Two unsuccessful efforts have been made to transmit typical *Plasmodium cynomolgi* to man. Sinton *et al.* (5) used infected mosquitoes and blood in one patient with general paresis and infected mosquitoes in another. Neither showed any evidence of infection. Coggeshall (7), using infected blood and sporozoites, also failed in four attempts

Note added in proof: After this report was submitted for publication we learned from Leon Schmidt, director of the Christ Hospital Institute for Medical Research, Cincinnati, Ohio, that one of his staff members (R.G.) had experienced an attack of malaria shortly after the second accidental infection was diagnosed at the Memphis laboratory. Parasitized blood from the Christ Hospital patient produced a typical *cynomolgi*-type infection in a rhesus monkey. Typical *Plasmodium cynomolgi* and the subspecies *bastianellii* are present in the Cincinnati laboratory.

DON E. EYLES*
G. ROBERT COATNEY†
MORTON E. GETZ‡
Laboratory of Parasite Chemotherapy, National Institute of Allergy and Infectious Diseases, National Institutes of Health

Science 1960;131:1812-3

THE TRANSMISSION OF *PLASMODIUM CYNOMOLGI* TO MAN*

L. H. SCHMIDT, ROBERT GREENLAND AND CLARA S. GENTHER

The Christ Hospital Institute of Medical Research, Cincinnati, Ohio

Am J Trop Med Hyg 1961

The successful transmission of the *bastianellii* strain[1] of *Plasmodium cynomolgi* from rhesus monkey to man via the bites of infected *Anopheles freeborni* was described by Eyles, Coatney, and Getz[2] in June, 1960. This report dealt with studies which had their beginning in April of that year with the demonstration that two of the staff of the Memphis facility of the Laboratory of Parasite Chemotherapy, National Institute of Allergy and Infectious Diseases, had acquired accidental infections with this simian plasmodium while working with large numbers of infected mosquitoes.

EXPERIMENTAL OBSERVATIONS

Accidental transmission of P. cynomolgi *to RG.* RG, one of the members of the Institute staff, developed chills and a fever which reached 102°F between 9 and 10 p.m., May 8, 1960. As shown in Figure 1, this initial reaction was followed at 48-hour intervals by three successive paroxysms with fever of increasing intensity; temperature elevations to 103°, 104°, and 104° occurred at almost precisely 10 p.m. on May 10, 12, and 14. The recurrent nature of these paroxysms, their severity yet relatively brief duration, suggested a diagnosis of malaria. This diagnosis was confirmed early in the morning of May 14 by examination of both thick and thin films prepared at 6 p.m., May 13. The parasites found on thin films were morphologically indistinguishable from either *P. vivax* or *P. cynomolgi*. The disease in RG was terminated promptly by a chloroquine-primaquine curative regimen initiated on May 14, 1960. There have been no recurrences of malaria symptoms since that date.

Prior to initiating therapy, 5 ml of blood was withdrawn from RG at his home, citrated, and returned to the Institute where 2-ml aliquots were injected intravenously into one normal and one splenectomized rhesus monkey (*Macaca mulatta*). This was done largely to satisfy RG who repeatedly questioned whether his disease might be due to *P. cynomolgi* rather than to *P. vivax* since he had had no known contact with human malaria but had been bitten by *A. freeborni* infected with the simian plasmodium while preparing such mosquitoes for shipment to the Naval Medical Research Institute. To the sur-

Ind Med Gaz 1932;67:301-320

Original Articles

A STUDY OF MONKEY-MALARIA, AND ITS EXPERIMENTAL TRANSMISSION TO MAN

(A PRELIMINARY REPORT)

By R. KNOWLES

LIEUTENANT-COLONEL, I.M.S.

Professor of Protozoology

and

ASSISTANT SURGEON B. M. DAS GUPTA, L.M.P.

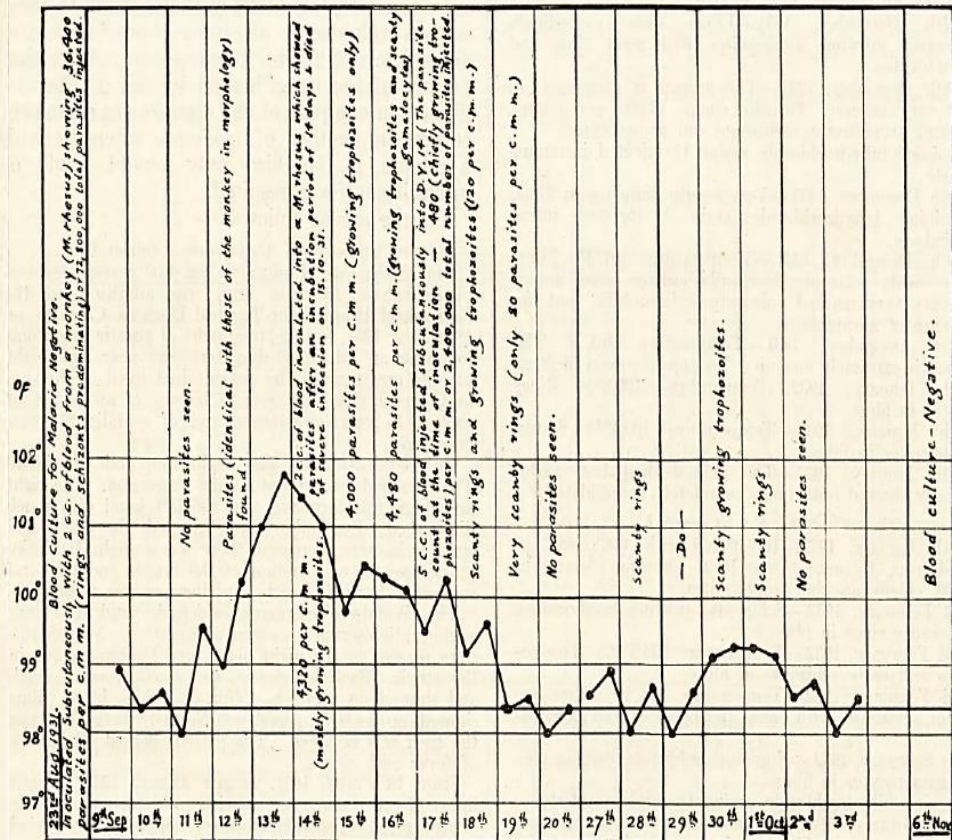
Assistant Professor of Protozoology, Calcutta School of Tropical Medicine and Hygiene

Introduction

Calcutta has the reputation of being a malarious city, but actually the reverse is the case. Its environs are malarious, and the further afield one goes the more intense becomes the endemicity of malaria in Lower Bengal.

CHART IV

Name M. D., age 33. Human volunteer V 1



OBSERVATIONS ON INFECTION BY PLASMODIUM KNOWLESI (APE MALARIA) IN THE TREATMENT OF GENERAL PARALYSIS OF THE INSANE

BY

C. E. VAN ROOYEN, M.D.Ed.

HALLEY STEWART RESEARCH FELLOW, AND LECTURER IN BACTERIOLOGY, UNIVERSITY OF EDINBURGH

AND

G. R. PILE, M.B., Ch.B.Ed.

SENIOR ASSISTANT MEDICAL OFFICER, MIDLOTHIAN AND PEEBLES ASYLUM, ROSSLYNLEE

(From the Midlothian and Peebles Asylum, Rosslynlee, and the Department of Bacteriology, University of Edinburgh)

three human volunteers in India. We have investigated the practical applicability of substituting this type of parasite for *Plasmodium vivax* in the treatment of G.P.I., and the following cases illustrate the application of this form of infection in the treatment of the disease. Clinical notes concerning the course of ape malaria occurring in man, the action of certain antimalarial remedies on this type of infection, and various experimental data are also incorporated.

The work has been carried out with a strain of parasite originally obtained from the Malaria Survey of India, and which was supplied to us by the courtesy of Sir Rickard Christophers of London, to whom we owe our thanks.

Case I

History.—The patient was a male aged 63, a coal miner.

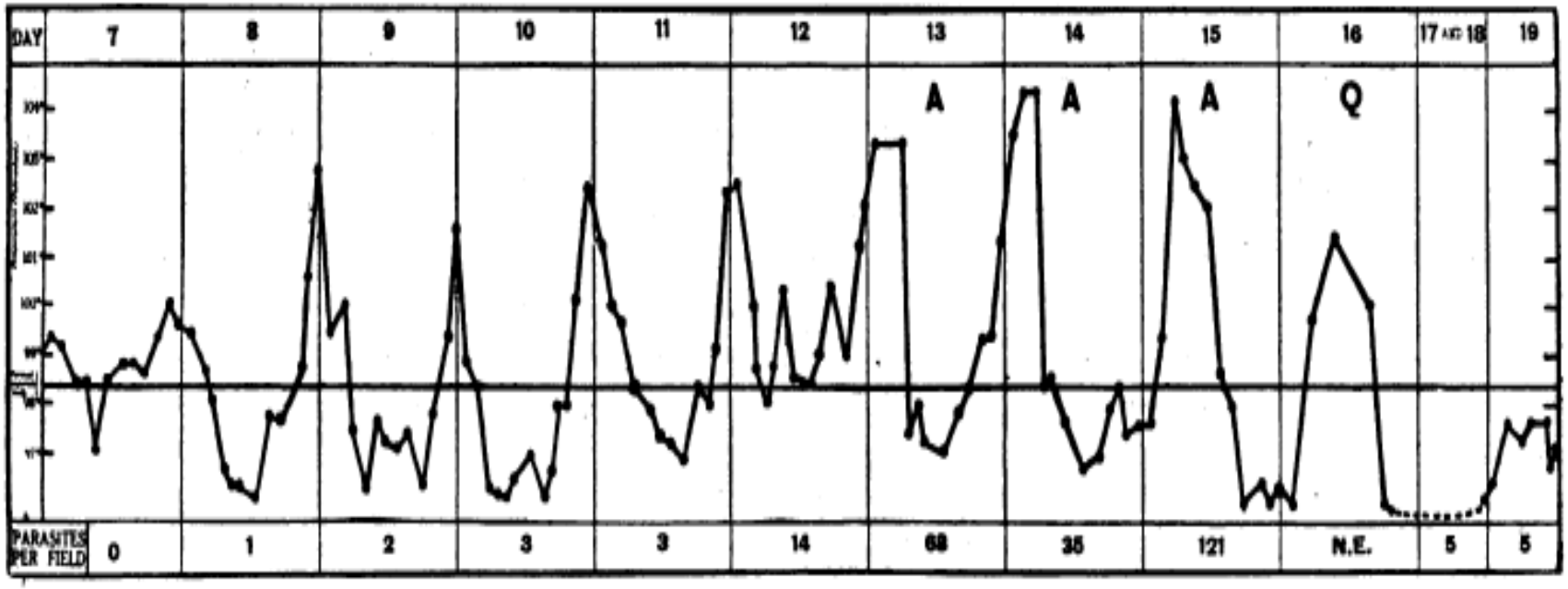
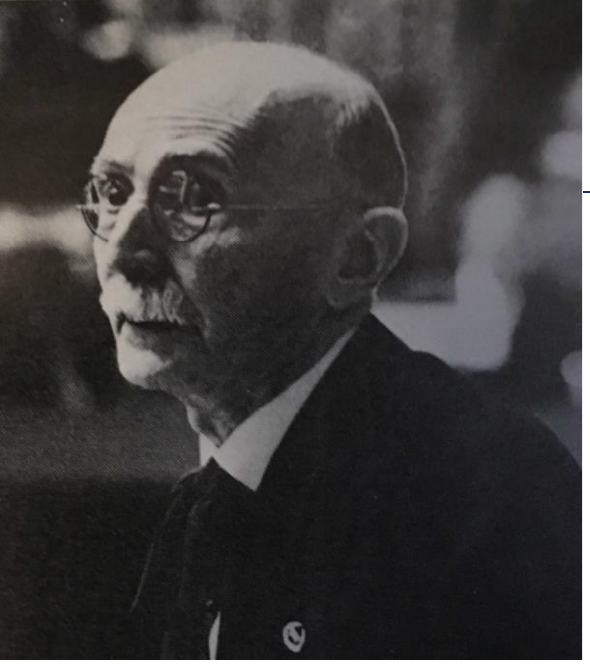


Chart 1.—A two-hourly temperature chart of Case I, showing pyrexia of quotidian type. Inoculation with 3 c.cm. infected blood was made six days before the chart begins. Antimalarial treatment commenced at day 13. A = atebrin given. Q = quinine started. N.E. = no examination for parasites.



Mihail Ciuca

P. knowlesi malariotherapy

Ciuca obtained knowlesi from Horton Hospital in the UK (where it had replaced vivax for malariotherapy) because of the difficult of using such therapy in the then malaria-endemic Romania

In the very large group of patients treated over many years by Ciuca et al., the virulence of the parasites increased over multiple blood passage (some 170) and its use was subsequently abandoned (1955)

Julius Wagner Jauregg

A systematic review of transfusion-transmitted malaria in non-endemic areas

Federica Verra[1*†], Andrea Angheben[1†], Elisa Martello[2], Giovanni Giorli[1], Francesca Perandin[1] and Zeno Bisoffi[1]

100 cases from 1911 to 2015

P. falciparum (45%); *P. malariae* (30%); *P. vivax* (16%); *P. ovale* (4%)

Mean incubation time (days): *P. falciparum* 25.7; *P. malariae* 63.9; *P. vivax* 29.3; *P. ovale* 19.0; *P. knowlesi* 15.5

Deaths: 14/91 (15.3%); 11 (12.1%) attributable

Malar J 2018;17:36

Alternative transmission routes in the malaria elimination era: an overview of transfusion-transmitted malaria in the Americas

1971-2016

Regina M. Alho[1,2], Kim Vinícius Amaral Machado[3], Fernando F. A. Val[1,3], Nelson A. Fraiji[2], Marcia A. A. Alexandre[1], Gisely C. Melo[1,3], Judith Recht[4], André M. Siqueira[5], Wuelton M. Monteiro[1,3*] and Marcus V. G. Lacerda[1,3,6]

Table 4 Epidemiological characteristics of 422 transfusion-transmitted malaria cases reported in the American continent

Characteristics	Number of cases	Proportion (%)
Country (n = 422; completeness = 100.0%)		
Mexico	214	50.7
USA	170	40.3
Brazil	28	6.6
Canada	4	0.9
Venezuela	3	0.7
Peru	2	0.5
Colombia	1	0.3
Gender (n = 355; completeness = 84.1%)		
Female	220	62.0
Male	135	38.0
Transfusion indication (n = 165; completeness = 39.1%)		
Gyneco-obstetrical conditions	111	67.3
Surgical procedures	34	20.6
Complications from neoplasias	10	6.1
Haemoglobinopathies	2	1.2
Nephropathy-associated anaemia	2	1.2
Other causes of anaemia	6	4.4
Blood product associated with TTM (n = 150; completeness = 35.5%)		
Packed RBCs	76	50.7
Whole blood	65	43.3
Platelets	9	6.0
Plasmodium species (n = 392; completeness = 92.9%)		
Plasmodium malariae	229	58.4
Plasmodium vivax	81	20.7
Plasmodium falciparum	70	17.9
Plasmodium ovale	11	2.8
Mixed *P. falciparum–P. vivax*	1	0.2

Malar J 2017;16:78

Transfusion-Transmitted Malaria in Countries Where Malaria Is Endemic: A Review of the Literature from Sub-Saharan Africa

Alex K. Owusu-Ofori,[1] Christopher Parry,[2] and Imelda Bates[3]

17 studies (1980-2009): median prevalence among 33,029 blood donors: 10.2%

Prevalence higher in 10 West African studies (median 30.2%)

88.7% *P. falciparum*; 9.2% *P. malariae*; 0.4% *P. ovale*; 0.3% *P. vivax*

Clin Infect Dis 2010; 51: 1192-8

Plasmodium Falciparum infection transmitted by living kidney donation: A case report from Iran

Behzad Einollahi

Nephrology and Urology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

We describe a case of malaria infection developed in a renal transplant recipient as early as 10 days after transplantation. The patient was 28-year-old man undergone living unrelated kidney transplantation. His donor was a 38-year-old healthy man who was laborer and has been long-term resident of malarious area (south of Iran).

The recipient experienced an episode of intravascular hemolysis, mild acute renal failure and fever 10 days after operation due to malaria infection which was confirmed by observation of the intraerythrocytic ring forms consistent with Plasmodium falciparum on blood film. He became afebrile and completely improved by antimalaria therapy.

To our knowledge, this is the first reported case of malaria transmission from donor after kidney transplantation in Iran.

Ann Transpl 2008;13:75-78

Nosocomial malaria

Between Nov 21 and Dec 28, 1917, 14 soldiers became ill and 10 died in a British military hospital at Portobello Barracks, Dublin.

All were being given weekly intravenous infusions of arsphenamine (Slavarsan), and all but one were treated on the same day of the week. Although the needle was changed between patients, other components of the infusion apparatus were not.

At necropsy, parasites of malignant tertian malaria were abundant in the tissue of internal organs and capillary spaces.

The Medical Research Council Salvarsan Committee noted in its report that one patient had been to a malarial area (Greece)….

Because indigenous malaria had last been described in Ireland in 1829 it was concluded that transfers of blood via the apparatus had occurred from the soldier……to other patients…. Causing spread of the infection

Mortimer PP, Lancet 1997;349:574

Hospital transmission

- Saline and heparin flushes of intravenous devices
- Incorrect capillay blood sampling techniques from blood-glucose measurement
- Contamination of gloves during the manipulation of drip lines and venous cannulae
- Needle-stick injuries
- Contamined catheters and contrast medium for computed tomographic scanner

Hospital-acquired malaria transmitted by contaminated gloves

S. Piro, M. Sammud*, S. Badi and L. Al Ssabi

Both patients, had had a venous cannula in situ since the day of admission and had had blood drawn for haematological investigations, plus daily infusion of saline or glucose solutions.

Case 1 underwent endoscopy for her gastrointestinal symptoms.

Case 2 had received a blood transfusion on a different medical ward, 10 weeks before the diagnosis of *P. falciparum* malaria was established.

Identification of the source of infection

Reviewing the medical records for recent cases of malaria, we established that on November 4th, 1997, during the time of admission of the two patients, a 45-year-old female had been admitted to the same ward and successfully treated with mefloquine for *P. falciparum* malaria acquired in Burkina Faso, where she had travelled a month earlier. On admission, her red blood cell count (RBCs) was 4 million/μL and a 5% parasitaemia cleared within the first 72 h of treatment. It was, concluded, therefore, that this was the probable index case, with Cases 1 and 2 residing in the adjacent room.

After reviewing the technique used by nurses during the insertion/removal of drip lines and cannulae, we concluded that malaria transmission might have occurred by accidental direct inoculation of infected RBCs of the index case through contaminated gloves.

If gloves are not changed after caring for a patient's intravenous line and when shortly afterwards the nurse operates a similar technique on another patient, transmission of live organisms is likely to occur because the contaminating blood, especially when mixed with the infusion fluid, is prevented from rapid clotting or drying, allowing survival of infectious agent on the glove surface.

J Hosp Infect 2001;47:156-8

Nosocomial Malaria and Saline Flush

Sanjay K. Jain,* Deborah Persaud,* Trish M. Perl,* Margaret A. Pass,* Kathleen M. Murphy,* John M. Pisciotta,* Peter F. Scholl,* James F. Casella,* and David J. Sullivan*

The Study

Abdominal pain, emesis, and a high fever developed in patient 1, a 9-year-old Gambian boy with sickle cell disease residing in the United States, during the flight home after a month in the Gambia; he had taken no malaria prophylaxis drugs. After diagnosis of *P. falciparum* malaria with 4% parasitemia and transfer to unit A of a tertiary care hospital, he responded well to antimalarial therapy and was discharged 2 days later.

Seven days before patient 1's admission, patient 2, a 14-year-old girl, with severe developmental delay, was admitted to unit A for placement of a surgical feeding tube.

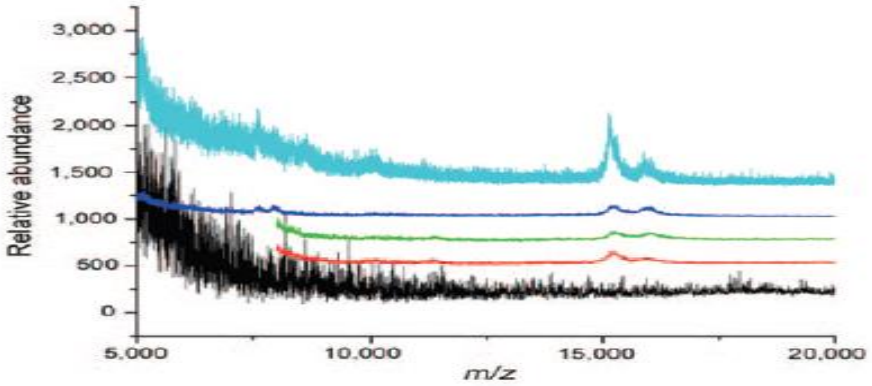
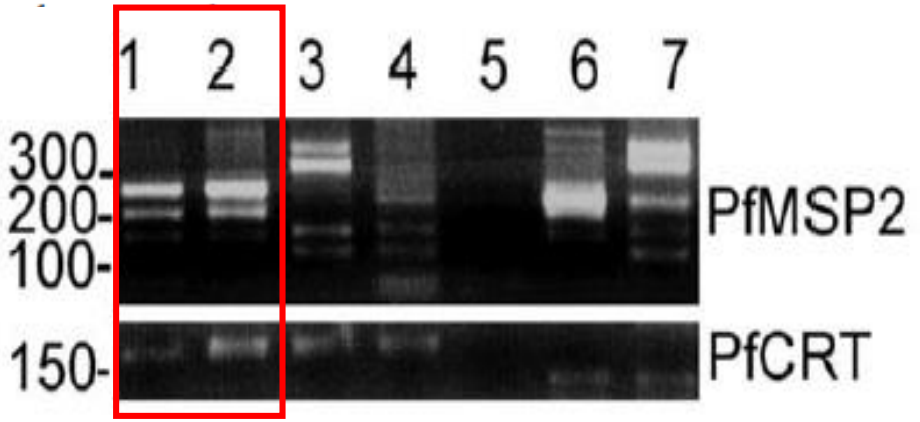


Figure 1. Mass spectroscopic analysis of sterile saline flush syringes after routine use. The contents of the used syringes were concentrated by centrifugation. Matrix-assisted laser desorption ionization detected the α and β chains of hemoglobin as the ions at mass/charge (*m/z*) 15,126 and 15,867, respectively, in samples A (red), B (green), C (blue), and J (aqua) that were absent in the matrix alone (black). The lower limit of sensitivity with matrix-assisted laser desorption ionization is ≈0.5 erythrocytes per mL.

Two potential sources of nosocomial transmission in unit A were identified: 1) heparin syringes, which were filled from multidose vials, and 2) factory preloaded 10-mL saline flushes, of which up to 3 mL was used per flush for intravenous lines not in use. Hospital policy had strict guidelines for using multidose devices and did not allow reusing single use devices. However, interviews of 7 nurses, including those who cared for the 2 patients, showed that 2 nurses admitted reusing saline flushes on the same patient, and 4 nurses had observed saline flushes being reused in unit A. Reusing multidose heparin vials was not

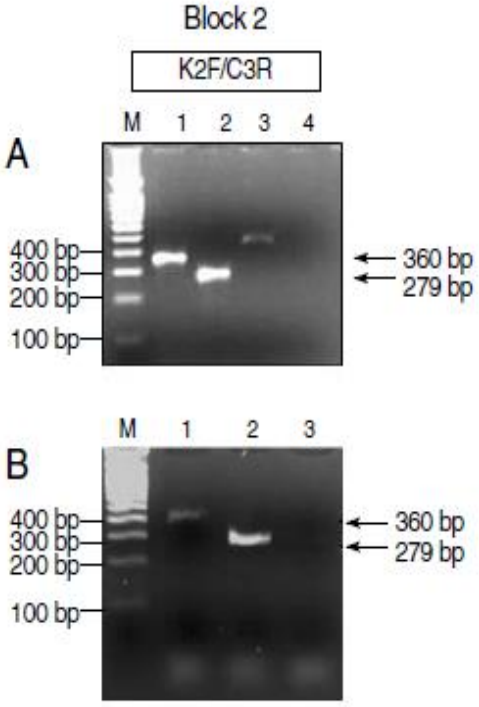


Emerg Infect Dis 2005;11:1097-99

A Locally Acquired Falciparum Malaria via Nosocomial Transmission in Korea

Jung-Yeon Kim[1,†], Jeong-Su Kim[2,†], Mi-Hyun Park[3], Young-A Kang[4], Jun-Wook Kwon[5], Shin-Hyeong Cho[1], Byeong-Chul Lee[1], Tong-Soo Kim[6] and Jong-Koo Lee[7,*]

Korean pt



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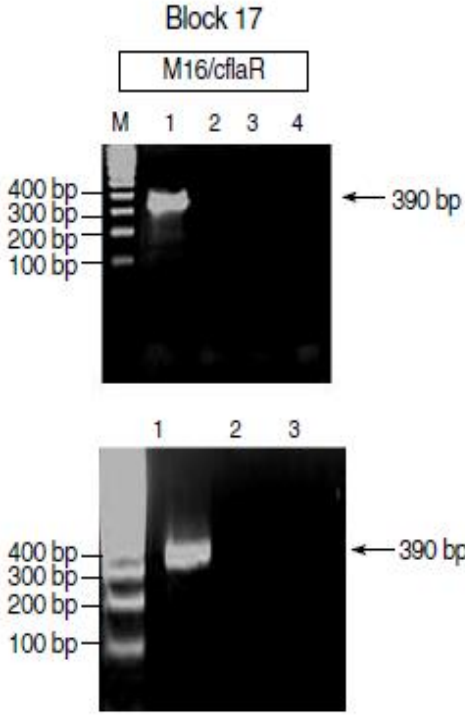


firmed through the family interviews. After reviewing all medical records from the hospital, we found that these 2 falciparum malaria cases were hospitalized in the emergency room at the same time. They were in the same emergency room for 9 hr and were given several emergency diagnostic and therapeutic treatments. The 2 patients were approximately 7 m apart. Case 1 received intravenous fluid via a peripheral vein and his gastrostomy incision site was disinfected and the dressing was changed. The interventions of Case 2 consisted of blood examination, central vein catheter insertion, intubation, mechanical ventilation, and cardiac massage. It is possible that several emergency room and internal medicine staff managed both patients. We

Korean J Parasitol 2009;47:269-73

Airport malaria

First cases of airport malaria were retrospectively diagnosed in 1969 in Le Bourget Airport , 6 km north of Paris (Doby JM & Guiguen C. Bull Soc Pathol Exot 1981;74:398-405).

Exclusion of any other mode of transmission (stay in a malarious area, transfusion, medical occupation, drug addiction, tattooing)

Possible exposure to bites from infected imported anopheles mosquitoes (occupation associated with aeronautics, visits to airport or houses near an airport, or to airports having contacts with countries whose levels of malaria or anopheles are high)

Two cases of falciparum malaria acquired in Britain

DONALD WHITFIELD, C F CURTIS, G B WHITE, G A T TARGETT, D C WARHURST, D J BRADLEY

The patient in case 1 was the landlord of a public house located 10 km west of the airport buildings at Gatwick airport. He had not visited the airport recently. Nevertheless, in spite of its rather isolated location, his public house was frequently visited by aircrew from Gatwick, who comprise over 5% of his numerous customers. The patient in case 2 lived further from Gatwick airport, 13 km south west, in a suburban area of north west Horsham. The countryside of this whole area is well wooded. Her husband worked at Gatwick airport but was concerned with furnishings for the aeroplanes and did not work on those in service. His blood showed neither parasites nor antimalarial antibodies. His wife accompanied him on a short visit to the airport on 14 July but did not visit it thereafter. She also travelled on the evening of 29 July (about the day on which she became infected) between Horsham and Reigate by motor scooter, passing close to the residence of case 1. The weather was very hot and her arms and legs would have been exposed to mosquito bites, though she did not stop appreciably on the journey, except presumably for traffic at intersections. The incubation period of falciparum malaria has a range of eight to 25 days with for most cases 10-14 or 10-16 days.[4] Possibly the two infections might have been contracted as little as three days apart if the range of incubation periods is used (as low as 14 days apart with a 10-16 day incubation period, and about 20 days apart on identical incubation periods for the two cases[4]). Both patients might have contracted malaria at almost the same site not less than 18 days apart. Moreover, it is difficult to disregard the proximity of Gatwick airport, as in spite of the long, hot summer no other indigenous cases of malaria were recorded in Britain, with the possible

Two additional British cases from the summer of 1983 did not appear to have been infected in known malarious areas. They were reported from London[15] and Durham[16] independently but were subsequently found to have travelled on the same flight from London (Heathrow) to Rome and may have become infected en route by a mosquito infected in Africa which could have boarded the aeroplane in Ethiopia.[5] It is now clear that the United Kingdom is not exempt from airport malaria. The methods of enzyme electrophoresis and other means of infraspecific taxonomy of both parasites and vectors, as used and attempted in these cases, may indicate the likely origin of the mosquitoes and the malaria, and efforts are needed to preserve both insects and parasites alive whenever the opportunity presents.

Countries where confirmed or probable cases of airport malaria have been reported,1969-2016

Country	Period					Total
	1969-77	1978-86	1987-95	1996-99	2000-16	
France	9	3	11	3	2+1+4	33
Belgium	0	9	7	1	0	17
Switzerland	3	0	5	1	0	9
United Kingdom	4	3	0	7	0	14
Italy	0	1	3	0	0	4
USA	0	0	3	1	0	4
Luxembourg	-	-	-	5	0	5
Germany	0	0	2	2	0	4
Netherlands	0	2	0	0	1	3
Spain	0	1	1	0	0	2
Israel	0	0	0	1	1	2
Australia	0	0	0	1	-	1
Tunisia	-	-	-	-	4	4
Total	16	19	32	22	13	102

Estimating the malaria risk of African mosquito movement by air travel

Andrew J Tatem*[1,2], David J Rogers[1] and Simon I Hay[1,2]

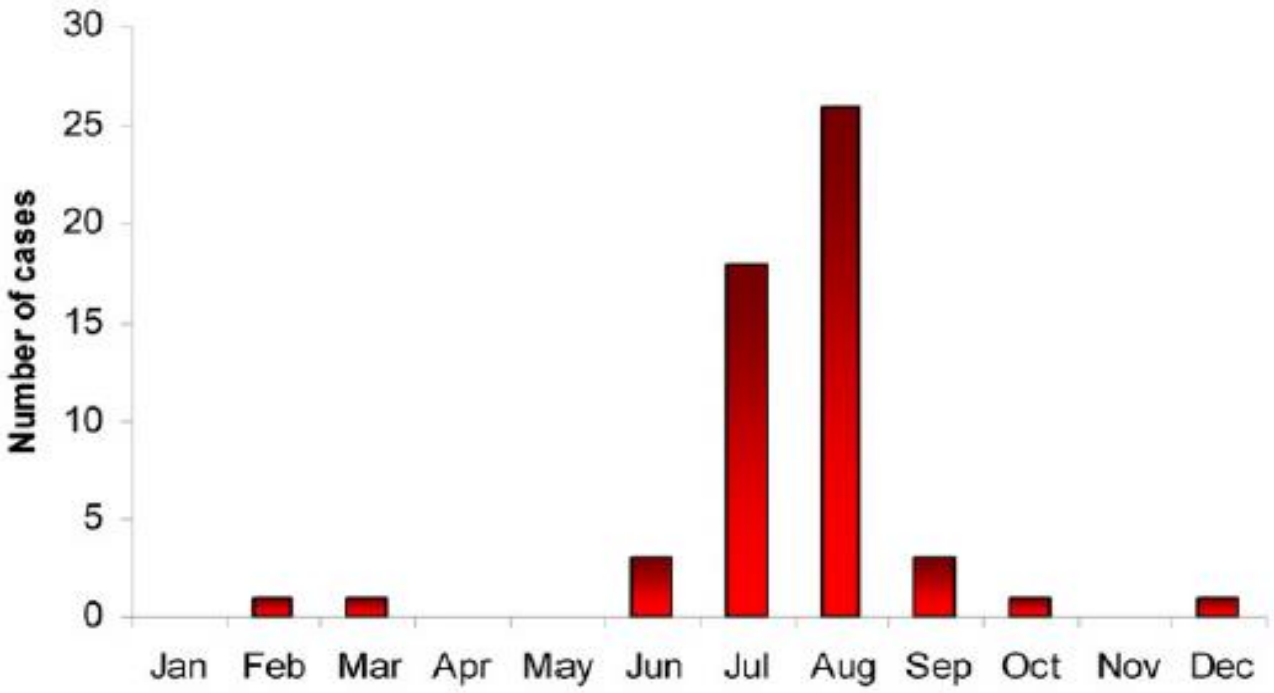


Figure 3
Month in which European airport malaria cases occurred [7, 8, 14, 25, 38-62] (where date is provided).

Estimating the malaria risk of African mosquito movement by air travel

Andrew J Tatem*[1,2], David J Rogers[1] and Simon I Hay[1,2]

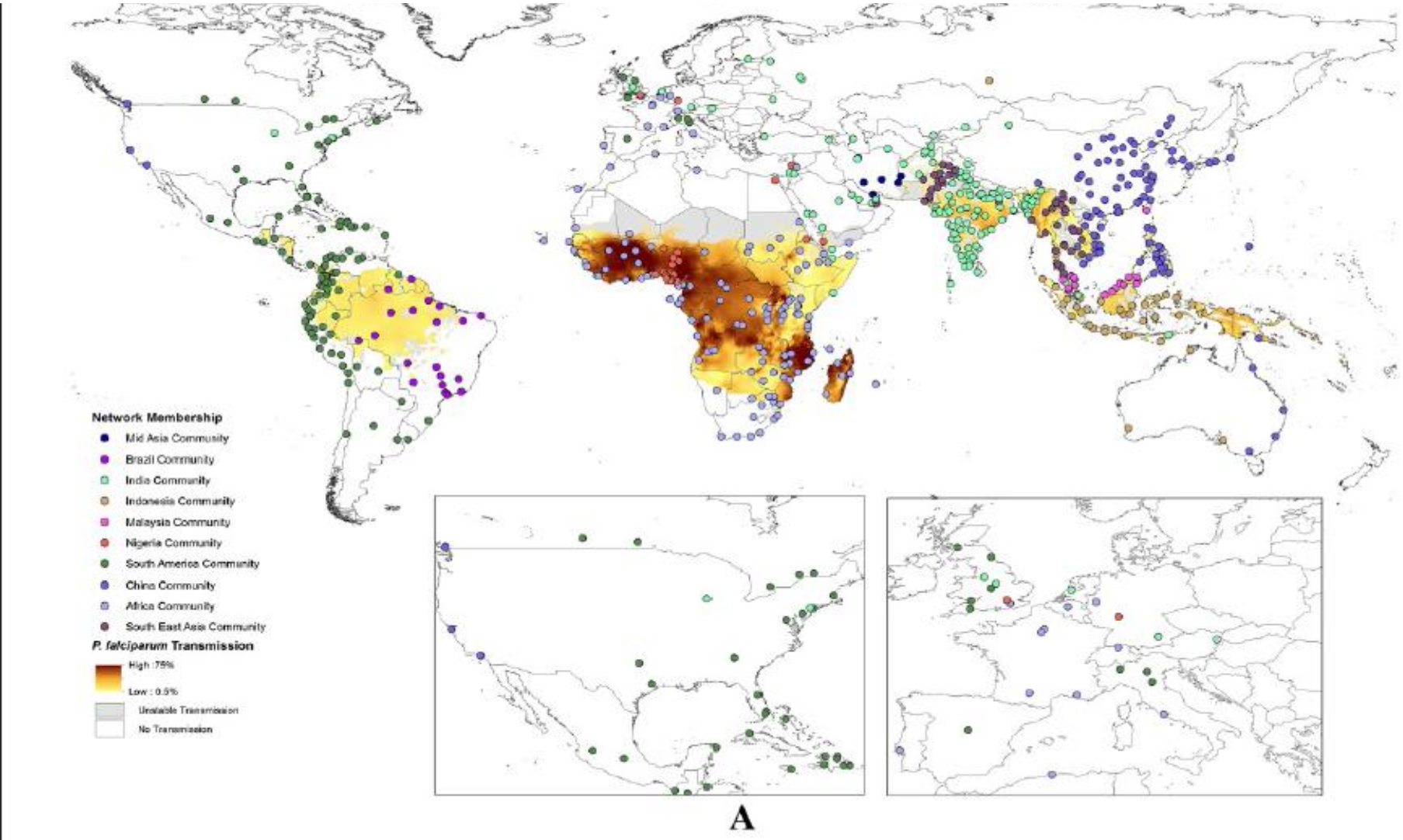
Table 1: Year 2000 top 10 air travel risk routes for *P. falciparum* infected *An. gambiae* invasion and subsequent autochthonous transmission.

	From		To			
Rank	Airport	Country	Airport	Country	Month	Annual No. Passengers
1	Abidjan	Cote d'Ivoire	Paris Charles de Gaulle	France	August	169,188
2	Accra	Ghana	Amsterdam Schippol	Netherlands	July	53,130
3	Entebbe/Kampala	Uganda	Brussels	Belgium	July	42,141
4	Accra	Ghana	Amsterdam Schippol	Netherlands	September	53,130
5	Abidjan	Cote d'Ivoire	Brussels	Belgium	August	58,021
6	Accra	Ghana	Rome Fiumicino	Italy	September	12,420
7	Abidjan	Cote d'Ivoire	Zurich	Switzerland	July	46,495
8	Accra	Ghana	Rome Fiumicino	Italy	August	12,420
9	Abidjan	Cote d'Ivoire	London Gatwick	United Kingdom	August	37,843
10	Cotonou	Benin	Brussels	Belgium	August	14,954

Malar J 2006;5:57

Global malaria connectivity through air travel

Zhuojie Huang[1,2,3,4*] and Andrew J Tatem[5,6]



Malar J 2013;12:269

Multiple reports of locally-acquired malaria infections in the EU

20 September 2017

Table 1. Number of cases of locally acquired malaria in the EU, by country of report, May-September 2017

Country of report	No.	*Plasmodium* species	Date of onset	Suspected mode of transmission, place of infection	Date of report
France	2	*P. falciparum*	26 August	Mosquito-borne, Allier, France.	7 September
Greece	5	*P. vivax*	2 May–22 July	Mosquito-borne, regions of Dytiki Ellada and Sterea Ellada, Greece.	18 May, 21 July, 17 August
	1	*P. falciparum*	17–23 July	Mosquito-borne or nosocomial, region of Ipeiros, Greece.	17 August
Italy	1	*P. falciparum*	29 August	Mosquito-borne or nosocomial, Trento l, Italy.	5 September
United Kingdom	3	*P. vivax*	29 August	Mosquito-borne, the northern part of Cyprus.	8 September

Table 1. **Cases of hospital malaria transmission in the EU, by country, 2016–2018**

Country of report	Age (years)	Date of onset	Place of infection	Suspected mode of transmission	Possible exposure	Outcome	*Plasmodium* species
Germany	33	2016	Nordrhein-Westfalen, Germany	Hospital transmission	Shared room with a malaria case	Alive	*P. falciparum*
Greece	39	18–20 Jul 2017	Ipeiros, Greece	Vector or hospital transmission	Shared ward with a malaria case	Alive	*P. falciparum*
Italy	4	29 Aug 2017	Trento, Italy	Hospital transmission	Shared ward with two malaria cases	Dead	*P. falciparum*
Italy	13	28 Oct 2017	Tuscany, Italy	Hospital transmission	Shared ward with a malaria case	Alive	*P. falciparum*
Spain	64	9 Mar 2016	Galicia, Spain	Hospital transmission	Stayed in emergency ward with a malaria case	Alive	*P. falciparum*
Spain	<1 (3 months)	19 Feb 2018	Madrid, Spain	Hospital transmission	Shared ward with a malaria case	Alive	*P. malariae* and *P. ovale*

Hospital-acquired malaria infections in the European Union

Malaria in Maremma, Italy

Marco Baldari, Angelo Tamburro, Guido Sabatinelli, Roberto Romi, Carlo Severini, Giampiero Cuccagna, Gabriella Fiorilli, Maria Pia Allegri, Cristina Buriani, Mario Toti

Patient and methods

On Aug 7, 1997, a 62-year-old woman who had had an intermittent high fever since July 30 was admitted to the Internal Medicine Unit of Grosseto Hospital. She had not travelled out of the country, nor had any of her family. She had not received any blood or blood products or used intravenous drugs. She lived in a sparsely populated rural area. The nearest international airport (Pisa) was 150 km away. On Aug 13, microscopy of her blood showed heavy parasitaemia with *P vivax* (10 200 parasites/μL; 5500 were gametocytes).

her daughter in May, 1997. She had had no feverish illness for 4 years. The daughter became feverish the day after her arrival from India. She was treated with antibiotics. Her fever subsided after 3 weeks. A week later she was found to be anaemic (haemoglobin 8·1 g/dL) and given iron. Malaria was not suspected at that time.

On August 18, the girl's blood was found to contain scarce *P vivax* blood forms (436/μL, of which 124/μL were gametocytes). No parasites were found in the blood of her father or mother. Blood samples were tested for malarial antibodies (bioMérieux, Marcy-l'Etoile,

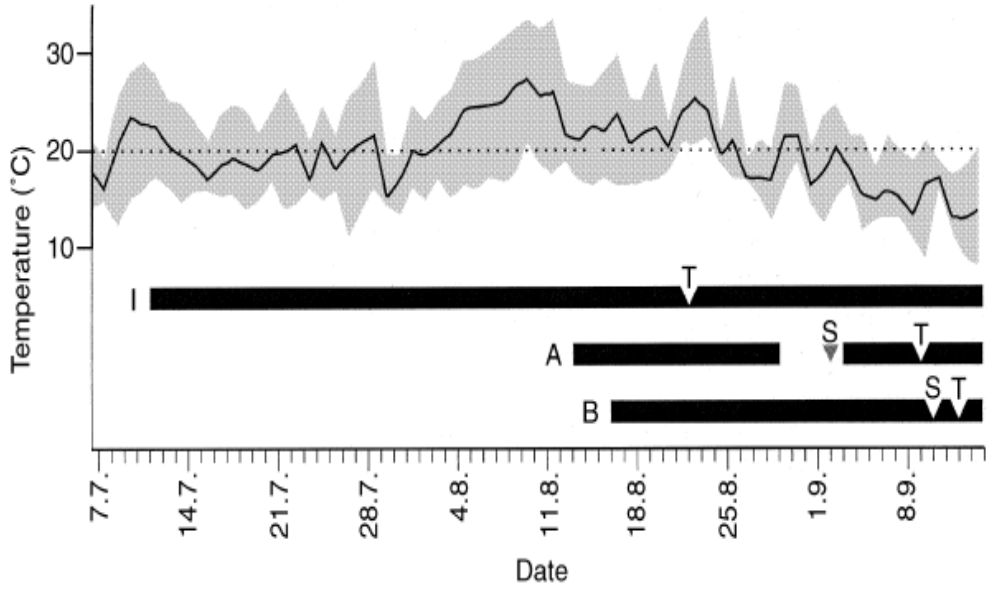
We believe that malaria in the Italian woman (and possibly in the Indian girl's father) were transmitted by Italian indigenous *An labranchiae*. They may represent the first cases of "introduced malaria" in Europe for 20 years. An alternative explanation is "luggage malaria" (introduction of an infected mosquito from an endemic area); but considering the low population of the rural area where the cases occurred and its distance from an airport, this possibility is unlikely. Malaria in the father could well be due to a primary attack or a relapse of an imported *P vivax* infection. Its timing and location, however, make it likely to be another case of introduced malaria.

Lancet 1998;351:1246-7

Short communication: **Two cases of autochthonous *Plasmodium falciparum* malaria in Germany with evidence for local transmission by indigenous *Anopheles plumbeus***

Andreas Krüger[1], Andreas Rech[2], Xin-Zhuan Su[3] and Egbert Tannich[1]

vectors. We report two cases of PFM in German children without travel history to malaria-endemic areas. Both infections occurred during a stay in a hospital where a child from Angola with chronic *P. falciparum* infection was hospitalized at the time. Known routes of transmission, such as imported mosquitoes or blood transfusion, were very unlikely or could be excluded, whereas evidence was obtained for transmission by the indigenous mosquito species *Anopheles plumbeus*.



only 700 m from the hospital, in a small forest, a flooded hole in an old beech tree was discovered containing larvae and pupae with characteristics typical for those of *A. plumbeus*. The species *A. plumbeus* was confirmed by morphological characteristics of adult mosquitoes reared in the laboratory from collected pupae, leaving no doubt that the potential *P. falciparum* vector *A. plumbeus* is breeding in the vicinity of the Duisburg hospital.

Probable autochthonous introduced malaria cases in Italy in 2009–2011 and the risk of local vector-borne transmission

R Romi (roberto.romi@iss.it)[1], D Boccolini[1], M Menegon[1], G Rezza[1]
1. Istituto Superiore di Sanità (ISS), Department of Infectious, Parasitic and Immune-Mediated Diseases (MIPI), Rome, Italy

Case 1

A 41-year-old Caucasian man living in the outskirts of Rome was admitted to the intensive care unit of the local Hospital for Infectious Diseases on 8 August 2009 with high remittent fever, peaking every 48 hours and classical paroxysms with alternate cold, hot and sweating stages. Clinical suspicion of malaria was confirmed by microscopic (blood smear observation, thick and thin films) and molecular (nested PCR analysis) [7] diagnosis as *P. vivax* malaria. The patient had no history of recent travel in malaria-endemic areas; he only reported a one-week holiday in 2003 in Santo Domingo, ous six years. In July 2009, the month before the onset of symptoms, he had spent two weeks in two different holiday farms, one in Terracina, between 4 and 5 July, and the other in Pontinia, between 25 and 26 July. Both sites are located in the former 'Pontine marshes', a rural coastal plain of Central Italy, where malaria was hyperendemic until 1946. Although long term

Case 2

A 39-year-old Caucasian man resident in the midtown of Rende, a residential district close to the town of Cosenza, in Calabria Region, southern Italy, was hospitalised on 15 September 2011 with the same symptoms as Case 1 (high remittent fever, peaking every 48 hours and classical paroxysms with alternate cold, hot and sweating stages), although the onset of symptoms had

Euro Surveill
2012;17:pii=20325

A local outbreak of autochthonous *Plasmodium vivax* malaria in Laconia, Greece—a re-emerging infection in the southern borders of Europe?

Panos Andriopoulos [a,b,*], Asimoula Economopoulou [c], Gregoris Spanakos [c], George Assimakopoulos [b]

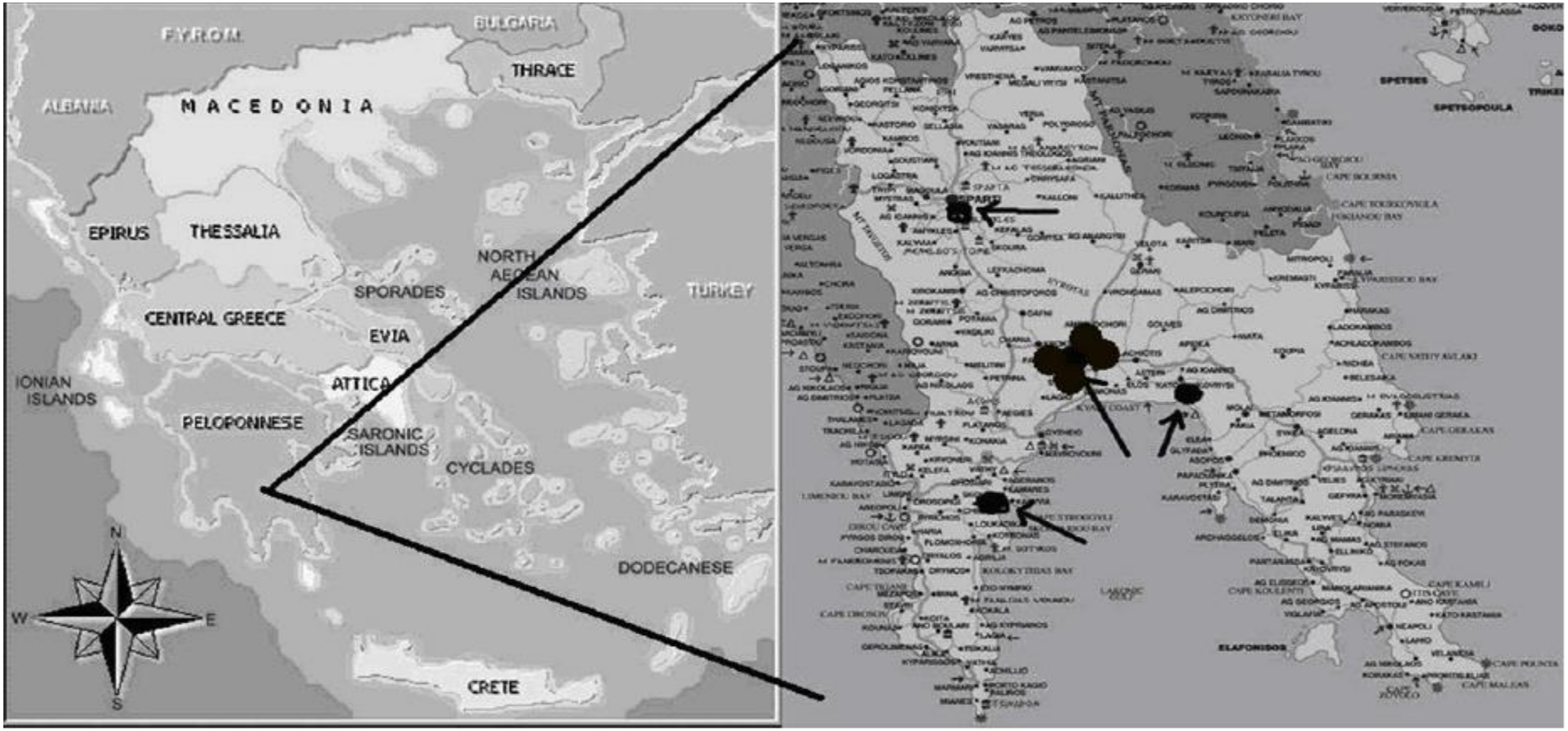


Figure 2. A spot map showing the area of residence of the cases in the region of the cluster of *Plasmodium vivax* infections.

Int J Infect Dis 2013;17:e125-e128

Source identification of autochthonous-introduced *Plasmodium vivax* Malaria, Spain

Infection (2017) 45:111–114

Laura Barrado[1,2] · Carmen Ezpeleta[2,3] · José Miguel Rubio[4] · Carmen Martín[2,3] ·

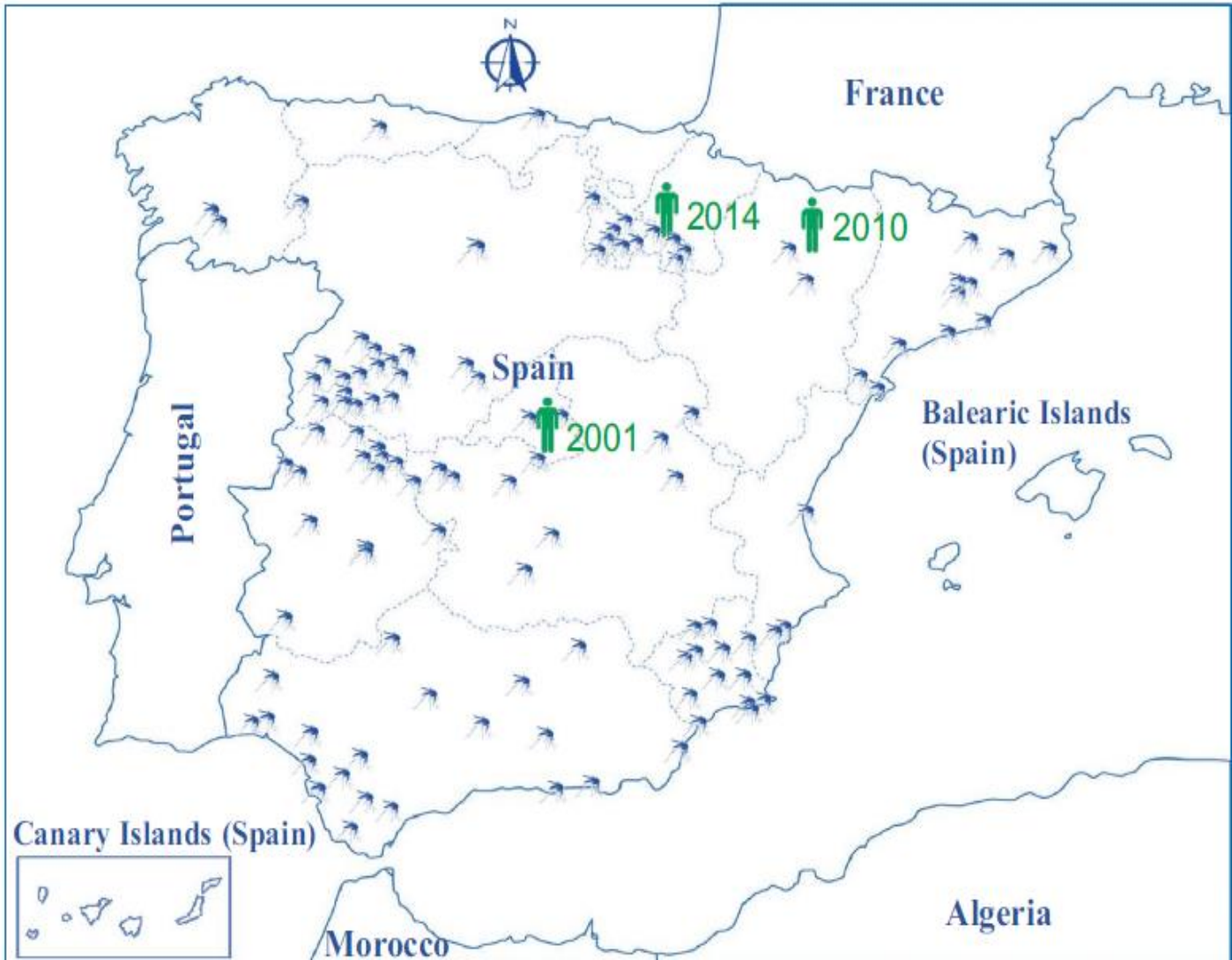


Fig. 2 Map of Spain where the geographical distribution of *Anopheles atroparvus* is represented by blue mosquitoes and three autochthonous malaria cases by *green person figures*. Source: References [2, 8, 9]

Letter to the editor: Is malaria re-emerging in southern Europe? Cryptic *Plasmodium falciparum* malaria in Malta, October 2018

Raquel Medialdea-Carrera[1,2], Tanya Melillo[1], Charmaine Gauci[1], Graziella Rocco[1], Maria Louise Borg[1]
1. Infectious Disease Control Unit, Health Promotion and Disease Prevention Directorate, Msida, Malta
2. European Programme for Intervention Epidemiology Training (EPIET), European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

Cryptic severe *Plasmodium falciparum* malaria in a Moroccan man living in Tuscany, Italy, August 2018

Lorenzo Zammarchi[1,2], Nicoletta Di Lauria[1], Filippo Bartalesi[2], Lorenzo Roberto Suardi[1], Giampaolo Corti[1,2], Jessica Mencarini[1], Daniela Boccolini[3], Carlo Severini[3], Luigi Gradoni[3], Carla Buonamici[4], Giorgio Garofalo[4], Anna Maria Bartolesi[5], Nunziata Ciccone[5], Andrea Berni[6], Loredana Poggesi[1,6], Fabrizio Niccolini[7], Gian Maria Rossolini[1,5], Roberto Romi[3], Alessandro Bartoloni[1,2]

Autochthonous falciparum malaria possibly transmitted by luggage-carried vector in Paris, France, February 2013

S Gallien (sebastien.gallien@sls.aphp.fr)[1], F Taieb[1], S Hamane[2], N De Castro[1], J M Molina[1]
1. Department of Infectious and Tropical Diseases, Paris Diderot University, Paris 7, Saint-Louis Hospital, Paris, France
2. Department of Parasitology, Paris Diderot University, Paris 7, Saint-Louis Hospital, Paris, France

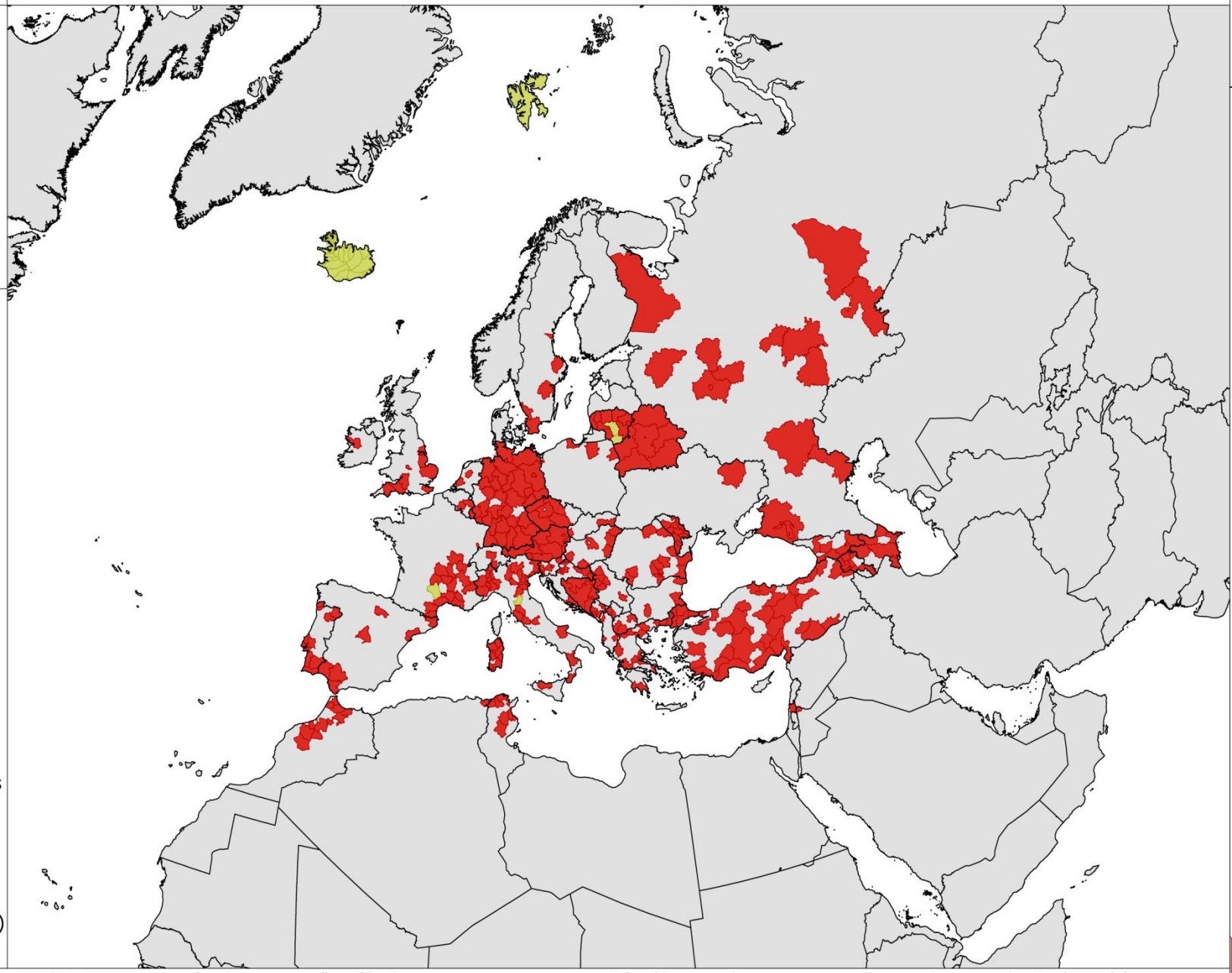
European Centre for Disease Prevention and Control

Cryptic malaria

Epidemiological update - indigenous Plasmodium falciparum malaria cases in the Apulia region, Italy

On 4 October 2017, Italy reported through the Early Warning and Response System (EWRS) the detection of four Plasmodium falciparum malaria cases in the Apulia region. Cases are 21 to 37-year-old men, originally from Africa. All stated that they had been in Italy for more than three months. Dates for onset of symptoms ranged from 20 to 27 September 2017. The cases are agricultural workers in Ginosa and Castellaneta. Malaria vectors such as Anopheles labranchiae and Anopheles superpictus are present in Italy.

Distribution* of *Anopheles maculipennis s.l.* complex, July 2018



ECDC and EFSA, map produced on 9 Jul 2018. Data presented in this map are collected by the VectorNet project. Maps are validated by external experts prior to publication. Please note that the depicted data do not reflect the official views of the countries. * Map takes into account distribution data from 1980. ** Countries/Regions are displayed at different scales to facilitate their visualisation.

Anopheles labranchiae - Factsheet for experts

Species name/classification: *Anopheles labranchiae* Falleroni, 1926

Common name/synonyms: Member of the *Anopheles maculipennis* complex. Synonym *Anopheles sicaulti* [17]

Current distribution:

Anopheles labranchiae is restricted to southern and south-eastern Europe [1], with reports from Corsica, coastal areas of Italy, Sardinia, Sicily and the Istrian peninsula and Dalmatian coast of Croatia (Merdic, personal communication) [1]. It has also been reported from the Czech Republic, Slovakia, and Bulgaria [2], although these reports have been questioned as the identification was based on morphology. *Anopheles labranchiae* is also distributed across North Africa [3]. It may occur in Hungary but this needs confirmation [4]. *Anopheles labranchiae* was once considered eradicated from Italy but has re-established in Sardinia, Sicily and the mainland in recent years [5], which has been suggested to be a result of the introduction of rice cultivation [6,7]. On the mainland it occurs in western, south-eastern and south-western coastal districts (Romi, personal communication). In Sicily and Sardinia, records of this species have been reported as high as 1000 metres above sea level [8].

Anopheles plumbeus - Factsheet for experts

SPECIES NAME/CLASSIFICATION:*Anopheles plumbeus* Stephens 1828

COMMON NAMES/SYNONYMS: *Anopheles corsicanus* Edwards, 1928; *Anopheles intermedius* Shingarev, 1928; *Anopheles nigripes* Staeger, 1839

Anopheles plumbeus is distributed throughout Europe, the Caucasus, the Middle East, Iran and Iraq and in North Africa [2]. This mosquito has been found in nearly all European countries, including Scandinavia and Italy, and also in the western Himalayas [3].

Anopheles plumbeus distribution: Albania, Austria, Belarus, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, France (including Corsica), Germany, Greece, Hungary, Ireland, Italy (including Sardinia and Sicily), Liechtenstein, Lithuania, Luxembourg, Macedonia, Moldova, Montenegro, Netherlands, Poland, Portugal, Romania, Russia, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, Ukraine and United Kingdom [1].

This mosquito species has begun to utilise artificial breeding sites which have helped it to expand into more suburban and urban areas in Europe.

Investigation on potential malaria vectors (*Anopheles* spp.) in the Province of Trento, Italy

Valentina Tagliapietra[1*], Daniele Arnoldi[1], Marco Di Luca[2], Luciano Toma[2] and Annapaola Rizzoli[1]

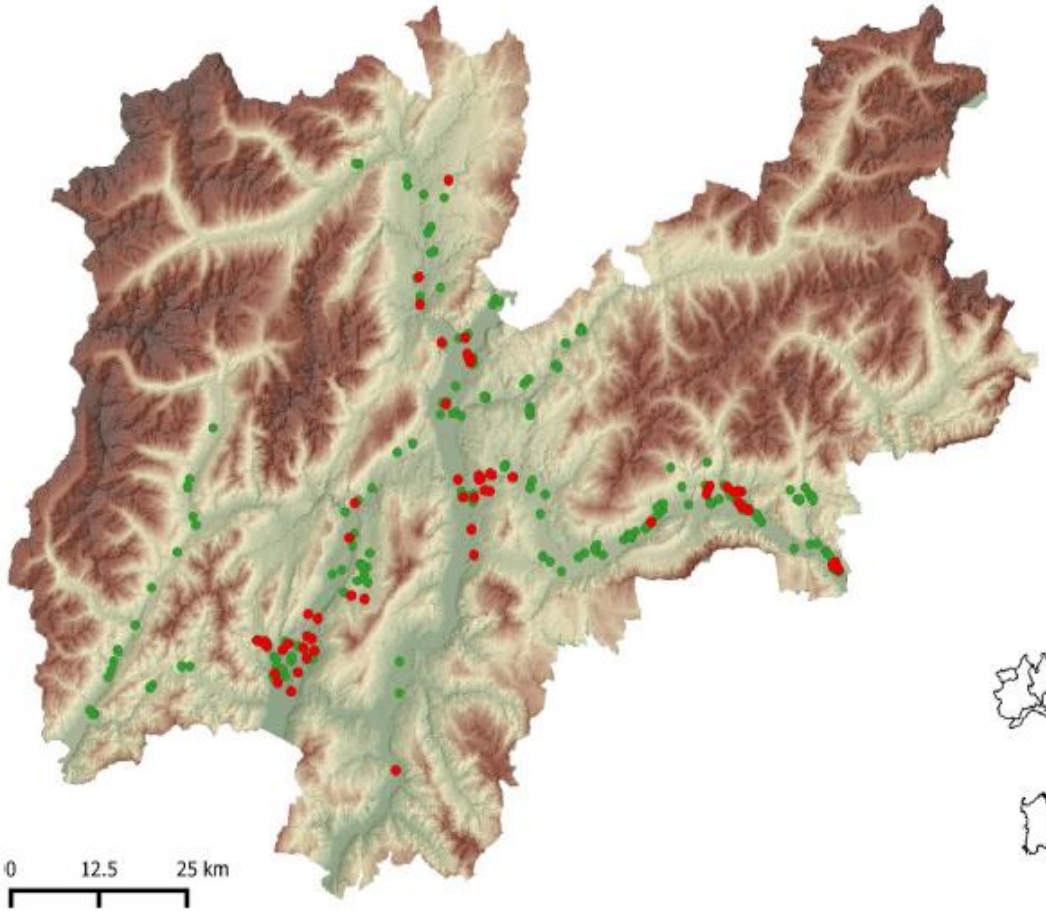


Fig. 1 Distribution map of *Anopheles* spp in the Province of Trento (Green circles = negative sites for *Anopheles* spp.; Red circles = positive sites for *Anopheles* spp.)

A total of 67 sites (23%; 67/287) resulted positive for the presence of immature or adult stages of *Anopheles* spp. (Fig. 1). In total 211 individuals were collected: 118 (56%) belonged to *An. plumbeus*, 56 (26.5%) to *An. maculipennis* complex, 10 (4.7%) to *An. claviger* and 27 were identified only at genus level (Table 1). Of note, the capture of *Anopheles* mosquitoes from our entomological surveillance, represents the 0.37% of all the mosquito samples collected. This is the first record for *An. plumbeus* in the study area.

Malar J 2019;18:151

Anopheles sacharovi

Species name/classification: *Anopheles (Anopheles) sacharovi Favre*, 1903

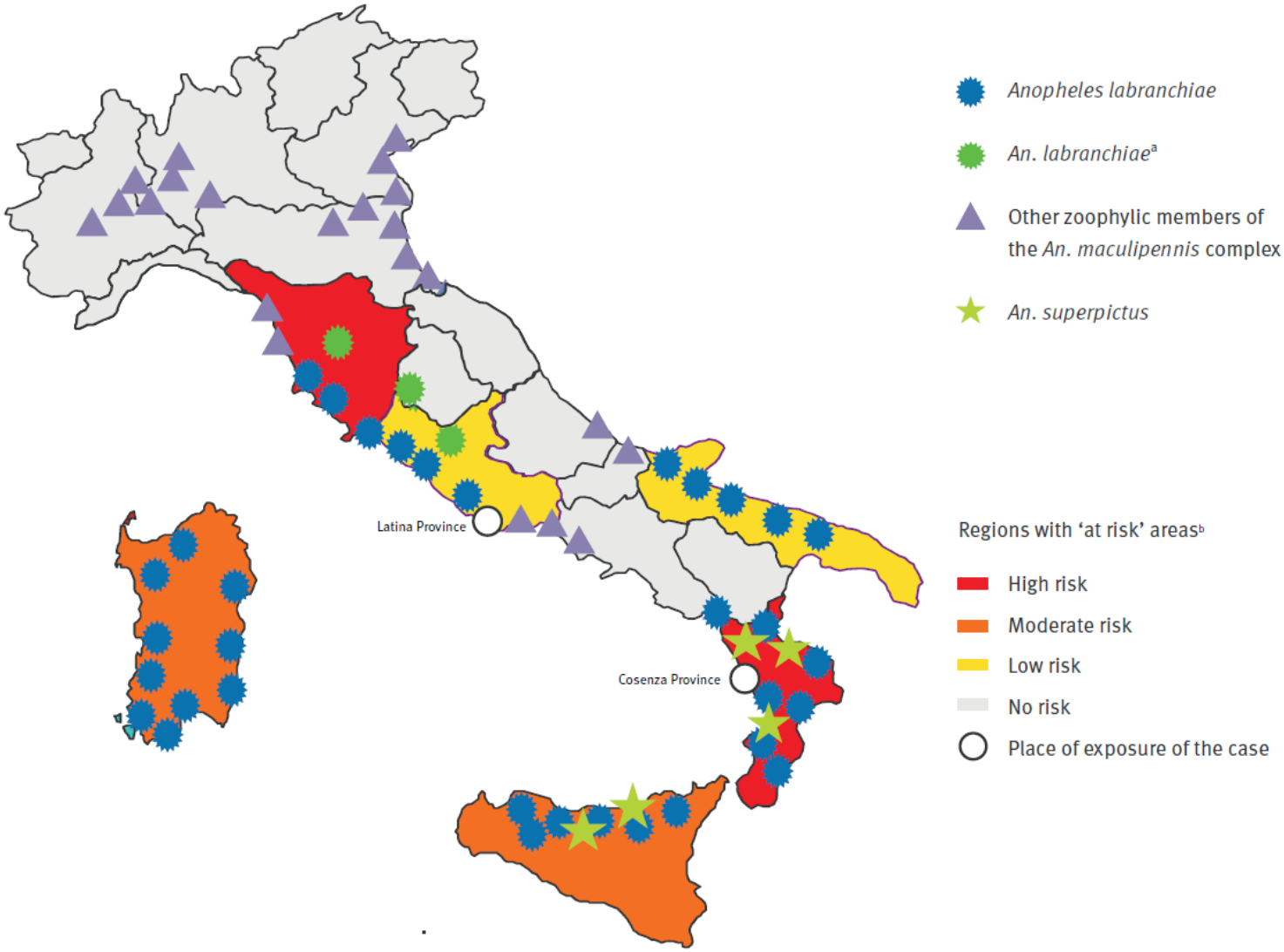
Common name/synonyms: Member of the *Anopheles maculipennis complex*

Anopheles sacharovi was reportedly distributed from coastal parts of Italy, Sardinia, Corsica, Croatia, the former Yugoslav Republic of Macedonia, Albania, Bulgaria, Romania to southern regions of the former USSR, and from Turkey to Lebanon, Israel, Jordan, Syria, Iraq, Iran [1-4]. Preliminary results from recent research in Moldova suggest that a large population of this species is present in the south of the country (Sulesco, personal communication 2012). It was first reported in Greece in 1928 and later found breeding in high densities in all coastal areas [5]. This species was previously present in Armenia in high numbers but disappeared in 1965. Recent studies suggest re-colonisation of some areas of Armenia [6]. There are also records from 2009 in Cyprus [7].

Anopheles sacharovi is no longer present in Italy; the last records were during the 1960s and 70s. The species was present in continental Italy, particularly along the north western coastal plain (delta of the Po river, where it acted as a malaria vector in the absence of An. labranchiae, previously the main malaria vector) and in northern Sardinia, where it probably played a secondary role in transmission. Aquatic habitats showed a preference for retro-coastal brackish swamps, but today it has almost disappeared from these habitats. It has

FIGURE 2

Distribution of the potential malaria vectors and regions considered at risk of malaria reintroduction, Italy, 2005-2011



[a] First detected in 2010–2011 in northern-central Italy.

[b] Areas with presence of foci and seasonal abundance of the potential vector and with seasonal climatic conditions favourable to malaria transmission.

Romi R et al, Euro Surveill 2012;17:pii=20325

Carta della malaria in Italia,

a cura del conte Luigi Torelli, 1882

The duration of *Plasmodium falciparum* infections

Elizabeth A Ashley[1,2*] and Nicholas J White[1,2]

Table 2 Non-transfusion cases of delayed presentation of falciparum malaria

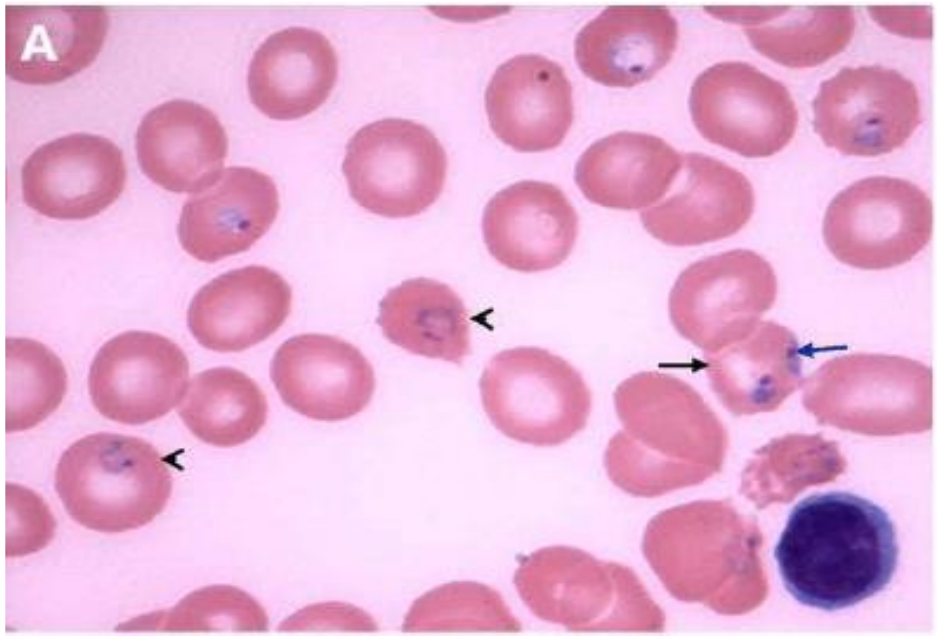
Author, country, reference	Case description	Time interval since last infection or exposure
Nagley *et al.*, UK [43]	49-years-old male, British soldier, in India from 1919 to 1928. History of malaria in India and one unconfirmed "relapse". Self-treated with quinine in 1932. No other relevant travel, or blood transfusions. Developed jaundice and then severe malaria in 1945. *P. falciparum* trophozoites and gametocytes on microscopy	13-17 years
Walters *et al.*, UK [44]	21-years-old pregnant female, originally from Nigeria. Asymptomatic. Diagnosis made by microscopy performed to investigate abnormal routine antenatal full blood count in 1958	19 months
Russell *et al.*, USA [45]	Medical student with annual episodes of smear positive falciparum malaria for 4 years after return from the Belgian Congo in 1934. Eventually cleared following a prolonged course of quinine	4 years
Revel *et al.*, France [46]	7-years-old male, originally from Comoros islands presenting with a febrile illness. *P. falciparum* trophozoites and gametocytes seen on microscopy, mixed with *P. ovale*.	3 years
Kyronseppa *et al.*, Finland [47]	46-years-old male sailor, last travel to endemic area was Jeddah 20 months previously. Other possible occupational exposure in late 1970s. Presented with fever after head injury (intracerebral bleed). *P. falciparum* diagnosed by microscopy	20 months
Krajden *et al.*, Canada [48]	30-years-old male, originally from Ghana. Presented with diabetic ketoacidosis. Malaria diagnosed by microscopy. Serology positive.	32 months
MMWR USA [49]	Obstetrician/gynaecologist admitted with fever. Last trip to a malarious area was 15 years before (Afghanistan). Diagnosed on microscopy. Labelled as cryptic malaria (occupational exposure cannot be excluded).	15 years (unless occupational exposure)

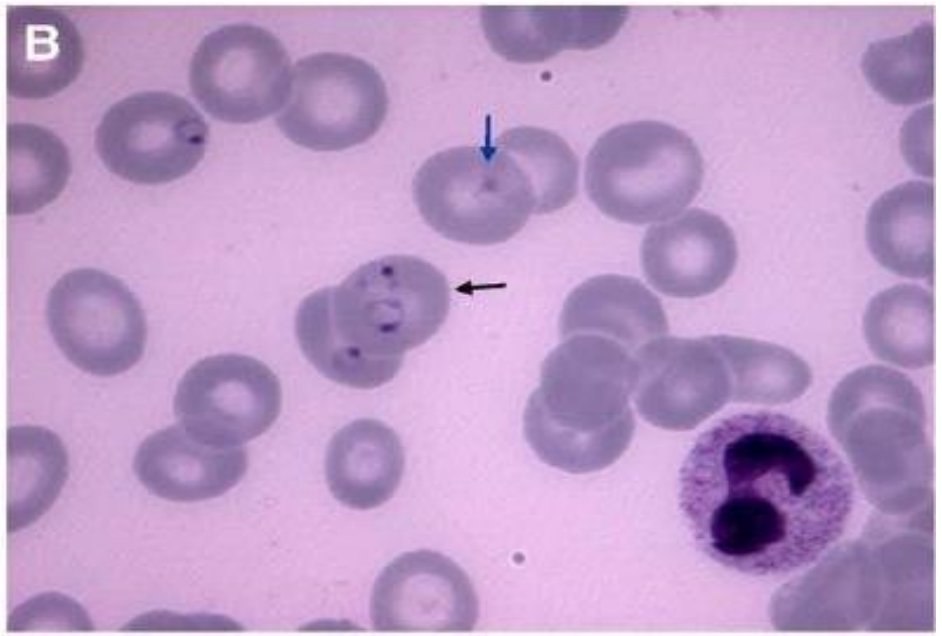
Malar J 2014;13:500

Plasmodium falciparum malaria occurring 8 years after leaving an endemic area

Paul E. Szmitko[a], Magdie L. Kohn[a], Andrew E. Simor[a,b,*]

A 29-year-old patient who was born in Angola developed *Plasmodium falciparum* malaria 8 years after leaving Africa. She had not returned to a malaria-endemic area, and there were no apparent risks of local or nosocomial acquisition of malaria in Canada. She recovered after treatment with oral quinine sulfate and doxycycline.





Diagn Microbiol Infect Dis 2009;63:105-7

Conclusions

Non-vector-borne malaria is an infrequent but difficult to diagnose malaria

Nosocomial malaria in non-endemic countries has been associated with different modalities of transmission but the exact mode is sometimes overlooked

Cryptic malaria is rare and can be associated with local mosquitoes although different pathogenic explanation can be exploited

Reintroduction of malaria has been recorded in several European countries (Greece, Italy, Spain, France) where Anopheles mosquitoes are still present