

Imported malaria in a hospital in Paris

M. GENTILINI, J. F. TRAPE,* M. DANIS, D. RICHARD-LENOBLE, G. BRUCKER AND H. FELIX

Central Laboratory of Parasitology and Consultation for Parasitic and Tropical Diseases, Pitié-Salpêtrière Hospital Group, 75651 Paris Cedex 13, France

Summary

The number of cases of imported malaria diagnosed by the Parasitology Laboratory of the Pitié-Salpêtrière Hospital Group in Paris has shown a significant increase in recent years. From 1970 to 1979, 443 cases were diagnosed and the annual number recorded during this period rose from seven to 93 cases. This is causing anxiety since *Plasmodium falciparum* is the principal species observed, affecting two out of three patients. The principal epidemiological characters of malaria imported into France, the diagnostic difficulties and the therapeutic schedules are shown in a study of 192 case histories of patients observed by the authors.

Introduction

For several years, in most European countries, there has been a significant increase in the number of cases of imported malaria (BRUCE-CHWATT *et al.*, 1974; ZULUETA, 1975; WHO, 1979). This, which has been notable in France since 1973, has recently been emphasized by several authors (LAPIERRE *et al.*, 1977; PENE *et al.*, 1977).

We have drawn attention to this phenomenon since 1975, and have tried to point out its principal epidemiological and clinical aspects (GENTILINI *et al.*, 1975; TRAPE, 1975).

Despite the rising cost of fuel, the significant reduction in the cost of air fares in the past ten years has played a major part in the spectacular development of tourism in the tropical regions of the world, and, at the same time, has encouraged more immigrant workers to fly home on holiday. Several factors have contributed to the increased number of recorded cases of imported malaria, including the setbacks suffered by eradication programmes in malarious areas of the world and the lack of information for tourists about the dangerous risks they run and the necessity for chemoprophylaxis.

Frequency

In the Pitié-Salpêtrière hospital group in Paris, 443 cases of malaria were diagnosed from 1970 to 1979. The annual number of cases has shown a steady progression during this period, rising from seven in 1970 to 93 in 1979 (Fig. 1).

Species of plasmodia

Plasmodium falciparum was the most commonly found species occurring in 308 cases (69.7%), followed by *P. ovale* in 64 cases (14.4%), *P. vivax* in 65 (14.6%), *P. malariae* in 24 (5.4%) and, lastly, an exceptional case of *P. cynomolgi bastianellii*. In four cases (0.9%) the species of *Plasmodium* could not be identified. The 23 cases of species associated

were included in this total number: *P. falciparum*—*P. malariae* (seven cases), *P. falciparum*—*P. ovale* (three cases), *P. falciparum*—*P. vivax* (12 cases) and *P. malariae*—*P. ovale* (one case).

Monthly breakdown

A seasonal peak is noted regularly each year from August to October (Fig. 2). This increase corresponds with the return to France of many summer holidaymakers and is explained by the seasonal peak for travel and the coincidence of the rainy season in the major part of Africa and tropical Asia, where the transmission of malaria resulting from the multiplication of the vectors is particularly active.

However, the fact that malaria cases are observed more and more frequently throughout the year is explained by the increase in intercontinental business trips and winter holidays and the frequently long incubation period of species other than *P. falciparum*.

Observations

Out of 443 patients diagnosed as malaria cases, 192 were observed by our services and their medical reports analysed. There were 123 cases of *P. falciparum*, 35 of *P. ovale*, 20 of *P. vivax*, seven of *P. malariae*, one of *P. cynomolgi bastianellii* and one unidentified case. In five, two species were associated — *P. falciparum* and *P. vivax* in three cases and *P. falciparum* and *P. malariae* in two.

Nationality

More than half of the patients were French (60.9%). Among the immigrants, the patients originating from Black Africa (including Madagascar and the Comoro Islands) were the most numerous (33.4%). A few patients came from other parts of the world (Table I). 97% of the African

Table I—Nationality of patients

Nationality	Number of cases	Percentage
French	117	60.9%
Black Africans	64	33.4%
North Africans	2	1%
Asians	3	1.6%
Latin-Americans	4	2.1%
Europeans (France excluded)	2	1%

*Present address: Office de la Recherche Scientifique et Technique Outre-Mer (O.R.S.T.O.M.), 70-74 route d'Aulnay, 93140 Bondy, France.

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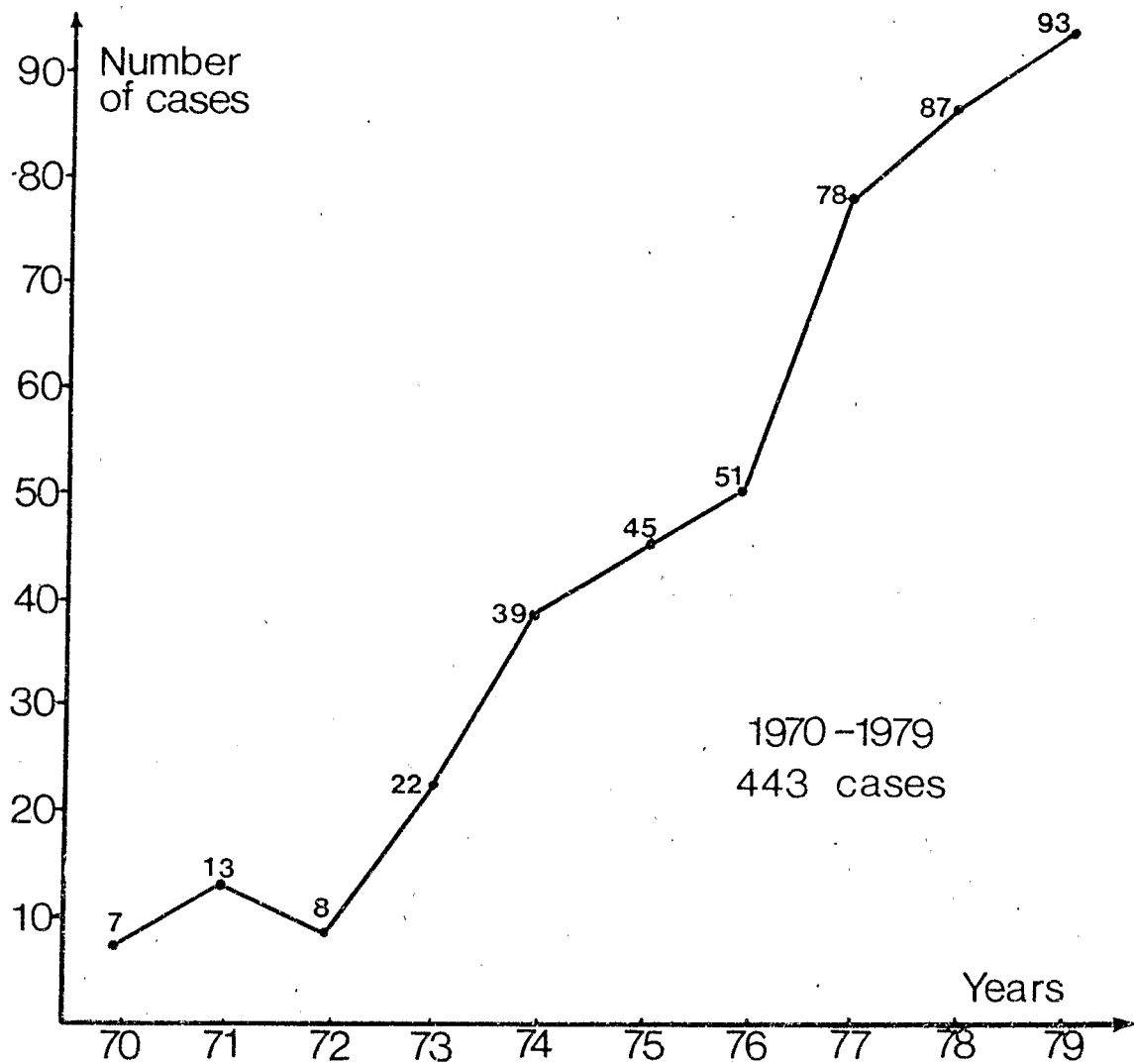


Fig. 1. Annual distribution of the malaria cases diagnosed between 1970 and 1979.

Table II—Origin of infection

Origin of infection	Number of cases	Percentage
Black Africa	160	83.3%
North Africa	2	1%
Asia	17	8.9%
Latin America	7	3.7%
France	3	1.5%
Unknown origin	3	1.6%

patients came from French-speaking countries, particularly Mali, Senegal, Congo, Ivory Coast and Camerouns. 80% of them were immigrants, workers or students, in France for two to 16 years

(average six years), re-infected during a holiday at home. 20% were "newcomers", living in Africa before their stay in France.

Origin of the infection

Black Africa (83.3%) is the area where malaria is most often contracted, especially in the French-speaking countries of West and Central Africa, and particularly in five (Gabon, Mali, Camerouns, Ivory Coast and Senegal) where 61.2% of the African cases originated (Table II). The important economic and cultural exchanges between France and Black Africa explain the role played by the African continent. A significant number (8.9%) came from Asia, most of the disease being contracted in Indo-China and Thailand. The few cases contracted in

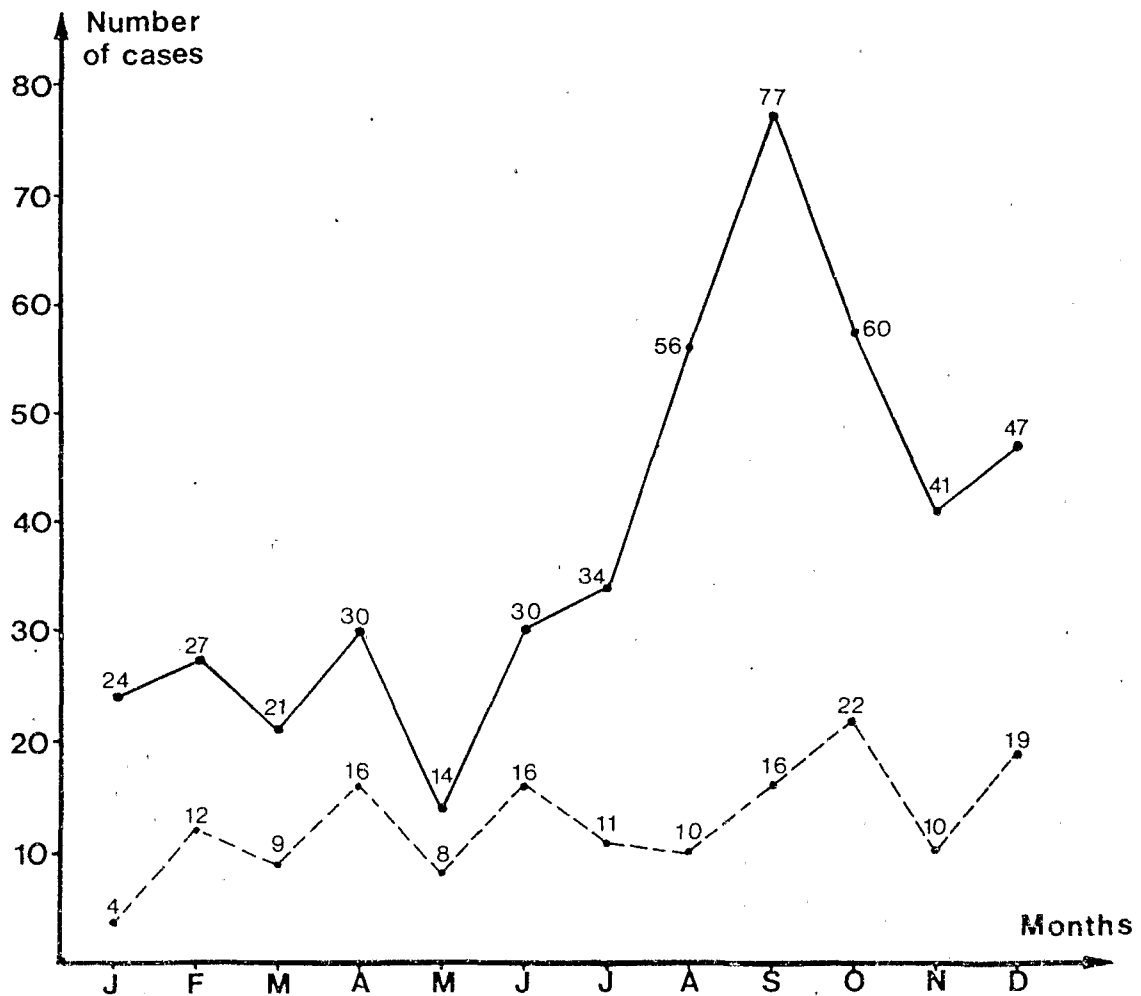


Fig. 2. Monthly distribution of the malaria cases diagnosed between 1970 and 1979. The plain line corresponds to the total number of cases, the broken line to *P. vivax*, *P. ovale* and *P. malariae*.

Latin America came from Guyana, Brazil and Haiti. Three native cases were observed. The first was an infant suffering from congenital malaria, the second an adult probably infected near Orly Airport by an *Anopheles* carried to France on an aircraft (GENTILINI *et al.*, 1978), and the third a laboratory technician who was accidentally infected by *P. cynomolgi bastianellii* (DRUILHE *et al.*, 1980).

Age and Sex

We noted that young adults (20 to 29 years) were clearly the most numerous. This was more significant in the case of French patients (56.5%) than in immigrants (41.9%) where patients aged from 30 to 39 years were equally involved (Table III). Male patients (72.5%) were almost three times as numerous as females (27.5%), a proportion which is slightly higher for immigrants than for French patients (75.5% instead of 69.8%).

Incubation

It is often difficult to establish accurately the incubation period because of the multiple variations in the duration of stay in endemic areas.

Table III—Age of Patients

Age group (years)	Natives		Foreigners		Total	
	No. of cases	%	No. of cases	%	No. of cases	%
0-9	2	1.8	6	8.1	8	4.3
10-19	3	2.6	4	5.4	7	3.7
20-29	65	56.5	31	41.9	96	50.8
30-39	15	13.0	21	28.4	36	19.0
40-49	11	9.6	10	13.5	21	11.1
50-59	16	13.9	2	2.7	18	9.5
≥ 60	3	2.6	—	—	3	1.6
Total	115	100%	74	100%	189	100%

Table IV—*Plasmodium falciparum*: time interval between departure from endemic zone and the onset of malaria symptoms

Time interval (days)	No. of cases	Percentage
Before departure	14	15.7
0-7	40	45.0
8-14	20	22.5
15-30	7	7.8
31-60	4	4.5
>60	4	4.5

Table V—Time interval between departure from endemic area and onset of malaria symptoms*

Time interval (months)	<i>P. ovale</i>	<i>P. vivax</i>	<i>P. malariae</i>
Before departure	0	3 (15.8)	1 (11.1)
1	4 (12.1)	7 (36.9)	4 (44.5)
2	3 (9.1)	1 (5.3)	0
3-4	14 (42.4)	2 (10.5)	2 (22.2)
5-6	5 (15.1)	2 (10.5)	1 (11.1)
7-8	3 (9.1)	2 (10.5)	0
9-10	2 (6.1)	0	1 (11.1)
≥10	2 (6.1)	2 (10.5)	0

*percentages are given in parentheses.

The time which elapsed between the departure from the endemic area and the first clinical symptoms—which therefore corresponds to the minimum incubation period—is nevertheless a very useful criterion for diagnosis and prophylaxis. In case of infection by *P. falciparum*, this period is less than 15 days in 83.2% of cases and over two months in only 4.5% (Table IV). The maximum period that we observed was eight months. This period is generally much longer for the other *Plasmodium* species (Table V). For *P. ovale* a period shorter than two months was observed in only 21.2% of cases. The onset of symptoms took place in the third or fourth month in 42.4% and later in 36.4%. The maximum period observed was 15 months. For *P. vivax*, 58% showed some signs before two months 10.5% during the third and fourth month and 31.5% after this period. For *P. malariae* five out of nine cases showed no symptoms before two months had elapsed.

Signs and symptoms

P. falciparum is generally discovered with a febrile syndrome (92%) and more rarely through a general check-up for the diagnosis of an isolated splenomegaly (2%) or for different symptoms presented by people who have taken holidays in tropical countries (6%). Serious digestive disorders (continuous vomiting, sometimes accompanied by abdominal pains) which can mislead the diagnosis occurred in 37% of cases. Sometimes examination showed splenomegaly (26%) and jaundice (11%). Eleven cases of cerebral malaria (9%) were observed but none were fatal. A febrile syndrome was constantly found in *P. ovale* infections, sometimes associated with splenomegaly (42%) and jaundice (11%). Digestive symptoms seemed to be the

exception: only one child suffered from vomiting. A febrile syndrome was always present in *P. vivax* infections, sometimes associated with splenomegaly (43%) and digestive symptoms (7%).

Diagnosis

Diagnosis was established by the presence of malaria parasites on thin or thick films; these two techniques were always associated. The thin smear, examined for 10 to 20 min by a trained technician or a physician, was negative in 20% of cases and it was the thick smear that enabled diagnosis to be made.

The proportion of negative thin films was higher for *P. ovale* (27%) than for *P. falciparum* (18%), *P. vivax* (17%) or *P. malariae* (20%). In 35% of cases the patients had taken chloroquine some days before the blood sample was taken. In 26% of cases the patients had lived for some years in the endemic area without taking any preventive medication. The parasite was only discovered when they had a check-up or when there was a change in their general condition. In 26% the blood sample was taken from the patients at the onset of symptoms, particularly fever (four cases of *P. ovale*, one of *P. falciparum*, one of *P. malariae*). In 13%, the sample was taken from the patient several days or weeks after the onset of symptoms which had spontaneously subsided.

Circumstances of appearance

Almost all cases of *P. falciparum* malaria were due to lack of chemoprophylaxis or to its premature interruption. Nevertheless, in three of our patients *P. falciparum* occurred in spite of a correct chemoprophylaxis. In these cases, the strains of *P. falciparum* originated from South-east Asia or the Amazon region of Brazil and were probably resistant to chloroquine. Many of the patients suffering from *P. ovale* and *P. vivax* malaria had correctly followed their chemoprophylaxis.

The length of the incubation period and the possibility of relapses shows that although the period of two months normally advised can prevent attacks of *P. falciparum* in almost all cases, it cannot provide protection for the more delayed attacks in cases of infection with other species of *Plasmodium*.

Treatment

As a general rule, chloroquine (Nivaquine[®]) was used (for 82%) and the most frequent regimen was five tablets of 0.100g per day for five consecutive days (intra-muscular injection was used when vomiting precluded the swallowing of tablets). Sometimes the association of sulphadoxine 0.50g and pyrimethamine 0.025g (Fansidar[®]) was preferred (11%). The serious cases (7%) were treated by an i.v. drip of quinine hydrochloride (25 mg/kg body-weight) followed by Fansidar (R) i.m. or Nivaquine (R) per os.

Comments

Species of malaria

A high incidence of *P. falciparum* infections (between 63 and 78%) has been recorded in all

recent reports published in France (CHARMOT *et al.*, 1979; COULAUD *et al.*, 1979; LAPIERRE *et al.*, 1977; PENE *et al.*, 1977; TRAPE, 1975). Some differences appear in the rate of infection by other species varying from 3.6 to 13.9% for *P. ovale*, from 10.2 to 25.2% for *P. vivax* and from 1.5 to 9.7% for *P. malariae*.

The rate of infection with *P. falciparum* is considerably less in Great Britain (46.3%) and West Germany (43.8%) than in France (BRUCE-CHWATT *et al.*, 1974; WHO, 1979). *P. vivax* was the most commonly found species in Birmingham (68.6%) (ANSDELL *et al.*, 1974) and its frequency is only slightly lower than that of *P. falciparum* in Great Britain (42.4%) and in West Germany (40.2%).

Patients' origin

A remarkably similar proportion of French patients (between 49 and 51%) has been reported by all authors (CHARMOT *et al.*, 1979; LAPIERRE *et al.*, 1977; PENE *et al.*, 1977; TRAPE, 1975). A slightly higher proportion (60.8%) was noted in our service, although a rate of 50.2% was also found in the group of 443 patients studied at the Pitié-Salpêtrière hospital group. The proportion of Black Africans is also similar (around 40%) throughout the series. Asians and Latin-Americans are usually less numerous and only the proportion of North Africans shows considerable variation since, in certain hospitals, they account for up to 11% of the patients (LAPIERRE *et al.*, 1977) compared with 1.3% in our service. The predominance of Black Africa as the source of the disease is stressed by all authors, other regions playing only a minor role. We found the differences already mentioned only in regard to North Africa.

In Great Britain, the proportion of infected immigrants reaching 77% in Birmingham seems to be higher than in France (ANSDELL *et al.*, 1974; BRUCE-CHWATT *et al.*, 1974). This figure comprises mainly Indians and Pakistanis, with a small percentage of Africans. Malaria is frequently contracted in Asia (63% for Birmingham, 34% for the whole of the country), hence the large number of *P. vivax* infections. However the role of Black Africa remains important (33 and 61% respectively) because of the African origin of a significant part of the Indian-Pakistani community.

In West Germany, the proportion of patients infected in North Africa, which was significant from 1963 to 1972 (78.3%) has since decreased (66.5%); this is due to the arrival of Asiatic refugees and the resurgence of malaria in Turkey, country of origin of many immigrant workers. However, over-all, the number of African cases has increased four times in 10 years (WHO, 1979).

Incubation

The period of time between departure from an endemic zone and appearance of the first clinical symptoms rarely exceeds one or two months for *P. falciparum* (CARME *et al.*, 1978). BRUCE-CHWATT *et al.*, (1974) in a study of 221 cases, observed that only 12 presented symptoms after one month (5.5%) and only two after five months. Of 111 patients observed by TRAPE (1975), three became ill after two months and one during the ninth

month. A much longer interval is noted in cases of *P. vivax*, *P. ovale* and *P. malariae* infections. Of 208 cases of *P. vivax* malaria reported by BRUCE-CHWATT *et al.* (1974), 60% showed some symptoms after one month and 27% after five months; out of 23 cases of *P. malariae*, 34.8% showed symptoms after five months. CHARMOT *et al.* (1979) noticed an incubation period longer than five months in 43.2% of 44 cases of *P. ovale* infection.

Incidence of imported malaria in France

The declaration of imported malaria in France became obligatory only in March, 1980. The evaluation of the number of cases observed each year is therefore hazardous. BRUMPT *et al.* (1978) estimated that the annual number of cases was 2000, 20 fatal. It is possible that the current incidence of imported malaria in France is much higher. 29 fatal cases were notified to the health authorities from 1971 to 1974, 13 for 1974 only (WHO, 1971, 1972, 1973, 1977).

In the series of cases reported in France in the last few years, the proportion of deaths is, one of 136, two of 96 and two of 204, respectively, (LAPIERRE *et al.*, 1977; PENE *et al.*, 1977; TRAPE, 1975). In our service however there were no fatal cases, even though 11 patients had cerebral malaria. Rapidity of diagnosis and treatment are essential requirements for preventing death. It often depends on the precision of the inquiries made by the first physician consulted as the patient often forgets to mention even a recent holiday. Once the possibility of a tropical disease is considered, the patient is generally transferred to specialists, enabling a diagnosis to be quickly established.

Conclusion

The current resurgence of imported malaria in Europe necessitates the creation of an improved information service for physicians who, in general, are not familiar with this disease and for travellers who, far too often, do not take the indispensable chemoprophylaxis or interrupt it prematurely.

For travellers, airlines could play an important role by providing the necessary information to those heading for the endemic zones. Several methods could be considered: booklets distributed to passengers, information sheets placed in the aircraft (similar to those which already exist for safety procedures) and information broadcasts on loudspeakers or through individual earphones. The recent initiative taken by some companies on their African lines should be encouraged and extended.

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