MEDICAL PRACTICE

Contemporary Themes

Malaria in the United Kingdom

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Over the past decade the United Kingdom had the second highest number of cases of imported malaria among European countries. There has been a substantial rise in recorded cases of malaria during the past three years though some of it may be due to improved notification. Fatal cases of malaria in visitors to Africa have averaged 6.5% of reported infections due to *Plasmodium falciparum*. Attacks of vivax malaria may occur several months after travellers return from a malarious country.

Introduction

The danger of imported tropical disease generally and malaria in particular has been repeatedly emphasized during the past decade.¹⁻⁵ Recently the World Health Organization drew attention to the problem of imported malaria and provided guidance for international travellers.⁶

Indigenous malaria, so common in the past, has now disappeared from Europe with the exception of a small zone of Greek Macedonia and parts of Azerbaidjan and Georgia of the U.S.S.R. Yet the latest reports indicate a striking rise in the incidence of imported malaria in several European countries,⁷ where the yearly number of notified cases has increased from 839 in 1967 to 1,240 in 1972. Over these six years the total number of cases of imported malaria in 25 European

countries was 5,704, with the highest figures in Portugal (2,447), the United Kingdom (1,201), the U.S.S.R. (444), Federal Germany (394), Italy (177), Sweden (157), the Netherlands (133), Spain (131), Greece (110), and Denmark (100).

Between 1962 and 1972 the yearly number of passengers carried by scheduled air services increased from 121 million to 450 million. Non-scheduled commercial air transport also now carries at least 25% of the passengers carried by the scheduled sector.⁸ Tourism plays an important part in this extraordinary mobility.⁹ Figures for world tourism rose from 70 million in 1960 to nearly 200 million in 1972. There was a considerable increase of visitors to Africa, where in 1970 the number of foreign tourists reached 3.9 million.¹⁰

Tourist arrivals in the U.K. rose from 200,000 in 1946 to 7.2 million in 1971. On the other hand the number of U.K. tourists travelling abroad rose from 1.5 million in 1951 to 8.5 million in 1972; of these nearly one million visited countries outside Europe and many went to tropical areas.^{9,10}

Findings in Great Britain**SURVEILLANCE**

In the U.K. regular surveillance of imported malaria was started in 1954 by the Malaria Reference Laboratory at Horton Hospital—a unit which over the past 48 years has played a prominent part in the development of malaria therapy and in malaria research.¹¹⁻¹³ The responsibility for collection, evaluation, and presentation of epidemiological data about malaria in Britain has recently been transferred to the London School of Hygiene and Tropical Medicine.

A 1969 review by Shute and Maryon¹² mentions some 2,000 cases of malaria reported in Britain in the past; the yearly number of cases of malaria in England and Wales contracted abroad during the period 1960-69 according to official reports^{14,15} is shown in table I. The trend of the occurrence of

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TABLE I—Number of Cases of Malaria in England and Wales 1960-9

Year	1960	61	62	63	64	65	66	67	68	69
No. of cases	82	88	128	93	88	71	62	92	130	113

Occurrence of imported Malaria in United Kingdom 1953-73.

imported malaria during the past 20 years is shown in the chart.

Though malaria has been a notifiable disease in Britain since 1919 it is not always reported even when the infection is diagnosed correctly. The mean figure of 100 cases per year during the decade 1960-9 is probably well below the actual incidence. The figures in table I do not include the data for Scotland and Northern Ireland even though international health organizations often quote the records for England and Wales as referring to the United Kingdom. In Scotland alone about 20 cases per year were notified during the period.¹⁶ The Public Health Laboratory Service reports are more complete and include notifications from Scotland and Northern Ireland.¹⁷

To assess the recent trends of imported malaria in this country we summarized the data for the period 1970-2 (table II). These figures represent only the cases of malaria confirmed by microscopical examination. Some notifications not supported by blood examinations are also recorded by the Registrar General. These cases (26 in 1972) represent about another 10% over and above the confirmed cases; they are not included in table II.

The table shows a striking increase of imported malaria in tourists, nearly 30% of all cases now, and in immigrants (who account for nearly 40%). These conclusions must be treated with caution because in one third of all cases the information is not available. Data for 1973 are not yet complete, but the provisional figures indicate a further rise in the incidence of imported malaria to 541 cases. The probable origin of malaria infection in 645 patients is shown in table III.

TABLE II—Occurrence of Malaria in the United Kingdom 1970-2 and Circumstances of Infection. Percentages have been calculated only from Cases for which Information was Available.

	1970	71	72	Total (%)
Short visits abroad:				
Schoolchildren visiting parents	5	10	8	23 (5.8)
Tourists	3	13	65	82 (20.4)
Business travellers	6	8	10	24 (6.0)
Travellers from non-malarious areas who call at malarious countries	9	10	7	26 (6.5)
Longer-term residents:				
Servicemen	10	12	12	34 (8.6)
Others	28	26	38	92 (23.1)
Immigrants from malarious areas	7	27	84	118 (29.6)
No information	33	155	112	300
Total	101	261	336	698

A case of transfusion malaria due to *Plasmodium falciparum* occurred in Britain in 1969 and was discovered only by perusal of existing records. The donor was a visitor from Africa and his blood, meant to be used only for preparation of plasma, was mistakenly used for whole blood transfusion. The recipient had a mild pyrexia with low parasitaemia and spontaneous recovery. The case had some unusual features and was not widely reported. It was the seventh case of accidental transfusion malaria recorded here since 1936.

MORTALITY FROM MALARIA

In view of the severity of undiagnosed and untreated cases of *P. falciparum* infections in non-immune individuals data on mortality from malaria are of particular interest (table IV). The pattern of these events is depressingly repetitive; the following note represents a typical death due to falciparum malaria in Britain:

TABLE IV—Mortality from Malaria United Kingdom 1970-2

Year	No. of Reported Cases of <i>P. falciparum</i> Infections	Deaths	
		No.	%
1970	49	5	10.2
1971	138	9	6.5
1972	136	7	5.2
Total	323	21	6.5

A man aged 55 was recently admitted who had been in Nigeria for two weeks, but was not offered or advised about prophylaxis for malaria. Ten days after his return he developed symptoms of a chest infection and was treated with antibiotics. Five days later he collapsed and was admitted to hospital in coma and profound shock. Cerebral malaria was considered, and the blood film showed heavy infection with *Plasmodium falciparum*. Despite intensive treatment his condition slowly deteriorated, and he died a week later.

Other cases have been described in reports of the Public Health Laboratory Service.¹⁷

TABLE III—Occurrence of Malaria in United Kingdom according to Species of *Plasmodium* and Origin of Infection 1970-2

	<i>P. vivax</i>			<i>P. falciparum</i>			<i>P. malariae</i>			<i>P. ovale</i>			Not stated			All Species		
	1970	71	72	1970	71	72	1970	71	72	1970	71	72	1970	71	72	1970	71	72
Africa	11	14	19	40	123	125	6	8	9	3	12	12	2	1	7	62	158	172
Middle East	2	5	15	—	—	1	—	—	—	—	—	—	—	—	—	2	5	16
Asia	18	54	127	2	5	3	2	—	3	—	3	1	—	1	1	22	63	135
South America	—	4	3	—	—	—	—	—	—	—	—	—	—	—	—	—	4	3
Other Areas	1	1	1	—	—	—	—	—	—	—	—	—	—	—	—	1	1	1
Not Stated	6	13	2	7	10	7	1	2	—	—	1	—	—	4	—	14	30	9
Total Cases	38	91	167	49	138	136	9	10	12	3	16	13	2	6	8	101	261	336
	37.6%	34.8%	49.7%	49.0%	52.9%	40.5%	8.9%	3.8%	3.6%	3.0%	6.1%	3.9%	2.0%	2.3%	2.4%	100%	100%	100%
Total Cases for 1970-2	296			323			31			32			16			698		
	42.4%			46.3%			4.4%			4.6%			2.3%			100%		

INTERVAL BETWEEN RETURN TO U.K. AND ONSET OF MALARIA

Information on the time interval between return to the United Kingdom and the onset of malaria is available in 484 cases (table V). In nearly 70% of these cases symptoms of malaria appeared within one month after return, particularly with falciparum infections. Delayed attacks of malaria are not uncommon, however, and in 15% of cases attacks may occur six months or later after leaving the endemic area. Not surprisingly this happens almost exclusively in infections with *P. vivax*, *P. malariae*, and *P. ovale*. The relevance of this phenomenon to the diagnosis of the disease, long after the exposure to the infection has been forgotten, needs no emphasis.

TABLE V—Time Interval between Return to United Kingdom and Onset of Malaria due to various Species of Plasmodia (1970-2). Percentages are given in Parentheses

Time Interval (Months)	<i>P. vivax</i>	<i>P. falciparum</i>	<i>P. malariae</i>	<i>P. ovale</i>	Species Not stated	Total
≤1	83 (40.0)	209 (94.5)	10 (43.5)	7 (30.4)	8 (89.0)	317 (65.5)
>1-5	69 (33.2)	10* (4.5)	5 (21.7)	11* (47.8)	0	95 (19.6)
6-11	44 (21.2)	2 (1.0)	5 (21.7)	3 (13.1)	1 (11.0)	55 (11.4)
≥12	12 (5.8)	0	3 (13.1)	2 (8.7)	0	17 (3.5)
Total	208 (100)	221 (100)	23 (100)	23 (100)	9 (100)	484 (100)

*Includes two cases of concomitant infection with *P. ovale* and *P. falciparum*.

DETECTION

Serological methods for detection of malaria infection are now increasingly used for epidemiological studies. The indirect fluorescent antibody (I.F.A.) test indicates with high probability present or previous infection with malaria while the titre of tests that gave positive results may differentiate between individuals recently infected and those who were infected fairly long ago. To assess the value of this test and because of the high proportion of cases of malaria found in 1971-2 in immigrants (see table II) we investigated in November 1972 nearly 1,000 Asian refugees from Uganda, housed temporarily at the Newbury reception camp (see table VI). Methods used in this study have been described before;¹⁸ only one antigen (*P. falciparum*) was used. Sixteen immigrants were sent to hospital with the diagnosis of malaria. Blood slides taken from the remainder of the group all gave negative results.

Interpretation of results of I.F.A. tests shown in table VI must be cautious, especially since only one antigen was used. The titre of the test which gave a positive result depends on several factors such as the degree and time of previous infection and the amount of treatment. Sulzer and Wilson¹⁹ using an I.F.A. test of comparable sensitivity to ours considered that in non-immune subjects a titre of 1/256 was highly suggestive of a current malaria infection. Some of the Uganda Asians would probably have been infected previously and this

would result in higher malaria antibody titres. Nevertheless, if one arbitrarily assumes a titre of 1/1024 in this group, indicating a recent infection, one may surmise that some 4% of these immigrants could show a recrudescence or relapse of malaria in the future.

Discussion

Malaria holds first place among the exotic diseases increasingly observed in countries with temperate climates. Some of the figures quoted for several European countries call for comment.

SOURCES OF IMPORTED MALARIA

The high number (2,447) of imported cases in Portugal during 1967-72 was due to repatriation of soldiers from African territories.⁷ The same situation occurred in the U.S.A. where during the same period 17,619 cases of imported malaria were recorded. This "fourth wave of imported malaria" in the U.S.A. was related to Vietnam war and 94% of cases occurred in servicemen.²⁰

In the U.S.S.R. during 1960-8 the number of imported cases was 1,382.²¹ Some 30% of these cases (mainly due to *P. vivax*) were seen in Soviet citizens while the remainder (usually *P. falciparum* infections) were diagnosed in visitors, many of whom were African students. All foreign students arriving in the Soviet Union undergo periodic blood examinations, and 20% of African students had clinical malaria on their return to Moscow after summer holidays spent in their own countries.²² In France 11 falciparum infections were found in 960 students, who came mainly from West and central Africa.²³

The United Kingdom had the second highest number of cases of imported malaria in Europe during the relevant period, and there has been a steady rise in these infections. Provisional figures for 1973 indicate that the number has further increased to 541, with *P. vivax* representing some 60% of identified species of the parasite and *P. falciparum* about 25%.

Over the past three years there has not been much difference between the proportion of imported malaria in short-term visitors to the tropics and in longer-term residents, the latter group being preponderant. In 1972, however, the number of cases among both tourist and immigrants showed a striking rise and contributed to the 25% increase in the total number of cases. Of patients with *P. falciparum* infection 95% came from tropical Africa while most (72%) cases of *P. vivax* originated on the Asian mainland.

It should be emphasized that the cases of imported malaria reported by the Public Health Service Laboratories, or otherwise notified, represent only a small proportion of persons visiting the U.K. or returning from abroad who are or who might have been carriers of malaria parasites. An unknown but substantial percentage of temporary visitors from highly malarial

TABLE VI—Indirect Fluorescent Antibody (I.F.A.) Tests on Blood Samples from Uganda Asian Refugees

Age Groups	No. Examined	No. of Sera with the Following I.F.A. Titres Against <i>P. falciparum</i> :					Titres		
							>1/16		≥1/1024
		<1/16	1/16	1/64	1/256	≥1/1024	% Positive	G.M.T.	% Positive
12-23 Months ..	6	0					0	0	0
2-4 Years ..	52	50	2				0	0	0
5-9 Years ..	141	132	5	2	2		2.8	39	0
10-14 Years ..	153	140	5	3	3	2	5.2	208	1.3
15-19 Years ..	110	91	9	5	3	2	9.1	169	1.8
20-39 Years ..	272	152	16	47	42	15	38.3	169	5.5
≥40 Years ..	174	69	18	39	34	14	50.0	168	8.0
Total	908	634	55	96	84	33			

G.M.T. = Geometrical mean titre.

ous areas of the world may have scanty parasitaemia with few if any clinical symptoms because of a high degree of acquired immunity.

GROUPS MOST AT RISK

Obviously not all travellers or long-term visitors to the tropics are equally exposed to malaria. Rural areas with lower standards of sanitation and housing are more likely to be highly malarious though several infections with *P. falciparum* have been traced to a few hours spent at an African airport. The risk of malaria infection in crews of civilian airlines has been repeatedly stressed.²¹ Missionaries, tourists, and children returning to school after holidays with parents living overseas are also particularly exposed to malaria.

In young people working in volunteer service programmes malaria with its overall incidence of 2% per year appears to be a lesser problem in comparison with gastrointestinal diseases, accidents, upper respiratory infections, skin diseases, and infectious hepatitis.²⁵ The 1971/2 reports of the British Voluntary Service Overseas indicate, however, that the annual contingent some 2,500 strong have had an average malaria incidence of 10.5% while abroad; in parts of Africa the incidence was 20% and 25% of volunteers returning from Papua New Guinea had relapses of vivax malaria.²⁶

MORTALITY FROM FALCIPARUM MALARIA

The number of deaths due to falciparum malaria in people who have been infected overseas causes much concern. During the period 1955-64 in 15 selected non-malarious countries of Europe, North America, and the South Pacific there were 468 deaths out of 4,075 notified cases of imported malaria.²⁷ A recent report prepared on the basis of W.H.O. data⁷ states that in Europe during the period 1967-72 there were 62 deaths from malaria, nearly all of them due to *P. falciparum* (1,709 cases). Because the disease is under reported the true fatality rate cannot be calculated with any degree of certainty.

Available records indicate that during the period 1954-72 there have been no fewer than 79 deaths due to *P. falciparum* infections, in the United Kingdom,^{2, 14, 15} giving an estimated fatality rate of about 11.6%; recently this rate has shown a decrease to 6% (see table IV). This high death rate in falciparum malaria is common in other European countries, including the Netherlands²⁸ West Germany,^{29, 31} and Switzerland.³²

The fact that the overall fatality rate of falciparum malaria in the U.S.A. over the period 1963-72 was only 1.4% may suggest a better standard of diagnosis and treatment than in many European countries.²⁰ When servicemen are omitted from this calculation, however, the fatality rate for civilians was about 6.0%.

A striking increase in imported malaria was recently observed in Cape Town, South Africa, where out of 47 hospital cases of malaria, 36 had falciparum infection and five died.³³

MERCHANT SEAMEN

Falciparum malaria in merchant seamen is a particularly serious problem. There are few areas of occupational health where statistical data are less complete and reliable. Health services for seafarers are an international problem,³⁴ and a study in the Swedish merchant navy has pointed out the difficulties of diagnosis and treatment of malaria on ships plying between Europe and the tropics: obviously many fatal cases of malaria were not reported or were misdiagnosed.

During 1960-71 13 deaths in the British Merchant navy were recorded in the annual reports of the Marine Division of the Department of Trade and Industry as due to malaria and blackwater fever. However, some of the 295 deaths oc-

curing at sea and ascribed to "ill-defined and unknown causes" were probably due to malaria.

Outbreaks of malaria on board ship with several fatalities during a voyage have been described before in Norway, the U.S.S.R., and other countries,^{6, 7, 8} and statistics given for Germany,^{39, 40} U.S.A.⁴¹ and Poland.^{42, 43} The explanation of the high incidence and fatality of malaria in seafarers is simple. In addition to a greater degree of exposure to the infection (especially in African ports) there are difficulties in consulting a doctor. Moreover, antimalaria discipline and chemoprophylaxis are notoriously lax among ships' crews. The German study³⁹ showed that out of 340 seamen with malaria only 20% were taking any antimalarial drugs while in the tropics. Moreover, only 20% of these patients were referred to hospital with the suspected diagnosis of malaria.

DIFFICULTIES IN DIAGNOSIS AND TREATMENT

Travellers exposed to malaria in tropical countries and particularly in Africa are often careless about preventive measures and especially about taking prophylactic drugs. The long interval (up to 30 days or longer) between the infection and the onset of symptoms adds to the probability of overlooking malaria in a febrile patient especially when gastrointestinal symptoms, myalgia, arthralgia, jaundice, etc., complicate the clinical picture.

Simple questioning of the patient about his movements during the previous months is often omitted by the doctor. The list of wrong diagnoses of malaria compiled by various authors^{5, 24, 44} includes dysentery, influenza, dengue, nephritis, hepatitis, heat stroke, etc. Often enough, within a few days after first seeing his doctor the patient suddenly shows signs of cerebral involvement or hyperpyrexia or renal failure. An emergency admission to hospital may lead to correct diagnosis and treatment, but by then a severe infection with *P. falciparum* may not respond to belated therapeutic measures.

The possibility of transfusion malaria in a patient who has never been abroad but has been infected by a symptomless blood donor should be kept in mind. A recent world wide survey showed that the number of 2,000 cases of transfusion malaria in published and unpublished reports is an underestimate.⁴⁴ In 1972 alone the notified number of cases of "induced" malaria in Europe was 19, and in 1971 Spain had an outbreak of 54 cases of vivax malaria, due to indiscriminate use of previously infected donors by a blood bank.

The problem of imported malaria may be complicated by the occurrence of chloroquine-resistant strains of *P. falciparum* in South East Asia and parts of South America.⁵ There is evidence of a few imported infections with *P. falciparum* resistant to 4-aminoquinolines, and consequently the knowledge of the place where the infection may have been contracted is of value.

Information on delayed attacks of malaria in people returning from the tropics (see table V) is of particular interest in view of recent observations in Denmark.^{45, 46} Hortsman⁴⁵ emphasized that attacks of vivax malaria may be seen in some people seven to nine months after their return from the tropics, and this is very important both clinically and from the point of view of public health. Data available in this country and in the U.S.A.⁴⁷ confirm this statement. The other important point is that the usual chemoprophylactic drugs taken by the traveller while in the tropics and for one month after his return may protect him from falciparum malaria but not from the true relapsing infections with other species of plasmodia. Many delayed attacks of vivax malaria may occur for up to one and a half years in spite of regular prophylaxis with proguanil, pyrimethamine, or chloroquine, and the radical cure can usually be obtained by the proper treatment with primaquine (15 mg daily for 14 days).

This delay is most probably due to the "abortive" action of antimalarial drugs on the primary infection with the sub-

sequent relapses appearing after a latent period. On the other hand strains of *P. vivax* with inherent long incubation periods are found in temperate countries,^{45, 46} though probably some such strains can also be found in the tropics.⁴⁸

The resurgence of malaria due to local transmission ("introduced malaria") is unlikely in Europe though a small outbreak of vivax infection in Corsica in 1971-2 was a reminder that this possibility cannot be excluded.⁷ In countries where the disease has been eradicated but where the anopheles vector persists surveillance of malaria is of particular importance. This has been done by setting up malaria reference centres in Portugal, the U.K., the U.S.A., and Australia.

Conclusions

The possibility of reintroduction of malaria into countries where the disease has disappeared was assessed by the W.H.O.,⁴⁹ the report stressed the need for better information from national and international sources, improvement of present diagnostic methods for screening potential malaria carriers entering a country, co-ordination between immigration and health authorities, etc. International health regulations cannot be applied to malaria even though they provide general rules that could be of value in unusual circumstances. Restrictions on travel or compulsory reporting of possible malaria infection are difficult to put into practice.

Protection from malaria infection when travelling in the tropics is to a large extent the responsibility of the individual concerned. The medical profession can only advise the public at large and organizations concerned with overseas travel of the risk of the infection. Details of protective activity have been described before and attention should be drawn to these "verités premières," so often ignored.

When it comes to the recognition of imported malaria three cardinal principles may provide the necessary guidance:

(a) malaria must be suspected in any patient with fever of unknown or doubtful origin who has ever been to tropical areas or who has had a blood transfusion up to three months before the start of a febrile illness; (b) the clinical picture of malaria is very variable and the best way of diagnosing the infection is by microscopical examination of the blood, preferably before any specific treatment is given; (c) *P. falciparum* malaria in a non-immune individual needs rapid and complete treatment—it must often be considered as a medical emergency.

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