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Paper

Imported malaria to Northern Ireland: improving surveillance for better intervention

GM Ong, B Smyth

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ABSTRACT

Malaria is a preventable disease, which is under notified in the UK. This study sought to evaluate the current surveillance arrangements in Northern Ireland (NI), describe the epidemiology of malaria and make appropriate recommendations.

A case was defined as a resident or visitor to NI with laboratory confirmed malaria, diagnosed by the NI haematology laboratories and/or the Malaria Reference Laboratory (MRL) from 1998-2003. Laboratory data were compared with notifications and hospital admission data.

One hundred and fourteen laboratory cases were identified compared with 63 notifications received by the regional surveillance centre. Six cases were associated with two episodes of malaria reflecting recurrence and or reinfection. *P. falciparum* was the most common infection with two fatalities reported; this was particularly associated with travel to West Africa. Most cases were associated with short visits to malarious areas. Thirty-three percent of all cases did not take prophylaxis and, of those that did, approximately half were taking a prophylactic regime appropriate to the region visited.

This study highlights the need for improved surveillance of malaria in order to capture risk factors and other relevant information to inform public and professional education. This would facilitate increasing local awareness, enhancing prescription of and compliance with appropriate chemoprophylaxis and enabling early diagnosis and treatment of malaria.

INTRODUCTION

Malaria is a disease that affects 40% of the world's population, mainly in tropical and subtropical countries. The World Health Organisation estimates that malaria accounts for more than 300 million acute illnesses and at least one million deaths annually.[1] Human malaria is caused by *Plasmodium falciparum, P. malariae, P. ovale* and *P. vivax. P. falciparum* has the highest fatality rate compared with the other three types of malaria infection.[2] The number of imported cases of *P. falciparum* in the UK has risen steadily since the 1970s.[3] Challenges to the prevention and control of malaria include raising public awareness and compliance with appropriate chemoprophylaxis. A further challenge is the development of antimicrobial resistance to common anti-malarial drugs such as chloroquine which are used for prophylaxis.

Malaria is a statutory notifiable disease in Northern Ireland requiring the clinician to notify the patient to the Director of Public Health of the Health and Social Services Board. In practice, these notifications are received by the Consultant in Communicable Disease Control (CCDC). Notifications are based on clinical suspicion and laboratory confirmation is not required for the purposes of the legislation. However malaria notifications are frequently under-reported.[4]

The aims of this study were (a) to evaluate the current malaria surveillance arrangements in NI; (b) to describe the epidemiology of imported malaria to NI between 1998-2003; and (c) to suggest appropriate recommendations to improve surveillance for better prevention and control of imported malaria.

METHODS

A case was defined as an individual who was a resident or visitor to Northern Ireland with malaria confirmed by the NI haematology laboratories and/or the London Malaria Reference Laboratory (MRL) from 1998-2003.

The current MRL patient report form was used for data collection. The data was entered on to Epi Info version 6.03 (Centres for Disease Control, Atlanta) and the analysis undertaken at the Communicable Disease Surveillance Centre, Northern Ireland [CDSC (NI)].

Grace Ong, Consultant Microbiologist, Department of Microbiology, Kelvin Building, Royal Hospitals Trust, Belfast BT12 6BA.

Brian Smyth, Consultant Regional Epidemiologist, Communicable Disease Surveillance Centre (Northern Ireland), Belfast City Hospital Trust, Belfast BT9 7AB.

Correspondence to Dr Ong.

Email: grace.ong@bll.n-i.nhs.uk

Data sources

Data was sought on age; gender; onset of illness; dates and reason for travel; countries visited; prophylaxis taken; method of diagnosis; species of parasite; and outcome of illness. Information on date of birth and gender was used to identify duplicate reports.

Data was obtained from the haematology laboratories, MRL, Regional Infectious Diseases Unit, CsCDC, Department of Health, Social Services and Public Safety (DHSSPS) Regional Information Branch, Registrar General and CDSC (NI).

RESULTS

Data Source

Requests for malaria tests originated from the Regional Infectious Diseases Unit, acute medical wards and general practitioners (GP). There were 1774 requests (including repeats) for malaria tests (1998-2003) submitted to the main Belfast laboratory of which the majority (approximately 80%) were from hospital sources. Of the 114 positive cases, 99 were from the hospital (i.e. Regional Infectious Diseases Unit and acute medical wards).

Laboratory reports refer to malaria confirmed reports from the haematology laboratories and/or MRL. Fig. 1 illustrates the number of laboratory-confirmed malaria cases per annum and the annual number of falciparum cases from 1998-2003. One hundred and fourteen laboratory confirmed cases were identified which equate to an average incidence rate of 1.1 per 100,000 population using the 2002 mid year estimate. These 114 cases involved 108 individuals as six patients had either a relapse and/or reinfection. Table I describes the proportion of laboratory confirmed malaria cases from each data source. There were 10 cases identified by the MRL with no corresponding haematology laboratory report.

Age, gender, ethnicity

The average age of patients was 33 years (age range 2-80, median 31 years, mode 22 years). The male to female ratio was 2:1 (78 males, 36 females). Ethnicity was available on 104/114 patients of whom 94/104 (90%) were Caucasian. The other ethnic backgrounds 10/104 (9%) included Black African (7) and South-East Asian (3).

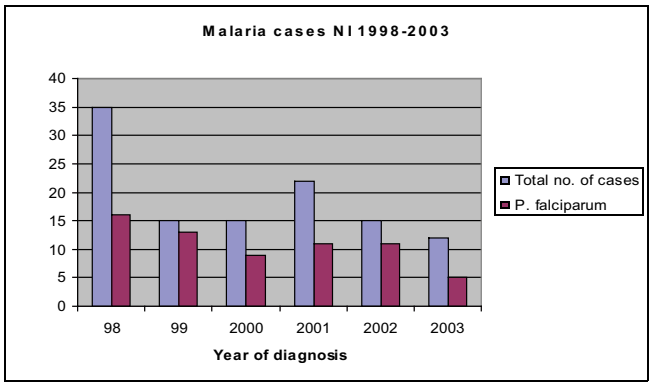

Fig 1. Annual number of laboratory-confirmed malaria cases and those of P. falciparum, 1998-2003, Northern Ireland.

Travel history

Travel history was available on 110/114 (97%) patients. The most frequently visited region was Africa (98/110, 89%), with West Africa being the region with the greatest number of associated cases (39/110, 36%). South-East Asia was visited by 8/110 (7%) of cases followed by India/Pakistan (4/110, 4%).

The reasons for travel were obtained from 52/114 (46%) cases (*Table II*) together with history of prophylaxis. The majority were short term travellers (29/52, 57%) comprising holiday makers or those on short mission trips (18/52, 35%) and business/professional travellers (11/52, 21%). Long term travellers (12/52, 24%) included expatriates living, studying and working abroad (including armed forces) and individuals visiting friends and relatives in their country of origin (4/52, 8%). In 1998 there was a cohort of nine patients infected with *P. ovale* following a church organised trip to Kenya. Seven cases (7/52, 14%) were visitors to NI including three members of an African children's choir.

The length of stay in malarious regions was available on 98/114 (86%) patients. The average duration was 7 months (206 days) but the most common period was two weeks (14 days). The length of stay ranged from five days to eight years with a median of two months (60 days). However there were four patients (UK citizens living abroad) whose length of stay was unknown.

Plasmodium species

The most common species of malaria was *P. falciparum* (65/114, 57%), followed by *P. vivax* (21/114, 18%), *P. ovale* (20/114, 18%) and *P. malariae* (2/114, 2%). The plasmodium species was not identified in three cases. A combination of two plasmodium species (*P. ovale* and *P. falciparum, P. vivax* and *P. falciparum, P. ovale* and *P. malariae*) was noted in three patients. A church group was associated with nine reports of *P. ovale* (see earlier).

Table III describes the number of cases, classified by species, associated with travel history. There were 65 cases with *P. falciparum* infection all of whom had visited Africa. Thirty-three (33/39, 85%) of those acquiring malaria in West Africa had infection with *P. falciparum* compared with 18 (18/37, 49%) visiting East Africa. All those presenting with malaria and travel to the Indian sub-continent and South East Asia had *P. vivax* infection. The time interval for presentation of disease as calculated from date of arrival into the UK to date of laboratory diagnosis is given in Table IV.

Prophylaxis

Prophylaxis history was available on 103/114 (90%) cases of which 65/103 (63%) reporting taking prophylaxis and 38/103 (37%) did not. The number of travellers who sought travel advice was not recorded as part of the data collection. However it is presumed that those who took appropriate prophylaxis probably did seek travel advice. Thirty-four (34/65, 52%) travellers took prophylaxis appropriate to the country they were visiting with 25/34 (74%) taking it regularly while abroad but only 13/34 (38%) continued prophylaxis for four weeks on return from travel as advised under current guidelines.

(Accompanying table)

Year	*Total cases*	*Plasmodium species*					
		falciparum	*vivax*	*ovale*	*malariae*	*unknown*	*combination*
98	16	6	12	0	1	0	35
99	13	1	1	0	0	0	15
2000	9	4	2	0	0	0	15
2001	11	4	4	0	2	1	22
2002	11	2	0	1	0	1	15
2003	5	4	1	1	0	1	12
Total	65	21	20	2	3	3	114

The type of prophylaxis taken and countries visited are shown in Table V. Of the 62/98 (63%) travellers to Africa who took prophylaxis, 26 took mefloquine which is one of the drugs of choice in malarious regions with chloroquine resistance. Chloroquine was used in combination with proguanil by 17 travellers to Africa and as a single agent by six cases. Five took doxycycline of which one took it in combination with chloroquine.

Twelve cases travelled to India/Pakistan, South-East Asia and/or Papua New Guinea of whom three took chemoprophylaxis. Each of the three took chloroquine and proguanil, doxycycline and mefloquine as part of the recommended chemoprophylaxis regime.

Table II shows that twenty four (24/29, 83%) short term travellers (previously defined) took prophylaxis of which 11/24 (46%) was consistent with current guidelines. Fourteen of the former (14/24, 58%) took prophylaxis regularly while abroad but only seven (7/24, 29%) continued the regimen for four weeks on return to NI. Eight (8/12, 67%) of the expatriates took prophylaxis of which 5/8 (63%) took the appropriate anti-malarial drug with four (4/8, 50%) taking it regularly while abroad but only one (1/8, 13%) completed the month's course on return. The foreign visitors to NI did not take any prophylaxis and three of the four visiting friends and relatives in their country of origin did not take prophylaxis (*Table II*).

Table I

Number and percentage of confirmed malaria cases by referring source, 1998 – 2003, Northern Ireland (n=114)

Data Source	No. reported (%)
NI haematology labs	104 (91.2)
MRL	33 (28.9)
CCDC	69 (60.5)
CDSC (NI) (notifications)	63 (55.3)
Regional information branch (RIB)	68 (59.6)
Regional Infectious Diseases Unit	80 (70.2)

Inpatient information

The 114 cases were associated with 99 hospital admissions. The inpatient length of stay was available on 88/99 (89%) cases. The mean length of stay was 4 days (range 1-20 days, mode and median of 3 days). Two patients required renal dialysis and three required ICU support. Among the 114 cases were two malaria related deaths (a case fatality rate of 1.8 %). Both were associated with travel to Nigeria and infection with *P. falciparum*. One had not taken chemoprophylaxis and information on the other was missing.

Recurrence

Incomplete treatment or drug resistance may lead to recurrence of malaria. Co-infection with *P. vivax* or *P. ovale* may result in these species lying dormant in a patient resulting in break-through infection if compliance to chemoprophylaxis is poor or inappropriate. Six (6/108, 6%) patients had two episodes of malaria. In this study each malaria episode was counted as one case. The average time interval between the two episodes was 14 months (range 3-46 months). Two had recurrence of falciparum malaria. The remaining four cases had combinations of falciparum malaria followed by infection with *P. ovale* (2), *P. ovale* followed by *P. vivax* (1) and *P. falciparum* and *P. vivax* followed by *P. ovale* (1).

DISCUSSION

This study demonstrated that statutory notifications of malaria were associated with an under-ascertainment rate of 45%. Possible reasons for under notifying include clinicians being unaware that malaria is a notifiable disease and the mechanism for informing the CCDC. It is not a statutory requirement for laboratories to notify all positive results to the CCDC or send laboratory reports to CDSC (NI). The annual incidence rate of imported malaria to Northern Ireland over this six year period (1.1/100,000) is much lower compared to other parts of the UK. This reflects the travel history and ethnicity of the Northern Ireland population, which is predominantly Caucasian. In a study in southeast London the incidence rate of malaria was 38.8 per 100,000 population, which accounted for 14% of all cases in England and Wales in 20004. In this London study only 6.8% of laboratory confirmed cases were formally notified.

Table II

Reason for travel of malaria patients and prophylaxis history, 1998 – 2003, Northern Ireland (n=52)

Reason for travel	*Frequency*	*Percentage %*	*Prophylaxis Taken*	*Prophylaxis Appropriate to region*	*Regularly abroad*	*4 weeks on return*
Short term traveller	29	56.8	24	11	14	7
Expatriates	12	23.5	8	5	4	1
VFR	4	7.6	1	No history	–	–
Foreign visitors to NI	7	13.7	0	n/a	n/a	n/a

VFR= visiting friends and relatives in country of origin.

Table III

Plasmodium species per patient by region of travel, 1998 – 2003, Northern Ireland

Region	*Plasmodium*						*Total*
	falciparum	*vivax*	*ovale*	*malariae*	*unknown*	*combination*	
Africa							
Central	8	2	3	0	0	0	13
East	18 [1]	3	14 [2]	0	1	1 (fal +vivax)	37*
West	33	0	3	2	0	1 (falc+ovale)	39
South	6	3	0	0	0	0 0	9
South East Asia (SEA)	0	8	0	0	0	0 0	8*
India/Pakistan	0	4	0	0	0	0 0	4
Unknown	0	1	0	0	2	1 (oval+mal)	4
Total	65	21	20	2	3	3	114

* 1 patient in each of these regions also visited South America,[1] One patient also travelled to South Africa,[2] One patient also travelled to SEA.

Table IV

Time of presentation (date of lab diagnosis-date of arrival in UK) to hospital/GP for malaria, 1998 – 2003, Northern Ireland (n = 76)

Plasmodium species	*Time interval between arrival to UK and lab diagnosis (days)*		
	Range	*Median*	*Mean*
P. falciparum	(-2)*- 35	8	10
P. vivax	1-365	90	104
P.ovale	14-244	116	116
P.malariae	36-112	74	74
Combination of 2 species	12-20	16	16

Note: *One patient diagnosed 2 days prior to return to UK

Malaria is a relatively uncommon diagnosis in Northern Ireland. Nevertheless the 114 cases reported between 1998 and 2003 contrast with 18 cases of Legionnaires' disease reported over the same period (CDSC (NI) – personal communication). With the growth in air travel, more independent travel, increased immigration and an increasing tendency to buy "last minute" breaks, there is likely to be more travel between Northern Ireland and malarious regions. A recent example is the increased number of patients returning to the UK from Gambia and developing malaria.[5] Travellers need therefore to be reminded of appropriate precautions and the importance of alerting their general practitioners to their travel history should they develop fever on return from a malarious region. Falciparum malaria usually presents early within two weeks of being bitten but can present up to 90 days later whereas ovale and vivax malaria has been reported to present from 20 days to 10 months on return.[6] Collation of risk factor information on imported malaria enables the development of targeted public and professional awareness programmes for this mainly preventable and curable infection.

Risk factor information on cases was incomplete particularly with respect to reasons for travel (55%) and chemoprophylaxis (12% either missing or unspecified). To ensure that relevant risk factors and epidemiological information are obtained it is suggested the MRL case questionnaire be routinely used by CsCDC when responding to a clinical notification of malaria. To improve ascertainment it is also recommended that haematology laboratories report positive blood films to CsCDC similar to the reporting arrangements developed with bacteriology laboratories for organisms of public health significance. Clinicians also need to be reminded that malaria is a notifiable disease.

Noting the changing epidemiology of malaria and drug resistance, clinicians also require access to updated guidance on chemoprophylaxis and treatment. There are several helpful telephone contact numbers and websites listed in the British National Formulary for healthcare professionals and travellers. These include the Health Protection Agency, the National Travel Health Network and Centre, Health Protection Scotland and the World Health Organisation. Travellers could also contact the London Hospital of Tropical Diseases or MASTA (Minding your Health Abroad) for a travel brief which incurs a charge. These and other sources of travel health advice should be promoted at GP surgeries and high street travel agents in order to raise awareness among intending travellers to malarious areas. Those taking trips abroad at short notice may not have time to consider taking preventative treatment or let appropriate therapeutic drug levels develop before travel. Hence the risk needs to be highlighted at the planning stage by the travel industry. A previous study showed 25% of travel brochures contained no health information at all.[7] Another study showed that spontaneous health warnings

TABLE V

Countries visited and prophylaxis history (n=114)

Drug	*Africa*			*South Asia*					*Total*
	Central	*East*	*West*	*South*	*India*	*Pakistan*	*SEA/ Oceania*	*Un-known*	
NONE TAKEN	5 SEA(1) WA(1)	8 SAM(1)	16	1 WA(1)	1	2	5 SAM(1)	0	38
Mefloquine	3 EA(1)	13	8	2	0	0	1	0	27
Chloroquine +Proguanil	2 SA(1)	10 SA(1)	3	2 EA(1)	0	0	1	0	18
No history available	2 SA(1)	1	3	0	1	0	0	4	11
Chloroquine	0	3 SEA(1)	2	1	0	0	0	0	6
Doxycycline	0	0	3	1	0	0	1	0	5
Medication unspecified	0	1	2 SEA(1)	0	0	0	0	0	3
Proguanil	1 SA (1)	0	0	2 EA(1)	0	0	0	0	3
Proguanil+ mefloquine	0	0	1	0	0	0	0	0	1
Chloroquine +Doxycycline	0	0	1	0	0	0	0	0	1
Fansidar	0	1	0	0	0	0	0	0	1
Total	13	37	39	9	2	2	8	4	114

The letters in superscript indicate the number of travellers that travelled to other places as well. EA= East Africa, WA= West Africa, SA=South Africa, SEA= South east Asia, SAM= South America

Table VI

Comparison of malaria species between studies 1998-2003 Northern Ireland, 1974-1983 Northern Ireland and HPA report 2004

Reports	*Plasmodium species*	
	P. falciparum	*P. vivax*
NI 1974-1983[10]	40% (27/67)	3% (2/67)
NI 1998-2003	56% (65/114)	18% (21/114)
HPA UK report[9] 1987	38% (696/1816)	55% (1005/1816)
HPA UK report[9] 2002	76% (1468/1944)	15% (284/1944)

were not given in 61% (123) of consultations for malarious destinations and, after prompting, only 37% of agents brought up the need for malaria prophylaxis for the journey.[8] This apparent low level of verbal and written advice needs to be addressed by local initiatives and collaboration between public health practitioners and the travel industry.

The epidemiology of imported malaria in Northern Ireland is interesting as it differs from the rest of GB particularly in the ethnicity of cases and reasons for travel. The majority of patients in this study were Caucasians in contrast to GB where the majority were non Caucasian with 50% of all cases visiting friends or relatives.[9] In Northern Ireland the majority were holiday makers and those on business/professional travel, noting that travel history was only available on 45% of cases. Differences were also noted when compared to an earlier study of 67 imported cases of malaria to Northern Ireland between 1974 and 1983 in which the majority of cases were long term residents working overseas (14/67, 21%) whereas short term travellers (29/52, 57%) made up the majority in 1998-2003.[10]

There are over 2000 cases of imported malaria annually in the UK of which the majority are secondary to *P. falciparum*. The predominant species in the UK has changed over the past 15 years from *P. vivax* to *P. falciparum*. In 1987 cases were mainly from the Indian Subcontinent secondary to *P. vivax* infection whereas in 2002 the majority of UK cases were from West Africa with *P. falciparum*.[9] However in NI the predominant species has not changed over the past 15 years.[10] In the UK (1987-2002) P. *falciparum* rates have increased by 38% and *P. vivax* decreased by 40%, whereas in NI the rates of both these species have increased by 15% after 15 years (Table VI).

The average number of malaria deaths from 1977 to 2002 in the UK was 8 per year (a case fatality rate of 0.4% for imported malaria and 1.0% for falciparum cases). In Northern Ireland there were two deaths in six years resulting in an overall case fatality rate (CFR) of 1.8%. The CFR for falciparum was nearly twice as high at 3.1%.

P. vivax and *P. ovale* have persistent liver stages and can give rise to relapses up to a year after the initial infection whereas *P. falciparum* rarely persists for more than two years. *P. malariae* may persist in the bloodstream for many years. The time interval between arrival in the UK from a malarious region and the date of laboratory diagnosis confirms that patients with *P. falciparum* tend to present early whereas those with *P. vivax* and *P. ovale* infection tend to present late. Four patients had two episodes of malaria with two different species. This would suggest breakthrough infection with a species in the dormant phase resulting from co-infection or not complying with the prophylaxis regime and acquiring repeated malarial infections from visiting malarious regions. These cases also illustrate that the physician needs to be aware that a patient treated for one malaria parasite may be infected with another parasite that may be lying dormant.

The current guidelines (2003) recommend four steps to prevent malaria in travellers:[11] (a) awareness of the risk of malaria; (b) preventing and avoiding mosquito bites by using appropriate insecticides, repellents, sleeping in a screened room and using bed nets; (c) compliance with appropriate chemoprophylaxis and (d) diagnosing breakthrough malaria swiftly and obtaining prompt treatment. A useful publication on malaria prophylaxis for long –term travellers was also published in the same year.[12]

Under current guidelines, mefloquine is the drug of choice for travel to Africa and chloroquine plus proguanil for South Asia (Indian subcontinent) and low risk places in South East Asia (Indonesia /Malaysia) or mefloquine, doxycycline or atovaquone/proguanil in Oceania (Papua New Guinea).[11] In this study mefloquine was the most common form of prophylaxis and mainly used for travellers to Africa. Nevertheless a third of cases did not take any form of chemoprophylaxis. Chloroquine and proguanil was the second most common chemoprophylactic drug regime. Over a third of travellers to Africa took chloroquine as prophylaxis despite chloroquine resistance being a major problem with *P. falciparum*. Travellers to the Indian subcontinent, South-East Asia and Oceania who took prophylaxis took the appropriate drug combination.

RECOMMENDATIONS

The following are recommended:

- increase awareness among clinicians that malaria is a notifiable disease through multidisciplinary educational meetings.
- haematology laboratories to report positive results to CsCDC for public health purposes as part of good laboratory practice
- enhanced surveillance (using a standard proforma such as the MRL case report form) to be used by CsCDC

to collect appropriate epidemiological and risk factor information which is essential for targeted public and professional education.

– CDSC (NI) should produce regular epidemiological reports to inform public and professional education including the travel industry.

– GPs and travel agents require information on accessing appropriate travel health advice.

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The authors have no conflict of interest

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Correction:

In the article by Lappin *et al* (Hox genes: seductive science, Mysterious mechanisms. *Ulster Med J* 2006; **75(1):** 23-31) there are two small corrections:

Page 23; Abstract: line 3– '... at 7p15, 17p21,' should read '... at 7p15, 17q21'

Page 26; Hox GENES IN VERTEBRATES, Line 5 '... at 7p15, 17p21, 12q13' should read '... at 7p15, 17q21, 12q 13'

This was amended on the website PDF online on 7th February 2006 and the correct PDF may be downloaded free from the website.

Patrick Morrison, Honorary Editor.

