UK experience regarding malaria antibody tests and their contribution to blood safety

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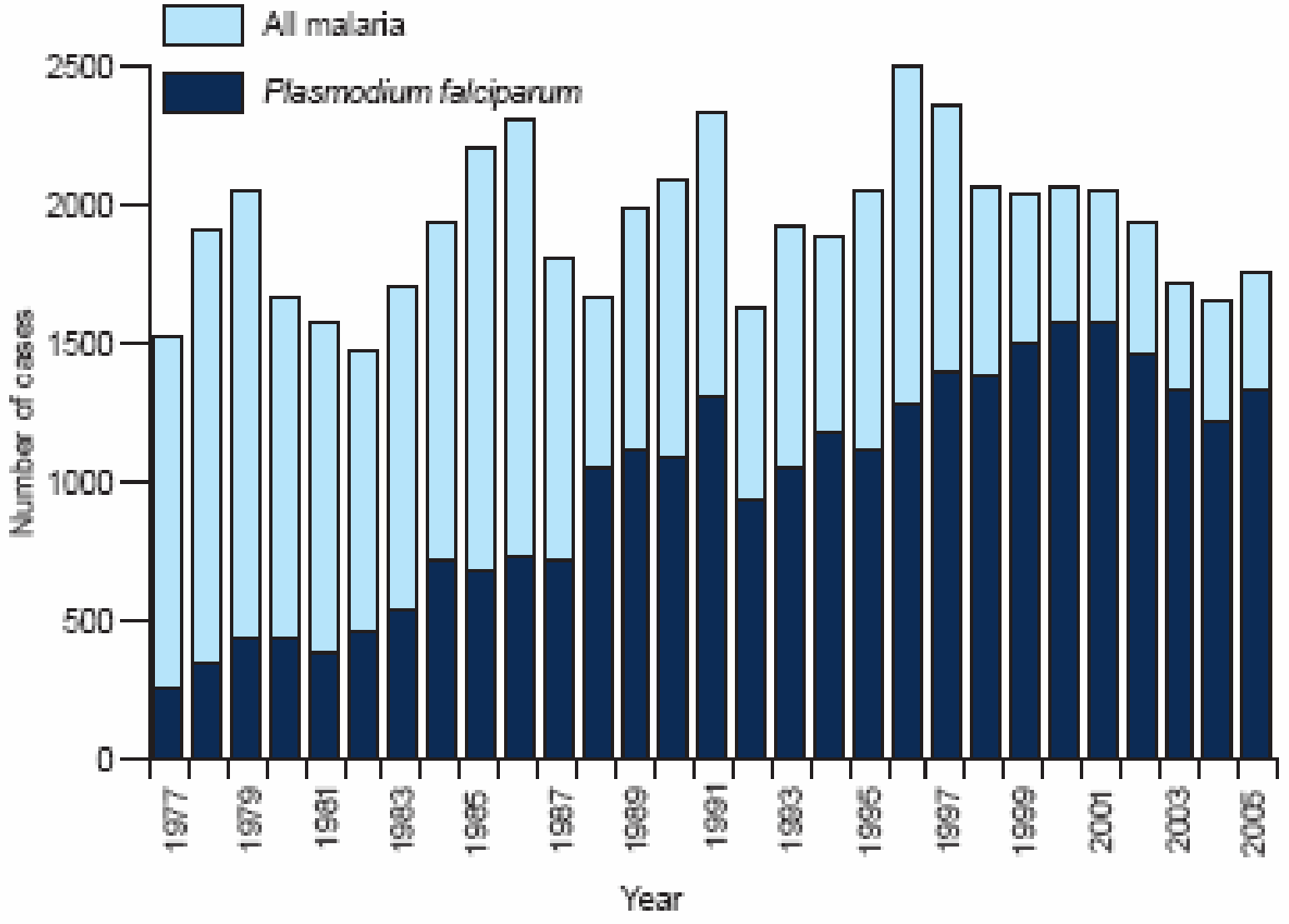
Figure 1 Cases of malaria in the United Kingdom: 2005



UK Malaria 2005

• Plasmodium falciparum	1338
• Plasmodium vivax	258
• Plasmodium ovale	116
• Plasmodium malariae	29
• Mixed infections	10
• Unspecified	3
TOTAL	**1754**

UK MRL Data 2005

	Species of malaria									
Geographic Area	P.f	P.v	P.m	P.o	Pf+Pv	Pf+Pm	Pf+Po	Po+Pv	P.unsp	Total
North Africa	–	–	–	–	–	–	–	–	–	–
Central Africa	35	–	2	12	–	1	1	–	–	51
East Africa	126	11	4	12	–	–	1	–	–	154
Southern Africa	46	1	–	2	–	–	–	–	–	49
West Africa	781	2	10	57	–	1	3	–	–	854
Africa - unspec.	26	–	–	3	–	–	–	–	1	30
Middle East	2	–	–	–	–	–	–	–	–	2
Asia	15	162	–	–	–	–	–	–	–	177
Asia -unspecified	–	–	–	–	–	–	–	–	–	–
Far East/S.E.Asia	2	1	–	–	1	–	–	–	–	4
Far East - unspec.	–	1	–	–	–	–	–	–	–	1
Central/S.America	1	17	2	1	–	–	–	–	–	21
Oceania	1	10	–	–	–	–	–	–	–	11
Not given	303	53	11	29	–	1	–	1	2	400
Total	**1338**	**258**	**29**	**116**	**1**	**3**	**5**	**1**	**3**	**1754**

UK MRL Data 2005

Population group	P. falciparum	P. vivax	Other	Total
New entrant	55	27	18	100
Visiting family in country of origin	482	58	27	567
UK citizen living abroad	15	2	2	19
Civilian sea/air crew	1	–	–	1
British armed services	8	2	5	15
Business/professional travel	46	4	6	56
Foreign student studying in UK	16	11	5	32
Holiday travel	59	19	5	83
Foreign visitor ill while in UK	66	22	6	94
Children visiting parents living abroad	2	–	–	2
Not stated	588	113	84	785

UK MRL Data 2004

Table 2 Ethnicity of travellers with malaria: 2004

Ethnicity, where stated	No of cases
White British	124
Other white	27
Black African	547
Black Caribbean	16
Other black	8
Indian sub continent	111
Southeast Asian	3
Other Asian	9
Other ethnicity	4
Categories – not on standard surveillance form*	
African descent *	365
Asian descent *	71
Ethnicity not stated	331
Total	**1616**

* These are not self-reported categories

Risk Groups for TTM

Travellers:

- No, or almost no, immunity to malaria
- Almost always symptomatic if parasites present; thus excluded from donation
- Almost all P.falciparum in this group occurs in the first 2 months; virtually none after 6m

Risk Groups for TTM

"Residents"

- Almost all brought up in sub-Saharan Africa
- Still partially immune to malaria disease
- May be asymptomatic but parasitaemic
- May harbour *P.falciparum* for years

TTM in the UK 1986-2006 (1)

- 5 cases, all due to *P.falciparum.* Donors:

1 Semi-immune European, 10y in Africa. History of travel not given. Blood film negative. IFAT strongly positive

2 West African. Blood collected for plasma usage, but inadvertently issued as whole blood after 19 days' storage at 4C in CPDA-1. IFAT strongly positive

TTM in the UK 1986-2006 (2)

3 West African. Donated 2 months after a visit there. Travel history not elicited. IFAT and ELISA positive.

4 African. Donated 2y11m after travel. Exclusion period at that time was 3y. ELISA & IFAT +ve

5 West African. Last visited 8 years previously. Exclusion period at that time was 5y. IFAT and ELISA positive. PCR positive.

Thus, UK Risk Factors for TTM are:

- Failure of history taking
- Administrative error (less likely now)
- “Semi-immune” individuals; both residents AND long-term expatriates

Strategies for Prevention of TTM

- Complete prevention may not be possible with current methodology
- Aim to minimise the risk of introducing malaria parasites into the blood supply, without excluding potential donors unnecessarily

Identifying Potential Malaria Risk in a Donor

- History taking
- Time exclusion
- Screening donor serum for antimalarial antibodies

History

- Geographical location
- Length of time resident; as adult **or** child
- Time elapsed since there
- History of past malaria

Problems with histories

- "Donors may give inaccurate information intentionally or unintentionally, or because they misunderstand the question posed, or because they are unaware or have forgotten that they previously have had malaria."

  Slinger *et al* (2001) *Can Med Assoc J.* **164**: 377

Time Exclusion:
UK Imported Malaria
Time to Presentation (2005)

	<1m	1-5m	6-11m
Falciparum	90%	98.9%	99.4%
Vivax	42%	75%	95.7%
Ovale	25%	76%	98.3%
Malariae	36%	100%	

Antibody Testing by IFAT (1)

Draper and Sirr (1980)

- UK residents and immigrants with malaria
- One week after onset of symptoms

  78% of UK residents

  100% of immigrants

  were **seropositive**

Antibody Testing by IFAT (2)

Draper and Sirr (1980)

- Immigrant patients had

1. Higher mean IFAT titres
2. Longer persistence of antibodies
3. Greater cross-reactions with other (non-falciparum) malarial antigens

Antibody Testing by ELISA (1)

Chiodini *et al* (1997)

ELISA (P.falciparum antigen-based) in UK donor population:

- 0.45% seropositivity in non-TA donors
- 1.5% seropositivity in TA donors
- Could safely retrieve 40,000 red cell units discarded each year in Great Britain

Antibody Testing by ELISA (2)

- But in 1999 the assay was withdrawn from use in the Blood Service due to concerns over its performance
- In 2001 the IFAT (Voller & O'Neill 1971) was introduced in NTML at NBS North London
- Alternative assays were evaluated

Malaria Antibody EIA (Newmarket Laboratories, UK)

- Sequential antibody sandwich EIA
- Recombinant protein antigens:

  P.falciparum MSP1 and 2 MSP2

  P.vivax MSP1
- Run in parallel to IFAT until May 2003

Malaria Antibody EIA and IFAT Testing

Serum samples tested:

- Acute malaria: within 7 days of 1st +ve film
- Follow-up: > or = 8 days after 1st +ve film
- Routine blood donations: no identified malaria risk
- Malaria-risk donations: malaria exposure history, returned 6 to 12 months ago

ACUTE Species	IFAT +ve	NMK +ve	Both +ve	IFAT +ve NMK neg	IFAT neg NMK +ve	Both neg
P.falciparum (n=138)	103 74.3%	114 82.6%	103	0	11	24
P.vivax (n=13)	8 61.5%	11 84.6%	8	0	3	2
P.ovale (n=10)	8 80%	7 70%	7	1	0	3

FOLLOW-UP Species	IFAT +ve	NMK +ve	Both +ve	IFAT +ve NMK neg	IFAT neg NMK +ve	Both neg
P.falciparum (n=46)	46 100%	44 95.7%	44	2 (Days 9 & 31)	0	0
P.vivax (n=5)	3 60%	4 80%	3	0	1	1
P.ovale (n=4)	3 75%	2 50%	2	1	0	1

DONOR CATEGORY	IFAT +ve	NMK +ve	Both +ve	IFAT +ve NMK neg	IFAT neg NMK +ve	Both neg
Low risk (n=880)	NT	0	N/A	N/A	N/A	N/A
Malaria risk (n=13,053)	550 4.21%	714 5.47%	262	288	452	12051

Learning Effect with IFAT

Date	Sera (n)	IFAT only +	EIA only +	Both +ve
Ja 02	792	8.96%	4.54%	2.52%
M 02	576	3.12%	3.3%	3.82%
A 03	917	1.09%	3.48%	1.31%
M 03	990	0.61%	2.92%	1.51%

EIA Negative, IFAT Positive Donor Sera January to April 2003

IFAT Titre	No of sera
1 in 10	1
1 in 20	7
1 in 30	13
1 in 40	7
1 in 60	3
	TOTAL 31

Additional data for non-falciparum malarias

- The following 2 slides show data for the Newmarket ELISA on acute and follow-up sera from patients with *P.malariae*, *P.vivax* and *P.ovale* infections. This information consists of results from the 2004 Vox Sanguinis paper (shown in the preceding slides in this presentation) and from samples tested since the 2004 publication combined into one data set.

ACUTE **Combined**	IFAT +ve	NMK +ve	Both +ve	IFAT +ve NMK neg	IFAT neg NMK +ve	Both neg
P.malariae (n=13)	12 92%	10 77%	10	2	0	1
P.vivax (n=47)	32 68%	40 85%	32	0	11	4
P.ovale (n=36)	32 89%	26 72%	26	6	0	4

FOLLOW-UP **Combined**	IFAT +ve	NMK +ve	Both +ve	IFAT +ve NMK neg	IFAT neg NMK +ve	Both neg
P.malariae (n=1)	1	1	1	0	0	0
P.vivax (n=8)	5 63%	7 88%	5	0	2	1
P.ovale (n=5)	3 60%	2 40%	2	1	0	2

NBS Donor testing for antimalarial antibodies

Year	No. tested	RR	%
2004	42947	1209	2.82
2005	66994	1368	2.04
J-M 06	11988	236	1.97

NBS Donor testing in England, March 2006

HBsAg	19140	[new donors]
Malaria	4258	

Universal testing for malaria antibodies would add another 14882 tests

UK Donor Selection Guidelines
Implemented November 2005

OBLIGATORY

Must not donate if:

- The donor has ever had malaria
- The donor has had an undiagnosed fever (which could have been malaria) while abroad or within six months of leaving a malaria endemic area

UK Donor Selection Guidelines
Implemented November 2005

OBLIGATORY

Must not donate if:

- The donor has lived in any malarial endemic area for a continuous period of six months or more at any time of life
- Less than 12 months after last leaving a malaria endemic area

UK Donor Selection Guidelines
Implemented November 2005

DISCRETIONARY

Donors who have had malaria diagnosed:

- If more than three years have passed since anti-malarial therapy has been completed and symptoms caused by malaria have resolved, perform a validated test for malaria antibody. If this is negative, accept

UK Donor Selection Guidelines
Implemented November 2005

DISCRETIONARY

For other donors:

- If at least six months has passed since the date of the last potential exposure to malaria, or the date of recovery from symptoms that may have been caused by malaria, a validated test for malaria antibody is negative, accept.

Conclusions (1)

- Antibody testing provides a safeguard which is both additional and complementary to history taking and time exclusion and should not be seen as a replacement for those measures in the prevention of transfusion-transmitted malaria

Conclusions (2)

- The UK policy of selective antimalarial antibody screening of donors with possible malaria exposure facilitates earlier donor reinstatement, without detracting from the current safety of the blood supply

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