

Prolonged incubation period of imported *P. vivax* malaria in London¹

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Summary: Between January 1976 and July 1979, 453 cases of malaria were seen at Hillingdon Hospital. The majority of cases were *Plasmodium vivax* infections in Asians from the Punjab in Northern India—either new immigrants or United Kingdom resident Asians returning from holidays. Twenty-four cases were contracted in Africa or the Middle East. Figures are presented showing a considerable increase in cases during the period of study. In *P. vivax* infections the time interval between arrival and development of the acute illness was significantly greater for those subjects entering the United Kingdom in autumn or winter.

Introduction

In recent years there has been a rapidly increasing number of cases of imported malaria in the United Kingdom, particularly from Asia. This has produced a considerable workload for general practitioners, diagnostic services and inpatient facilities. Although in 1969 Shute & Maryon suggested that primary or relapsing cases of *P. vivax* could be a source of local infection in the United Kingdom of *Anopheles maculipennis* and *Anopheles plumbeus*, no transmission by insect vector in this country has been reported since 1954 (Shute 1954). The last outbreak reported in Europe was in Corsica in 1970–1972 (Britt & Hutchinson 1971, De Zulueta 1974).

Hillingdon Hospital serves a community of about 25 000 Asians in West London and has been in an unique position for surveying the morbidity of this population. Over one-tenth of the reported cases of malaria in the United Kingdom in recent years were seen at this hospital (176 of a total of 1738 reported cases in 1978). Many Asians living in Southall are employed at nearby Heathrow Airport and, together with their families, receive the benefit of concessional air travel. A large number spend their holidays visiting relatives in the villages of Northern India from which they originally emigrated. The majority of cases of malaria seen at this hospital were contracted in these villages. The patients were thus either new immigrants who were partially immune to malaria due to previous multiple reinfection or London resident Asian tourists and their children with reduced or no acquired immunity.

The opportunity to study a large number of cases of *P. vivax* malaria in Britain where there is no vector transmission has made it possible to study certain aspects of the natural history of the disease in man. It is apparent that there is a great variation in the incubation period and almost complete absence of clinical attacks of malaria in the winter months. Possible explanations for this are considered.

Methods

This study included all patients diagnosed as having malaria between January 1976 and June 1979 at Hillingdon Hospital. Some of these have previously been reported (Warwick *et al.* 1979). At the time of diagnosis a proforma was completed giving the information detailed in

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this report. The patients were referred by general practitioners, from the Accident & Emergency Department and from St John's Infectious Diseases Hospital, Uxbridge. The patients' peripheral blood was examined in a thin film stained with Giemsa at pH 7.2. All diagnoses were confirmed by the Malaria Reference Laboratory of the Ross Institute at the London School of Hygiene and Tropical Medicine. About one-third of the patients were admitted (e.g. 59 out of 144 total in 1977). The remainder were treated as outpatients. *P. vivax* infection was treated with oral chloroquine 600 mg base and 300 mg base 6 hours later, followed by 150 mg base twice daily for two days. This was followed by a ten-day course of primaquine 7.5 mg base twice daily. Dosage was modified according to body weight in children. Some general practitioners have treated occasional obvious clinical cases without laboratory diagnosis, despite the danger of not identifying *P. falciparum*. The total number of cases may thus be underestimated.

Results

From 1976 to 1978 there were large annual increases in cases of imported malaria. These cases increased from 81 in 1976 to 176 in 1978, representing over 100% increase. Those cases of malaria in newly-arrived Asian immigrants, predominantly from the Punjab, almost doubled from 50 to 97 cases. The largest increase occurred in Asian tourists with almost a three-fold increase from 25 to 72 cases between 1976 and 1978 (Table 1). Our figures for 1979 ceased to be representative of this increasing trend, due to diversion of some cases to a new hospital in the vicinity. The total for the first six months of 1979 was 52. Over the study period the ratio of male to female was 1.13:1. The average age was 26 years reflecting the large numbers of

Table 1. All cases of malaria seen at Hillingdon Hospital from January 1976 to June 1979

	1976	1977	1978	To end of June 1979	Total
Asian immigrant	50	87	97	25	259
Asian tourists	25	50	72	23	170
Asian total	75	137	169	48	429
Others	6	7	7	4	24
Total	81	144	176	52	453

children. There were 84 cases under 16 years of age, representing 19.2% of the total. Of the 429 cases of malaria imported from the Asian subcontinent, all but three were *P. vivax*. There was one case of *P. falciparum* and one of *P. ovale*. The remaining patient has *P. malariae* and also suffered chronic renal failure. All those cases (24) contracted in Africa and the Middle East were due to *P. falciparum* except for a single case of *P. ovale* from Saudi Arabia.

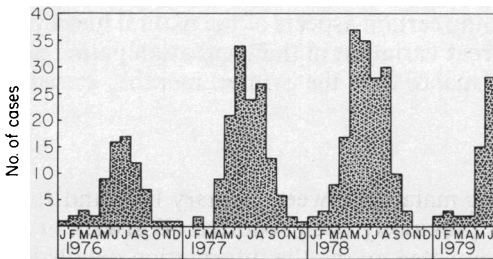


Figure 1. Time of presentation by month and year of all cases of *P. vivax* malaria in the study

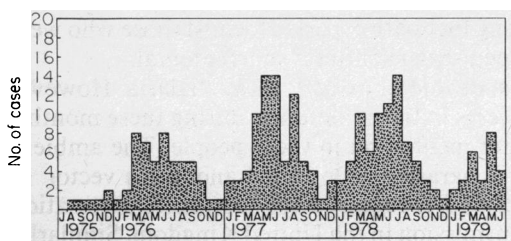


Figure 2. Month of entry into the United Kingdom of all patients who developed an acute attack of *P. vivax* malaria within four months of arrival

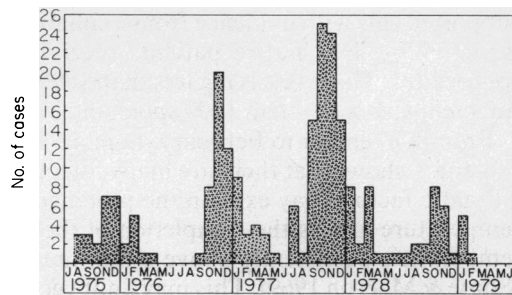


Figure 3. Month of entry into the United Kingdom of all patients who developed an acute attack of *P. vivax* malaria more than four months after arrival

The majority of patients with *P. vivax* malaria presented clinically in the summer months (Figure 1). However, the time of the year these patients left the endemic area did not follow the same distribution. The largest numbers returned to the UK in October and November, although there were also considerable numbers spread throughout the rest of the year. Approximately half the patients (242 out of 426) presented within four months of arrival in the United Kingdom (Figure 2). The remainder all presented within thirteen months (Figure 3). The majority of the former patients, with apparent incubation periods of less than four months, left the endemic area in the summer. They thus presented with their 'attack' of malaria in the same season. However, patients who left the endemic area in the autumn and winter had long 'latent periods' between four and thirteen months and presented in the summer of the following year.

All patients were questioned regarding the taking of malaria prophylaxis, although as would be expected it was only in occasional tourists that this was found. In all, only 7 subjects claimed they took protection and some of these were unable to recall the name of the drug or duration of treatment. There was no evidence indicating transmission of malaria in this country during the 3-and-a-half years covered by this survey.

Discussion

The considerable increase in malaria in West London in recent years has partly been a reflection of an increase that has occurred in Northern India (Professor B Cowan, personal communication). It is also related to the increasing numbers of Asians living in London who spend their holidays in the Punjab. Very few of these tourists take malaria prophylaxis. However, the community health services, travel agencies, etc., are encouraging the use of such prophylactic drugs by travellers to endemic malarial areas. There is no doubt that this would considerably reduce the number of imported cases of *P. falciparum* malaria. However, unless drugs were continued for up to two years after return from the endemic area, *P. vivax* cases would continue (Jopling 1979).

Prolonged incubation periods from 4 to 13 months were found in a large number of patients (196 out of 426) with *P. vivax* in this study. The phenomenon of prolonged incubation in this type of malaria was first described by Korteweg in Holland from observations between the autumn of 1901 and the spring of 1902 (see Swellengrebel & de Buck 1938). The subject has been reviewed more recently by Professor L J Bruce-Chwatt (1977).

Various malariologists have propounded explanations for this phenomenon. Nicolaev (1949) proposed that there were two strains of *P. vivax* with different incubation times. He gave to the variety with a long incubation period a subspecific taxonomic name of *P. vivax hibernans*. It was suggested that this sub-species has adapted to more northern latitudes where the anopheles vector is absent for much of the year. Shute (1946) propounded that the incubation period varied with the sporozoite dosage in the infective bite. He subsequently

supported this with evidence from a collaborative study with Rumanian malariologists (Shute *et al.* 1976). Psychiatric patients receiving malaria therapy were given graded doses of sporozoites. Those receiving less than 1000 had long incubation periods whilst those who were infected with more than 1000 sporozoites developed malaria after a short interval.

From November to February, London is almost devoid of overt *P. vivax* malaria. However this study shows that there are many infected subjects in the community during these months. Climatic factors may explain the prolonged winter incubation in these people. The ambient temperature affects the completion of the malaria parasite cycle in the anopheles vector. A temperature persistently above a minimum of 23.9°C is required for sporozoite maturation (Shute & Maryon 1969). This may limit vector transmission in the United Kingdom. Similarly, a winter inhibition may occur in the human host. Collins and his colleagues (1977) used body surface thermistors to record skin temperatures as a measure of the shell body temperature. They found this to be as low as 29.37°C (± 1.82) in fit young adults wearing light clothing after only 16 minutes at an ambient temperature of 15°C. Far lower ambient temperatures for more prolonged periods are usually experienced in English winters. The relationship between ambient winter temperatures, body shell temperatures and the extended incubation period of *P. vivax* remains to be elucidated.

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References

- Britt R P & Hutchinson R M** (1971) *British Medical Journal* **ii**, 206–208
Bruce-Chwatt L J (1977) *Protozoology* **3**, 143–148
Collins K J, Dore C, Exton-Smith A N, Fox R H, Macdonald I C & Woodward P M (1977) *British Medical Journal* **i**, 353–356
De Zulueta J (1974) *Journal of Tropical Medicine and Hygiene* **76**, 279–282
Jopling W H (1979) *Lancet* **i**, 1340
Nikolaev B P (1949) *Doklady Academy of Sciences, USSR* **67**, 201–204
Shute P G (1946) *Transactions of the Royal Society of Tropical Medicine and Hygiene* **40**, 189–200
Shute P G (1954) *Monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service* **13**, 48–51
Shute P G & Maryon M (1969) *British Medical Journal* **ii**, 781–785
Shute P G et al (1976) *Transactions of the Royal Society of Tropical Medicine and Hygiene* **70**, 474–481
Swellengrebel N H & de Buck A (1938) *Malaria in the Netherlands*. Scheltema and Holkema, Amsterdam; p 57
Warwick R, Swimer G and Britt R P (1979) *Lancet* **i**, 1242