EOSINOPHILIC RESPONSE TO FALCIPARUM MALARIA INFECTIONS

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Abstract. Eosinophilia was a frequently detected incidental finding during a prospective study of malaria seroepidemiology in Thailand. Blood eosinophil counts were performed every 3 months for a year in 823 Thai soldiers on border guard duty in a malaria endemic area. Soldiers developing malaria were admitted to hospital and more frequent eosinophil counts were done. *P. falciparum* parasitemia suppressed preexisting eosinophilia but eosinophilia returned following treatment. *P. vivax* and mixed infections had a similar but less marked effect on the peripheral blood eosinophil count. Eosinophilia in persons from a malaria endemic area may represent a normal late response to malaria infection.

INTRODUCTION

Eosinophilia is a common manifestation of tropical parasitic disease. Increased numbers of circulating eosinophils are well known to be associated with metazoan parasitic infestation (Beeson and Bass, 1977) but an association with malaria and eosinophilia is not generally made. Studies of soldiers with malaria have shown a characteristic pattern of acute eosinopenia followed by eosinophilia after successful treatment (Lowe, 1944; Reiley and Barrett, 1971). Severely ill Thai patients exhibit similar changes in eosinophil count (Davis *et al,* 1991). We report a study of over 800 Thai soldiers stationed on the Thai-Cambodian border in which changes in blood leukocyte counts during prophylaxis and treatment of malaria were prospectively evaluated.

MATERIALS AND METHODS

Four battalions of Thai Military recruits were enrolled into a prospective malaria seroepidemiology study after giving informed consent. The four separate battalions were sequentially enrolled from 1985 to 1987. 823 men entered the study and 642 (78%) completed one year follow-up. A positive history of previous malaria was given by 26% but only 18% had serologic evidence of previous *P. falciparum* infection on enrolment (HK Webster, personal communication).

Blood samples were obtained routinely on all soldiers on entry and every 3 months for one year. While in the endemic area all had thick blood films examined for malaria every 10 days. One tablet of pyrimethamine 12.5 mg and 100 mg dapsone (Maloprim, Wellcome Foundation PLC, UK) was administered weekly. Soldiers developing malaria were hospitalized and treated with quinine and tetracycline. Daily venous blood samples were taken from all hospitalized soldiers. On each sample, a total leukocyte count was performed using a hemocytometer and a differential count was determined from Giemsa stained blood smears. Total eosinophil counts were derived by multiplying the percent eosinophils by the total leukocyte count.

RESULTS

During the period of study 95 soldiers contracted falciparum malaria and these soldiers had at least three separate leukocyte measurements during their illness. A further 60 soldiers had mixed infections with *P. falciparum* and *P. vivax,* and 23 developed vivax malaria alone. Fig 1 shows the eosinophil response following falciparum malaria in 95 soldiers. A progressive increase to levels above 1,000 eosinophils/mm^3 occurred over 13 weeks. One individual soldier's serial results are shown in Fig 2. In this case, falciparum parasitemia repeatedly suppressed eosinophilia but recovery

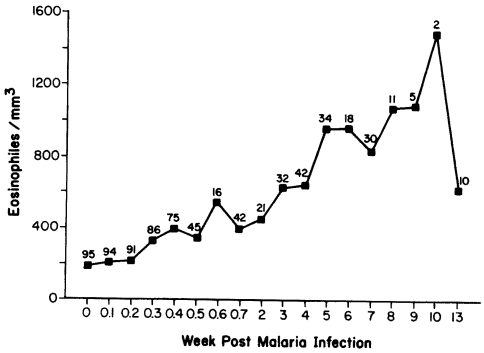

Fig 1—Mean eosinophil counts shown as a function of time since malaria infection in 95 *P. falciparum* patients. Number above point denotes number of separate patients contributing data to the mean.

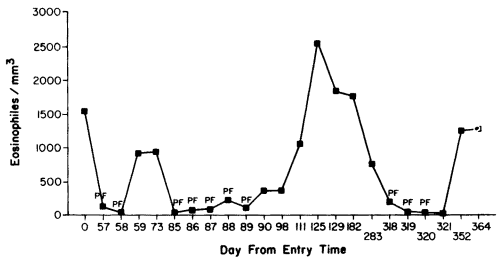

Fig 2—An individual soldier showing progression of eosinopenia and eosinophilia during three falciparum malaria infections. PF designates a positive malaria smear at that point.

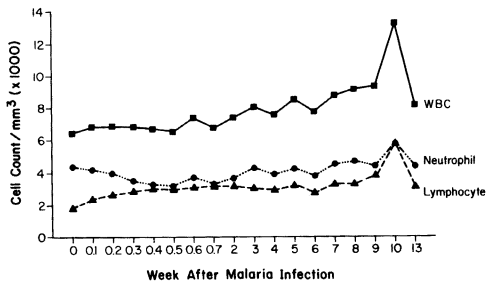

Fig 3—Mean white blood cell, neutrophil and lymphocyte counts in 95 *P. falciparum* patients identical to Fig 1.

of high eosinophil levels occurred over several days post-infection. Similar eosinophil responses were seen in soldiers with mixed or vivax infections

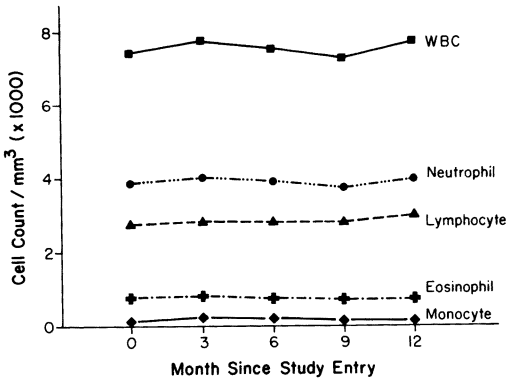

Fig 4—668 uninfected Thai soldiers were routinely screened every 3 months to produce this hematologic profile.

but usually to a lesser extent.

Other leukocyte types remained stable during and after malaria. A mean increase in leukocytes from 6,000 to 8,000/mm^3 during the 10 weeks post infection was due almost entirely to the increase in eosinophils (Fig 3). Uninfected soldiers demonstrated very stable leukocyte and differential counts which did not vary over 12 months (Fig 4).

DISCUSSION

Eosinopenia followed by eosinophilia in response to an acute infection is a general phenomenon seen in many infectious diseases such as pneumonia, meningitis, typhus, typhoid, measles, varicella and dengue (Beeson and Bass, 1977). That malaria can demonstrate this same pattern was shown when Australian soldiers were studied during World War II (Lowe, 1944). Eosinophilia was a common observation in convalescent soldiers who contracted malaria in Vietnam (Reiley and Barrett, 1971).

The observations reported here are an extension of previous studies since eosinophil counts were available prior to malaria infection and length of follow up was long. The lower level of eosinophilia seen with mixed infections and vivax malaria suggests that these infections produce less inflammation. The use of malaria chemoprophylaxis did not contribute to the eosinophilia since the uninfected men demonstrated no change in their eosi-

nophil counts while receiving the same drugs. Previous studies in Thai soldiers have shown a high prevalence of helminth infestation, but this too does not explain the eosinophilia specifically related to malaria.

Eosinophilia is often seen as an incidental finding in a patient returning from the tropics. This can generate concern that a tropical parasitic infection is being suppressed or missed. It is worth remembering that eosinophilia can often be a normal reaction to a previous malaria infection. In this setting, undue attention should not be given to eosinophilia in the absence of other signs of illness.

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