AN ESSAY

ON

MALARIA IN INFANCY AND CHILDHOOD

Submitted for partial fulfilment of the

Mastership Degree in Pediatrics

By

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Cairo

1984

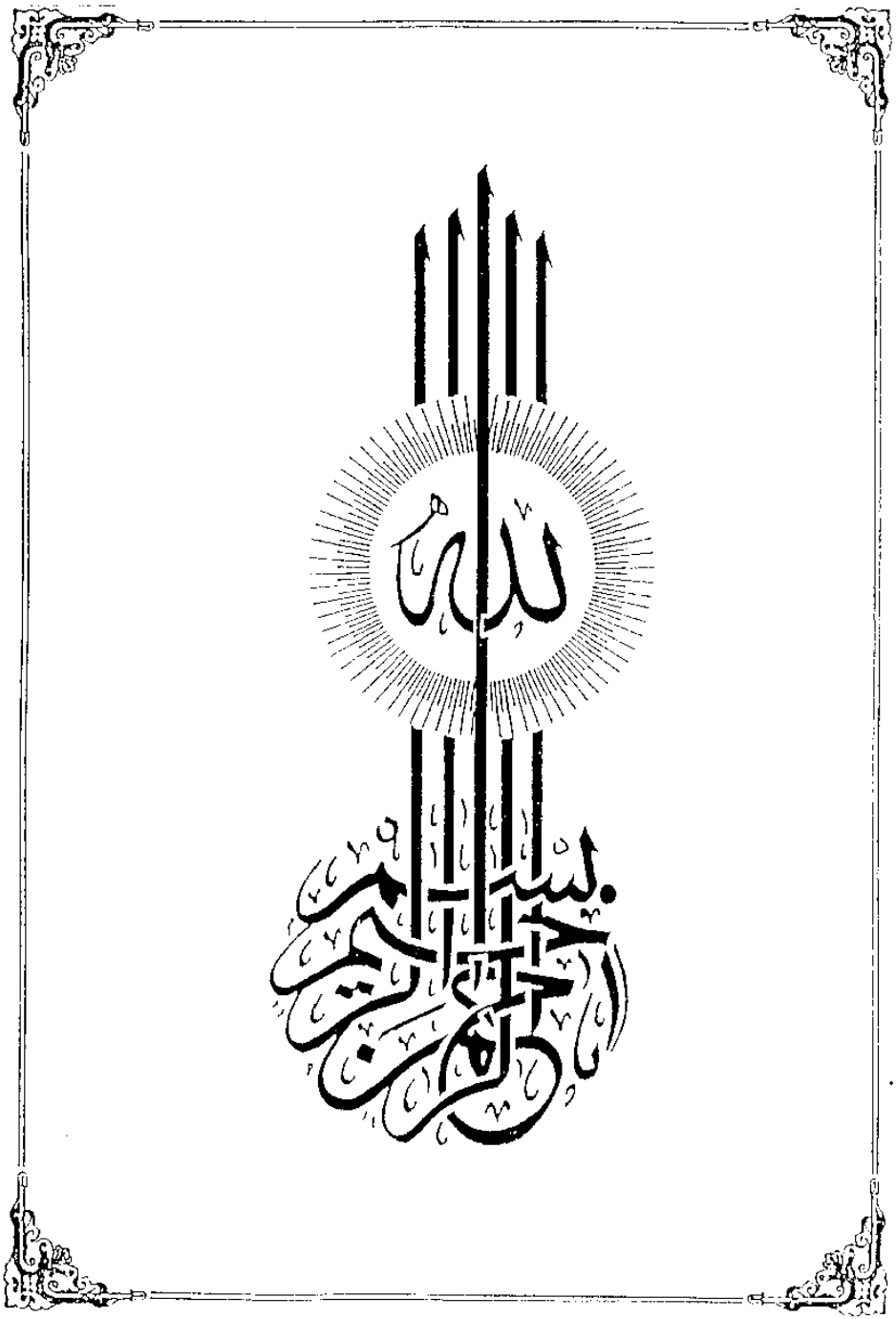
ACKNOWLEDGEMENT

I would like to express my sincere and deep gratitude to my Professor

DR. KHALIL ABD-EL HADI MOURAD

Professor of Paediatrics
Faculty of Medicine
Ain Shams University

For his valuable help, close supervision, maximum accuracy and expert guidance and Supervision.



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INTRODUCTION

Worldwide, malaria is one of the most common infectious diseases of man, causing much morbidity and significant mortality (Louis, 1982).

The first malarial work in Egypt was organized by Ross, who described 300 malaria cases at Ismailia in 1877 (Madwar, 1936). In 1899, John Pole reported in the Kharga and Dakhla Oases, fever usually occurring in late of summer and autumn, that took lives and left most of the population bed-ridden (Madwar, 1936).

The mosquitoes in Egypt were surveyed by Kirkpatrick (1925). Madwar (1936) had shown that Anopheles Pharoensis act as a malaria vector in Egypt noted after the high Nile flood, also Barber and Rice (1937) demonstrated the vector role of Anopheles Pharoensis in Egypt.

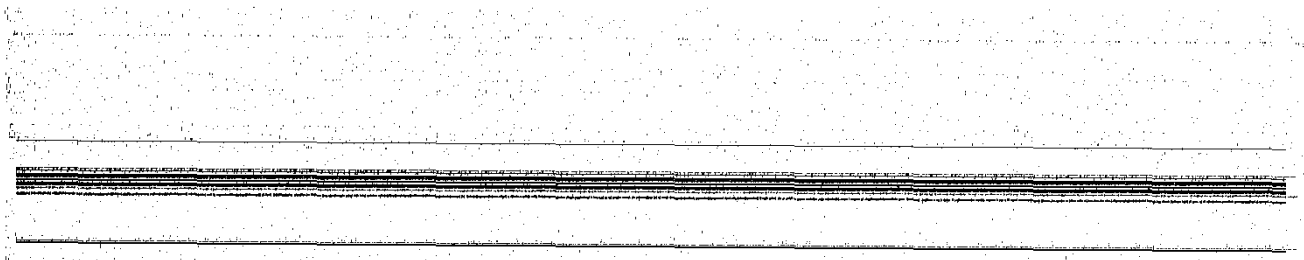
Over 23 thousand deaths occurred during the outbreak of malaria caused by the introduction of a foreign mosquito; Anopheles Gambia in Egypt in the year 1942 (Hassan et al., 1973). This was due to invasion of Anopheles Gambia from north of Sudan to Egypt "Upper Egypt" mainly in Nubia (Sadek, 1973). The species of plasmodium that occurred in Egypt between 1950-1960 are P. Vivax, P. falciparum and P. malaria in the ratio 31:18:1 (Halawani, 1957).

The disease results from invasion of erythrocytes by 1 of 4 species of Protozoan parasites of genus plasmodium

(P. falaparum, P. ovale, P. vivax, P. malariae). It is characterized by high fever, which is often intermittent, and by anemia and splenic enlargement (Gilles, 1966). Of these, P. falciparum most often causes serious morbidity and extensive mortality, and it provides a challenge, because it is resistant to some antimalarial drugs.

With P. falciparum, early therapy is essential, and its effectiveness depends on immediate diagnosis by examination of blood films (Louis, 1982).

Despite worldwide campaigns aimed at eradication of malaria through interruption of its life cycle in the intermediate host (female mosquitoes of the genus Anopheles) malaria continues to be a major cause of morbidity and mortality in many developing nations (Louis, 1982).



LIFE CYCLE OF PLASMODIUM SPECIES

Of the four species pathogenic to man; P. falciparum and P. vivax occur most frequently. All have complex life cycles involving man and mosquitoes (Louis, 1982) (Fig. 1). The usual evolution of disease is as follows:

1. An asexual cycle in the body of man:

This cycle, known as schizogony, consists of the pre-erythrocytic and erythrocytic phases (Antina, 1978).

a) The Pre-erythrocytic phase:

Infection is initiated when sporozoites that have developed in the mosquito are injected into the host during a blood meal. Sporozoites rapidly circulate to the liver within one hour and develop within hepatocytes as exoerythrocytic forms (David, 1982).

After entering the cytoplasm of hepatic cells, growth and nuclear division are rapid, and microscopic cysts (Schizonts) are formed which contain merozoites, some of the cysts of P. vivax and P. ovale persist in the liver for weeks or months, years, paving the way for relapses (Young, 1976), relapses may occur after months to years after initial infection (Yoshida et al., 1979).

The merozoites are released from the liver into the circulation, invade erythrocyte (Young, 1976).

b) Erythrocytic phase (cycle):

Once inside the erythrocytes, plasmodia ingest 25 to 75 percent of the hemoglobin content of the host red cell and begin to grow (Pasvol et al., 1982).

The process of growth and replication in the erythrocyte referred to as schizogony, within 48-72 hours depending on the species of plasmodium. The infected erythrocytes rupture, liberating six to twenty four merozoites, each capable of invading other erythrocytes (Sherman, 1979).

2. Sexual cycle in mosquitoes:

The life cycle is completed when a small percentage of intra-erythrocytic parasites develop into the sexual stages known as gametocytes and are taken up by susceptible feeding anopheline mosquitoes (Trigg, 1979).

In the mosquito's gut, infected red cell lyse, releasing male (microgamate) and female (macrogamate) gamates that unite to form the zygote which subsequently develop as an oocyte in the gut wall (Trigg, 1979). The nucleus of the oocyst divides repeatedly forming sporozoites (Antina, 1978). When oocyst rupture sporozoites released from the mature oocyst migrate to the salivary glands of the mosquito, whence they are injected into host during blood meal (David, 1982).

Invasion of the erythrocytes by the merozoite:

The invasion of erythrocytes by merozoites is initiated at specific receptors on the erythrocyte surface (Louis, 1982). Plasmodium falciparum is the only human malaria parasite found in erythrocytes of all ages, although it preferentially invades young red cells. In contrast, P. vivax primarily invades reticulocytes.

The interaction of merozoites and host cell is highly specific. Merozoites attach to and invade erythrocytes selectively.

Specificity also restricts the interactions of plasmodial species to erythrocytes of susceptible species of hosts (Miller et al., 1975). Some species of plasmodia (e.g. P. vivax in man) invade only the young erythrocytes of the susceptible host. In addition, within a species, genetic host determinants may dictate the susceptibility of the erythrocytes to invasion. Thus, for example, blacks are generally resistant to malaria caused by P. vivax. These considerations suggest that the initial interactions between parasite and host cell entail recognition of specific surface receptors (David, 1982).

Merozoites attach to susceptible erythrocytes via their apical end and induce marked deformations in the erythrocyte membrane, waves of deformations spread out from the initial

site of attachment. Thereafter the merozoite enters the erythrocyte by a process resembling endocytosis and comes to reside in a parasitophorous vacuole created by the invaginated erythrocyte to membrane (Miller et al., 1975).

A parasitophorous vacuole created by the internalization of host membrane envelops the merozoite.

The mechanism by which the infection "slides" over the merozoite is presently unclear, and whether its energy requirements are derived solely from the parasite or also from the host is unknown.

It has been postulated that the histidine-rich protein that may be contained in rhoptries might empty through a common duct during the invagination process and might somehow alter the erythrocyte membrane to permit the deformations involved in the process of invasion (Miller et al., 1975). The invasion process, lasts a mere 20 seconds (David, 1982).

Intracellular Growth:

Epidemiologic evidence indicates that patients with certain erythrocyte abnormalities may be protected from lethal infection with P. falciparum malaria (Pasvol et al., 1982). The plasmodia themselves serve as oxidant stress by oxidizing erythrocyte reduced in nicotinamide adenine dinucleotide

or reduced nicotinamide adenine dinucleotide phosphate or both, thereby hindering the regeneration of reduced glutathion.

Infected cells that were inherently deficient in G-6-p-PD. would therefore be expected to be impaired in their ability to counter these oxidant effects and to lyse prematurely, since they have a decreased ability to regenerate reduced nicotinamide adenine dinucleotide phosphate, and glutathione as a result of the enzymatic lesion. The recent finding, (David, 1982), that P. falciparum parasites possess their own G-6-PD casts some doubt on the pleasibility of this explanation (David, 1982).

Fetal hemoglobin may also retard the intracellular growth of P. falciparum (David, 1982), and help to explain why, during the first six months of life; children living in areas where the disease is endemic are relatively protected from malaria (Wernsdorfer, 1981).

Other hemoglobin variants (HbC, HbE, and thalassemia and abnormal erythrocytes have been studied in malaria cultures in efforts to understand various aspects of invasion and intracellular growth and to provide a cellular explanation for the distribution of the red cell abnormalities in malarious areas (Miller, 1979).

Infectivity is high in the early days of parasitaemia and falls abruptly when the crisis of a sexual forms begins, presumably because antibodies are formed (Manson, 1982).

In the tropics children are probably the most prolific source of infective gametocytes (Manson, 1982).

Transmission other than by mosquitoes:

Malaria can, however, be transmitted in other ways. By design or by accident, by the inoculation of blood from an infected person to a healthy person. In this way the asexual blood forms continue to develop in their own periodicities in the peripheral blood, producing attacks of fever in the recipients, but pre-erythrocytic and erythrocytic shizonts are not formed in the liver, because these forms originate only from sporozoites inoculated by mosquitoes (Manson, 1982).

Malaria transmitted by inoculation of blood is easily cured and relapses do not occur. Nevertheless, P. falciparum infection transmitted in this way can be fatal (Bruce, 1980). The chief operations by which such transmission is affected are: Unintentional infection through transfusion of blood which unknown to the physician, contains malaria parasites. In this way, P. vivax has been transmitted in temperate climates from donors infected three years before

(Chin and Contacos, 1966). P. malariae from donors infected as many as 17 years before and not exposed to infection since, and P. falciparum present in blood from donors who were exposed twenty months to three years earlier (Bruce, 1980).

The subject of the transmission of malaria by blood transfusion has been well reviewed by Bruce 1970, 1974). Such infections are frequently due to P. vivax or P. falciparum, but P. malariae accounts for many causes and is of special importance because of its chronicity in blood donors and the difficulty in detecting it (Anderson et al., 1974). Most infections occur when the blood has been stored for less than five days, infections with blood stored for two weeks or more are exceptional. Dried plasma prepared from malarial blood is safe (Manson, 1977). Microscopic examination of blood is not very helpful in the detection of infected donors, but in special circumstances the immunofluorescence (IFA), test has proved a useful screening test for this purpose (Campbell et al., 1979). In malarious countries donors should be treated with antimalaria drugs before blood is withdrawn and non-immunorecipients should also receive a course of these drugs (Beale et al., 1972).

A single dose of chloroquine (600 mg base), given to the recipient 24 hours before transfusion, will prevent infection, but it may be easier to give the standard three day course (Campbell et al., 1979).