DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Centers for Disease Control
Atlanta GA [illegible]

To: The Record

From: Chief, Malaria Branch, DPD, NCID
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Subject: Induced Malaria Infection for the Treatment of HIV/AIDS

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Recently, the Centers for Disease Control and Prevention (CDC) has received inquiries regarding a proposal entitled "IMT (induced malariatherapy): A Potential Cure for AIDS". This proposal has been circulated by The Heimlich Institute Foundation for the purpose of investigating the use of induced malaria infection to cure HIV infection in 10 HIV seropositive patients. Based on our involvement in both ongoing discussions of induced malaria infection for the treatment of Lyme disease in the United States and in assessing the possible interaction between Plasmodium falciparum malaria and HIV/AIDS in subsaharan Africa, we offer the following comments on this proposal:

I. Induced malaria infection for neurosyphilis and Lyme disease

Malariatherapy is the induction of symptomatic malaria infection through the inoculation of malaria parasites typically through intramuscular or intravenous injection of blood from a malaria infected donor. Induced malaria infection was used to treat neurosyphilis before the advent of antibiotics. However, controlled studies were never performed to evaluate this mode of treatment, and published reports suggest that the clinical response was unpredictable. Whether or not induced malaria infection was beneficial in the treatment of neurosyphilis remains unknown.

Since 1990, the Heimlich Foundation has encouraged the use of induced malaria infection for Lyme disease in the United States.[2] CDC has officially gone on record opposing this therapy.[3] Reportedly, patients with purported Lyme disease have been injected with blood from individuals in Panama and Mexico infected with Plasmodium vivax. However, induced malaria infection for Lyme diseases has never been proven effective; despite reported "cures", there are no published data to show that patients had documented Borrelia burgdorferi infection or that these patients were either cured of their infection or had resolution of clinical signs attributed to Lyme disease.

CDC opposes induced malaria infection for the treatment of Lyme disease because: 1) there is no scientific evidence that malaria infection is effective in the treatment of Lyme disease; 2) induced malaria causes iatrogenic morbidity and carries a direct risk for death from complications of P. vivax infection or from co-infection with other, undetected, blood borne pathogens (see III below); and 3) there is a small but finite potential for local transmission of malaria from parasitemic persons in the United States.[3]

II. The relationship of Plasmodium falciparum malaria and HIV/AIDS

Several studies have examined the relationship between HIV/AIDS and malaria, that is, whether HIV infected patients are more susceptible to malaria, or whether malaria alters the course of HIV-1 disease. Studies in Kinshasa have shown that there was no statistically significant difference in the incidence of malaria in HIV-1 positive children who developed AIDS during the course of a two year study when compared to HIV-1 positive children who did not develop AIDS.[4] If malaria had a beneficial effect on the course of HIV infection, we would expect that fewer children would progress to AIDS among the study children who were infected with malaria when compared to those who were uninfected. Other studies have also failed to find any association between malaria and HIV-1 disease.[5]

In fact, substantive concerns have been raised regarding the possibility that malaria infection could potentiate the course of HIV infection. P. falciparum infection can cause a transient decrease in CD4 lymphocytes.[6] In addition, Plasmodium infection is a potent stimulator of cytokines, which enhance viral replication in HIV positive individuals.

Considerable published experience in Africa, where malaria is hyperendemic and where AIDS has reached epidemic levels, suggests that malaria has no protective effect against HIV infection or the progression to AIDS.

III. Lack of evidence for beneficial effects of malaria infection

No evidence currently exists to indicate that malaria infection would beneficially effect the course of HIV infection, either through induction of fever or alterations in immunologic parameters. The perceived benefit of malaria infection for neurosyphilis was believed to be attributable to the destruction of the causative spirochete by repeated high fevers (40-42°C). Induced fever is unlikely to have any benefit in the treatment of HIV/AIDS since temperatures in

this range have little effect on the HIV virus[7]. In 1990, the National Institute of Allergy and Infectious Disease (NIAID) investigated the use of systemic hyperthermia for the treatment of HIV/AIDS and concluded that there was no basis for the use of hyperthermia in the treatment of HIV disease.

IV. Risks associated with malaria or other blood-borne pathogens

Infection with P. vivax in non-immune individuals leads to an acute fever illness with potential multisystem involvement (renal, cardiac, pulmonary, etc.) and carries a small but finite risk of death from splenic rupture. Donor blood used to induce malaria may also be infected with agents other than malaria. While many infectious agents can be identified through screening (e.g. HIV, hepatitis B and C), laboratory error could allow infected blood to be considered safe. Additionally, other infectious agents for which screening is not performed, such as cytomegalovirus, could lead to further illness and debilitation in persons who may be already immunocompromised.

V. Ethical considerations

Any protocol involving the use of humans in research should undergo thorough ethical review and approval by a human subjects review board prior to initiation.

Without evidence, either in-vitro or in-vivo, to support the hypothesis that malaria suppresses HIV infection or delays the development of AIDS, and with the risk of adverse health consequences associated with induced P. vivax infection or other blood borne pathogens, the use of induced malaria infection in HIV infected individuals can not be justified.

1. Austin SC, Stolley PD, Lasky T. The history of malariotherapy for neurosyphilis: modern parallels. JAMA 1992;268:516-9.

2. Heimlich HJ. Should we try malariotherapy for Lyme disease? [Letter] N Eng J Med 1990;322:1234-5.

3. Centers for Disease Control. Imported malaria associated with malariotherapy of Lyme disease-New Jersey. MMWR 1990;39:873-5.

4. Greenberg AE, Wato N, Ryder RW, et al. Plasmodium falciparum malaria and perinatally acquired human immunodeficiency virus type 1 infection in Kinshasa, Zaire: a prospective, longitudinal cohort study of 587 children. New Eng J Med 1991;325:105-109.

5. Greenberg AE. HIV and malaria; interactions of AIDS and other diseases. in AIDS in the World: a Global Report. eds Mann J, Tarantola DJM, Netter TW. Cambridge, MA: Harvard University Press; 1992 pp. 143-8.

6. Ho M, Webster HK. Immunology of human malaria. A cellular perspective. Parasit Immunol 1989;11:105-116.

7. McDougal JS, Martin LS, Cort SP, Mozen M, Heldebrant CM, Evatt BL. Thermal inactivation of the acquired immunodeficiency syndrome virus, human T lymphotropiv virus-III/lymphadenopathy-associated virus with special reference to antihemophilic factor. J Clin Invest 1985;76:875.