West African Malarial Prophylaxis Initiative (WAMPI)

4 FERN WOODS LANE
PHOENIXVILLE, PA 19460
UNITED STATES OF AMERICA
TEL: 610.783.0849
FAX: 610.783.0880

LIBERIAN HEALTH CENTER
ROCK CHURCH INT'L COMPLEX
ROBERTS FIELD HWY.
DUAZOHN CITY, SCHEFFLIN TWP.
REPUBLIC OF LIBERIA
TEL: (231) 651 4627

E-MAIL: mumpi@comcast.net

"Wherever the art of medicine is respected,
there is also respect for humanity"
Hippocrates 400 BC

ACTION PLAN:

MALARIA PREVENTION (PROPHYLAXIS) INITIATIVE FOR CHILDREN IN SUB-SAHARA AFRICA ©

George Herman “Babe” Ruth was and will remain one of the legends of American sport. As a New York Yankee he was affectionately known as the “Sultan of Swat” and held the major league single season home run record for nearly fifty years. He became the first true American sports superstar and his fame transcended baseball. What is little known about “The Babe” is that he struck out over sixty percent of his time at bat. But he never stopped swinging for the home run and earned immortality.

We are in a life-and-death game with malaria and we are clearly falling behind. We have no option but to swing for the home run. It’s the bottom of the ninth and the “good guys” are at bat. We’re behind 2 to 1, two outs with one man on base and the count is 3 and 2. The pitcher (*Anopheles*) winds up….

CONTENTS

Malaria: An infectious disease… caused by a parasitic protozoan of the genus *Plasmodium* in red blood cells, which is transmitted to humans by the bite of an infected female *anopheles* mosquito.

PROLOGUE

Probably at no time in history has malaria been so prominently at the forefront of world consciousness. In defiance of the triumphant march of medicine and science in many important areas, this pernicious disease has mushroomed out of control in known venues and has surprisingly arisen in venues where it had never been seen before. According to some estimates, over half of the population of Sub-Sahara Africa may be transporting one or more of the four malaria protozoans in their blood -- although many of them never exhibit symptoms associated with the disease.* If the estimates about the number of malaria parasite "carriers" is accurate there is an almost limitless resource pool of "attractive" parasite-infected blood** for the *anopheles gambiae* mosquito to draw from to infect previously-untainted victims.

In response, health organizations throughout the world are in high gear attempting to "stem the tide" of this insect-borne epidemic including undertaking extensive research to find an effective and affordable anti-malaria vaccine. However, in the best case, this will be some time in coming and in the interim the two most prominent weapons being arrayed against malaria are ITN's (Insecticide Treated Nets – "bednets"), and large-scale spraying with DDT. In both instances, there are heartening results in terms of reduction of the incidence of the disease and children's deaths. However, both of these resources working in concert cannot account for saving more than a minority of lives.

<u>Insecticide spraying</u>

Insecticide spraying is employed in Sub-Sahara Africa in both large-scale outdoor aerial spraying and interior spraying of the walls of huts and houses. Interior spraying has produced a significant short-term reduction in the incidence of malaria. However, the most frequently used agent, DDT, is an insecticide that has been prohibited in the US (and the European Community) for the past thirty five years due to toxicity issues. In addition, mosquitoes have shown the ability to develop a surprisingly robust resistance to various pesticides in a relatively short time. Studies in India on mosquito resistance to DDT demonstrate this conclusively. Many health organizations perceive that indoor spraying (the most often used form of spraying) represents an acceptable balance between effectiveness and toxicity risks. Because the US and European Community prohibit domestic use of DDT, many developing nations that suffer from malaria are reluctant to use DDT for fear (largely unjustified) of losing aid support from these sources. At any rate, cost-effectiveness studies suggest that insecticide-treated nets may exhibit a cost/reward advantage over insecticide spraying. The "risk vs. benefit" arguments revolving around the potential toxic impact of pesticides are likely to continue in the near term.

<u>ITN's (bednets)</u>

Bednets have been used for generations in tropical areas to avoid the discomfort of continuous insect intrusion, even before science was aware that the mosquito is a disease-bearing insect. In recent years, the pyrethroid insecticides – permethrine,

---

*Host resistance is a recognized phenomenon although the reason(s) underlying this may not be well understood in science.

**Children who harbor gametocytes (the stage transmissible to mosquitoes) of the parasite *Plasmodium falciparum* attract about twice as many mosquitoes as children who do not harbor these gametocytes[1].

deltametrhrin and alphacypermethrin -- have been approved by the World Health Organization for the impregnation of bednets to enhance their effectiveness (hence the expression “Insecticide Treated Nets” -- ITN’s). Unfortunately, in Benin, Nigeria and Thailand, resistance to pyrethroid insecticide has been reported in *Anopheles gambiae* and *Anopheles minimus*, the two *anopheline* species representing the major vectors of malaria in these regions. This is considered a major setback to vector control using bednets.

Bednets are relatively inexpensive. In venues where they have been used, there has been a gratifying reduction in the incidence of malaria. However, by themselves, they cannot provide the needed full-time protection against malaria. To begin with, bednets (logically) require beds. In many African huts and homes there simply are no beds – family members sleep on mats or on the floor. When there are beds, several members of the family may be using the bed and rigging a bednet so that everyone is properly protected may represent a small engineering task. If someone’s arm or leg sticks out from under the net, it becomes a target. Anyone leaving the bed during the night also becomes an immediate target for mosquitoes. Nets also make the sleeping area underneath them noticeably warmer and the additional discomfort discourages many people from using them. It is disheartening that bednets that have been distributed free by either governmental agencies or international humanitarian organizations have a rate of user compliance (actual usage) of only 30%. Moreover, neither adults or children can lead their lives under bednets, even during the high risk evening hours. Thus, although the consistent use of bednets has been shown to reduce the incidence of malaria, they alone cannot provide the comprehensive, full-time, “go anywhere” protection that children need to avoid the deadly bite of the *anopheles* mosquito.

<u>A New Methodology</u>

It is difficult for a new methodology to gain acceptance in face of long-held trust in existing methodologies – particularly if these methodologies demonstrate benefit. It also seems characteristic of human nature to be skeptical of something new or of a different way of doing something. This is likely true for the mosquito-avoidant patches which provide the long-term “anywhere/anytime” protection against malaria that is so clearly needed. Both adults and children, accustomed to applying mosquito-repellant lotions on every square centimeter of exposed skin, have difficulty accepting the fact that a small (less than two inch square) patch can protect the entire body. There is the feeling that a significant portion of the skin should be covered by the patches to provide the same level of protection provided by insect-repellant sprays and lotions. Reflecting another dimension of attitude toward something new or unusual, several children in a Ghanaian school having observed that a child wearing a patch seemed invulnerable to mosquito attacks insisted that he was being protected by a form of voodoo. Old habits die hard….

Nevertheless, the insect avoidant patches were designed and executed based on good science and using an effective and well-documented route of administration. It is important to review what follows with the mindset that there can be a “better mousetrap” to add to the mix in the battle against the world’s deadliest killer.

---

[1] Lacroix R, Mukabana WR, Gouagna LC, Koella JC (2005) Malaria Infection Increases Attractiveness of Humans to Mosquitoes. PLoS Biol 3(9): e298

EXPLAINING THE WAMPI PROJECT

*In the 1990's Residents of Asembo Bay (in Western Kenya) were bitten 60-300 times a year by a malaria-carrying mosquito**

*National Center for Infectious Diseases, Division of Parasitic Diseases, Centers for Disease Control and Prevention, April 11, 2007
Photo taken in Tanzania. Published online by IHDRC, University of Brighton, Mayfield House, Falmer, BN1 9PH, United Kingdom

West African Malarial Prophylaxis Initiative (WAMPI)

4 FERN WOODS LANE, PHOENIXVILLE, PA 19460, U.S.A.
TEL: 610.783.0849 FAX: 610.783.0880
E-MAIL: mumpi@comcast.net

WHAT WE ARE ATTEMPTING TO DO

In the early years of the twenty first century, Africa faces grave problems unlike any other continent in their intensity and extensiveness. Political instability, despotism, genocide, human trafficking, poverty, hunger and disease top the list. The western Sudan region of Darfur immediately comes to mind but is by no means unique. Unfortunately, world resources seem to have made only a marginal impact in many of these areas.

In terms of disease, malaria and HIV/AIDS easily top the list. The incidence of these two diseases appears to be out-of-control in Sub-Sahara Africa. And, unfortunately, there is a malevolent tie-in between them. According to the African Medical and Research Foundation (AMREF), online newsletter, May 10, 2007, people infected with HIV/AIDS are more prone to severe malaria, and malaria infection can contribute to an increased incidence of HIV virus. In addition, both HIV and malaria are fast-reproducing microbes which gives them the ability to develop resistance to medications.

No single program, project, or organization can realistically tackle more than one specialized part of the problem. Having discovered a “new technology” approach to combating malaria, we have spent the past two years testing it in the field and acquiring licenses and governmental approvals in West Africa. We are now proposing this practical and effective approach to the number one killer of children and adults in Africa. However, the issues of increased mutual disease susceptibility existing between malaria and HIV/AIDS suggests that malarial prophylaxis could be an important component of HIV/AIDS prevention, control and amelioration programs as well.

With this in mind, please take a careful look at our proposal for limiting if not defeating one component of human misery in Sub-Sahara Africa.

Thank you for giving this program your kind attention.

A NEW APPROACH TO AFRICA'S DEADLY MALARIA PROBLEM

Worse Than You Imagined

Although malaria is a worldwide dilemma afflicting as many as 500 million persons per year, 90% of those afflicted live in Sub-Sahara Africa[1]. In Africa, *3,500 people die from malaria every day, most of whom are children.* Shockingly, it is estimated that *a child dies from malaria every 30 seconds* in this region and it is the leading cause of death of children there. The disease kills more than one million children each year in Africa alone. *In regions where the disease is hyperendemic 40% of toddlers may die of acute malaria*.

Unfortunately, most African children do not receive treatment save for unregulated herbal remedies. Although the Ministry of Health in Ghana has approved a significant number of herbal medicines, on a local level most of the herbal treatments utilized are more a product of folk culture than science. The estimated annual cost to Africa for malaria is approximately $12 billion. In addition, people infected with HIV/AIDS are more prone to severe malaria, and malaria infection can contribute to an increased incidence of HIV virus.[2]

Sometimes, the attempted solution becomes the problem. The *inappropriate use of anti-malarial medications* is one of the highest contributors to the increasing morbidity. Recently, health researchers, working from Togo but gathering data from Senegal eastward and southward have observed the *emergence of drug-resistant strains of malaria* in West Africa.*

In attempting to combat hunger, urban agriculture projects have been initiated in West Africa. Unfortunately, these appear to be breeding-grounds for the *anopheles* (malaria-bearing) mosquito. At the pilot project in Kumasi, Ghana, researchers have noted higher biting rates at night in areas of urban agriculture. The evaluation of these programs is under careful investigation by entomologists in both Kumasi and Accra.

Attempted Solutions to the Present

The most visible approach to the problem is the use of treated bed nets, which have demonstrated efficacy but require a careful installation and cannot protect children when they are not in bed (very often the case) or when they leave their beds at night. To compound the problem, the Noguchi Memorial Institute for Medical Research in Ghana[3] indicates that mosquitoes appear to adapt to the nets: "their [the mosquitoes'] behavioral changes in biting patterns in response to insecticide treated nets (ITNs) continue to present a great challenge against control efforts."

The large-scale use of insecticides has been questioned due to their potential human and environmental toxicity issues and – surprisingly – the ease with which insects develop resistance to them.* As has been reported earlier, studies have shown the

---

* In the early 1960's only 10% of the world's population was at risk of contracting malaria. This rose to 40% as mosquitoes developed resistance to pesticides and malaria parasites developed resistance to treatment drugs. Malaria is now spreading to areas previously free of the disease. Sources: The Malaria Control Programme, World Health Organization, *Third World Network Features, Health Canada* and The Centers for Disease Control and Prevention (US).

anopheles mosquito's uncanny ability to develop resistance to the most widely-used insecticides for both area spraying and impregnating bednets (ITNs).

Topical mosquito repellants [avoidants] can be effective but have definite limitations. Their efficacy period is generally in the three to eight hour range. Due to toxicity concerns, it is strongly recommended that they are not reapplied often (or at all), leaving adults unprotected a large portion of the day. Because topical agents must not come into contact with the eyes, mouth or open wounds and are toxic if swallowed, they are risky for use with children; moreover, their concentration level (dosage) is highly critical for children. In addition, every square centimeter of exposed body surface must be treated to afford full protection. Topical sprays and lotions also lose their effectiveness due to perspiration, exposure to rain, bathing or swimming or rub-off from contact.

As there are several species of malaria parasites (*Plasmodium vivax, ovale, malariae and falciparum*), it should be observed that *no single drug* is capable of protecting against all of them. Multi-compound drugs that protect against all of these species are available but are expensive. Moreover, anti-malarial medications are also under-produced relative to need, often exhibit deleterious side effects and are dosage-critical for children. Many of these medications *cannot be tolerated by children* even in substantially reduced dosages. In households where written instructions may not be understood, dosage-critical medications for children may be dangerous.

A Viable Alternative

The anti-mosquito patch represents a viable, affordable and individualized solution to the problem. The patches contain no dangerous or toxic substances, are safe for children and are not dosage-sensitive. They attack the root cause of malaria infestation -- the bite of the *Anopheles* mosquito -- by generating a body action that keeps the mosquito away from the person using the patch. The active agent is B-1 thiamin which has no toxicity issues and is not dosage-critical for either children or adults. The transdermal route of administration offers a controlled, sustained release of the active agent, allowing continuous 36 hour protection. They are not subject to falling off or loss of potency due to perspiration, exposure to rain, bathing or swimming. The mosquito-avoidant patches are widely marketed in the US and the European Community. The Ghana Food & Drugs Board, the National Agency for Food & Drug Administration and Control (NAFDAC) in Nigeria and the Ministry of Health of the Côte d'Ivoire have approved the use of the patches after extensive review and testing. On-the-ground efficacy testing in a variety of settings in West Africa has produced consistently positive results and the testing regimen remains ongoing. In sum, the transdermal mosquito-avoidant patches appear to offer the needed full-time "go anywhere, do anything" protection that will help African children avoid the deadly bite of the *anopheles* mosquito and intervene the cycle of infection and death that has prevailed for so long.

---

[1] Compared to 31 million people who are infected with HIV in Sub-Sahara Africa. Sources: (1) UNAIDS 2006 Report on the Global AIDS Epidemic; (2) Until There's A Cure Foundation [HIV/AIDS], © 2004, 2006.

[2] African Medical and Research Foundation (AMREF), online newsletter, May 10, 2007 update

[3] *Evaluation of the Efficacy of Impregnated Thiamine-Based Formula Adhesive Tape Against Mosquito Bites in Malaria-Endemic Areas*. Preliminary report by the Department of Parasitology of the Noguchi Memorial Institute for Medical Research, Legon, Ghana, September, 2006.

West African Malarial Prophylaxis Initiative (WAMPI)

4 FERN WOODS LANE, PHOENIXVILLE, PA 19460, U.S.A.
TEL: 610.783.0849 FAX: 610.783.0880
E-MAIL: mumpi@comcast.net

AN OPEN LETTER TO HELPING AGENCIES SERVING AFRICAN CHILDREN

"The test of the morality of a nation is what it does for its children."
Dietrich Bonhoeffer, Theologian

Although malaria is the number one killer of children throughout Africa (exceeding HIV), there are limited means for protecting them. Due to problems and shortcomings exhibited by many traditional anti-malarial methodologies, we are introducing the anti-mosquito patch to Sub-Sahara Africa as a practical, inexpensive and efficacious means of preventing children from being bitten by parasite-bearing mosquitoes. The patches are easy to use, offer continuous 36 hour efficacy and are totally safe for use with children. The active agent is vitamin B1-thiamin. The action of the patches is wonderfully simple.

Like other biting insects the *anopheles* mosquito (which transmits the malarial parasite) relies on olfactory cues (smell) to detect its human targets. The specific smell that attracts these insects is the carbon dioxide (and lactic acid) expelled in breath and perspiration. To intervene in this process, the patches introduce B-1 thiamin into the system via a transdermal (through the skin) route of administration. Within a short time the B-1 passes through the system and begins to be excreted through the sweat glands. This becomes a continuous process. The smell of the unmetabolized B-1 masks the odor of the carbon dioxide in the breath and perspiration. As a result, the person becomes "invisible" to mosquitoes and other biting insects. It is analogous to stealth technology for military aircraft (becoming invisible to enemy radar). In addition, the odor of B-1 thiamin is repugnant to biting insects. The patches offer a surprisingly simple, safe, inexpensive yet effective means of disease prevention by protecting children from being bitten wherever they go. Their insect-repellant action is similar to the well-known DEET-based topical applications except that they offer a significantly longer efficacy period (36 hours vs. 8 hours), ease of application, freedom from toxicity concerns and immunity from loss of potency due to perspiration, rain, bathing or swimming.

The patch sees use in the US for avoiding Lime ticks as well as West Nile Virus-bearing mosquitoes and is also marketed and used extensively in Europe. The respected Noguchi Memorial Institute for Medical Research in Ghana undertook an initial field study of the B-1 thiamin patches with follow-up studies currently underway. Other efficacy studies conducted in "real life" settings in Ghana and Liberia have yielded consistently positive results.

The patches have been licensed by the Ghana Food & Drugs Board, the National Agency for Food & Drug Administration and Control (NAFDAC) in Nigeria and the Ministry of Health of the Côte d'Ivoire. They have been recommended by the Ghana Schools Health Education Program for use in that nation's schools.

We are strongly interested in working closely with concerned humanitarian and philanthropic organizations to implement an anti-malarial prophylaxis campaign for school-age children in Africa using this "new technology" approach.

TECHNICAL AND RESOURCE SECTION

The mosquito has been characterized as the most dangerous animal on earth.
One out of every 17 people on the planet will die from a mosquito-borne disease.[1]

[1] Mark S. Fradin MD. *Mosquitoes and Mosquito Repellents: A Clinician's Guide*. Annals of Internal Medicine 1998; Vol. 128; Issue 11: pp 931-940 [1].

THE SEARCH FOR AN IDEAL MOSQUITO-AVOIDANT

"Ultimately, the best cure for malaria is not to get bitten."
History Channel Documentary, July 26, 2007

The World Health Organization advocates protection against mosquito bites as the first line of defence against malaria. David N Durrheim, Peter A Leggat. *Prophylaxis against malaria*. BMJ 1999;318:1139 (24 April).

The difficult part has been finding that means. Numerous authors argue that there has been an over-emphasis on insecticides as an insect avoidant, and that a variety of mosquitoes in different locales have developed resistance to several widely-used insecticides – as well as citing the human toxicity and environmental concerns linked with insecticides.

> The researchers hope that these kinds of discoveries will eventually suggest new and effective ways to keep mosquitoes from preying on people that will be less poisonous than the insecticide and repellent sprays now in common use. For example, a compound might be found that reduces the mosquitoes' response to human odors. Laurence J. Zwiebel *et a*l, *Proceedings of the National Academy of Sciences* online Nov. 27, 2006.

As a result many authors endorse alternative methods of "vector" control. They argue that the potential opportunities inherent in the use of attractants [or repellants] in the control of the mosquito vector have not been fully utilized and that the search for the ideal insect repellant to the present has been disappointing:

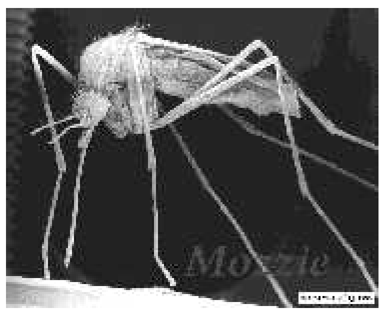
> Use of personal protection measures may have been compromised by widely publicised reports of encephalopathic reactions in children associated with the most widely used insect repellant, diethyltoluamide (DEET), and the nonchalance of many travellers. David N Durrheim, Peter A Leggat. *Prophylaxis against malaria*. BMJ 1999;318:1139 (24 April)

> Insect repellents must cover *all* exposed skin; mosquitoes will attack just a few centimeters beyond the area coated with repellent. Swimming, sweating, and hot weather require frequent reapplication. J Scott*. Mosquitoes Bite*. Journal Watch Emergency Medicine. August 1, 1998

> …the search for the perfect topical insect repellent continues. This ideal agent would repel multiple species of biting arthropods, remain effective for at least 8 hours, cause no irritation to the skin or mucous membranes, cause no systemic toxicity, be resistant to abrasion and rub-off, and be greaseless and odorless. No available insect repellent meets all of these criteria. To be effective, a repellent must show an optimal degree of volatility, making it possible for an effective repellent vapor concentration to be maintained at the skin surface without evaporating so quickly that it loses its effectiveness. Abrasion from clothing, evaporation and absorption from the skin surface, wash-off from sweat or rain, higher temperatures, or a windy environment all decrease repellent effectiveness [17, 34-37]. The repellents currently available must be applied to all exposed areas of skin; unprotected skin a few centimeters away from a treated area can be attacked by hungry mosquitoes [33, 35]. Mark S. Fradin MD. *Mosquitoes and Mosquito Repellents: A Clinician's Guide*. Annals of Internal Medicine 1998; Vol 128; Issue 11: pp 931-940.

The B-1 thiamin transdermal patches rectify these concerns. Application is easy. They are resistant to abrasion and rub off and will not wash off the skin as a result of sweat, rain, bathing or even swimming. Their uniquely long (36 hour) efficacy period permits protection all day and night without re-application. They have no toxicity or dosage-sensitive issues. There is no problem maintaining B-1 vapor concentration at the skin as the B-1 supply is continually being replenished from the stores in the patch. And they are effective with multiple species of mosquitoes and other biting arthropods.

Clearly, the disappointments exhibited by topical applications and sprays do not apply to the patches and no longer remain an issue with their use. In addition to avoiding the negatives, recent efficacy studies of the patches attest to their ability to protect the user against biting in a variety of mosquito-rich environments in West Africa. In accomplishing these things, the patches appear to meet the requirements for the ideal mosquito-avoidant.



B-1 THIAMIN PATCHES AS AN INSECT REPELLANT AND ANTI-MALARIAL PROPHYLAXIS:
A Physician's Commentary

Following discussions with parties involved in an anti-malarial program in West Africa, I have investigated B-1 thiamin serving as an insect avoidant (repellant) in the form of a transdermal patch. These patches are being used as an anti-malarial prophylaxis in afflicted areas by "insulating" people from the bite of the *anopheles* mosquito.

It is accepted that biting insects use olfactory receptors as a primary means of locating their "prey". It follows that disrupting the olfactory signaling process deprives them of their ability to do this. This is the methodology employed by B-1 thiamin as an insect repellant and is similar in concept (but not action) to widely-used topical insect repellants such as DEET (see *Selected Documentation: Olfactory Cues..*). An important distinction is that the thiamin B-1 patch is completely non-toxic when used as directed.

The first step in disrupting the signaling process is delivering the agent into the blood stream. Transdermal delivery of B-1 thiamin into the blood stream is facilitated by an established mechanism and the small size of the B-1 molecule. This route of administration also allows for a well-regulated, sustained delivery of the agent.

The method by which B-1 thiamin disrupts the olfactory signaling process is easily understood. Unmetabolized B-1 in the system is excreted at the skin surface as a volatile gas capable of overwhelming the odor of the naturally-emitted olfactory cues needed by biting insects to locate their targets. This is more thoroughly discussed in *"Explanation of the Action and Efficacy of B-1 Thiamin Transdermal Patches as an Insect Repellant".*

A brief history of the use of B-1 thiamin as an insect-repellant presents the context from which the patches evolved (*History of B-1 Thiamin As An Insect Repellant*).

It is not uncommon in science to discover new and non-traditional applications for familiar substances and technologies. For example, there are a number of pharmaceuticals that have been found to be therapeutically helpful in treating conditions other than those for which they were developed. In addition, we see the use of vitamin D, a known treatment for osteoporosis, showing good research in the prevention of many cancers. From this vantagepoint, it is interesting to examine B-1 thiamin serving a function that is very different from its accustomed role in health and nutrition.

Respectfully submitted,

Robert J. Zieve, MD, Director
PineTree Clinic for Comprehensive Medicine
Prescott, AZ

EXPLANATION OF THE ACTION AND EFFICACY OF B-1 THIAMIN TRANSDERMAL PATCHES AS AN INSECT-REPELLANT

1. <u>Transdermal Medications:</u>

The skin has evolved to minimize entrance of noxious chemicals and UV radiation into the body. But from a pharmacological perspective, delivering drugs across the skin is an important goal. Transdermal delivery would avoid numerous problems with the oral route, including drastic pH changes, the deleterious presence of food and enzymes, variable transit times, pulse entry (rapidly fluctuating drug plasma concentrations), side effects and inadequate patient compliance, while also eschewing needle delivery and its associated inconvenience and even patient phobia. (*Journal of Nature Biotechnology* 22, 165-167 [2004]).

Impregnated polymers (transdermal patches) can safely store and deliver controlled amounts of medication across the epidermis for systemic distribution.

Transdermal medications have been in clinical use for many years. Some of the products that have been medicated in this fashion include: nitroglycerin, estradiol, clonidine, fentanyl, nicotine and scopolamine. (Deputy for Acquisition and Advanced Development, USAMRMC). Recently, the FDA has approved the use of transdermal patches to deliver medications for treating Parkinson's Disease, Alzheimer's Disease, menopause and osteoporosis as well as the delivery of stimulants for treating Attention Deficit Hyperactivity Disorder (ADHD), hormonal contraceptives, antidepressants and painkillers (especially for the preipheral pain of shingles).

An advantage of transdermal patches is ease of compliance. It is generally accepted in the medical community that the less frequently a drug is dosed, the higher [patient] compliance is. Because of its sustained release capability, a single patch can be used in place of several repeated doses of oral medications, leading to better compliance. In fact, it may be said that transdermal administration combines the relative ease of oral medication with many of the advantages of IV administration (see above).

Another advantage of transdermal patches is that a lower total dose of the medication is required and that the patches maintain an even level of medicine within the blood.

However, many substances are not amenable to the transdermal route of administration. The substance to be transmitted in this fashion must be composed of small enough molecules (low molecular weight) that it can be absorbed across the skin. There is a limited number of drugs and chemicals that are candidates for such delivery because *few molecules yield skin permeability coefficients sufficiently high to develop clinically active plasma levels***.** An example of a molecule that is <u>not</u> capable of being medicated in this fashion is insulin. Clearly, the transdermal route of administration would be preferable to injection; however, the insulin molecules are simply too large to be absorbed across the skin. By comparison, thiamin hydrochloride (B-1 thiamin) molecules are of sufficiently low molecular weight to be medicated across the skin.

In sum, transdermal medication offers a readily accepted, non-toxic dosing system that eliminates the need for multiple dosings while offering protection over a sustained period.

For a small number of persons who are allergic to adhesive, patches may cause skin irritation.

2. <u>Toxicity of Thiamine</u>

Upper limits for B-1 thiamine ingestion have not been set because there are no known toxic effects from the consumption of thiamine in food or through long-term oral supplementation (up to 200 mg/day).

Emergency medicine toxicology texts state that in supplement doses of 50-500 mg this vitamin is generally non-toxic. The patches contain ≥100 mg. of B-1 thiamin which is released in uniform, gradual fashion over a period exceeding 24 hours, insuring that dosages at any time fall well below the published potential toxicity level.

Thiamine toxicity is extremely rare, and requires doses far greater than that presented in the patches.

Poison control medical source books do not even contain a listing for specific treatment for thiamine toxicity. It is generally the *fat soluble vitamins*, such as A, D, E, and K, as well as Vitamin B3 that require specific antidotes or treatments. (Mark Rosenbloom, MD, MBA, FACEP, Adjunct Associate Professor of Medicine, Emergency Medicine, Feinberg School of Medicine at Northwestern University).

3. <u>B-1 Thiamine Transdermal Patches</u>

Thiamine is a is a water-soluble vitamin needed to process carbohydrates, fat, and protein. Vitamin B1 is nontoxic, even in very high amounts.

B-1 thiamin has sufficiently small molecules to be transmitted across the skin. Some other vitamins are given safely through the transdermal route, such as B12.

It is well established that excess B-1 thiamine, as well as all water-soluble vitamins, are excreted and flushed from the body by urination or perspiration. It is the excretion of unmetabolized B-1 thiamine through perspiration as a volatile gas that overwhelms the olfactory receptors of mosquitoes hence impairing their ability to locate their prey.

Over a period of years, the Australians were reported to have used both tablets and liquid B1-thiamin for repelling biting insects. However, unlike the oral form which is often passed through the body too quickly, the impregnated polymer patch allows for uniform, sustained transmission of its B-1 thiamine stores, delivering up to 36 hours of medication.

<u>The Action of B-1 Thiamine Patches</u>

The action of the B-1 thiamin-based insect-repellant patches is based on biting insects' use of olfactory cues as their primary means of locating their human targets. This is widely documented in the literature. Current approaches to deterring mosquitoes involve "cloaking" the required olfactory cues to prevent the insect from identifying its target. The two principal olfactory stimuli used by biting insects are the carbon dioxide and – to a lesser degree – lactic acids expelled as volatile gases through human breath and perspiration ("host attractants"). The action of the patches is to introduce a safe, non-toxic agent into the system that will be expelled through the sweat glands as a volatile gas which will present an odor capable of overwhelming ("cloaking") the odor of the carbon dioxide and also the lactic acid. This interrupts the olfactory signaling needed by the biting insect to detect its "target".

B-1 thiamine is an ideal agent to accomplish this: (1) Thiamin hydrochloride molecules are low molecular weight (i.e., small enough) to be medicated transdermally; i.e., pass through the skin unimpaired and into the bloodstream; (2) Thiamin B-1 introduced in excess of the system's nutritional needs (≈ 1.2 mg./day) is expelled through the sweat glands and urine. Thiamin B-1 is water soluble but not fat soluble and is able to pass through the system and into the sweat glands unmetabolized, thus reaching the skin surface as thiamin B-1 in the form of a volatile gas; (3) Thiamin B-1 has an odor that – although largely undetectable to humans – is strong and repugnant to biting insects and is capable of "overwhelming" the odor of the carbon dioxide and lactic acid normally expelled by humans as described above; and (4) Thiamin B-1 is non-toxic in doses far exceeding that required to accomplish the "cloaking".

The insect-avoidant action of B-1 thiamine is therefore similar to that of the widely-used topically-applied insect repellant DEET (N, N-Diethyl-Meta-Toulamide) in a specific way. Both agents interrupt the olfactory signaling needed by biting insects to detect their targets by "cloaking" the odor of carbon dioxide and lactic acid with a substitute – repugnant – odor. However, there are large differences in action, efficacy and risk between the two repellants.

Topically-applied repellants must show an optimal degree of volatility, making it possible for an effective repellent vapor concentration to be maintained at the skin surface without evaporating so quickly that they lose their effectiveness (short efficacy period). However, with the patches, the long-term sustained release of the active agent into the system ensures a continuous replenishment of B-1 as a volatile gas at the skin surface, making this issue less critical.

It has been recommended to use DEET in concentrations of 30% to balance efficacy period and toxicity avoidance. Although the literature varies on this issue it appears that the maximum safe efficacy period for this agent is approximately eight hours; however, it is not recommended to apply a second coating of the agent in the same day to achieve an extended coverage period.

The sustained release patches have an efficacy period of 36 hours. Data to the present suggests that, with continuous use of the patches, the system accumulates a surplus of B-1 so that by the end of a week's usage it is possible to continue receiving coverage for 24 hours or more after the expected "life" of the last patch has been exceeded.

4. <u>Secondary Nutritional Benefits of B-1 Thiamin Supplement</u>

Our bodies use dietary thiamine as a cofactor in energy metabolism. Every cell of the body requires vitamin B1 to form the fuel the body runs on - adenosine triphosphate (ATP). Nerve cells require vitamin B1 in order to function normally. However, thiamine deficiency is rampant in many parts of the world, including areas of Africa. An article in the *American Journal of Clinical Nutrition*, 1979 Jan;32(1):99-104., found biochemical deficiency of thiamine in young Ghanaian children. The article states that this evidence of widespread biochemical thiamin deficiency is indicative of an at-risk population among young children for clinical thiamin deficiency.

A study from 2001 in the *American Journal of Clinical Nutrition* states that reports of a high incidence of thiamine deficiency during pregnancy and lactation were previously reported in India, Malaysia, and Ghana, where, in some cases, the consumption of foods rich in thiaminases was also implicated.

5. <u>Summary</u>

Thiamine transdermal patches are an extraordinarily simple, effective, virtually non toxic, and inexpensive way to prevent mosquito bites that are the vector for malaria organisms. It is not a treatment for those who have malaria. But it is an important investment in prevention, far less expensive in the long term and even in the medium term compared to hospitalization and drug treatment for the disease.

Selected Documentation:

OLFACTORY CUES ARE THE PRIMARY MEANS THROUGH WHICH BITING INSECTS FIND HOSTS

There are numerous and often redundant references in the literature to biting insects' use of olfactory cues as their primary means of "targeting" their prey. The listing below provides a sampling of representative entries.

1. "Mosquitoes are attracted to people by skin odors and carbon dioxide from breath. The active ingredients in repellents make the person unattractive for feeding." U.S. Department of Health & Human Services, Centers for Disease Control and Prevention.

2. "The mosquito is the most dangerous animal on the planet. It relies on its sense of smell to find the source of its blood meals." Laurence J. Zwiebel. *Exploration*. The online research journal of Vanderbilt University. November 26, 2001.

3. "The specific smell that attracts these insects is the carbon dioxide (and lactic acid) expelled in breath and perspiration." CDC National Center for Infectious Diseases, Division of Vector-Borne Infectious Diseases. Online Newsletter.

4 "The factors involved in attracting mosquitoes to a host are complex and are not fully understood [6-11]. Mosquitoes use visual, thermal, and olfactory stimuli to locate a host. Of these, olfactory cues are probably most important.

Carbon dioxide and lactic acid are the two best-studied mosquito attractants. Carbon dioxide, released mainly from breath but also from skin, serves as a long-range airborne attractant and can be detected by mosquitoes at distances of up to 36 meters [3, 13-15]. Lactic acid, in combination with carbon dioxide, is also an attractant. Mosquitoes have chemoreceptors on their antennae that are stimulated by lactic acid, important for in-flight orientation….

DEET is believed to work by blocking insect receptors (notably those which detect carbon dioxide and lactic at acid long ranges) which are used to locate hosts." Mark S. Fradin MD Mosquitoes and Mosquito Repellents: A Clinician's Guide. *Annals of Internal Medicine*, 1 June, 1998; Vol 128; Issue 11: pp 931-940.

5. "There is a plethora of evidence to suggest that host seeking in mosquitoes is mediated by info chemicals emanating from the host. Info chemicals are synonymous with semiochemicals. Mosquitoes have evolved a wide range of host-oriented responses. As Gibson & Torr (1999) reported, 'carbon dioxide appears to be universally attractive to mosquitoes, and is probably the most understood of the volatile host cues' (p. 2)." Abstracted from: *Mosquito Host Attractants*. A scholarly paper by Jason Pike.

6 Abstract: Olfactory cues play an important role in the attraction of major disease vectors towards their host. A.O. Oduolaa & O.O. Aweb. *Behavioural biting preference of Culex quinquefasciatus in human host in Lagos Nigeria.* Jnl Vector Borne Diseases 43, March 2006, pp. 16–20

HISTORY OF B-1 THIAMIN AS AN INSECT REPELLANT

The earliest reference to the use of B-1 thiamin as insect repellant apparently traces to Australia approximately 50 years ago. The data are anecdotal and describe that the route of administration was oral with daily dosage varying between 25 to 100 mg. Since that time, additional anecdotal data reflect the use of B-1 thiamin in this capacity in various parts of the world. In 1958, the first scientific article dealing with the use of B-1 thiamin as an insect repellant appeared in a learned journal in Switzerland:

> *Insect repellant properties of vitamin B1*.] [Article in German] Schweiz Med Wochenschr. 1958 Jun 28;88(26):634-5. RAHM U.MeSH Terms Insects* PMID: 13568728 [PubMed - OLDMEDLINE for Pre1966].

Since that time, additional anecdotal reports in a similar vein continued to appear. The route of administration apparently remained oral, dosages remained within the same range and there was no systematic attempt to promote B-1 thiamin as an insect repellent in any commercial way. Reportage remained anecdotal until mention of the insect-repellant quality of B-1 thiamin appeared in 1969 in a US medical journal along with a brief explanation of its action:

> “Some studies suggest that taking thiamine (vitamin B1) 25 mg to 50 mg three times per day is effective in reducing mosquito bites. This safe vitamin apparently produces a skin odor that is not detectable by humans, but is disagreeable to pregnant mosquitoes.” (*Pediatric Clinics of North America*, 16:191, 1969).

Apparently, the use of B-1 thiamin as an insect-repellant continued on the part of individuals who had heard of this application for the vitamin. However, there was no systematic attempt to organize the body of anecdotal reports bearing on the efficacy of B-1 utilized in this manner until 1995 when a brief reporting appeared in *Handbook of Dietary Supplements*: “Some individuals appear to find thiamin effective as an insect repellant (1).” Pamela Mason. *Handbook of Dietary Supplements*. Blackwell Science, 1995.

Although there appeared to be a solid constituency of people who used B-1 as an insect repellant and were pleased to share their success in doing so on the internet, there appeared little interest on the part of the major pharmaceutical companies to develop or market B-1 thiamin as a prophylaxis against malaria. Hence, there were none of the efficacy studies that typically attend such large-scale commercial efforts. Further mention of the action of B-1 thiamin as an insect repellant did not appear in the literature until 2006 in the newsletter of the American Academy of Anti-Aging Medicine which stated that vitamin B-1 helps repel insects and mosquitoes.

Various internet services focusing on travel to parts of the world where insect-borne diseases are prevalent (e.g., Africa), invariably address the issue of mosquito-avoidance and discuss numerous methodologies for accomplishing that. Most of them include at least a brief discussion of B-1 thiamin as an insect-avoidant agent. Two typical entries follow.

The International Travel Healthline Supplemental Health Recommendations states:

> "Vitamin B-1 (thiamine) is often an effective insect repellant for some people (the smell can repel biting insects). Take one Vitamin B-1 (100 milligrams) tablet by mouth each morning and evening …."

This is echoed by an on-line travel advisory service for students, International Service Learning. In their on-line document *Getting Ready to Go to Tanzania; Health Issues* they state:

> "As an optional prophylaxis for mosquito control, you can take 100 mg of Vitamin B-1 (Thiamin) daily to give your skin a mosquito repulsive 'flavor'."

A recent New Zealand Dermatological Society internet posting (DermNet) states:

> "Thiamin (vitamin B1) can be used as a systemic insect repellant (the skin has a characteristic smell)." Extracted from: Textbook of Dermatology. Eds.: Rook, A., Wilkinson, D.S., Ebling, F.J.B., Champion, R.H., Burton, J.L. Fourth Edition. Blackwell Scientific Publications

For some time, German pharmacies have been vending ampoules containing liquid B-1 thiamin for topical application use. Its purpose is to create a skin surface odor that will repel biting insects.

In 2003, a US company with extensive experience producing impregnated polymer (transdermal) patches for various applications, developed a B-1-based, sustained-release patch as an insect repellant and has successfully marketed it domestically and internationally. Their distributor in the UK was granted European Community registration for the patches as an insect-repellant and is actively marketing the product throughout the European Community.

The patches were also provided the Israeli military through their mission at the United Nations for trial utilization in the desert as a means of protection against sand fleas.

The highly-respected Noguchi Memorial Institute for Medical Research in Legon, Ghana recently concluded an initial study of the B-1 thiamin patches in a mosquito-intense environment with follow-up studies in process Other efficacy studies conducted in Ghana and Liberia in several geographic locales have yielded consistently positive results. After extensive review, the Ghana Food & Drugs Board, the National Agency for Food & Drug Administration and Control (NAFDAC) in Nigeria and the Ministry of Health of the Côte d'Ivoire have all approved the TPI B-1 thiamin mosquito patches for sale and they have been recommended by the Ghana Schools Health Education Program for use in the schools there.

A recent initiative – *the West African Malarial Prophylaxis Initiative* – has been undertaken in Ghana, Liberia, Nigeria and Côte d'Ivoire (expanding to other West African nations) which represents an attempt to protect children against the bite of the *anopheles* mosquito by large scale use of the B-1 patches.

FIGURE EXCERPTED FROM THE PRELIMINARY REPORT BY THE DEPARTMENT OF PARASITOLOGY OF THE NOGUCHI MEMORIAL INSTITUTE FOR MEDICAL RESEARCH:

“Evaluation of the Efficacy of Impregnated Thiamine-Based Formula Adhesive Tape Against Mosquito Bites in Malaria-Endemic Areas”

The findings from this study revealed a nearly 2:1 ratio between the number of mosquitoes collected by the collectors wearing patches and the number collected by those not wearing the patches (2,353 collected *without* the patch vs. 1,361 collected *with* the patch). As there were errors in the field implementation protocols, NMIMR is undertaking a new round of field trials throughout the country using revised protocols. It is anticipated that this could yield heightened differences between the “*with patches*” and “*without patches*” groups.

EFFICACY STUDIES IN LIBERIA AND GHANA

The Need for the Studies:

Because malaria represents the most prominent and vexing health issue in Africa, it is clear that a product which promises breakthrough protection against the bite of the *anopheles* mosquito demands serious on-the-ground testing in "real life" situations. In its report dealing with the mosquito-avoidant patches, the highly-regarded Noguchi Memorial Institute for Medical Research observes:

> "…species *Anopheles gambiae* and *An. funestus* that transmit malaria… also transmit the parasite that causes lymphatic filariasis. It was thought that if the repellence of the adhesive patch could be demonstrated in the field its value would not be restricted to malaria but also against other mosquito vector-diseases of medical importance, e.g., haemorrhagic fevers, etc. in the tropics".

In the same report, the Institute further asserts:

> "…novel vector control tools are required to compliment existing measures for synergy to subsequently reduce the disease burden."

A review of the action and history of B-1 thiamin as an insect repellant coupled with the commercial success of the B-1 transdermal patches in the USA, Europe and the Caribbean suggests the potential for these patches to become the "new technology" mosquito-avoidant ("novel vector control tools") alluded to in the Noguchi report and a leading anti-malarial prophylaxis. For this reason, several rounds of efficacy testing for the patches was undertaken in different locales in West Africa and with different populations.

Study Design:

An everyday "real life" test of the efficacy of the patches as a mosquito-avoidant was evolved that compared the amount of mosquito biting experienced: 1) by subjects using the patches for protection; and 2) by subjects not using the patches for protection. For both ethical and logistical reasons it was decided to use "pre-treatment" and "post-treatment" measures with the same subjects rather than employ experimental (using patches) and control (not using patches) groups. Subjects using the patches would go about their everyday lives in the usual places with no changes.

Lacking practical objective or third party means for quantifying the frequency of biting (e.g., consistent observation or recording of subjects), a structured, non-anecdotal self-reporting design was selected. This design permitted relatively uncomplicated implementation and feedback. Since mosquitoes are a persistent everyday problem and rank high in the awareness of everyone living in West Africa, subjects had a realistic basis on which to report their mosquito-biting experiences.

To address the issue of the generalizability of the findings the study was replicated in various locales with different populations to see whether or not a clear and consistent pattern of results emerged. Accordingly, studies were conducted with six diverse and geographically dispersed groups: two in Ghana and four in Liberia. These groups exhibited a wide diversity in subjects' ages and environments: young adults in a university setting in Accra, Ghana, residents of a Liberian refugee camp in Ghana, adults and children in schools and clinics in the Salvation Army program in Monrovia, Liberia, adult church members and school children and teachers in two different settings in Monrovia and adult staff members in a leading newspaper in Monrovia. Additional studies are ongoing in another newspaper in Monrovia and in a large outdoor industrial program in Ghana.

Instrumentation:

The data-collection instrument developed was a structured, objective self-reporting form. It consisted of a two-part questionnaire, the first part to be completed by subjects before their use of the patches and the second part after their use of the patches. In the first part, subjects were asked to rate the frequency with which they were bitten by mosquitoes in normal, everyday life using no anti-mosquito prevention (pre-treatment) and in the second part they were asked to rate the frequency with which they were bitten by mosquitoes after they had begun or completed usage of the mosquito-repellant patches (post-treatment).

For each of the items, subjects were instructed to respond by selecting one of the discrete options along a five-point rating scale. The rating scales for both items were identical. The options ranged from no biting on the low end ('None") to a high frequency of biting on the high end ("A Lot").

Item number one asked subjects to identify the amount (frequency) of mosquito biting that they experienced *before* receiving the patches. They were given five options: "None", "Very Little", "Some", "More" and "A Lot". The least possible frequency of biting ("None") was given a value of 1 on the rating scale, the next point ("Very Little") a value of 2 and upward to the greatest possible frequency of biting ("A Lot") which was given a value of 5 on the rating scale. Hence, the lower the number, the less amount of biting experienced; the higher the number the greater amount of biting experienced.

Item number two asked subjects to identify the amount of biting that they experienced *once they had begun or completed using the patches* using the same rating scale, ranging from the least amount ("None", value of 1) to the greatest amount ("A Lot", value of 5).

Procedure:

Subjects were volunteer participants living and working in typical West African mosquito-intense environments. They were asked to rate the frequency of biting that they experienced in everyday life prior to using the patches.

The subjects then received a one-week's supply of four TPI mosquito-avoidant patches, each containing ≥ 100 mg. of B-1 thiamin in controlled release (transdermal) form and the standard instructions for use. They were asked to follow the instructions and remain alert to the amount of mosquito biting that they experienced. At the conclusion of the week using the patches, they were asked to record the frequency of mosquito biting that they experienced while using the patches, using the same rating scale as the pretest measure.

Treatment of the Data:

In each study, the responses from all subjects to the "*before*" item were pooled and a mean computed. This represented the baseline, pre-treatment mean for that study. The lower the number, the less biting experienced. Similarly, the responses from all subjects in each study to the "*during or after*" item were pooled and a mean computed. This represented the post-treatment mean for that study. The lower the number, the less biting experienced.

An inspection was made of the distribution of the responses for each of the items in each study and standard deviations computed for those studies for which statistical analysis was applied (Valley View University and the Liberian Refugee Camp).

Findings: Central Tendency and Variability:

Subjects' response patterns were nearly identical across all of the studies. Pre-treatment means fell at or slightly above 4.0 on the rating scale ("More"), while post-treatment means fell between 1.5 and 1.77 (between the lowest and second lowest points on the rating scale). There was also consistency among the studies in the distribution of the responses. In all cases, the pre and post-treatment response patterns were heavily skewed in opposite directions. The pre-treatment responses were heavily clustered at or next to the high end of the scale (high frequency of biting) while the post-treatment responses were heavily clustered at or close to the low end of the scale (low frequency of biting). The means and standard deviations for the Valley View University and Liberian Refugee Camp studies are presented below:

Table I:
Pretest and Posttest Means and Standard Deviations
Valley View University Study

Pretest Mean: 4.000	Pretest Standard Deviation: 1.114
Posttest Mean: 1.667	Posttest Standard Deviation: 0.758

Table II:
Pretest and Posttest Means and Standard Deviations
Liberian Refugee Camp Study

Pretest Mean: 4.563	Pretest Standard Deviation: 0.512
Posttest Mean: 2.188	Posttest Standard Deviation: 0.403

Three-dimensional bar graphs for each study displaying both the pre and post treatment means follow. Each study's bar graph is followed by a chart displaying the rating scales for the two questionnaire items and indicating the mean response for each item by a large "X" on that rating scale. A brief explanation accompanies each study's chart. Due to the unique conditions under which the study was conducted in the Liberian Refugee Camp and their possible impact on the results for that study, a more comprehensive discussion is provided with that study's chart.

Statistical Analysis:

The data from the Valley View University and the Liberian Refugee Camp studies were subjected to parametric statistical analysis. As a direction for the results was predicted, a one-tailed *t*-test for unpaired data was applied. Under the assumption that the variances for the pretests and posttests were not equal Welsh's correction was applied. Although the data were not dispersed in a "normal" (Gaussian) pattern it was believed that *Student's t* could be applied with the Welsh correction with little likelihood of a Type I (α) error.

In the Valley View University study, the difference between the means of the pre and post treatment measures was statistically significant (t = 9.483 with 51 df) in the predicted direction (less biting post-treatment) at a extremely high level of confidence ($p < .0001$; "extremely significant").

In the Liberian Refugee Camp study, the difference between the means of the pre and post treatment measures was statistically significant (t = 14.572 with 30 df) in the predicted direction (less biting post-treatment) at a extremely high level of confidence ($p < .0001$; "extremely significant").

Interpretation of Findings:

The visibly large pre vs. post-treatment mean differences (representing reduced frequency of biting after using the patches) were shown to be extremely significant. These results were consistent across both of the studies subjected to statistical analysis.

Although the *n*'s in the studies were small (≤ 30) and the distributions skewed, the extremely significant differences ($p < .0001$) vindicated the application of statistical analysis.

Because of the uniformity of the response patterns across all of the studies and the extremely significant differences shown between the pre and post treatment means in the two studies subjected to statistical analysis it was decided not to subject the remaining four studies to statistical analysis while maintaining an assumption that the difference between the pretest and posttest means in each of these studies was significant.

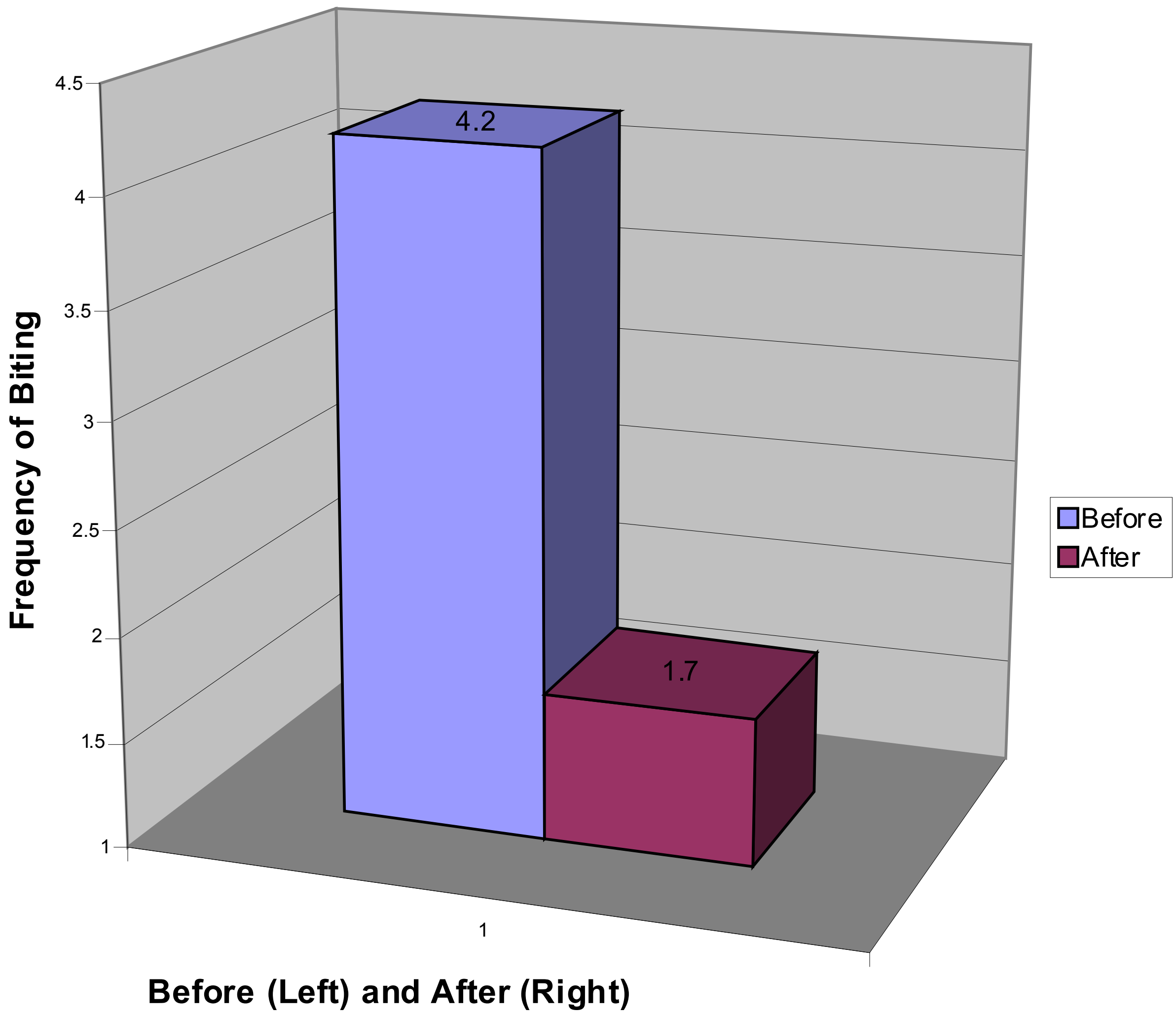
Discussion:

A criticism of self-report studies (pre and post-treatment) is the "placebo effect", whereby subjects believe that they experience changes because they were subjected to a treatment (whether or not that treatment did, in fact, engender any real changes). In this study the placebo effect was not believed to have been an issue in subjects' response patterns: being bitten by a mosquito is a vivid, tangible event. There are no subjective degrees of being bitten: each mosquito bite is a digital, not analogue, experience. One is either bitten or is not bitten. Hence, although subjects received an anti-mosquito treatment, the reality of being bitten is vivid enough as to not being masked by their having received a treatment.

The selection of a design and instrument that were "field friendly"; i.e., easy to implement and adaptable to varied settings proved very helpful, especially in undertaking the study in the Liberian Refugee Camp.

The consistency of the results from setting to setting is compelling. The closely-matched results from diverse study populations in widely different settings and geographic areas show a persistent pattern that is difficult to explain other than in cause-and-effect terms. The follow-up study at the Noguchi Memorial Institute should provide additional important insights in the efficacy of a product that shows so much promise in the ongoing fight against the largest and most pernicious health problem in Africa.

SALVATION ARMY - MONROVIA



COMPARISON OF MEAN FREQUENCY OF MOSQUITO BITING:
BEFORE USING PATCHES AND DURING/AFTER USING PATCHES

Study: Salvation Army, Monrovia, Liberia

1. *Before* using patches:

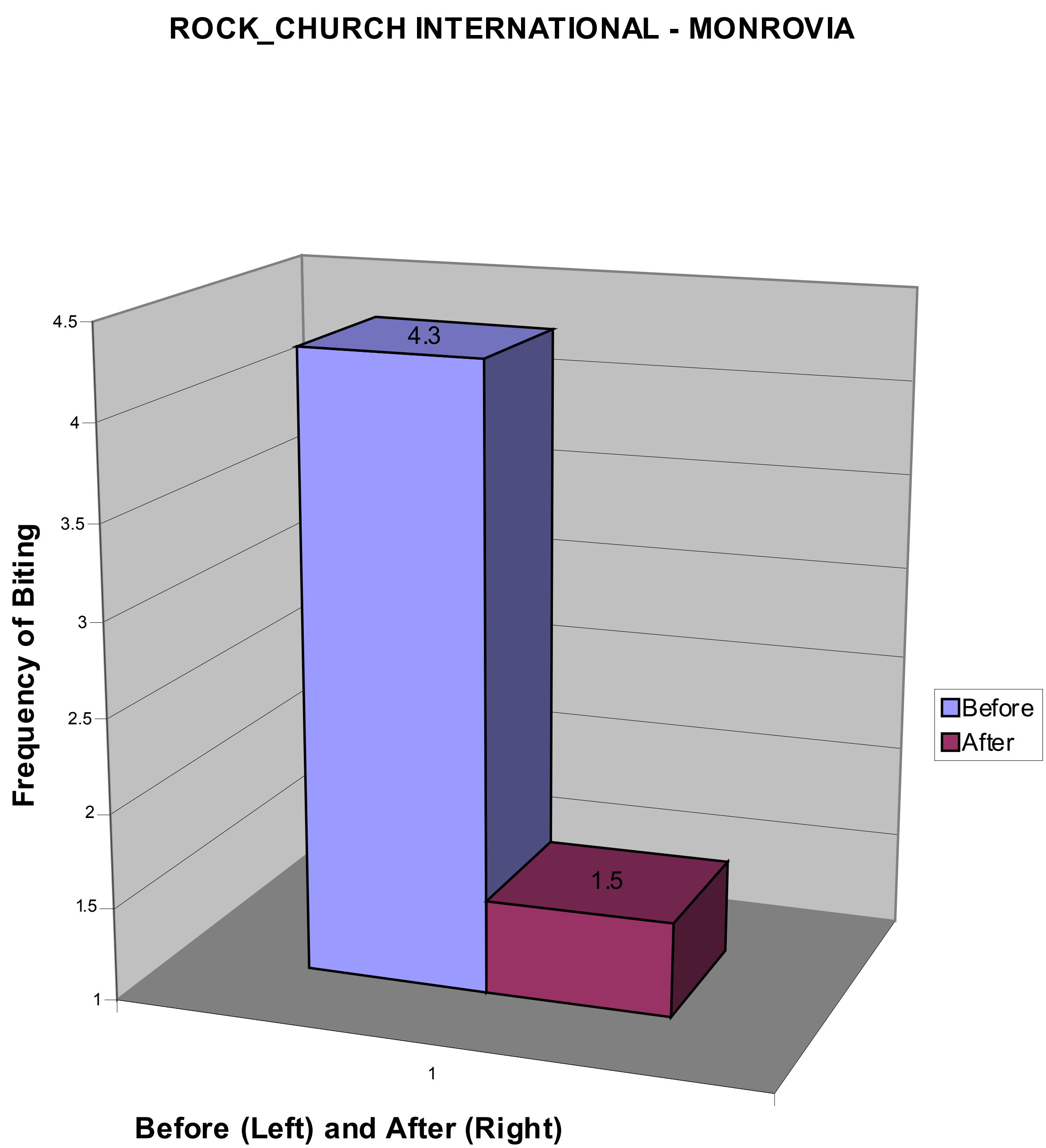
```
  1              2              3              4               5
  I______________I______________I______________I_X_____________I
None           Very           Some           More            A Lot
               Little
```

2. *During or after* using patches:

```
  1              2              3              4               5
  I__________X___I______________I______________I_______________I
None           Very           Some           More            A Lot
               Little
```

EXPLANATION:

Before using the patches, participants in this study reported being bitten – on average – on the high end of the scale, above "More". After applying the patches, they reported being bitten – on the average –on the low end of the scale, between "None" and "Very Little", slightly closer to "Very Little".



ROCK_CHURCH INTERNATIONAL - MONROVIA
4.5
4
3.5
3
2.5
2
1.5
1
Frequency of Biting
4.3
1.5
1
Before
After
Before (Left) and After (Right)

COMPARISON OF MEAN FREQUENCY OF MOSQUITO BITING:
BEFORE USING PATCHES AND DURING/AFTER USING PATCHES

Study: Rock Church International, Monrovia, Liberia

1. *Before* using patches:

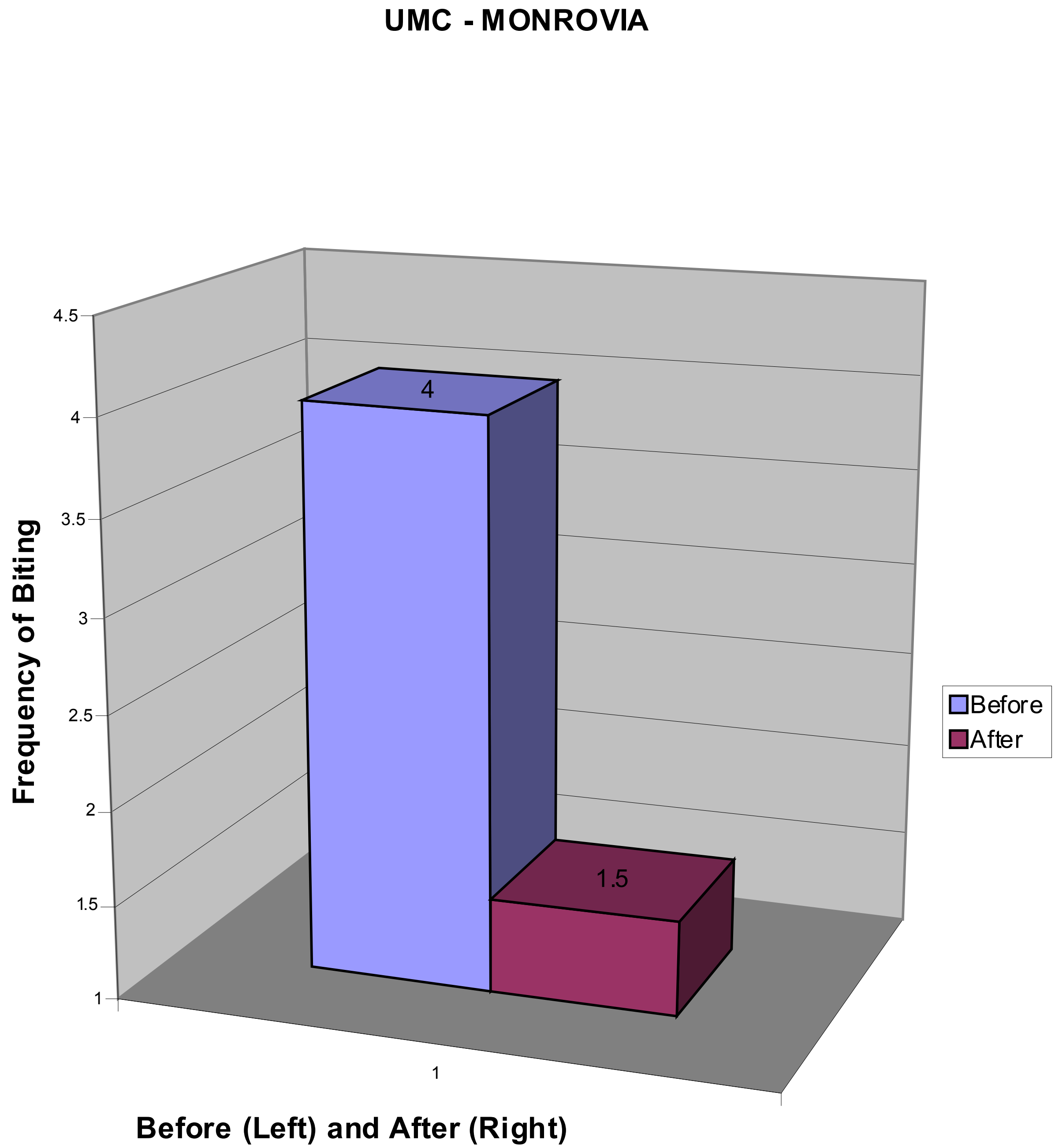
```
 1            2            3           4           5
 I____________I____________I___________I_X________I
None         Very         Some        More        A Lot
             Little
```

2. *During or after* using patches:

```
 1            2            3           4           5
 I_____X_____I____________I___________I___________I
None        Very          Some        More        A Lot
            Little
```

EXPLANATION:

Before using the patches, participants in this study reported being bitten – on average – on the high end of the scale, above “More”. After applying the patches, they reported being bitten – on the average –on the low end of the scale, between “None” and “Very Little”.



UMC - MONRIVIA
4.5
4
3.5
3
2.5
2
1.5
1
Frequency of Biting
4
1.5
1
Before (Left) and After (Right)
Before
After

COMPARISON OF MEAN FREQUENCY OF MOSQUITO BITING:
BEFORE USING PATCHES AND DURING/AFTER USING PATCHES

Study: United Methodist Church, Monrovia, Liberia

1. *Before* using patches:

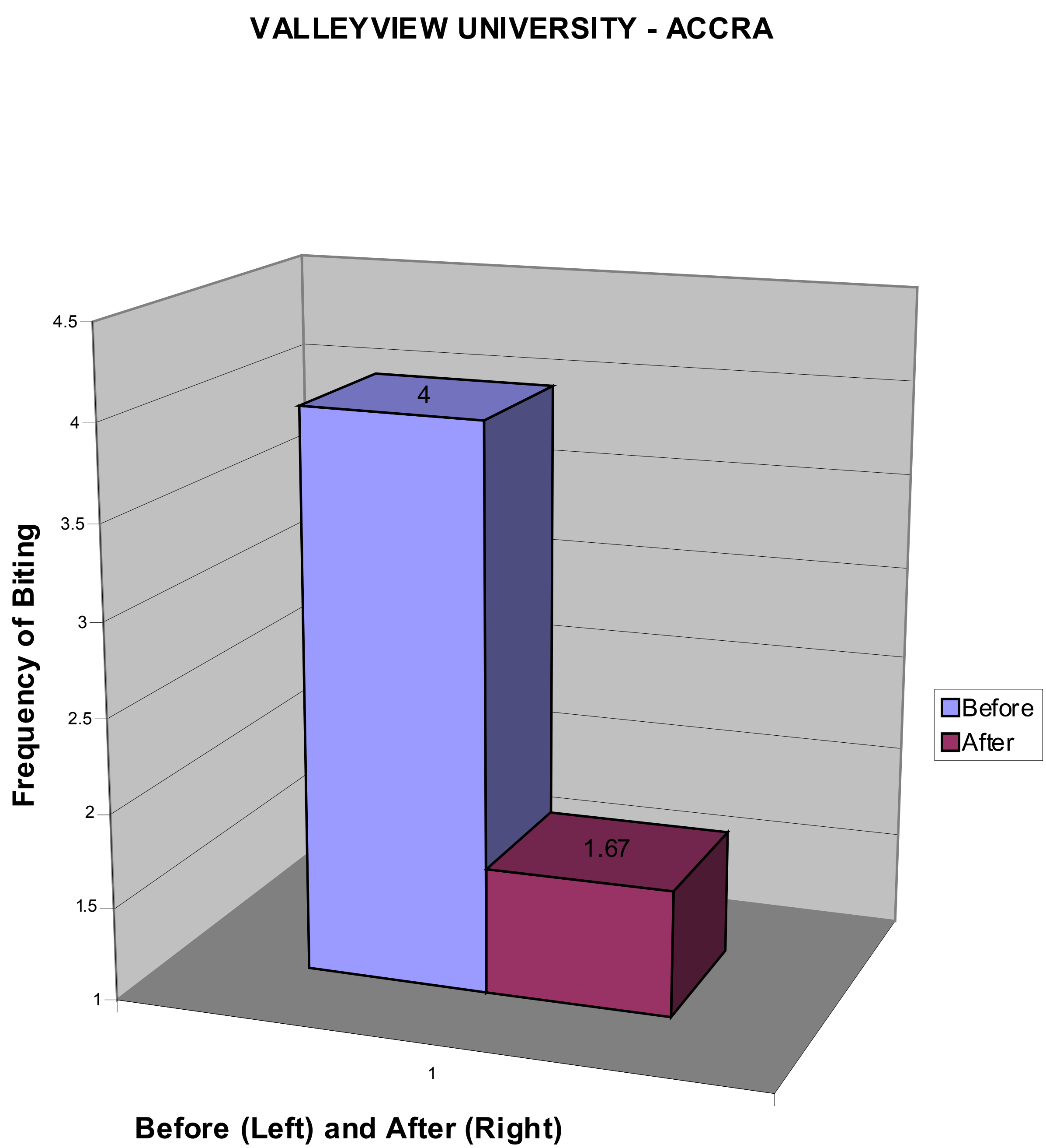
```
1            2            3            4            5
I____________I____________I____________X____________I
None         Very         Some         More         A Lot
             Little
```

2. *During or after* using patches:

```
1            2            3            4            5
I_____X______I____________I____________I____________I
None         Very         Some         More         A Lot
             Little
```

EXPLANATION:

Before using the patches, participants in this study reported being bitten – on average – on the high end of the scale, slightly above “More”. After applying the patches, they reported being bitten – on the average –on the low end of the scale, between “None” and “Very Little”.


VALLEYVIEW UNIVERSITY - ACCRA
Frequency of Biting
4.5
4
3.5
3
2.5
2
1.5
1
4
1.67
1
Before
After
Before (Left) and After (Right)

COMPARISON OF MEAN FREQUENCY OF MOSQUITO BITING:
BEFORE USING PATCHES AND DURING/AFTER USING PATCHES

Study: Valley View University, Accra, Ghana

1. *Before* using patches:

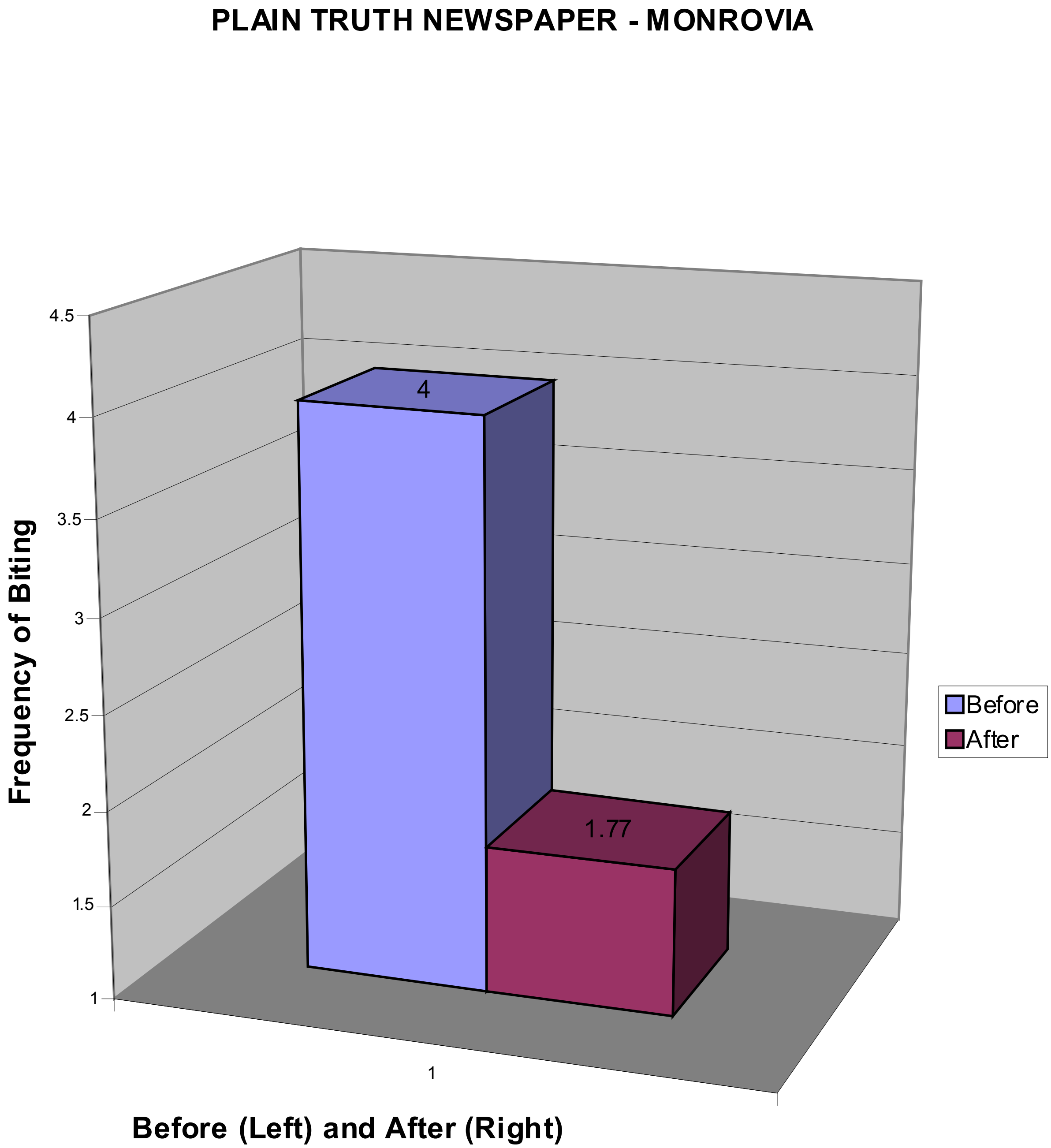
1 2 3 4 5
I___________I___________I__________X_________I
None Very Little Some More A Lot

2. *During or after* using patches:

1 2 3 4 5
I_______X__I___________I___________I__________I
None Very Little Some More A Lot

EXPLANATION:

Before using the patches, participants in this study reported being bitten – on average – on the high end of the scale, slightly above "More". After applying the patches, they reported being bitten – on the average –on the low end of the scale, between "None" and "Very Little", closer to "Very Little".


PLAIN TRUTH NEWSPAPER - MONROVIA
Frequency of Biting
4.5
4
3.5
3
2.5
2
1.5
1
4
1.77
1
Before (Left) and After (Right)
Before
After

COMPARISON OF MEAN FREQUENCY OF MOSQUITO BITING:
BEFORE USING PATCHES AND DURING/AFTER USING PATCHES

Study: The Plain Truth (Newspaper), Monrovia, Liberia

1. *Before* using patches:

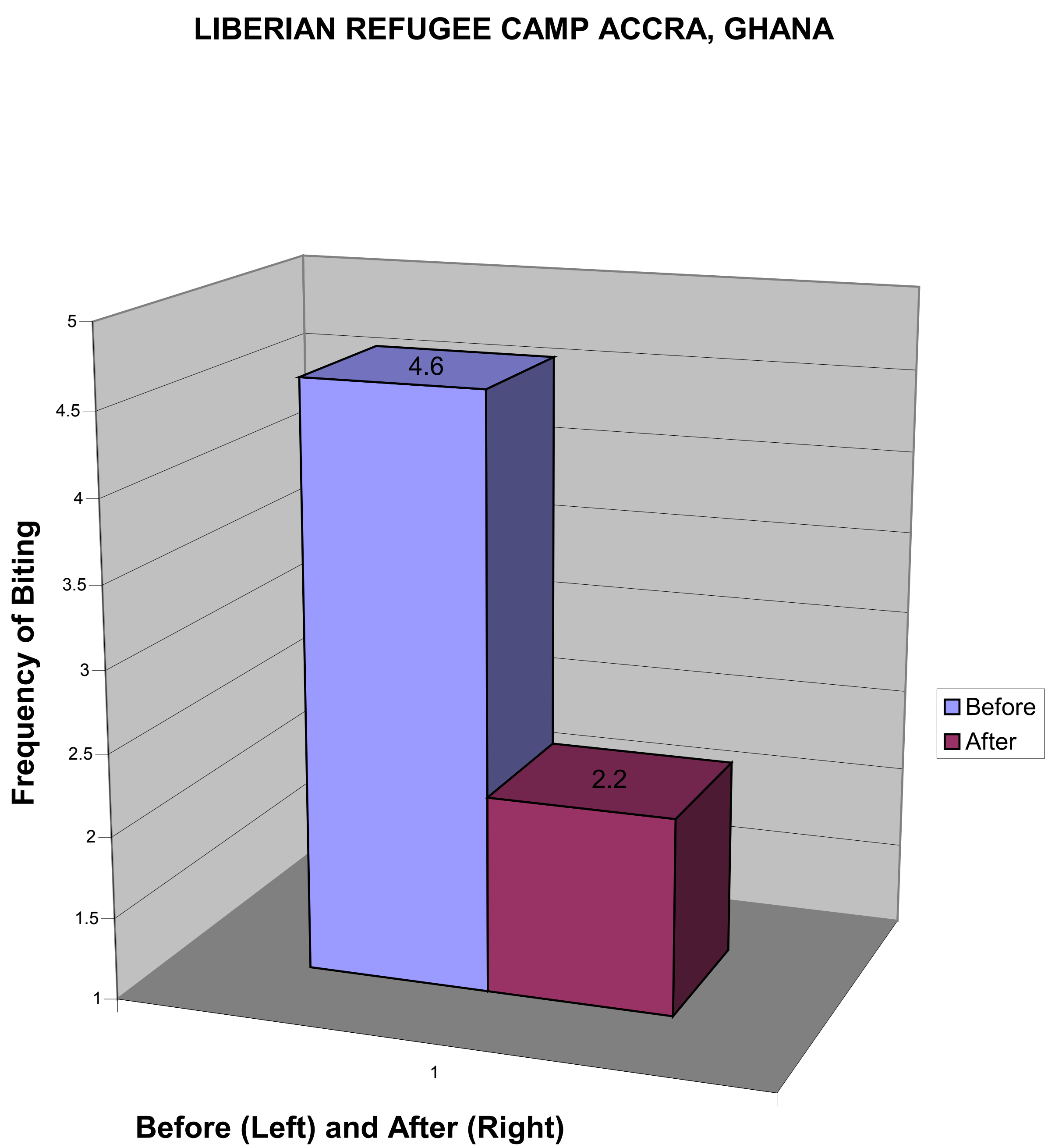
1	2	3	4	5
I	I	I	X	I
None	Very Little	Some	More	A Lot

2. *During or after* using patches:

1		2	3	4	5
I	X	I	I	I	I
None		Very Little	Some	More	A Lot

EXPLANATION:

Before using the patches, participants in this study reported being bitten – on average – on the high end of the scale, at “More”. After applying the patches, they reported being bitten – on the average –on the low end of the scale, between “None” and “Very Little”, closer to “Very Little”.


LIBERIAN REFUGEE CAMP ACCRA, GHANA
Frequency of Biting
5
4.5
4
3.5
3
2.5
2
1.5
1
4.6
2.2
1
Before (Left) and After (Right)
Before
After

COMPARISON OF MEAN FREQUENCY OF MOSQUITO BITING:
BEFORE USING PATCHES AND DURING/AFTER USING PATCHES

Study: Liberian Refugee Camp, Accra, Ghana

1. *Before* using patches:

1 2 3 4 5

I___________I___________I__________I______**X**__I

None | Very Little | Some | More | A Lot

2. *During or after* using patches:

1 2 3 4 5

I___________I_**X**________I___________I__________I

None | Very Little | Some | More | A Lot

EXPLANATION AND DISCUSSION:

Before using the patches, participants in this study reported being bitten – on average – on the high end of the scale, close to the maximum -- "A Lot". After applying the patches, they reported being bitten – on average – on the low end of the scale, slightly above "Very Little".

The range between the "before" and "after" means is nearly identical to those exhibited in the other field studies. However, in the present case, it is evident that both of these measures are elevated in comparison to the other studies; i.e., the frequency of biting -- both "before" and "after" -- is higher. This is believed to reflect several phenomena unique to the refugee camp.

First, the living and sanitary conditions in the camp are abysmal and malaria is rampant. The refugees have marginal shelter and there is standing water all around, breeding ground for mosquitoes. Due to the lack of shelter and refugee immobility, the subjects in this study represent a veritable "food supply" for the mosquitoes. In addition, sanitary practices are nearly nonexistent. Thirdly, several participants reported sharing the patches amongst family members, essentially negating their efficacy in these instances (i.e., product design and efficacy is based on one person using all four patches in sequence over a one week period).

Statistical analysis of the data reveal that the difference between the mean frequency of biting before using the patches and mean frequency of biting after using the patches is extremely significant ($p < .0001$).

Provisional conclusions that may be drawn from this study suggest that: 1) even under "worst scenario" conditions the patches exhibited efficacy; and 2) for maximum protection against biting in similar settings, shelter and sanitation issues should be addressed and that sufficient patches be made available to families in order that the "sharing" seen in this study does not take place, thus permitting their intended and most efficacious usage.

POSTLOGUE

An Inclusive Approach to Combating Malaria

In the fight against malaria, the B-1 thiamin mosquito-avoidant patches have been characterized as a “new technology” for protecting children against the bite of the *anopheles* mosquito. They provide a uniquely long (36 hour) efficacy period and a “go-anywhere/do anything” comprehensiveness of coverage that is so important for active children. They are also safe for young children.

While awaiting a breakthrough in medicine that will produce a safe, economical and long-term effective vaccine against malaria on a large scale, this dread disease remains a constant threat and reasonable people should adopt all appropriate measures to combat it. Unfortunately it is very human to think in “either/or” terms – choosing one approach over another -- even when there are definite advantages to employing multiple resources.

With this in mind, the WAMPI program is committed to an inclusive approach to combating malaria. Children and adults using the patches are encouraged to adopt other appropriate measures against malaria such as clearing land and eliminating standing water, teaching and encouraging sanitation and implementing personal hygiene measures. In addition, insecticide-treated nets (bednets) are inexpensive and are becoming more widely available. Although their scope of protection has limitations their use as an allied prevention measure is strongly recommended. Pesticide spraying inside homes has shown efficacy, although it is necessary to “change off” from one pesticide to another to avoid mosquito resistance from developing. In deference to toxicity concerns, caution in usage must be observed. However, the whole coterie of popular insect-avoidant measures such as insect-repellant lotions and sprays, smoking coils and like devices are unnecessary when using the patches. Parents are advised that care should be exercised in dispensing anti-malarial medications to children. Several of the adult drugs (when available) – particularly compound drugs that protect against all four malaria protozoans – cannot be tolerated by children even in reduced dosages.

The battle against malaria is a complex and difficult one and all practical and realistic weapons should be employed to combat it. In this battle the patches can provide the safe, day-by-day comprehensive coverage that forms the nucleus of a prevention program which incorporates the other measures recommended above.

Cost

The patches see widespread usage in the US, Europe and the Caribbean as a consumer item (vacationers, campers, fishermen, hikers, picnickers, etc.) as well as sporadic seasonal use against biting insects. In those markets, their use is occasional rather than continuous and they are priced accordingly. However, their role in Africa is as a necessary health item, their use is continuous and their cost in country must be consistent with economic realities there. Fortunately, WAMPI sources the patches directly from the manufacturer, eliminating the “middlemen” in the usual retail chain. As a result, the patches are less expensive than some measures, more expensive than others. Even in small quantity purchases their annual cost for protecting a child is far less than a single hospital visit for an infected child.

Bednets and Treatment Kits

WAMPI works closely with one of the three manufacturers of insecticide treated nets (ITN's) approved by the World Health Organization (WHO) and can provide bednets in all sizes and colors. In addition, net treatment kits -- primarily used to convert untreated nets into ITN's but also used to re-treat older ITN's – are available very economically. These kits come complete with a discardable roll-up plastic container, throw-away latex gloves and a sachet of active agent (WHO-approved insecticide) that is mixed with water in the container. The nets simply need to be soaked and dried. The insecticide permits the nets to be made with a more open weave which makes them lighter but most importantly, less of a "heat trap" for the sleeping environment. This should contribute toward better user compliance.

Summing It Up:

As discussed in the Prologue and earlier in this document, medical researchers, with generous grants from the Bill and Melinda Gates Foundation, NGO's and philanthropic organizations around the world are "pulling out the stops" in the race to find an effective, safe, child-friendly and economical anti-malaria vaccine. Unfortunately, they are facing the same task that their predecessors faced over the decades (this is an old battle): that the four malaria protozoans are what are called "fast-reproducing microbes", which gives them the ability to "adapt" to new medications very quickly. By the time you have read this explanation the protozoans that were "newborns" in the first sentence likely have grandchildren. In addition to the difficult scientific challenge, bringing a new, apparently viable vaccine to market involves substantial testing followed by regulatory approvals, followed by the production funding process, manufacturing, packaging, shipping, distributing, etc. And, hopefully, most of the vaccine reaches its target population rather than the black market. All of this means – in a practical sense – that we cannot afford to accept the *status quo* while waiting for "the cure" to come along to save lives. Everything that can be done to defeat malaria must be done. And all parties agree that the best way to accomplish this is prophylaxis – preventing children and adults from being bitten by the *anopheles* mosquito.

It is also clear that depriving the *anopheles* mosquito of its blood supply has the potential for making a dramatic impact on the fight to defeat malaria. This is accomplished by keeping mosquitoes away from their intended victims. Easy to say, difficult to do. The mosquito-avoidant patches, used in concert with the other measures recommended above, are positioned to play a unique and special role in accomplishing this.

Thank you for your consideration of our program. Keep safe and well.

“I pray God look with favor upon your journey and deliver you safe back.”

Geoffrey de la Tour-Landry, 1371

About Us

NMIMR

University of Ghana

The Noguchi Memorial Institute for Medical Research is a semi-autonomous I
the University of Ghana established in 1979; and a constituent member of th
Health Sciences, University of Ghana. The Institute was built and donated to
Ghana by the Japanese Government. It's history cannot be told without maki
of Dr. Hideyo Noguchi, a Japanese scientist who died in Ghana in 1928 while
into yellow fever.

The Institute is a biomedical research facility and conducts research mainly i
communicable diseases and nutrition. It is made up of nine Academic Depart
has several facilities. The facilities are also used for training both undergradu
postgraduates from tertiary institutions in the country and abroad. It has stro
the Ministry of Health and provides high end laboratory support to public hea
programmes of the Ministry. The Institute also provides training in laboratory
technicians of the Ministry of Health.

Principal Research Areas

- Malaria
- Schistosomiasis
- Onchocerciasis
- Filariasis
- Diarrhoeal Diseases
- Buruli ulcer
- Tuberculosis
- HIV/AIDS
- Sexually Transmitted Disease
- Food Security
- Micronutrients
- Parasite Immunopathology
- Viral Haemorrhagic Fevers
- EPI Diseases

Key Facilities

- General Laboratories
- Electron Microscopy
- Biosafety Level 3 Labo
- Animals Experimentati
- Conference Hall
- Clinical Research Facil
- Electron Microscope
- Mercury Analyser
- Liquid Nitrogen Plant
- Staff Canteen
- Sample Collection & St Facility
- Research project office
- Administrative Block fo
- Health Support Centre

- Sickle Cell Disease
- Plant Medicine
- Antioxidants
- Environmental Pollution
- Infant and Maternal Mortality
- Molecular Biology

- Health Support Centre

[Noguchi] [About Us] [People] [Departments] [Projects] [Library] [WACIPAC] [Ac

Contact director@noguchi.mimcom.net with comments or questions reg site.

.Site Last Updated July 2006