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A Physician's Commentary:

B-1 THIAMIN PATCHES AS AN INSECT REPELLANT AND ANTI-MALARIAL PROPHYLAXIS

Following discussions with Dr. Fred Honigman, a former research director, author and consultant, 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". 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 (*Appendix A*). 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 (*Appendix B*).

It is not rare 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 11/13/06

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APPENDIX A

SELECTED DOCUMENTATION:

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

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 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 long ranges, whereas olfactory stimuli become more important as a mosquito nears its host.dioxide and lacric acid) 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.

3. 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.

4. 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

APPENDIX "B":

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 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 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'."

In 2003, a US company, Transdermal Products, drawing on several years' 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. Because the active agent is a vitamin, in the US it falls under the Vitamin and Cosmetic Act and is not subject to regulation as a drug by the US Food and Drug Administration and is traded freely. Transdermal Products' distributor in Sheffield, England, Medi-Patch Clinic, Ltd., a subsidiary of Medi-Tech Industries, LTD, was granted European Community registration for the patches as an insect-repellant (CE registration number CA008413) and is actively marketing the product throughout the European Community through their web-site at http://www.medi-patch-clinic.co.uk .

Patches were provided the Israeli military through their mission at the United Nations for utilization in the desert as a means of protection against sand fleas. Recently, patches were obtained by Walter Reed Army Hospital in Washington, DC for trial utilization there. A recent initiative has been undertaken in West Africa – *the West African Malarial Prophylaxis Initiative* – which represents an attempt to protect children against the bite of the *anopheles* mosquito by large scale use of the B-1 patches.