A sustainable strategy for eliminating DDT from disease vector control programs and reducing malaria: the Mexican Model

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INTRODUCTION

Malaria continues to be one of the most significant health problems, causing approximately 200 million cases a year with between one and two million deaths. World efforts have been focused on vector control through the use of insecticides, applied residually on the walls of homes or impregnated in bednets, and through early diagnosis and treatment of those infected with this illness. In response to the resistance of mosquitoes and parasites to insecticides and respectively, there is increasingly more research on these phenomena and some important advances have been made, although these threats have not been erased.1

A different perspective asserts that one of the fundamental problems that must be resolved in order to control malaria is whether actions aimed at vector control and early diagnosis and treatment are ongoing and sufficient in nature. There are other problems that are no less important, specifically: 1) The need to update the natural history of the illness and its epidemiology, 2) The need to discuss whether such large amounts of insecticides are actually necessary to control transmission, 3) Whether it is truly necessary to return to the use of DDT, 4) Whether we can improve diagnosis and treatment of those infected with this illness, 5) To better recognize the dynamics of vector populations and to use principles other than Insecticide use, 6) The need to truly work together with communities, 7) Whether only these mosquitoes are controlled with malaria vector control measures, and 8) The fact that even if this illness is brought under control, the risks associated with that control remain in most situations. In addition, one of the problems analyzed most recently is that the prices of the inputs used in controlling malaria are inaccessible, and while the incidence of malaria has increased, resources have diminished while costs have risen. Together, all of this confirms that malaria is indeed a neglected disease.

The scientific information produced and published since the beginning of the last century has still not been analyzed at the international level. Some examples of relevant information include: the findings indicating that zoonotic illnesses are transmitted in concentrated sites where the animals involved have found their niches;2 and references on malaria in Panama indicating that most infections were found in the same homes and some individuals had repeated infections, leading to the conclusion that the most important types of P. vivax malaria cases to be monitored are those in which the same individuals have numerous repeated infections.3,4 Nevertheless, the information in all of these reports was disregarded when strategies for eradicating malaria were designed in the mid-1950s.5

More recently, a range of evidence on the epidemiology of malaria in different parts of the world has been published. It has been confirmed, for example, that there are homes and families in which malaria infections are constantly present, and it is assumed that the
transmission in these homes is more intense than in other homes.6,7,8,9,10,11,12,13,14 Along this line it is very important to consider the definitions of ecological habitats and niches. If we are to reflect upon this information, it is necessary to consider the possibility that the transmission of malaria is concentrated in certain places where it only takes place in the presence of the elements playing a part in the niches established by vector mosquitoes. It is perhaps for this reason that there are certain contradictions in the scientific information on this topic, such as the failure of zooprophilaxis or bednets impregnated with insecticides, to mention two examples.15

Insects in general engage in three major activities that assure their survival. The first is mating (which takes place in two stages, specifically the actual mating and then oviposition). The second major activity is feeding, and the third consists of protection and rest. In all of these processes, temperature seems to be a fundamental element, as well as the substances that regulate mosquitoes’ interaction with the hosts from which they obtain their food, and geomorphological conditions such as vegetation, valleys, caves, plus some of the characteristics of the homes where the vectors arrive. The feeding processes of plant-eating insects (phytophagous) have been described in a scheme that seems to coincide universally with other insects, such as blood-sucking insects like mosquitoes.16,17 In these feeding schemes, the insects’ sensory organs are fundamental for detecting smells, seeing shapes and colors, and perceiving temperatures, for example. Several scientific documents have been written on this.18,19,20,21

In conclusion a “niche is a place where there is a prevailing group of ecological conditions that can be exploited effectively and sufficiently by a species in order to assure its survival” (Hutchinson).16 From this perspective, the nids of malaria transmission and the transmission of many other illnesses and vectors could be the result of the coincidence of a group of variables in which these living beings can survive well enough to assure that their species survives, and to assure that the extrinsic incubation periods are completed—and thus, illnesses can be transmitted. Therefore, the vectors that do the best job of adapting biologically and identifying their niches may be those responsible for transmitting illnesses—and not all vectors—and these would not seem to be random processes.

In the 1930s Hoffman described the breeding grounds of nearly all the anophelines in the Americas. There are three in reference to An. Pseudopunctipennis that are especially worth mentioning from his studies in Mexico. He not only described the biology of this malaria vector, but also suggested some logical control measures such as eliminating filamentous green algae from breeding sites and streams, to achieve effective larval control.22,23,24 Unfortunately, his suggestions were not implemented in malaria control programs, or at least not until the 1990s when some studies were published on the impact from eliminating algae on larvae in breeding sites.25

**General characteristics of malaria in Mexico**

In Mexico malaria has been considered to be a disease of unstable transmission during the fifty years in which government programs have addressed this health problem. Nevertheless, the Mexican Model for Malaria Control has been carried out on the basis of epidemiological and entomological foundations, in which insecticides are used only as a complementary element, since vector control is achieved by physically modifying breeding sites through community participation. With this model the use of drugs has been adjusted to the life cycle of the primary prevailing parasite and the transmission of this disease is controlled with emphasis on focalized treatment for clinically symptomatic, atypical and
asymptomatic cases. This model has been used during the last seven years. With these efforts the incidence of malaria has been reduced to historically low levels and government costs have been reduced, since spraying operations have been practically suspended in the entire country, and responsibility for vector control activities has been transferred to communities. Government brigades have been in charge of detecting, diagnosing and treating persons with this illness, as well as providing training to communities and supervising community actions in high-risk areas. The purpose of this article is to describe the Mexican Model for Malaria Control that was developed in 1999 and then implemented nation-wide beginning in 2000, and to analyze its successful impact in the years up until 2006.

In the mid-1950s malaria was found in all the coastal areas of Mexico with the exception of Baja California, and also in the country’s central regions located at less than 1,800 meters above sea level. Overall it was estimated that nearly 50% of the population and nearly 60% of national territory were at risk (Map 1). Beginning in the year 2000 the transmission areas had been reduced by more than 80% of those originally established, corresponding to scattered rural localities, nearly all of which had less than a thousand inhabitants and were among those most remotely located in the country. Originally, this endemic disease of the 1960s was found in 27 of the country’s 32 states, and by 1997 it had been diminished to 24 states still characterized by endemic transmission.

Map 1

Risk areas of malaria in Mexico

99% of the cases correspond to *Plasmodium vivax*, and only a few cases of *Plasmodium falciparum* are found in localities bordering with Central America and along the routes of migration by Mexican and Central American populations from the south to the north. The most recent intense outbreaks of *P. falciparum* in the country took place during the 1980s. The strains of both species are susceptible to treatment with chloroquine and primaquine. The main vectors in Mexico are *Anopheles pseudopunctipennis* and *An. albimanus*, although there are at least four others that have been involved in transmission, however with less intensity.

Between 1959 and 1988 the guidelines suggested for eradicating malaria were implemented, obtaining varying degrees of control over the disease, depending on
whether adequate resources were available. The reasons for this situation included changes in administration, different priorities in policies, plus national and international financial crises and decentralization. Between 1989 and 1997 a new scheme was designed, based on activities for controlling the disease taken from eradication guidelines. The new scheme was given the name of Simultaneous Intensive Actions Program, and was implemented only in hyperendemic localities. The program managed to combat the transmission of malaria to a considerable degree, particularly malaria transmitted by An. albimanus. DDT was used in Mexico from the beginning of eradication efforts up to 1999. Due to the success from a new scheme for working on malaria control, the use of DDT was eliminated from the Malaria Program in 2000 and its production in Mexico was also cancelled during that year.\textsuperscript{28,29}

From the beginning of eradication efforts, varying actions were taken to eliminate malaria in some cases, and in others, to achieve better control over this disease. Among these efforts, a treatment for controlling an outbreak caused by \textit{P. vivax} and \textit{P. falciparum} in the state of Chiapas was used for the first time in 1981. It led to the elimination of the \textit{P. falciparum} endemic disease and a 50\% reduction in the \textit{P. vivax} endemic disease. The treatment was referred to as the Massive Single Dose Treatment (\textit{Tratamiento de Dosis Única Masiva}—TDUM in spanish) and consisted of administering chloroquine at 10 mg/kg of body weight and primaquine at 0.75 mg/kg of body weight.\textsuperscript{30} The TDUM treatment has been fundamental in eliminating \textit{P. falciparum}, due to primaquine's antigametocyte effect. It has also been used as a preventative, suppressive dose, and to date there are no reports of secondary problems or resistance to medicines.\textsuperscript{31}

In 1998 there was a \textit{P. vivax} outbreak along the Pacific Ocean coast in the state of Oaxaca, causing 18,000 cases of malaria. The outbreak occurred after the area had been affected by two hurricanes the previous year, but also due to a change in government authorities. Another significant antecedent was that health services in Oaxaca had been decentralized the year before. The Mexican Model of Malaria Control currently being implemented in the entire country was based on experiences from that particular outbreak, and it was also an opportunity to update the natural history of malaria. Epidemiological, entomological and strategic intervention studies were conducted, to control the outbreak and seek new forms of assuring more permanent control. The latter was considered to be of utmost importance, since the success of control measures is always threatened not only by resistance to drugs and insecticides by parasites and vectors, respectively, but also due to the lack of sufficient resources, changes in labor routines, administrative changes and changes in government officials, labor problems—and now, also due to climatic changes that are increasingly more frequent and more intense.

One of the most important premises was the definition of risk factors accompanying malaria transmission, with the objective of seeking to modify this transmission, and not only controlling mosquitoes and parasites. In 1998 DDT was still used in the country, however its use had diminished between 1989 and 1998, from 1,840,300 to 651,200 homes sprayed with DDT. This reduction was possible since most of the intense outbreaks in the country had been controlled through the Simultaneous Intensive Actions Program, which had controlled the endemic disease, reducing the 101,241 cases of malaria in 1989 to 4,805 cases in 1997. However, there was once again an outbreak of more than 25,000 cases in 1998. This was caused by the fact that even though the transmission of malaria had been controlled, all the other conditions persisted, with the exception of the parasites. In this article I will be describing the experiences in Oaxaca and the results around the country when the model was expanded.
METHODS

STRATIFICATION METHODOLOGY

A process was undertaken to establish the stratification of malaria in Oaxaca, selecting the localities with the highest levels of transmission. Out of a total of 1,040 localities testing positive in 1998, the 733 corresponding to the region with the highest level of transmission were selected. Extraordinary measures were implemented in those localities, and initially the usual measures were implemented in the rest of the sites, characterized by lesser degrees of transmission. The following variables were used for a previous ten-year period: Localities Testing Positive, Number of Cases, and Years with Transmission. Secondly, the years of transmission were grouped into 1-2, 3-4, 5-6, 7-8 and 9-10 years. The localities testing positive and their cases were distributed using this scheme. Three levels were established, according to the number of cases per locality and the number of years of the transmission's persistence. The first level corresponded to 7-10 years of transmission, the second to 3-6 years of transmission, and the third to 1-2 years of transmission.

In Level 1 the distribution of cases among individuals and homes in the most affected localities was verified, with the objective of identifying those with repeated infections and the intensity of the transmission within each home. Initially, epidemiological studies were conducted in the majority of Level 1 localities, to establish the distribution and frequency of cases in these communities, and to make a comparison between homes with confirmed cases and homes in which transmission did not generally occur. The period of analysis for the nominal lists of confirmed cases was for the prior three years in Level 1 localities, and for the prior five years for the localities in Levels II and III.

DESIGN OF CONTROL MEASURES

On the basis of the stratification process, two major strategies were designed:

**Intensive control of outbreaks.** The objective was to control the transmission of malaria in Level 1 localities through the application of a massive single dose treatment (TDUM) of chloroquine at 10 mg/kg of body weight, and primaquine at 0.75 mg/kg of body weight. Those excluded from the strategy were pregnant women, children under the age of five, individuals with concurrent illnesses, older adults and those refusing treatment. The measures were implemented in Level 1 localities through three TDUMs, with a one-month interval between each treatment. At the same time the first TDUM dose was given, permethrine was applied using a ULV nebulizer, for three consecutive days at night and in the morning, with the objective of diminishing the density of mosquito vectors. These actions were carried out in the months of January and June 1999, which are those with the highest levels of transmission. The objective was to rapidly diminish the density of parasites in populations with the highest levels of transmission, thus making the outbreak more manageable.

**Elimination of focal transmission.** While intensive actions aimed at controlling the outbreak were underway, epidemiological studies were conducted in Level 1 localities. The variables were defined as the confirmed cases of malaria during the prior three years, individuals with more than one case of infection during the same period, the number of cases per household, and the mapping of cases in households. The same variables were analyzed in Level II and III localities, however covering the previous five years. Repeated
cases were defined as individuals who were determined through diagnostic studies to be positive for malaria parasites in the observed period of three or five years, and repeated households were defined as those in which more than one individual with malaria was diagnosed during the same period under study. Based on the above, entomological, cultural and household studies were conducted, in order to attempt to explain the persistence of the disease in individuals and in households, and at the same to use the documented information to determine if there were control measures for infected individuals or vector and risk control measures that were in need of modification.

In line with the results from epidemiological studies of repeated cases and households, the administration of a Single Dose Treatment (Tratamiento de Dosis Única—TDU) was designed for all individuals living in the households where malaria had been detected, with the following scheme: one monthly dose for three months, followed by no treatment for three months, and then a monthly dose repeated for the next three months, and consecutively following this same scheme over a period of three years. The scheme was referred to as TDU 3x3x3 (Scheme 1). TDU 3x3x3 was able to not only make parasites disappear from the blood during the following 24 hours, but it could also cover possible \textit{P. vivax} relapses. The objective of this treatment was to rapidly eliminate the parasitemias of typical fever cases and atypical (sub-clinical and sub-microscopic) fever cases, to eliminate the parasitemias of asymptomatic infections and to prevent parasitemias due to \textit{P. vivax} relapses. It is known that relapses from \textit{P. vivax} strains in Mexico and Central America can occur up to three years later, and consequently the treatment was extended to cover a three-year period. The decision was made to include all households with confirmed transmission from the three prior years. With this action, two premises were proposed: first, that even though vector mosquitoes continued to persist, these households would not be infected, and secondly, that the transmission was “nested” or localized only in the households where infected persons would be detected.

**Scheme 1 Treatment with Single Dosis (TSD) 3x3x3**

1st year

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3nd year

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<td>13</td>
<td>14</td>
<td>15</td>
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<td>-</td>
<td>16</td>
<td>17</td>
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</table>

- The first dosis coincide with the first febril access.
- The relapses can present at 30 days, 3, 6 or 9 months, and the dosis coincide with the relapse time (R)
- The vivax malaria parasites can persist little be more than 3 years

\[ A \text{ sustainable strategy for eliminating DDT from disease vector control programs and reducing malaria: the Mexican Model} \]
In addition some entomological observations were made. There are studies on mosquito behavior that suggest that certain smells produced in the environment could result in increased attraction by vector mosquitoes to human hosts. Other studies have concluded that certain environmental conditions could favor greater longevity for mosquitoes in households characterized by a significant level of transmission. It was determined that further studies are needed, based on the premise that in order for transmission to take place, mosquitoes must survive the extrinsic incubation period, and then survive even longer in order to eat and transmit parasites. Consequently, complementary studies were designed to determine the association of variables in positive households with those in negative households, with regard to the attraction of mosquitoes, the longevity of mosquitoes and variations in vector density.

In order to identify the environmental characteristics produced in households, a preliminary study was conducted by applying a questionnaire for identifying 42 variables corresponding to the habits and customs of families, and housing and vegetation characteristics, with emphasis on those related to the ways in which water, trash and human and animal excrement are managed. These interviews were conducted in households with positive identification of malaria within the prior three years, and at the same time, in households in which malaria had not been detected during this same period. Also, mosquitoes were collected between 6:00 p.m. and midnight, using human bait, and their ovarioles were dissected to determine their physiological age, using the Detinova technique. Results were analyzed comparatively for six households with transmission during the prior three years and six households with negative transmission in the same period. The selection of households was based exclusively on the presence of abundant cases during the prior three years, and the absence of cases during the same period for the control group, since we assume there must be relevant factors other than construction materials used in housing or the presence of domestic animals, or the number of rooms and inhabitants. The results from these studies should assist us in developing adequate control measures.

In the area of vector control, filamentous green algae were eliminated up to a distance similar to the average flying range of the prevailing mosquitoes in Mexico (2 kilometers), for control of *An. pseudopunctipennis*. Various tests were conducted to evaluate the possible impact of algae removal, by collecting adult mosquitoes at midnight during the two weeks prior to clean-up efforts, then skipping a week, and collecting mosquitoes for two more weeks, to determine if there were any changes in the density of mosquitoes biting humans. It was suggested that this activity could be designed so that the population would carry it out on a monthly basis, and it was proposed that local basic sanitation committees be formed in localities where transmission occurs. Personnel from the Official Malaria Program would make visit to communities to provide advice and training, and to evaluate these activities.

Six hyperendemic Level I localities were selected for follow-up, in order to evaluate impact on illness and for entomological observation. Nevertheless, more localities were included in the evaluation, and the information presented here corresponds to that evaluation:

Based on this information, FOCALIZED TREATMENT for malaria in Mexico was designed and has been implemented since 1999. It has been defined as follows:

1. The elimination of Sources of Infection by using TDU 3x3x3 with families and other individuals living together with those infected with malaria.
2. Secondly, vector control through the physical modification of vector breeding grounds, by cleaning up filamentous green algae in mosquito breeding grounds identified in the area within a perimeter of approximately two kilometers from the localities with malaria transmission. This is to replace the use of insecticides.

3. Lastly, improvement in family hygiene, in basic household sanitation (collection and disposal of trash and excrement, care in water use and trimming vegetation growing within ten meters of the housing structure), and in housing modifications. Examples of the latter are: at least whitewashing the walls of homes or painting them with insecticide-containing paint, covering dirt floors with cement, setting aside a specific space for domestic animals, and improving ventilation. The purpose of all of these actions is to prevent nearby mosquitoes from identifying attracting smells, and identifying potential sites for taking refuge and protection.

Focalized Treatment was extended to the entire country between 2000 and 2002, and since 1999 information has been exchanged with the seven Central American Malaria Programs, with the Eritrea Malaria Program, and with PMAFRO in the Andean countries in 2006, discussing principles, conducting field observations and developing Guidelines

**RESULTS**

**Epidemiological and entomological studies.** In the 733 localities analyzed, there were 27,267 cases registered between 1992 and 2001. 73.3% of the cases registered in the ten years were concentrated in 189 localities (15.7%), and consequently, these localities were selected for Level I (Table 1). The epidemiological studies conducted demonstrated that at least half of the homes in the Level 1 localities tested negative. The Annual Parasite Incidence varied between 150 and 832 cases per thousand inhabitants in the different localities analyzed during the ten-year period. In Levels II and III, 85% of the localities were found to have less than five cases and most of them had only one case.

**Table 1. Stratification of malaria in Oaxaca, Mexico, 1992-2001**

<table>
<thead>
<tr>
<th>Strata</th>
<th>Years with transmission</th>
<th>Positive localities</th>
<th>%</th>
<th>Total of cases</th>
<th>%</th>
<th>Average of cases for locality</th>
</tr>
</thead>
<tbody>
<tr>
<td>III 1-2</td>
<td>1,094</td>
<td>4.01</td>
<td>320</td>
<td>43.66</td>
<td>3.42</td>
<td></td>
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<tr>
<td>II 3-4</td>
<td>1,683</td>
<td>6.17</td>
<td>120</td>
<td>16.37</td>
<td>14.03</td>
<td></td>
</tr>
<tr>
<td>II 5-6</td>
<td>3,679</td>
<td>13.49</td>
<td>104</td>
<td>14.19</td>
<td>35.38</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>27,267</strong></td>
<td><strong>100.00</strong></td>
<td><strong>733</strong></td>
<td><strong>100.00</strong></td>
<td><strong>37.20</strong></td>
<td></td>
</tr>
</tbody>
</table>

Cases of repeated infections varied between 3.8% in 1997, 12.7% in 1998 and 25.2% for 1999. Also, 43% of all the cases corresponded to the same homes in nearly all the localities registering malaria transmission (Table 2). Those infected with the typical fever pattern of malaria are only part of the problem, since there are also sub-clinical, sub-microscopic and asymptomatic infections. It was assumed that these infections must be in the same homes as the typical fever cases. For many years there has been reference to the localized of certain illnesses, especially zoonotic diseases and those transmitted by vectors.
Table 2. Classification of cases in the outbreak of Oaxaca, Mexico, 1997-1999

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Single</th>
<th>Repeater</th>
<th>%</th>
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<tbody>
<tr>
<td>1997</td>
<td>677</td>
<td>651</td>
<td>26</td>
<td>3.8</td>
</tr>
<tr>
<td>1998</td>
<td>15,500</td>
<td>13,539</td>
<td>1,961</td>
<td>12.7</td>
</tr>
<tr>
<td>1999</td>
<td>4,439</td>
<td>3,321</td>
<td>1,118</td>
<td>25.2</td>
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</tbody>
</table>

In seven of the follow-up localities, the distribution of the cases of infections in homes indicated that most of the homes have no evidence of malaria transmission, while for example in San Rafael Toltepec, 78% of the cases registered between 1997 and 1999 were concentrated in only 21% of the homes—or in other words, the cases were indeed focalized, as expected. It is also important to point out that the distribution of homes in which malaria has been detected is not homogenous, and these homes are dispersed among homes without malaria transmission. Only in some homes are there many cases of infection, and instead, most have only between one and two cases (Figure 1).

In three of the follow-up localities, it was found that the proportion of homes testing positive for malaria varied between 22% and 37% in 1999, and of these homes, between 39% and 52% had more than one case. And, among the cases registered in these localities, the percentage of individuals who had been infected more than once varied between 11% and 34% (Table 3).

Table 3. Distribution of cases of malaria in three communities in Oaxaca, Mexico, 1999

<table>
<thead>
<tr>
<th></th>
<th>Yerbasantá</th>
<th>Rate</th>
<th>Las Cuevas</th>
<th>Rate</th>
<th>Tototlapa</th>
<th>Rate</th>
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<tbody>
<tr>
<td>Population</td>
<td>863</td>
<td></td>
<td>319</td>
<td></td>
<td>872</td>
<td></td>
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<tr>
<td>Houses</td>
<td>256</td>
<td></td>
<td>199</td>
<td></td>
<td>234</td>
<td></td>
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<tr>
<td>Total of cases</td>
<td>169</td>
<td>195.8</td>
<td>133</td>
<td>416.9</td>
<td>166</td>
<td>190.4</td>
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<tr>
<td>Positive houses</td>
<td>77</td>
<td>30%</td>
<td>44</td>
<td>22%</td>
<td>87</td>
<td>37%</td>
</tr>
<tr>
<td>Houses with + than 1 case</td>
<td>40</td>
<td>52%</td>
<td>20</td>
<td>45%</td>
<td>34</td>
<td>39%</td>
</tr>
<tr>
<td>Persons with more than 1 infection</td>
<td></td>
<td>26%</td>
<td></td>
<td>34%</td>
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<td>11%</td>
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In terms of entomological studies, it was observed that the density pattern of *An. pseudopunctipennis* varied according to the season of the year. In six follow-up localities the density of mosquitoes was studied between 6 p.m. and 6 a.m., and from February to
November of 1999. Between February and March it was observed that 75% of the mosquitoes arrived at homes before 10 p.m., and coincided with the period of highest transmission. Mosquitoes arrived at homes later in the night, as months passed by, and their density diminished until October or November, when it began to recuperate and they began to enter homes earlier in the night again (Figure 2).

Altitude is a determining factor in the presence of this vector, because of the rainy season, since only during the first half of the year are mosquitoes found above 400 meters above sea level, and the variations in density between 200 and 400 meters above sea level are defined by the driest time of the year (February and March) and the rains (July and October). Below 200 meters above sea level, cases of *An. pseudopunctipennis* are few, and density is low (Figure 3).

Mosquitoes were collected using human bait during the early hours of the night in six homes with intense transmission, and results were compared with six other homes with no report of malaria transmission during the prior three years. This took place in two different months (March and June). A total of 1,341 *An. pseudopunctipennis* specimens were collected, of which 60.1% or two out of every three were from homes with malaria transmission (Figure 4). In terms of physiological age, it was found that only 35.7% of the mosquitoes could transmit malaria since they had five or more ovarian dilatations. However, 71.5% of the mosquitoes with between 8 and 10 dilatations were from homes
with malaria transmission (Figure 5). Without a doubt, the vector capacity of the two populations will be a determining factor in assessing homes with malaria transmission.

**Figure 4. Human bite in houses with and without malaria transmission.**

March – June 2005

![Graph showing human bite density in 6 houses with malaria and 6 without malaria.](image)

- **Human bite density in 6 houses with malaria and 6 without malaria**
- **Total number of mosquitoes: 1,341**
- **806 mosquitoes in malaric houses (60.1%)**
- **535 mosquitoes in non malaric houses (39.9%)**

**Figure 5. Physiological age of mosquitoes in houses with and without malaria transmission.**

March – June 2005

![Graph showing physiological age of mosquitoes in 6 houses with malaria and 6 without malaria.](image)

- **Physiological age of mosquitoes in 6 houses with malaria and 6 without malaria**
- **Total of dissected mosquitoes: 1,052**
- **675 mosquitoes in malaric house (64.1%)**
- **377 mosquitoes in non malaric house (35.9%)**

In 45 homes with malaria, there were 35 that tested negative to malaria transmission. Although the sample was small, it was observed that homes testing positive for malaria and having abundant vegetation in the first 20 meters surrounding the walls of the home had a 27.9 odds ratio, meaning there was a greater risk of transmission. Of the homes testing positive, the odds ratio was 21.8 for those in which inhabitants did not bathe daily; and the odds ratio was 7.4 for those in which the indoor area and outdoor patio areas were not swept. It is especially noteworthy that for homes with malaria in which domestic insecticides in spray form were not used, the odds ratio was 7.6 (Table 4).

**Table 4. The malaria frontiers.**

In a case-control type study we found:

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR</th>
<th>IC 95%</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No take a daily bath and</td>
<td>21.8</td>
<td>2.5-182.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>No daily change of clothes</td>
<td>3.5</td>
<td>1.0-11.9</td>
<td>0.041</td>
</tr>
<tr>
<td>No sweep the house and patios</td>
<td>7.4</td>
<td>1.4-39.2</td>
<td>0.007</td>
</tr>
<tr>
<td>No cut the peridomestic vegetation</td>
<td>27.9</td>
<td>5.8-133.5</td>
<td>0.0000</td>
</tr>
<tr>
<td>No use of bednet</td>
<td>3.7</td>
<td>1.5-8.8</td>
<td>0.003</td>
</tr>
<tr>
<td>No use a commercial insecticides</td>
<td>7.6</td>
<td>1.0-60.9</td>
<td>0.027</td>
</tr>
<tr>
<td>Discontinuous walls</td>
<td>5.6</td>
<td>2.1-14.5</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

*A sustainable strategy for eliminating DDT from disease vector control programs and reducing malaria: the Mexican Model*
A transmission model was constructed on the basis of this information, and another control model was developed in line with the results. It was confirmed that approximately 70% of the homes in localities with malaria transmission continue to test negative, despite the presence of cases; and that there are some homes with very intense transmission, however most homes in the hyperendemic localities have between one and two cases a year. It would appear that this transmission is defined by biological processes linked to the attraction for mosquitoes (carbon dioxide, lactic acid and phenols, probably) more than to housing characteristics per se. Also, that higher densities of mosquitoes arrive at homes testing positive for malaria than those testing negative; and that mosquitoes in homes testing positive are characterized by more longevity and are more able to transmit malaria parasites. Together, this evidence indicates that the Focalized Model should be modified to eliminate sources of parasite infection, and consequently TDU 3x3x3 was selected for implementation.

**Intensive outbreak control.** During February, March and April of 1999, 254 Level I localities were selected in Oaxaca from a population of 35,000 inhabitants registered in the initial census, and TDUMs and nebulizations were applied in those localities. The decision was made to apply three consecutive doses with a one-month interval between each dose, and coverage was 87%, 78% and 65% for the three doses of TDUM, respectively, and coverage was 100% for nebulizations. In Level II and III localities, only those with malaria and the people living with them were treated, using the radical cure treatment scheme of chloroquine and primaquine doses taken for five days.

**Focalized treatment.** Beginning in May 1999, a new control scheme referred to as Focalized Treatment (FT) was defined at the three levels, and the application of insecticides as well as the use of previous radical cure schemes were suspended. FT consists of the following measures:

1. TDU 3x3x3 administered to the entire family of confirmed cases from the prior three years, with the objective of eliminating parasites (nests and pockets of infection) and covering the period of time for possible \( P. \) vivax relapses, specifically at one, three, six and nine months, and up to three years, since that is the length of time parasites can survive.
2. Monthly elimination of filamentous green algae in all vector mosquito breeding grounds in localities with malaria transmission, with the work to be organized and carried out by the communities.
3. Improving basic hygiene and sanitation in all localities testing positive for malaria, and whitewashing walls of homes.

With the use of this model in Oaxaca, it was possible to diminish malaria transmission from 17,540 cases in 1998 to less than 5,000 in 1999, equivalent to a 71% reduction. And between 1998 and 2002 malaria transmission was diminished by 98.4%, with only the use of Focalized Treatment (Figure 6). The TDUM was administered at a rate of 80% in all Level 1 localities, and there were no reports of any adverse reactions to the medicine. Nebulizations were carried out simultaneously with the administering of the TDUM in all localities, without any negative effects reported.
Figure 6. Impact of Focalized Treatment in the outbreak of Oaxaca Mexico, 1998-2002

SDTM: Single Dosis Treatment Massive
FT: Focalized Treatment

TDU 3x3x3 was applied to all persons in homes where a case of malaria had been detected. While in most cases the application of TDU 3x3x3 was not above 80% of the programmed objective, the rates for the first doses were above 80%, with more than 100,000 people receiving this treatment in the first cohort, consisting of inhabitants of homes with malaria detected in the prior three years.

The impact from the elimination of filamentous green algae was surprising. In the first evaluation conducted with the human bait technique for twelve hours in two localities in the Oaxaca Coast region, a 92.6% reduction was noted in the number of mosquitoes entering the homes studied, representing $\chi^2=67.8$; O.R. = 14.3; $p=>0.0000$; and C.I. = 6.04-36.33 (Figure 7). A reduction in larvae was also evident, with a 93% decrease observed in breeding sites below 300 meters above sea level, and a 72% decrease in the sections of the valley region at higher altitude, between 300 and 600 meters above sea level. The reason for the latter is that it is more difficult to eliminate the filamentous green algae from the waterfalls in the higher-altitude valleys (Figure 8).

Figure 7. Pre and post mosquito density index of An. pseudopunctipennis, Paso Limón, Oaxaca. 1999

\[x^2 = 67.84\]
\[\text{OR} = 14.33\]
\[p = >0.0000\]
\[\text{CI}\ 95\% = 6.04-36.33\]
Lastly, in order to assure the elimination of filamentous green algae, it was considered adequate to train the community and supervise its work once a month. The number of larvae was substantially reduced, and the sustained densities of vector larvae were also reduced, making it possible to establish consistent management of adult mosquito densities (Figure 9, Photo 1). This type of evaluation has been systematized, and currently the population recognizes that cleaning up filamentous green algae is related to the presence or absence of mosquitoes in the evenings/night.

Expanding focalized treatment (FT) to the entire country. Between 2000 and 2002 FT was expanded to all the affected areas in Mexico. DDT applications were eliminated as of 2000, and only Deltametrine was used for spraying in the Mexican states bordering with Guatemala and Belize. However, due to the positive results from FT, the systematic application of insecticides was suspended, and spraying was only used during outbreaks.
As a result of the FT implemented in 800 communities with significant malaria transmission, the incidence of malaria dropped from 25,023 cases, most of them *P. vivax*, in 21 states in 1998, to 7,362 cases in 16 states in 2000, and to 2,514 cases in ten states in 2006. In this same time period, the number of homes sprayed with insecticides decreased from 560,000 to fewer than 20,000 homes, between 1998 and 2006 (Figure 10 next page).

**COLLABORATION WITH CENTRAL AMERICA.** Mexico and the Central American countries of Belize, Costa Rica, Guatemala, El Salvador, Honduras, Nicaragua and Panama all have practically the same type of malaria. While there is a greater prevalence of *falciparum* malaria cases in Central American countries, the dynamics and tendencies of transmission are similar. In addition, regional south-north migration facilitates the spreading of the same strains of parasites. Mosquitoes are resistant to insecticides in all the countries, and to date parasites of the two species are sensitive to chloroquine and primaquine.

**Figure 10. Malaria cases, house sprayings and strategies of control, Mexico, 1959 - 2006**

In response to the results obtained in Mexico, and through the joint efforts of Mexico’s Ministries of Health and Foreign Relations, as well as those by the Mexican delegation of the North American Commission for Environmental Cooperation (CEC), an agreement was reached between all the countries to establish a “Regional Program for Action and Demonstration of Sustainable Alternatives for DDT-free Malaria Control in Mexico and Central America.” This program involves developing Demonstration Areas for applying the Mexican Model. Once the agreement was reached, the decision was made to ask PAHO/WHO to participate by coordinating the project’s implementation, and the Environmental Health Department of this international organization agreed to do so in 2001. Consequently, a technical group representing Mexico and PAHO/WHO elaborated a basic document that served to firmly establish a multinational agreement. The document was presented to the GEF/UNEP, which granted funding in the amount of more than US $13 million. The funding was targeted for eliminating the DDT stockpiles in the eight countries, and for following the Mexican model for controlling malaria in the selected Demonstration Areas.
Guidelines were developed for the Implementation and Demonstration of Sustainable Alternatives for Integrated Malaria Control in Mexico and Central America, and have served to orient operations for controlling malaria without the use of insecticides in each country. The work carried out in the Demonstration Areas in all the countries has resulted in effective control of malaria without insecticide use, while integrating effective community participation.

Discussion

Traditional strategies for controlling disease vector mosquitoes have been focused on their direct elimination through the use of insecticides, attacking the various life stages of these arthropods. Most research efforts have therefore been dedicated to mosquito resistance to pesticides, and the development of new formulas and new products. Little attention has been paid to the knowledge obtained from research studies conducted primarily in the 1930s, 1940s and 1950s. In these studies an association between families and individuals was observed in the malaria cases detected.

With regard to malaria infections and the strategies for detecting them, it is important to note that malaria may be symptomatic or asymptomatic, depending on the individual’s immune status and background of previous infections. In the case of those who frequently experience repeated infections, it is likely that the symptoms will disappear. Therefore, when some family members suffer from malaria every year, they will develop immunological tolerance, and the illness will no longer manifest itself. However, these asymptomatic infections will coexist with symptomatic infections suffered by other members of their families. Thus, we can see the importance of eliminating the parasites in all those who are infected by this disease. Also, in the case of \( P. \) \( vivax \) malaria, there is also the problem of relapses and the possibility that various members of a single household characterized by a significant level of malaria transmission may test positive for these parasites, however may be in a latent period between relapses. These elements indicate that a focalization strategy for eliminating the sources of mosquito infections must be designed to effectively treat persons with asymptomatic infections, with manifested illnesses and those experiencing a latent period between relapses.

There are two reasons that malaria cases are grouped into clusters. First of all, the homes with malaria transmission conserve and are constantly emitting odors that attract mosquitoes, and consequently mosquitoes can easily identify these homes when they go out in search for food. Secondly, mosquitoes find favorable ecological conditions and can survive better when there is vegetation located very close around homes. This vegetation protects the mosquitoes, and provides them with adequate shelter for prolonging their lives. These considerations are supported by data obtained from comparing mosquito populations between homes with and without malaria--which indicate that the age and number of dilatations in the accumulated number of mosquitoes is greater in homes with malaria. This suggests that these mosquitoes live longer, and consequently the likelihood of transmitting malaria is greater (Figure 11). This may be the reason that malaria cases are grouped together more in some families and homes than in others, and it is possible that controlling the mosquitoes in these homes could be sufficient for malaria control. In a publication regarding a project conducted in the Mexican state of Chiapas in the 1990s, it was concluded that spraying insecticide and administering medicine to families in homes with malaria transmission in a certain locality was sufficient to obtain the same results in controlling malaria transmission as in another locality, where all the homes
were sprayed and medicine was distributed to everyone in all the homes, including those without malaria transmission—as indicated in the guidelines for eradicating malaria.\textsuperscript{34}

**Figure 11. Cumulative number of ovarial dilatations in mosquitoes captured in malaric and no-malaric houses, Oaxaca, Mexico, 2005**

The use of TDU3x3x3 applied only to families in malaria-positive homes in Mexico has brought successful results, since the number of persons experiencing relapses, representing approximately 30%, was reduced to close to zero (Méndez, Betanzos et al., in preparation). In addition there was a very significant decrease in the appearance of new cases. Illnesses that originate from a common source of infection behave in a particular way, and control of these illnesses can be achieved through actions taken at the sources producing the infectious agents. In the case of malaria, it appears that its transmission originates in common sources, and even though all inhabitants of a locality may be susceptible to contracting the illness, its transmission is restricted to specific sites where mosquitoes can survive long enough to transmit the illness and where they can easily identify the location of their sources of food.

Pampana referred to the possibility that mosquitoes can be domesticated, and consequently, after one person suffering from malaria is detected, another will surely appear.\textsuperscript{5} Evidence that explains the mechanisms used by mosquitoes to locate their sources of food has been documented. The pattern we can infer from this information consists basically of the lack of hygiene and sanitation as important elements that greatly increase the emission of odors detected by mosquitoes.\textsuperscript{18,35,36,37} Also, according to biological studies of these arthropods, their niches are determined by temperature levels, the location of their breeding areas and the location of their hosts. We should also include a degree of protection as one of the elements to consider here, since in the case of mosquitoes, for example, they need areas for rest and protection. This element will ultimately allow them a greater level of survival, as they develop habitats with adequate temperature, light intensity and humidity. Obviously, the insects that are able to best exploit the sources of energy around them will be those with the greatest survival rates.

The Mexican model for controlling malaria has placed importance on, first of all, returning to an epidemiological focus in order to identify the chain of transmission—before predetermining that certain control measure such as insecticides should be used. In this way it was established that if good treatment is available, the sources of infection by mosquitoes can be eliminated. We know that mosquitoes prefer certain environments over others. Thus, we can infer from the grouping of malaria cases in the same individuals and the same homes that the latter have proven to be ideal habitats for the mosquitoes, and
thus the places where they can best survive. If mosquitoes are able to survive longer, then
they will have the opportunity to maintain malaria parasites for a longer period of time, and
produce repeated infections, asymptomatic infections, relapses and new cases within the
same homes and the same families. The potential for receptivity will depend on whether
the habitats of families and homes are compatible with the mosquitoes’ needs, since if
conditions in such habitats are adverse, the mosquitoes will die. We would also note that
favorable conditions for the survival of mosquitoes appear to prevail due to the persistence
of poverty and ignorance—which are not the same, since while a family may be poor,
there are no obstacles preventing such a low-income family from maintaining themselves
clean and living their lives modestly. More healthy living spaces can assure that malaria
transmission does not become focalized, in the terms established by Pavlovsky, specifically that certain niches are preferred because of the conditions they offer and are
thus characterized by persistent illness. The occurrence of illnesses that become focalized
in families and homes has been addressed in different ways, however there is agreement
regarding the need to study certain variables, in models such as microepidemiology, and it
is also agreed that many diseases would disappear if the habitats where they occur would
be modified.

Secondly, the Mexican Model includes actions to reduce the densities of mosquitoes,
through the elimination of their breeding grounds by physical means—organized and
carried out by communities. According to our results, a reduction in larvae translates into a
very significant reduction in adult mosquitoes, and consequently a reduction in the risk of
transmission. It is also concluded that the combination of eliminating parasite-filled niches
and decreasing the number of mosquitoes also translates into a very important reduction
in new cases.

The third and last point has been directed at improving homes, by painting walls, sweeping
floors and outdoor areas, pruning the vegetation growing around homes and correctly
disposing of trash. When these aspects of basic sanitation and hygiene are contemplated
and assumed by communities, the effects from a reduction in parasites and mosquitoes
will be more persistent, or minimally, there will be a more significant decrease in long-living
mosquitoes—which are those responsible for transmitting malaria.

Nearly all the malaria-control programs around the world have been vertical in their
structure, and only rarely have their strengths been shared or their coverage been
extended to other health programs. The insecticide sprayed on the walls of homes for
more than 50 years not only produced a decrease in malaria-transmitting mosquitoes, and
in some cases, their disappearance. It also surely reduced the numbers of transmitters of
the Chagas disease in the Americas, and the intra-home vectors of rickettsias and
arbovirus, in addition to many other bothersome insects and arachnids. Therefore,
maintaining a malaria control program unidirectional in nature would signify continuing to
think of the program as only useful in controlling malaria. Consequently, the Mexican
Model has been based on the idea of not only fighting malaria, but in addition, through
sanitation and hygiene measures, it can also control other illnesses such as dengue and
rickettsiosis, and poisoning from arachnid bites. And it can also have a positive impact on
efforts to correctly dispose of trash in rural, marginalized areas, and to disinfect water for
family use, and thus it can eventually include the control of diarrhea. This focus will surely
improve health and enhance the quality of life—as opposed to only expecting to reduce
illness from malaria. In addition, this investment in health may avoid excessive
expenditures.
One last aspect to mention here is that the use of insecticides, and even DDT, should be limited to a defined time period. An important conclusion from the Mexican Model for malaria control is that we are not facing a crisis in the selection of insecticides or a return to the use of DDT—which has produced polarization in international forums—but rather, what we need is to implement a new focus in our programs. It is important to remember that control over diseases is not only obtained through vaccinations or insecticides, for example. If the conditions for transmission of immune-preventable and vector-transmitted diseases remain in the environment, there will always be a latent risk, and it is necessary to continue to use vaccinations over an indefinite period of time—and to continue to use insecticides. It is very likely that insecticides or bednets impregnated with insecticides may be included in models such as the Mexican model, in order to accelerate efforts to eliminate persistent, focalized areas of transmission, and will therefore be used for a determined period of time.

The current threats we are facing in maintaining control over diseases are not only due to the lack of financing or because control measures are losing their effectiveness, or due to climate change or the resistance of parasites and vectors to medicines and insecticides. Outbreaks also occur when there are changes in government administration, and when there are changes in administrative and operational personnel in health programs—when outgoing personnel take their training with them, while those filling their positions lack the necessary information. And outbreaks also occur when there are labor problems in health programs. These variables are generally ignored in health program planning, and must be discussed and addressed in order to prevent these problems as much as possible.

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