Vectors Control Importance on Leishmaniasis Transmission

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We reviewed the control of transmission of leishmaniasis regarding chemotherapy, reservoirs elimination, vaccination and insect control through the use of chemical insecticides. We also discussed complementary measures like monitoring traps, impregnated bednets and curtains, repellents, pheromones, biological control, etc. A cost comparison of insecticide interventions through the use of products belonging to the four main chemical groups was also done, comparing together conventional formulations versus a slow-release insecticide developed by the Núcleo de Pesquisas de Produtos Naturais, Universidade Federal do Rio de Janeiro. We finally did recommendations on the situation that would justify an insecticide intervention to control sandflies.

Key words: leishmaniasis - sandflies - vector control - insecticides and formulations - entomological evaluation techniques

In Brazil, and in most countries where it is endemic, the control of transmission of leishmaniasis relied mostly on the elimination of infected hosts, mainly dogs, and in chemotherapy through the identification and treatment of infected people. This is true almost only for American visceral leishmaniasis (AVL) to which the Brazilian Ministry of Health has been giving more attention. Cutaneous and muco-cutaneous forms have only been treated by chemotherapy of diagnosed human cases.

Data reported by the Brazilian National Health Foundation (FNS 1993) show an average of 1000 new cases of AVL each year, during the past ten years. However, since 1988 this number is progressively increasing to show 1500 new cases in 1990, the last year for which FNS has the complete set of data (Fig.). If we consider people who have not yet search for assistance or asymptomatics, these numbers will certainly grow. Kala-azar has also spread to larger areas in Brazil showing what is being called the urbanization of this disease. By now, a real bad situation can be exemplified by Terezina, State of Piauí, where active transmission of AVL can be found everywhere, independing of socio-economic conditions of the population, and where some fatal cases have already been registered. This picture indicates that we are loosing control of the situa-

![Number of cases of human kala-azar registered in Brazil between 1981 and 1990 (FNS 1993).](image)

curtaetion and much more attention should be given to this disease. Stronger measures are necessary to help the control of transmission. The common or under development tools employed are chemotherapy, vaccination, reservoir and insect control, including the use of insecticides and complementary measures like monitoring traps, bednets and curtains, repellents, pheromones, biological control, insect growth regulators (IGRs), etc.

Observing the present situation of chemotherapy we must look to the past to see that not much progress has been achieved since sodium antimonyl gluconate started to be used in the treatment of Kala-azar in China, 50 years ago. According to Croft and Neal (1989) the drugs used nowadays are still the pentavalent antimonial derivatives of "Solu-stibosan" - the sodium stibogluconate "Pentostan" (Wellcome) and meglumine antimoniate "Glucantime" (Rhonepou-

lenc). New alternatives such as the pyrazolopyrimidines allopurinol and allopurinol riboside,

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the antifungal imidazole ketoconazole and the 4-methyl-8-aminquinoline WR602 have been or still are under study. However, it is not expected that pharmaceutical companies will support the high cost of development of a new drug due to the limited market. This mean that in the near future the continuation of use the antimoniais, even with the toxicity problems and limited efficacy, is likely to occur.

Regarding vaccination, it is known that leishmaniasis infections give life-long protection against new infections, what is a strong demonstration that a vaccine is possible. However besides all studies performed and progress achieved, a safe and efficient product that can be recommended for human mass protection is not available (Liew 1989). Field trials of a dog vaccine are presently being performed in Brazil, which gives hope of immunization of these reservoir hosts instead of their elimination.

Any strategy for leishmaniasis control is likely to include mammal reservoirs control. In spite of poorly documented and rigorous evaluation of consequences for humans of operations directed solely to the elimination of infected dogs, this method seems to be effective in certain circumstances (Ashford 1989). Recently Badaró et al. (1994) reported a new method for the fast diagnosis of AVL (Dipstick) that takes only 30 seconds. This method when applied to dogs could make the elimination of hosts much more effective, avoiding the period of time necessary for processing the diagnostic in the laboratory and coming back to the same place. A dog vaccine, still under development, would be welcome to avoid all the constraints generated by the elimination of pets or valuable animals. It is also worthwhile to think about the use of systemic insecticides in dogs that would eliminate biting sandflies, avoiding transmission to man and other animals, even if not protecting the treated dog itself.

The lack of well designed and performed field assays against flebotomine sandflies is still one of the main constraints in the evaluation of vector control actions in the transmission of leishmaniasis. In general there are only assumptions in this respect referring to the consequences of malaria control programmes and, furthermore, referring only to insect density and not on the impact on clinical disease.

Eggs, larvae and pupae of sandflies have rarely been found in nature turning the biology of these insects in natural conditions poorly understood. Studies performed in India by Smith et al. in 1936, in Panama by Hansen in 1961, in Sudan by Quate in 1964 and again in India (Dhiman et al. 1983) collecting soil samples indoors or outdoors, allowed the identification of some preimaginal stages. Even the use of emergence traps in a more recent study done by Bettini in Italy (Killick-Kendrick 1989) resulted in little help when referring to the possibility of using antilarval measures. According to Dhiman et al. (1983) *Phlebotomus papatasi*, *P. argentipes* and *Sergentomyia babu* lay their eggs preferentially in the loose soil close to the floor surface in the corners inside the houses, but can also be found in cattle sheds. In these conditions it seems that it would probably be worthwhile treating the soil near the walls with a control agent even though it is the same residual insecticide being used for adult control, probably rendering the treatment more effective not allowing adults to come up from young stages.

Referring to biological control through the use of entomopathogens, from which Bacillus thuringiensis israelensis (B. t. l.) and B. sphaericus are already known, and Clostridium bifermantans malaysia and B. t. medellin are other promising bacterial species under study, there is at present no hope of use. The last report on this matter from WHO (1993) does not even mention the possibility of use of these tools for sandflies control. However it is a matter of fact that sandfly larvae are susceptible to B.t.i. The problem remain in putting both, bacteria and larvae, in close contact in real natural conditions in a cost-effective manner, due to the poor present knowledge of young stages of sandflies in nature. The same situation is appliable to the IGRs, including juvenile hormones, precocenes and chitin inhibitors.

An alternative approach to the control of transmission of leishmaniasis is the use of bed-nets or curtains, to avoid sandflies biting. This has been an important approach for malaria control all over the world (Rozendaal 1989). However as sandflies are tiny insects, those nets and curtains should have a too fine mesh, which would result in discomfort due to poor air circulation. Itoh et al. (1986) has developed and tested a wide mesh treated with insecticides, that could avoid most of bites by mosquitoes transmitting malaria. Maroli and Lane (1989) and our group (Oliveira Filho et al. 1994) performed preliminary studies on the effects of permethrin impregnated large mesh nets respectively on Phlebotomus and Lutzomyia, showing significant results that can recommend this technique as a complementary approach to other measures of insect control.

Insect repellents are only palliatives mostly used by persons on their skin when entering an endemic area to stay a few days. To prolong their usually short duration they should be formulated in an oil base. The most common active ingredient is DEET (n-Diethyl-m-toluamide) but there are some others, including synthetic
pyrethroids in low concentrations, used for the
impregnation of clothes.
Some kinds of monitoring traps are already in
use, like CDC light traps, and those based on it,
animal baited traps and sticky traps. Nowadays
pheromone traps are under study but they are not
yet available (Ward et al. 1990).
As phlebotomines young stages cannot yet be
cost-effectively controlled in practice, the few
papers published refers to adults control and
some of them deal with insecticide resistance
mainly to DDT in areas generally treated for
malaria control.
The first report on the use of insecticides
against sandflies in Brazil was done by Nery-
Guimarães and Bustamante (1954) in a focus of
ACL in the State of Rio de Janeiro. Five years
after periodic domiciliary spraying with DDT
they noticed a decrease in both the sandfly
population and disease incidence. Seyedil-Rashiti
and Nadim (1975) reported the re-establishment
of cutaneous leishmaniasis in some areas of Iran
after the cessation of DDT spraying for the con-
rol of vectors of malaria.
In an attempt to reduce transmission of Leish-
mania braziliensis guyanensis in a periurban
rainforest, Ready et al. (1985) sprayed the lower
part of trees with DDT. They reported, 11 months
after, that these places were no longer occupied
by Lu. umbratilis. In Bolivia Le Pont et al. (1989)
reported the control of Lu. longipalpis from
dwellings and chicken houses until nine and ten
months, respectively, after one deltamethrin treat-
ment.
Falcão et al. (1991) studied the effect of del-
tamethrin in the sandfly population (mainly Lu.
intermedia and Lu. migonei) of an area of State
of Espirito Santo in Brazil. Application of 25mg
a.i./m² of a 5% flowable formulation, on the in-
ternal and external walls, roofs and buildings plus
the trees within 10m from the houses promoted a
reduction in the number of sandflies captured in-
side houses, but not in the peridomicilium, during
a period of 12 months.
More recently Rashiti et al. (1992) showed in-
creased tolerance, or maybe resistance, of Ph.
papatasi to DDT in Iran, even in areas where the
application of this insecticide has been discon-
tinued for more than 15 years. This is not the first
time resistance has been reported on this part of
the world, with many references already been
made in India.
In an informal report Silans (1991) showed
through the bioassay of treated house walls, ex-
posing Lu. longipalpis at intervals until six
months post-treatment, the comparative results of
the residual effect of DDT, deltamethrin and
cypermethrin. The only one that kept residual ef-
fect enough to kill 100% of the sandflies after
six months over mud surfaces was DDT, applied
as wettable powder at 2g a.i./m². Deltamethrin
5% FW sprayed at 25mg a.i./m² and cyper-
methrin 20% WP sprayed at 125mg a.i./m² didn’t
achieve this performance.
The last Technical Report released by WHO
(1990) on the control of leishmaniasis, reported
data collected on insecticides, formulations and
doses, probably derived from the literature and
practice on the control of other insect vectors
(Table). If not precise these data can help us to
make the assessment of part of the products that
could be used nowadays and at which cost/ratio
when compared with the commonly used DDT.
We added to this Table the results obtained with
the Slow Release Emulsifiable Suspension
(SRES) formulation developed in the NPPN-
UFRRJ when used against triatomines. We also
compared cost of operations, based on the real
costs determined during the campaigns against
Chagas’ disease vectors in Brazil (Oliveira Filho
1989). DDT is still one of the most cost/efficient
products in use, being cheaper than the represen-
tatives of organophosphorus, carbamates and
pyrethroids. The only exception was for the or-
ganophosphorus malathion or fenitrothion when
formulated in the slow-release formulation PVA
based, developed in our laboratories, which gave
an estimated cost ratio of 0.9, becoming cheaper
than DDT, due to its long residual effect
(Oliveira Filho 1988, Oliveira Filho & Melo
1994a). Deltamethrin would be the third product
of choice, however WHO data assume six
months residual effect for deltamethrin over mud,
what it is not in accordance with most of data
available (Silans 1991).
Anyway, as there are no conventional for-
mulation that can resist in non-protected
peridomíccium, the advantage of the SRES is
obvious because its film coating of the surfaces
assure its presence for longer than any other. This
will certainly save operational work and with the
same spraymen larger areas will be allowed to be
 treated, turning this kind of treatment even more
attractive. This have to be proven in real field
situation, comparing concomitantly other can-
didate products. By now a field trial is aproved
and will be supported by WHO/TDR in India, in
collaboration with the Rajendra Memorial In-
tstitute of Medical Sciences-Patna (India). An-
other field assay is being planned, together with
FNS, PAHO and WHO/TDR, to happen in
northeastern Brazil. In recent laboratory ex-
periments Oliveira Filho and Melo (1994b in press)
showed that the dose of this slow-release for-
mulation and also of some other insecticides in
conventional formulations can still be reduced
when compared with those recommended for the
control of other vectors like those of Chaga-
s’disease and malaria.
TABLE

Cost comparison of insecticide interventions of various products and formulations in the recommended doses
(Oliveira Filho 1989, WHO 1990)

<table>
<thead>
<tr>
<th>Insecticide and formulation</th>
<th>Dosage (ga. i./m²)</th>
<th>Residual effect on mud (months)</th>
<th>Approx cost/tonne (US$)¹</th>
<th>Insectic. cost ratio (DDT=1)</th>
<th>Cost/house 18 months + insectic operat. (US$)²</th>
<th>Insectic. cost ratio (DDT=1)³</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDT 75% WP</td>
<td>2.0</td>
<td>6</td>
<td>3,000</td>
<td>1.0</td>
<td>42.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Melathon 50% WP</td>
<td>2.0</td>
<td>3</td>
<td>2,100</td>
<td>2.1</td>
<td>84.6</td>
<td>2.0</td>
</tr>
<tr>
<td>Fenitrothion 50% WP</td>
<td>2.0</td>
<td>3</td>
<td>7,500</td>
<td>7.5</td>
<td>117.0</td>
<td>2.8</td>
</tr>
<tr>
<td>Propoxur (20% EC)</td>
<td>2.0</td>
<td>3</td>
<td>9,300</td>
<td>23.2</td>
<td>211.5</td>
<td>5.0</td>
</tr>
<tr>
<td>Deltamethrin (2.5% WP)</td>
<td>0.025</td>
<td>6</td>
<td>25,000</td>
<td>3.1</td>
<td>54.7</td>
<td>1.3</td>
</tr>
<tr>
<td>Permethrin (25% WP)</td>
<td>0.125</td>
<td>3</td>
<td>30,000</td>
<td>3.7</td>
<td>94.3</td>
<td>2.2</td>
</tr>
<tr>
<td>Melathon or Fenitrothion (10% SRES)</td>
<td>2.0</td>
<td>18</td>
<td>5,400³</td>
<td>13.5</td>
<td>39.0</td>
<td>0.9</td>
</tr>
</tbody>
</table>

¹: WP: wettable powder; EC: emulsifiable concentrate; SRES: slow-release emulsifiable suspension (NPPN).
²: international prices reported by WHO, not including freight.
³: cost of a visit US$ 12.00/house (250m² estimated treated area/house).
⁴: Brazilian price (Ilhãs, Sorocaba, SP).

Of course even if an insecticide is very effective against sandflies this does not mean that it should be applied in every situation. During the two last meetings on leishmaniasis that happened in Brazil (Natal 1991 and Recife 1993) the discussions among the experts lead to some general recommendations to help decision making. In short terms that would be the presence of autogenous human cases of AVL and of *Lu. longipalpis* in the same area, the only situation that would justify an insecticide intervention, together with the other tradicional measures. The application should be residual, covering walls and roof surfaces inside the houses, the eaves outside, all the peridomicaliary structures and tree trunks that often harbour domestic animals like chickens.

The methods of evaluation should be standarized. To assess the effect of control measures on sandfly populations many standard sampling methods can be used to measure population densities. Of course all of them refer to adult population due to the strong difficulties found in the capture of young stages in nature. According to the World Health Organization (WHO 1990) the mostly used are:

*Man-landing rates* - Expressed as number of sandflies/person/hour, where collectors working in pairs sucks into glassubes the adults coming to bite each other. Catches are made at night in previously set dates, in the same sites, during the same period of time. The collectors, preferentially selected among local population, should have had a previous infection and already recovered from it, to avoid the risk of becoming infected.

*Light traps* - Expressed as number of sandflies/trap/night, where CDC light traps are fixed at previously decided places and left running from before nightfall until just after dawn. Catches can be greatly affected by the species. They differ in their response to light, and the place where the traps are installed, accordingly to the endophilic or exophilic behaviour. Protected places (houses, chicken houses, stables, etc.) are preferred for being less affected by weather changes and intervals between observations can be longer.

*Active catches* - Expressed as number of sandflies/person/day, where all sandflies inside a given place are caught by skilled collectors. This method can only be used for endophilic sandflies
and must be done as repetitive as possible (same
days of the week, same buildings and, if possible,
same persons).

Knock-down catches - Expressed as number
of sandflies/room/night, where those insects are
collected after spraying selected places with an
appropriate insecticide (generally a synthetic
pyrethroid). It is also used only for endophilic
sandflies. The floor and furniture of a room are
covered with papers or plastic sheets, the place
is sprayed generally at dawn, and all insects falling
on to the sheets are collected.

Sticky-paper traps - Expressed as number of
sandflies/m²/night, where the flies are captured
onto pieces of paper or cards recovered with oil
(castor or engine oil), grease or a non-drying
glue, placed overnight in possible resting places.
These traps, measuring around 20x25cm can be
fixed in supports or onto the walls, should be
used in the same numbers and exposed area on
every occasion to make the results quantitative.

Pheromone traps, e.g. for Lu. longipalpis -
Can also be added to WHO list, however they are

For all the techniques mentioned the
specimens must be identified because usually
more than one species are caught.

It must be recognized that no universal
strategy is likely to be effective against all kinds
of leishmaniasis, even when dealing with the
same Leishmania species. Primary health care
services should be involved in control measures,
allowing popular participation but respecting
local traditions. Recurrent effort may be needed
in many circumstances what means the need of
continuous supply of funds. Controlled areas
must be surveyed on a long term basis to avoid
the reinstalation of transmission.

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