Methods for vector control

Michele Maroli

Istituto Superiore di Sanità, Rome, Italy
MIPI Department
Vector-Borne Diseases and International Health
michele.maroli@iss.it
Tools for *Leishmania* vector control

Sandflies are haematophagous pests, so their control may be required even where they are not active as disease vectors.

- Sandfly breeding-sites are generally difficult to find, and therefore control measures oriented specifically against immature stages are not feasible.
- At present, there are few effective methods other than chemical control against adult sandflies.
Control measures aimed at reducing sandfly populations and host-vector contact

1. Insecticide residual spraying (IRS) in houses and animal shelters
2. Insecticide treated nets for human use (ITNs)
3. Repellents applied on people’s skin exposed to sandfly bites
4. Topical application of insecticides on dogs for prevention of canine leishmaniasis
IRS implementation

- The effectiveness of IRS may depend on the degree to which sandflies have adapted to man-made environments.

- Thus IRS will be much more effective in urban situations, where every house and animal shelter is treated, than in rural areas, where relatively few, widely dispersed dwellings are sprayed.
Prerequisites for IRS implementation

- IRS campaign depends also on the availability of a suitable public health infrastructure, including adequate supplies of insecticide, spraying equipment and trained personnel.

- Moreover, such personnel should be trained not only in insecticide application, but also in safety procedures as well as monitoring techniques.
Monitoring techniques for IRS implementation

**Pre-intervention**
- Insecticide base-line susceptibility
- Vector density

**Post-intervention [periodically]**
- Vector density
- Evaluation of IRS residual effect on the treated surfaces

**Graph:**
- % Mortality (% MORTALITA')
- TEMPO (min)
- PAP-A-RM
- PAP-A-RO
- PERNI-VE

**Graph:**
- % MORTALITY vs TEMPO (min)
- PAP-A-RM
- PAP-A-RO
- PERNI-VE
Monitoring the residual effect by test cones
# Examples of IRS field interventions

<table>
<thead>
<tr>
<th>Insecticide</th>
<th>Efficacy or duration</th>
<th>Country</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDT</td>
<td>9 months</td>
<td>India</td>
<td>1996</td>
</tr>
<tr>
<td>Malathion</td>
<td>8-9 months</td>
<td>India</td>
<td>1985</td>
</tr>
<tr>
<td>Permethrin</td>
<td>50% reduction</td>
<td>Egypt</td>
<td>1993</td>
</tr>
<tr>
<td>Deltamethrin</td>
<td>Not significative</td>
<td>Colombia</td>
<td>1995</td>
</tr>
<tr>
<td></td>
<td>Significative</td>
<td>Brazil</td>
<td>1991</td>
</tr>
<tr>
<td>Lambda-cyhalothrin</td>
<td>90% reduction</td>
<td>Brazil</td>
<td>1997</td>
</tr>
<tr>
<td></td>
<td>Only 3 months</td>
<td>Perù</td>
<td>2000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Venezuela</td>
<td>2001</td>
</tr>
</tbody>
</table>
Malaria and sandfly control

There are several examples of sandfly populations being affected by IRS directed against other pest species.

The malaria control in Italy based on the use of DDT, reduced significantly the *Leishmania* transmission. The same occurred in India, Iran, Syria, and Greece.
Nowadays IRS campaign

Countries reporting the insecticide use for leishmaniasis vector control [indoor residual spraying]

- 2 from Americas (Brazil and Paraguay)
- 3 from the Mediterranean Region (Morocco, Syria, Iran)

Insecticides most extensively used, by class (2003-05)

- Organophosphates, Chlorpyrifos-methyl;
- Carbamates, Propoxur;
- Pyrethroids, Alpha-cypermethrin, Cypermethrin, Deltamethrin, Lambda-cyhalothrin.
Environmental and practical restrictions for IRS

✓ Needs of periodical interventions
✓ Skilled personnel and suitable equipment
✓ Limitation to treat all sandfly resting sites
✓ Cost/benefit
✓ Risk of the appearance of insecticide resistance
Susceptibility of sandflies to insecticides

- Sandflies remain susceptible to all the major insecticidal groups and there is no pressing need to develop new compounds specifically for sandfly control.

- To date most records of resistance refer to DDT in only three species: P. papatasii, P. argentipes, and S. shorti in one country (India), although there are reports of increased tolerance to this compound in several countries.

- Sandflies have been shown to possess detoxification mechanisms that could confer protection on other groups and insecticide resistance may arise in other populations, as a result of leishmaniasis control measures or indirect exposure to compounds used to control malaria or dengue.
Insecticide treated nets (ITNs)

- Insecticide treated nets (ITNs) have proven efficacy in protecting humans against arthropod vectors of malaria, lymphatic filariasis, Chagas disease and leishmaniasis.
ITNs use and Leishmaniasis

- The use of ITNs may represent the most sustainable method of reducing intradomiciliary transmission of *Leishmania*

- ITNs are easy to use and require less technical and capital resources to implement, compared to other vector control methods

- They are cost-effective, which has led to their extensive implementation by countries on a large scale
Advantage of ITNs use

- An advantage of ITNs use is that members of affected communities can treat the nets themselves, whether these are manufactured locally or supplied by health authorities.

- ITNs currently represent a key malaria control strategy, however, low insecticide retreatment rates remain problematic.
ITNs re-impregnation & LLINs

- During recent years, long-lasting insecticide-treated nets (LLINs) have been developed to overcome the problems of:

  ✓ low re-treatment rates,
  ✓ washing,
  ✓ and erratic dose of the insecticide

- Two methods are used for producing LLINs:

  ✓ incorporation of insecticide into fibers, and
  ✓ surface treatment of net fibers or finished nets
Commercially produced LLINs (bednet)

- **Olyset®**
  a.i. = 2% permethrin
  incorporated within fibers

- **PermaNet® 2.0**
  a.i. = deltamethrin
  The target dosage is 55 mg/m².
Synthetic pyrethroids

- Pyrethroids used for the treatment of the nets combine the properties of low to moderate mammalian toxicity, low volatility and high insecticidal activity.

- Are fast acting insecticides and show irritant properties against sandflies.
Effect of pirethroids on poisoned sandflies

- **Anti-feeding** = female sandflies unable to feed on the host

- **Knock down** = sandflies fall to the ground unable to move. These sandflies could regain movement in 1 h

- **Toxic** = sandflies die within 24 h

- **Functional** = sandflies disabled beyond the point of survival
Functional effect [similar to toxic effect]

- Sandflies exposed to pyrethroids lose some legs before dying
- Surviving sandflies able to fly with several lost legs, sometimes up to 4, are also commonly observed
- It is probable that this phenomenon occurs also in the field and that mutilated flies are unlikely to survive
### Standard WHO cones with a 3 min exposure time to ITNs

**Alive P. papatasi 24 h post-exposure showing leg losses**

<table>
<thead>
<tr>
<th>Test</th>
<th>ITNs Code</th>
<th>No.</th>
<th>Dead</th>
<th>Alive</th>
<th>Alive showing leg losses [No. of legs]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>[1] [2] [3] [4]</td>
</tr>
<tr>
<td>1</td>
<td>901-0</td>
<td>50</td>
<td>13</td>
<td>37</td>
<td>6  10  9  7</td>
</tr>
<tr>
<td>2</td>
<td>901-1</td>
<td>50</td>
<td>9</td>
<td>41</td>
<td>6  12  10  5</td>
</tr>
<tr>
<td>3</td>
<td>901-2</td>
<td>51</td>
<td>9</td>
<td>42</td>
<td>7  8  13  2</td>
</tr>
<tr>
<td>4</td>
<td>901-3</td>
<td>51</td>
<td>7</td>
<td>44</td>
<td>10  9  11  0</td>
</tr>
<tr>
<td>5</td>
<td>901-4</td>
<td>50</td>
<td>6</td>
<td>44</td>
<td>11  8  9  0</td>
</tr>
<tr>
<td>6</td>
<td>901-5</td>
<td>52</td>
<td>5</td>
<td>45</td>
<td>10  9  9  0</td>
</tr>
<tr>
<td>7</td>
<td>901-10</td>
<td>50</td>
<td>3</td>
<td>47</td>
<td>18  3  2  0</td>
</tr>
</tbody>
</table>
### Encouraging results on use of ITNs against sandflies have been obtained from several field intervention

<table>
<thead>
<tr>
<th>Country</th>
<th>Authors</th>
<th>Pyrethroid used</th>
<th>Impact</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Afghanistan</strong></td>
<td>Reyburn et al, 2000</td>
<td>Permethrin (0.5 g/m²)</td>
<td>-</td>
<td>Significant</td>
</tr>
<tr>
<td><strong>Colombia</strong></td>
<td>Alexander et al, 1995</td>
<td>Deltamethrin</td>
<td><em>L. youngi</em> (100.0)</td>
<td>3 months</td>
</tr>
<tr>
<td><strong>Iran</strong></td>
<td>Nadim et al, 1995</td>
<td>Deltamethrin 25 mg/m²</td>
<td><em>P. sergenti</em></td>
<td>6 months</td>
</tr>
<tr>
<td><strong>Kenya</strong></td>
<td>Basimike &amp; Mutinga, 1995</td>
<td>Permethrin 0.5 g/m²</td>
<td><em>P. martini</em> (88.8)</td>
<td>6 months</td>
</tr>
<tr>
<td><strong>Sudan</strong></td>
<td>Elnaiem et al, 1999a</td>
<td>Permethrin 0.5 g/m²</td>
<td><em>P. papatasi</em> (significant)</td>
<td>3-4 months</td>
</tr>
<tr>
<td><strong>Venezuela</strong></td>
<td>Feliciangeli et al, 1995</td>
<td>Deltamethrin 60 mg/m²</td>
<td><em>L. ovallesi</em> (not significant)</td>
<td>7 weeks</td>
</tr>
<tr>
<td></td>
<td>Kroger et al., 2002</td>
<td>Lambdacyhalothrin 12.5 mg/m²</td>
<td><em>Lutzomyia</em> sp</td>
<td>High reduction</td>
</tr>
</tbody>
</table>

Encouraging results on use of ITNs against sandflies have been obtained from several field intervention.
Community-based trials

- The efficacy of ITNs against leishmaniasis has been demonstrated by few community-based trials focused on Old World sandfly species,

- principally *P. sergenti*, peridomestic/urban foci

**Afghanistan**

**Iran**

**Turkey**

**Syria**
ITNs to prevent ACL in Aleppo governorate, Syria (Jalouk et al., 2007)

Active ACL lesions rates recorded before and after intervention in treated (A) and control villages (B).
Ongoing community-based trials aimed to assess the effectiveness of LLINs in the prevention of visceral leishmaniasis (VL)

Session 5. Control and update on interventions

- MSF and VL control in East-Africa
- KALANET EU project in *L. donovani* endemic areas of the Bihar region
Chemical repellents

- The use of insect repellents or protective clothing may be the only prophylactic measures in areas where *Leishmania* transmission is extra-domiciliary.

- They should be considered for use also by people who are only temporarily at risk of *Leishmania* infection, such as tourists, soldiers etc.
Commercial repellents

Among the synthetic repellents, the gold standard is **DEET**, which is highly effective against haematophagous insects and in use for more than 50 years.

Its efficacy has been also proven against *Leishmania* vectors.

Recently, the efficacy of a new piperidine compound [KBR 3023] has been demonstrated also against phlebotomine vectors.
Laboratory tests on human volunteers showed 100% protection (until the 7th hour) by 20% KBR 3025 commercial formulation against the bite of *P. papatasi* and *P. perniciosus*.
Preventative measures for dogs

- Although certain wild animal species may be involved in the epidemiology of ZVL, domestic dogs appear to be the principal reservoir host of *L. infantum* throughout the world.

- Much of the focus on control of ZVL is currently placed on these animals and preventing sandfly bites is a priority to protect dogs from leishmaniasis.
Researches have been carried out on chemical compounds to be used on dogs as an effective measure in controlling CanL.

In particular, the impact of mass use of:

- Deltamethrin 4%
- Permethrin 50% - Imidacloprid 10%
- Permethrin 2% - Pyriproxyfen 0.02%
- Permetrin 65%

have been evaluated in controlling CanL.

**Pyrethroids used as biocides against ectoparasites**

- Topical application
- Protector band
Anti-feeding and insecticidal effect by contact

**Protective**
- [Irritancy effect]
- Anti-feeding
  - [>90%]

**Toxic**
- Knock-down
- Leg losses (alive flies)
- Mortality [>25%<90%]
- 100% blood fed
Anti-feeding + insecticidal effects

Anti-feeding effect >90%

Individual protection

Mortality = 100% blood fed

Mass protection

healthy

infected
The anti-feeding and insecticidal effect have been demonstrated experimentally for a limited number of *Leishmania* vectors

<table>
<thead>
<tr>
<th>Species</th>
<th>Active ingredients (%)</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. perniciosus</em></td>
<td>- Permethrin (2)+Pyriproxyfen (0.02)</td>
<td>Asher et al 1998; Molina et al 2001; Mercier et al 2003</td>
</tr>
<tr>
<td></td>
<td>- Permethrin (65)</td>
<td>Molina et al 2001; Reithinger et al 2001</td>
</tr>
<tr>
<td></td>
<td>- Permethrin (50)+Imidacloprid (10)</td>
<td>Mirò et al 2005</td>
</tr>
<tr>
<td></td>
<td>- Deltamethrin (4)+Trifenilphosphate</td>
<td>Killick-Kendrick et al, 1997; Lucientes et al 1999;</td>
</tr>
<tr>
<td><em>L. longipalpis</em></td>
<td>- Permethrin (50)+Imidacloprid (10)</td>
<td>Mencke et al 2005</td>
</tr>
<tr>
<td></td>
<td>- Deltamethrin (4)+Trifenilphosphate</td>
<td>David et al 2001</td>
</tr>
<tr>
<td><em>L. intermedia</em></td>
<td>- Permethrin (65)</td>
<td>Reithinger et al 2001</td>
</tr>
<tr>
<td><em>L. migonei</em></td>
<td>- Deltamethrin (4)+Trifenilphosphate</td>
<td>David et al 2001</td>
</tr>
<tr>
<td><em>P. papatasi</em></td>
<td>- Deltamethrin (4)+Trifenilphosphate</td>
<td>Mencke et al 2003</td>
</tr>
</tbody>
</table>
## The impact of preventative measures on CanL and VL incidence

<table>
<thead>
<tr>
<th>Measures</th>
<th>Country</th>
<th>Reference</th>
<th>No. of dogs (control)</th>
<th>Intervention period</th>
<th>% of reduction CanL - VL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advantix</td>
<td><strong>Italy</strong></td>
<td>- Otranto et al 2007</td>
<td>209 (1) 204 (2) + (218)</td>
<td>8 months</td>
<td>89 (1) and 93 (2) CanL</td>
</tr>
<tr>
<td></td>
<td><strong>Brasil</strong></td>
<td>- Giffoni et al 2002</td>
<td>150 + (146)</td>
<td>4 months</td>
<td>50 CanL</td>
</tr>
<tr>
<td>Expot</td>
<td><strong>Italy</strong></td>
<td>- Maroli et al 2001</td>
<td>354 + (371)</td>
<td>2 seasons</td>
<td>50 (3) - 86 (4) CanL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Maroli et al 2002</td>
<td>49 + (150)</td>
<td>1 season</td>
<td>52 CanL</td>
</tr>
<tr>
<td></td>
<td><strong>Iran</strong></td>
<td>- Mazloumi Gavgani et al 2002</td>
<td>466 + (354)</td>
<td>6 months</td>
<td>54 CanL - 43 VL</td>
</tr>
<tr>
<td></td>
<td><strong>Brasil</strong></td>
<td>- Oliveira-Lima et al 2002</td>
<td>1246 + (1267)</td>
<td>1 year</td>
<td>49 CanL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Reithinger et al 2004</td>
<td>136 + (97)</td>
<td>5 months</td>
<td>50 CanL</td>
</tr>
</tbody>
</table>

(1) Treatment each 4 weeks;  
(2) Treatment each 2 weeks;  
(3) First sandfly season;  
(4) Second sandfly season
Perspectives

- Large-scale interventions based on IRS are no longer sustainable in most situations.

- In rural areas where dwellings are more dispersed and surrounded by large, untargeted "reservoir" populations of sandflies, IRS of houses may be both unpractical for logistic reasons and ineffective.

- ITNs [LLINs] may offer the best solution in rural areas where transmission is largely intradomiciliary.
Conclusions

- More focalised measures are required which may require increased community participation and education in preventative measures against leishmaniasis.

Improved information on aspects such as,

- biting behaviour and
- resting/breeding sites

would make delivery of existing compounds more efficient, resulting in lowered costs of interventions, higher efficacy and fewer detrimental effects to the environment.
Thank you for your attention