Development of a Global Strategy against Insecticide Resistance in malaria vectors

Vector Control & Prevention
Global Malaria Programme
World Health Organisation
Global Malaria Programme

Outline

• The current situation – the threat of pyrethroid resistance for malaria control
• Strategies to find new molecules for nets and walls
• Strategies to slow down the spread of resistance
• The policy process
GLOBAL MALARIA PROGRAMME
Insecticide Resistance - 1

1. Already a major issue in Africa – some reports from India

1. \textit{kdr} genes are already widespread – but other metabolic mechanisms are spreading rapidly – oxidases & esterases
   - too little data about distribution or importance of these mechanisms
   - may be more powerful as causes of control failure

2. Big gaps in the data – but consolidated regional databases do exist.

1. Disconnection between data and insecticide choice decisions: e.g.
   - Zanzibar, Kagera
Impact of insecticide resistance

- Very little data on impact of insecticide resistance on malaria control

- Most studies have used experimental huts and impact on entomological parameters

- Mozambique/KZN case (*An. funestus*) showed potential impact on malaria cases (although there are confounding factors as always)

- Urgent need for well conducted studies on epidemiological impact of resistance (multi-country study about to be launched, funded by BGMF & coordinated by GMP)
Summary points

- Pyrethroid resistance is widespread in *An gambiae* (and perhaps even more so in *An funestus*).
- Resistance to DDT also common.
- Carbamate and OP resistance so far restricted to W. Africa.
- *kdr* alone has not yet been shown to be a cause of control failure.
- But combination of *kdr* and other mechanisms is potentially much more serious – focus on *kdr* may have led to a false sense of security?
Insecticide Resistance - Response

1. **Recommend** that in GF (and other donor) proposals, resistance data should be quoted (for large-scale IRS or ITNs) and used to justify insecticide choice (for IRS) - as a condition for funding.

1. Expert consultation planned for March to review the current situation and recommend global policies – roll out via WIN / VCWG
   - Acceptance by the 3 or 4 main donors is necessary…. and probably sufficient!

2. Options for management:
   - Likely to recommend rotations - but mixtures are probably much more effective
   - Need more mixture (combination) products esp for nets
   - Reserve pyrethroids for ITNs? (NOT for IRS? Agriculture?)
Strategies to find new molecules for walls

- Chemical companies are the key source – they have the experience and knowledge

- IVCC – critical support, stimulus

- IVCC and Chemical companies
  - a few compounds new to public health are coming through
  - in the pipeline and medium-term prospects
  - but as IRS and/or wall-sheeting products

- But IRS needs repeated application once or twice a year

- Wall-sheeting last much longer but need elaborate fitting
Strategies to find new molecules for nets

- RBM needs effective ITNs! Nets have many advantages as a medium for insecticide!
  - between mosquito and the host
  - even untreated nets protect if intact
  - distribution at long intervals, village-scale or through EPI (don’t have to visit every house)
  - can’t cover 450m people at risk any other way!

- Nothing in the pipeline for nets
  - a molecule discovered tomorrow would take >5y to develop

- Much less incentive for primary chemical companies
  - they take 30% to 60% of expenditure on IRS
  - but only ~ 5% of expenditure on LLINs
  - They stand to gain from a shift to IRS from LLINs !!

- Need to find a solution to this unbalanced incentive !!
Strategies to slow down the spread of resistance

• Rotations - yes
  • but not reliable, not enough?
  • depend on fitness disadvantage of R, so only effective when R is rare?

• Combined products - yes
  • e.g. roof and walls with different products
  • Encouraging preliminary results

• Mixtures - yes
  • The most robust approach - less dependent on assumptions about resistance
  • industry ready, but little experience so far
  • Issues of tox, regulation, barriers to market entry

• Must act early -
  • Waiting for proof of control failure is no strategy at all !!
Strategies to slow down the spread of resistance

Reserve pyrethroids for use on Nets?
• From IRS? Would greatly reduce cost of IRS
  • e.g. at current prices would reduce IRS coverage from 29m to 11m population
  • might still be worthwhile, if it helped to slow down resistance enough…
• From agriculture? Desirable if feasible, at least for some applications (rice)

• The Lesson from Agriculture? Don’t do it like they do it in agriculture = ‘scramble competition’, i.e. a race to maximise profit!!

• All Resistance-delaying strategies raise short-term costs
  • Co-operation - Everyone must join in – Solid consensus needed
  • But some will lose out!!
  • but strategies not guaranteed!

• Evidence Issues - Current evidence is indirect & argumentative:
  • Problem: Evolutionary events are large-scale – can’t do village scale trials with R gene frequency change as the outcome
  • Need better evidence on sources of selection, methods to evaluate management strategies
## Two populations: 25% are resistant; sporozoite rate = 1%

<table>
<thead>
<tr>
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<th>Negative Sporozoite</th>
<th>Positive Sporozoite</th>
<th>Sporozoite rate</th>
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<tbody>
<tr>
<td>Susceptible</td>
<td>800</td>
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<tr>
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<tr>
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Fisher's exact test P = 0.0006
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<td>500</td>
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Fisher's exact test $P = 0.057$

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<td>Human blood</td>
<td>Animal blood</td>
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<tr>
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<tr>
<td><strong>Inside</strong> treated net with holes</td>
<td><strong>Outside</strong> net</td>
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<thead>
<tr>
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<th>Parous</th>
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The policy process

1. Review now being completed
   • Current situation
   • Strategy options

1. Techical Consultation on this issue - 1st qtr

2. Roll-out to RBM constituencies via Vector Control Working Group (VCWG)
   • Need for careful consensus building
   • New Products
   • Choosing insecticide / strategy based on subregional data
   • M & E tools