The VHEMBE study: A birth cohort study investigating potential health effects of indoor residual spraying

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April 25, 2013
Indoor Residual Spraying (IRS)

- At least 42 countries use IRS
- Main IRS insecticides DDT and pyrethroids (deltamethrin and cypermethrin)
- Malaria incidence reduced by 90% through a combination of IRS and other measures.
- Numerous studies have shown that IRS has substantially reduced infant and child mortality.
Unintended Exposures
Comparison of DDT/DDE Levels

**Serum Concentrations (μg/g lipids)**

- **DDT**
  - Current U.S. Women ('01-'02)
  - DDT-Era U.S. Women (CA '59-'67)
  - Limpopo Men Living in Non-IRS Areas ('03-'05)
  - Limpopo Men Living in Unsprayed Huts ('03-'05)
  - Limpopo Men Living in Sprayed Huts ('03-'05)

- **DDE**
  - Current U.S. Women ('01-'02)
  - DDT-Era U.S. Women (CA '59-'67)
  - Limpopo Men Living in Non-IRS Areas ('03-'05)
  - Limpopo Men Living in Unsprayed Huts ('03-'05)
  - Limpopo Men Living in Sprayed Huts ('03-'05)

**Comparison Values**

- DDT: 54 times
- DDE: 140 times

*References:
CDC, 2005; Bhatia et al., 2005; Aneck-Hahn et al., 2007*
Comparison of Pyrethroid Levels in Breast Milk

![Bar chart showing comparison of pyrethroid levels in breast milk from Switzerland and South Africa.](image)

- **Deltamethrin**
  - Switzerland ('01)
  - South Africa ('06)

- **Cypermethrin**
  - Switzerland ('01)
  - South Africa ('06)

**South Africa ('06)**
- 8.5 times

**Switzerland ('01)**
- 2.5 times

Sources:
- Zehringer et al., 2001
- Bouwman et al., 2006
Should we continue to use DDT?

There are different opinions held by well-intentioned organizations and their opinions vacillate:

- Stockholm Convention on POPs
- WHO International Programme on Chemical Safety
- President’s Malaria Initiative
- WHO Global Malaria Programme
Changing position of WHO vs. DDT

2000

2001
Stockholm Convention on POPs

2006
WHO recommends scaling up IRS

2007
WHO announces reevaluation of DDT safety and calls for ultimate elimination

2010

2011
WHO concludes exposure in IRS areas below levels of concern
“...exposures in treated residences have been higher than potential levels of concern...”

“Of particular concern would be women of childbearing age ... and transfer of DDT and DDE to the fetus in pregnancy and to the infant via lactation.”
Excerpts from WHO Report (2011)

“The strongest epidemiological study suggests an association of elevated maternal serum DDE levels with reduced gestational age and increased rates of small-for-gestational-age babies.”

“Consistent evidence for perinatal exposure having neurocognitive effects on a population level, particularly for DDT.”
Health effects of pyrethroid exposure

- Animal studies report effects on reflexes, locomotor activity, learning and memory

- Human studies of acute exposure also found neurological effects (paraesthesia, numbness, vertigo and rarely coma and death)

Virtually no data on chronic exposure to pyrethroids
An Important Piece of the Puzzle is Missing: Health Effects in IRS Populations

- IRS populations may be more susceptible to health effects due to malnutrition, poverty, and poor health.
Balance Cost/Benefits of IRS
The VHEMBE Study

Venda Health Examination of Mothers, Babies and their Environment

A birth cohort study in Limpopo, South Africa
Study Site

Thohoyandou
Varied Topography
Study Objectives

- **Enroll 750 women** at delivery
- Measure **DDT and pyrethroids** in maternal serum
- Follow children to **2 years of age**
- Assess exposure **determinants and sources**
- Assess relation of DDT and pyrethroids with child **neurodevelopment and mediators**
- **Compare** the impacts of DDT and pyrethroids on development
## Data Collection

<table>
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<td>Child Anthropometric Measurement</td>
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<td>Child Neurobehavioral Assessment</td>
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## Potential Confounders

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<th>1-Week 08 / 2013</th>
<th>1-Year 08 / 2013</th>
<th>2-Year 08 / 2014</th>
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<td>Basic demographics</td>
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<td>Food Frequency Questionnaire (QFFQ)</td>
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<td>Stressful Life Events</td>
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<td>Growth measurements</td>
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<td>Breastfeeding</td>
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<td>Home Assessment</td>
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<td>Maternal Cognitive Abilities (Raven’s Matrices)</td>
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<tr>
<td>Child Food Frequency Questionnaire</td>
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<td>Life Events (Coddington)</td>
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<td>Mother and Children Interaction (HOME)</td>
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<tr>
<td>Maternal Depression (CES-D)</td>
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<td>Lead</td>
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<td>Hemoglobin and Hematocrit (Anemia)</td>
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</table>
Progress to Date (since August 2012)

- Enrolled 452 participants
- Completed 406 home visits
- Building bio-repository
  - Blood (venous and heelstick)
  - Breast milk
  - Urine
  - Meconium
  - Saliva
Thanks to our funder

United States
National Institutes of Health

National Institute of Environmental Health Sciences
... and a special thanks to the Venda community in Vhembe, Limpopo
EXTRA SLIDES
Main health outcomes of concern

- Reduced gestational age
- Increased rates of preterm birth
- Neurocognitive effects
Study Collaborators
Limpopo, South Africa
DDT Use Under Stockholm Convention 2010

Grey: Not party to Stockholm Convention
Green: Party to Stockholm Convention
Pink: Countries notifying of DDT use
History of Pyrethroids

1800’s...

Early 19th Century
Natural pyrethrum is widely available in Europe

1920’s
Active structure of pyrethroids is discovered

1960
1st generation synthetic pyrethroids created

1970
2nd generation pyrethroids are created

1980
Pyrethroids comprise of 20% of the total insecticide market

2002...

Today
Sales of pyrethroids are at their highest level in history
Tshilidzini Hospital
For more information…

- Center for Environmental Research and Children’s Health (CERCH)  [www.cerch.org](http://www.cerch.org)
- Environmental Working Group  [www.ewg.org](http://www.ewg.org)
- Pesticide Action Network  [www.panna.org](http://www.panna.org)
- Collaborative on Health and the Environment  [www.healthandenvironment.org](http://www.healthandenvironment.org)
- Environmental Health News  [www.environmentalhealthnews.org](http://www.environmentalhealthnews.org)
Study Aims

Determine whether in utero exposure to IRS insecticides is associated with:

- Neurobehavioral development at 12 and 24 months of age
- Premature birth
- Intrauterine growth restriction
- Low birth weight
- Neonatal thyroid hormone disruption
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<tbody>
<tr>
<td>Venous Blood</td>
<td>X (Mom)</td>
<td></td>
<td>X (Child)</td>
<td></td>
</tr>
<tr>
<td>Urine</td>
<td>X (Mom)</td>
<td>X (Child)</td>
<td>X (Child)</td>
<td>X (Child)</td>
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<tr>
<td>Heel Stick</td>
<td></td>
<td>X (Child)</td>
<td></td>
<td></td>
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<tr>
<td>Breast Milk</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Hair</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
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<tr>
<td>Saliva</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Meconium</td>
<td>X</td>
<td></td>
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<tr>
<td>Buccal Cells</td>
<td></td>
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**ENVIRONMENTAL SAMPLE COLLECTION**

<table>
<thead>
<tr>
<th>Sample Collection</th>
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<tbody>
<tr>
<td>House Dust</td>
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</tbody>
</table>

BIOLOGICAL SAMPLE COLLECTION

- Venous Blood
- Urine
- Heel Stick
- Breast Milk
- Hair
- Saliva
- Meconium
- Buccal Cells

ENVIRONMENTAL SAMPLE COLLECTION

- House Dust
Maternal DDT/E & Bayley Mental Scores in the CHAMACOS Population

β (95% Confidence Interval) for every 10-fold increase in serum DDT/DDE

6 Months 12 Months 24 Months 6 Months 12 Months 24 Months

DDT

DDE

Eskenazi et al., 2006
Key Areas For Feedback from Malaria Experts

- What other factors should we consider?

- How can we assure information is most useful to you and other policymakers?

- Cost/benefit analysis
- Focused interventions
- Determine where to spray based on population characteristics and geographical characteristics
In summary, we designed our study to:

1. Identify the levels and pathways of DDT and pyrethroid exposures to infants in IRS communities

2. Uncover the mechanisms (i.e. thyroid hormone, fetal growth) which may underlie neurodevelopmental effects

3. Study the health impact of exposure to pyrethroid insecticides, a key alternative to DDT in malaria control efforts

4. Compare the impacts of DDT and pyrethroids on development

5. Identify susceptible subpopulations