Environmental Epidemiological study related to aerial spray of Endosulfan on Cashewnut plantations in Kasargode district of North Kerala

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How was the problem recognized?

• Since Feb. 2001, a number of reports appeared in national dailies, popular magazines and TV channels regarding health problems being linked to aerial spray of Endosulfan, in Kasargode district of Kerala.
• This pesticide had been sprayed twice a year for more than twenty years to control the tea mosquito on cashew nut plantations located in the area.
• A wide range of illnesses such as neurological disorders, congenital malformations, allergies, reproductive disorders and cancers were reported.
• The National Human Rights Commission initiated suo moto action and asked a number of agencies including ICMR to investigate the matter and submit a report.
List of confirmed cases of various diseases reported by Dr. Y.S. Mohankumar from Padre village.

<table>
<thead>
<tr>
<th>Disease</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>49</td>
</tr>
<tr>
<td>Mental retardation</td>
<td>23</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>9</td>
</tr>
<tr>
<td>Psychiatric cases</td>
<td>43</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>23</td>
</tr>
<tr>
<td>Suicide</td>
<td>9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>156</strong></td>
</tr>
<tr>
<td><strong>Total (by January 26)</strong></td>
<td><strong>197</strong></td>
</tr>
</tbody>
</table>

NOTE: * - cases counted by January 5, 2001
** - break-up not available
As regards the role of Endosulfan in causation of these morbidities, there are no published reports linking similar illnesses with Endosulfan exposure in human beings. However, there are some conflicting reports of endocrine disruption, congenital malformations and carcinogenicity in experimental animals.
Geographic location of the area
Planning of the Study

- Local contacts made
- Visits to the area for first hand information about location of plantations, types of other crops and pesticides used, location of residential areas, population size
- Preliminary inquiries from District collectors office, panchayat, schools, nearby medical college, local residents and medical practitioners
- Literature survey on Endosulfan toxicity
CASHEW NUT PLANTATION
Plantation is at the top and people live in the valley.
Mental retardation and epilepsy in one family
Udaya, eldest son of Sundara Shetty and Shailaja, living in Vannimagar, Padre is suffering from Cerebral Palsy.
Important points considered at the time of designing the study

- In the case series reported by Dr. Mohan Kumar, there was no denominator.
- The types of diseases reported are not unusual and could be due to other causes.
- The houses were scattered and detailed house to house survey was very difficult.
Probability of endosulfan exposures

- It is very difficult to associate chronic health effects with pesticide exposures because most of the times there are mixed exposures. This was a unique situation because only one pesticide – Endosulfan had been sprayed for more than twenty years.

- The topography of the area was peculiar with plantations on hill tops and residential areas in the valley
Probability of endosulfan exposures

- Endosulfan is known to bind to soil particles. The area has a rainfall of 140 inches per annum and run off water is likely to carry the soil sediments into the valley.
- People living in valley use water from streams which originate from the plantations.
- There is no source of water supply other than Surangas, wells or streams.
- Maximum number of diseases were being reported from people living near a stream - Kodenkiri.
Suranga, a peculiar source
Of water supply for people
Living in the valley
Environmental Epidemiological Study was undertaken with the following Objectives:

1. To confirm the reported disease pattern in the exposed populations and evaluate the magnitude of the problem by comparison with control populations through a well designed epidemiological study.

2. To search for etiological factors if the exposed populations show abnormal disease patterns and generate a hypothesis.

3. To analyse endosulfan residues in environmental and biological samples.
Methodology and plan of work:
After preliminary visits it was decided to select school children for the study
Material and Methods:

**Exposed Group:** School children of a village near cashew plantations where endosulfan was sprayed for over 20 years. (619 children).

**Control Group:** Children of a similar school of a village about 20 KM away where endosulfan has been never sprayed. (416 children)
Why children were selected as the exposed population

- Many of the diseases reported were in the children such as epilepsy, cerebral palsy, congenital malformations etc.
- Due to high literacy, most of the children attended school and school records were well maintained
- It was possible to get full cooperation from schools through district health authorities
Why children were selected as the exposed population

- Parents were asked to accompany the children and family details could be recorded at the same time.
- It was possible to get information about siblings who were not able to attend the school due to physical or mental health problems.
Selection of control group

Our major criteria for the selection of control population was the similarity in ethnic background, climate, food habits, occupations, crops and socio-economic status and absence of aerial spray of endosulfan.
Parameters selected for the study

Parameters of exposure and effect were selected after detailed discussions with members of the SAC and the Dept of Pediatrics, KMC, Mangalore, literature survey for toxicity of endosulfan and availability of standard techniques.
Study Parameters

Questionnaire
Physical Examination by a Pediatrician.
Sexual Maturity Rating (Tanner’s Classification) by Pediatrician.
Blood Samples Analysed for:
   Endosulfan residues.
Hormonal Analysis:
   Thyroid Hormones: T3, T4 and TSH
   Sex Hormones: Testosterone, Oestradiol, Progestrone, FSH, LH, Prolactin and growth hormone.
Cytogenetic Studies
In children

- The questionnaire included details of birth history and other factors which could have caused the illnesses besides those which could be due to endosulfan toxicity.
- The pediatricians were requested to give a definite diagnosis wherever possible.
- Any case showing an abnormality was reexamined by a senior pediatrician.
Illnesses and deaths in the family were enquired from the parents

Parents were requested to bring any relevant papers related to illness in the family members e.g. reports of investigations, medicine strips etc

Details of cattle owned and any illnesses were also recorded

Source of water, food habits, occupation, use any herbal remedies were recorded
Investigations (contd..)

Satellite based assessment of physiographic disposition of villages in the cashew plantation area of Kasargod district: The Regional Remote Sensing Service Centre (RRSSC), Bangalore
Estimation of Endosulfan residues in environmental samples.
Some precautions taken during the study

- The field study was carried out in one stretch over a period of 20 days
- The questionnaires were completed by qualified social scientist conversant with the local languages
- Exact date of birth of each child was checked from the school records
- Same pediatricians did the examination of the study and control groups
- Same instruments were used (weighing machine, skin calipers etc.)
Some precautions taken during the study

- Methodologies for estimation of endosulfan residues and serum hormone levels were well standardized at NIOH and analysis was carried out by trained persons.
- The completed questionnaires were checked everyday by one senior team member who was present in the field all the time.
Results

- The exposed and study group children were similar when compared by anthropometric parameters, parents occupations, ethnicity and food habits.
- Prevalence of bronchial asthma, allergic skin disorders was similar in both groups (not high as reported by media).
- Chromosomal aberrations did not show any difference between the two groups.
- Cancer cases reported by Dr. MK could not be confirmed.
Results (contd.)

- There was significantly higher prevalence of neurobehavioural disorders, congenital malformations in female subjects and abnormalities related to male reproductive system in the study group children.

- Serum endosulfan residue levels were significantly higher in study population as compared to the control group showing that the study population had much higher exposure than reference population.
Mean ± SEM levels (ppb) of Serum Endosulfan in study and control subjects

<table>
<thead>
<tr>
<th></th>
<th>Control (n=45)</th>
<th>Study (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-Endosulfan</td>
<td>0.87 ± 0.23</td>
<td>4.24 ± 0.74**</td>
</tr>
<tr>
<td>β-Endosulfan</td>
<td>0.40 ± 0.17</td>
<td>1.77 ± 0.36**</td>
</tr>
<tr>
<td>Endosulfan</td>
<td>0.10 ± 0.08</td>
<td>1.47 ± 0.33**</td>
</tr>
<tr>
<td>Sulfate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Endosulfan</td>
<td>1.37 ± 0.40</td>
<td>7.47 ± 1.19**</td>
</tr>
</tbody>
</table>

** p < 0.001
Prevalence of scholastic backwardness (learning disability) as reported by the class teacher and the results of annual examinations.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Exposed (619)</th>
<th>Control (416)</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Learning disability</td>
<td>66 (10.7%)</td>
<td>11 (2.60%)</td>
<td>P&lt;0.001 4.03 (2.16 – 7.54)</td>
</tr>
<tr>
<td>Retained in the Same class</td>
<td>126 (20.40%)</td>
<td>56 (13.50%)</td>
<td>P=0.0055 1.51 (1.13 – 2.02)</td>
</tr>
</tbody>
</table>
IQ evaluation by “Draw A Man Test” in Exposed and control population.

<table>
<thead>
<tr>
<th>IQ range</th>
<th>Control</th>
<th>Exposed</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;84</td>
<td>155/239 (64.90%)</td>
<td>398/511 (77.90%)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>84 – 115.99</td>
<td>68/239 (28.50%)</td>
<td>107/511 (20.90%)</td>
<td></td>
</tr>
<tr>
<td>116+</td>
<td>16/239 (6.70%)</td>
<td>6/511 (1.20%)</td>
<td></td>
</tr>
</tbody>
</table>
Comparison of male children participating in the SMR study

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control (n=90)</th>
<th>Study (n=117)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>13.10 ± 2.12</td>
<td>12.80 ± 2.07</td>
</tr>
<tr>
<td>Height (cms)</td>
<td>141 ± 10.60</td>
<td>139 ± 13.30</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>30.70 ± 7.44</td>
<td>29.50 ± 8.93</td>
</tr>
<tr>
<td>BMI</td>
<td>15.30 ± 1.98</td>
<td>15.00 ± 2.11</td>
</tr>
<tr>
<td>Skin fold thickness (mm)</td>
<td>7.31 ± 2.15</td>
<td>7.40 ± 2.28</td>
</tr>
</tbody>
</table>
The graph illustrates the relationship between age in years and serum testosterone levels (ng/mL) in two groups: Study and Control. The regression lines are as follows:

- Study: Rsq = 0.5163
- Control: Rsq = 0.4626
SMR Score for Pubic Hair

Age in years

- Study
  Rsq = 0.4358

- Control
  Rsq = 0.4815
SMR Score for Testes

Age in years

Study
Rsq = 0.3611

Control
Rsq = 0.4786
SMR Score for Penis Development

- Study: Rsq = 0.3631
- Control: Rsq = 0.4520

Age in years
# Prevalence of Congenital Abnormalities in Male Control and Exposed Subjects

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Control (n=233)</th>
<th>Exposed (n=361)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital Hydrocele</td>
<td>0 (0.00)</td>
<td>4 (1.11)</td>
</tr>
<tr>
<td>Undescended Testes</td>
<td>0 (0.00)</td>
<td>2 (0.55)</td>
</tr>
<tr>
<td>Congenital Inguinal Hernia</td>
<td>1 (0.43)</td>
<td>1 (0.28)</td>
</tr>
<tr>
<td>Cerebral Palsy</td>
<td>0 (0.00)</td>
<td>1 (0.28)</td>
</tr>
<tr>
<td>Macrocapheley</td>
<td>1 (0.43)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>4 (1.72)</td>
<td>2 (0.55)</td>
</tr>
<tr>
<td>Congenital skeletal disorder</td>
<td>1 (0.43)</td>
<td>3 (0.83)</td>
</tr>
<tr>
<td>Congenital Cataract/ retinopathy</td>
<td>1 (0.43)</td>
<td>3 (0.83)</td>
</tr>
<tr>
<td>Total Cases</td>
<td>8 (3.43)</td>
<td>14 (3.88)</td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td>1.43 (0.48 – 2.65) NS.</td>
<td></td>
</tr>
</tbody>
</table>
Illnesses in the families

- Our data does not support higher prevalence of bronchial asthma, skin problems and suicides in the exposed population
- Cancer cases reported by Dr. Mohan Kumar could not be confirmed
- There was a significantly higher prevalence of convulsive disorders in the exposed group families
Conclusions

1. There is a close similarity between the spectrum of health effects observed in the study population and those described in animal experiments. This supports the hypothesis of endosulfan as a causative factor for the endpoints observed in the study.

3. The physiography of Padre village had been a major factor responsible for continued exposure of the population.
4. It was found that the two groups differed mainly with respect to aerial spray of endosulfan. Therefore the most probable cause for the health problems in the study area could be relatively high and continued exposures to endosulfan through various environmental media such as food, water, soil and air.

5. The detection of endosulfan residues in the reference area does not antagonize our hypothesis and in fact this may have masking effect on the observed health effects.
Limitations of the SMR study

(3) Non participation in SMR study - 57% of the exposed and 33% of the control participants did not agree for SMR examination. However, growth related end points (height, weight and skin fold thickness) were comparable amongst the non participating groups.

(4) One time collection of blood samples for hormone analysis - The sex hormone secretion is pulsatile in nature with lot of diurnal variation.
Difficulties

- Deadlines set by NHRC
- Pressure by Pesticide Industry
- Controversies created by Expert group set up by Ministry of Agriculture
- Contradictory reports submitted by KAU and FIPPAT
Participating scientists

- Principal Investigator, Dr. H.N. Saiyed, Director
- Co-Investigator, Dr. (Mrs.) A. Dewan, Dy. Director (S.G.)

- Analytical Work
  - Dr. T.S. Patel, Dy. Director
  - Dr. V.K. Bhatnagar, S.R.O.
  - Dr. Rekha Kashyap, S.R.O.
  - Dr. V. Krishnamurthy
Analytical Work
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Mr. M.R. Varia, R.A.
Mr. N.M. Desai, R.A.
Mr. M. M. Mansoori, Lab. Asst.

Cytogenetic Assay,
Mr. B.C.Lakkad, AD
Mr. A.M. Suthar, T.O.
Mr. M.M. Patel, R.A.
Mr. A.K. Gautam, R.A.
Hormone Assay

Dr. K. G. Patel.
Dr. S.S.A. Zaidi, Asst. Director
Mrs. S.J. Gandhi, T.O.

Statistical Analysis: Mr. P.K. Kulkarni, DD

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Mrs. Lalitha Nagaraj, R.A.
Prof. U.V. Shenoy
Dr. Rathika D. Shenoy
Dr. RoshanAnn Oommen
Dr. Sangeetha Mahesh
Dr. Duggabatti Anjaneya Prasad

Dr. Vasanth
Dr. Prathiba Kamath
Dr. Siddharthanan S.
Dr. E. Venkatakamalakar Rao
Participating staff from Department of Pediatrics, Kasturba Medical College, Mangalore.

Dr. Habib Alam Raza
Dr. Bodla Hari Prasad
Dr. Syed Mohamed Omran
Dr. Venkatagiri Praveen Kumar
Dr. Podalakur Madhusudhan Rao
Dr. Venkata Ravanamma
Dr. Vadlamudi Radha Madhavi
Dr. Maya Menon
Publications

- Report to NHRC (July, 2002)
- **Publication of Endosulfan Study**
- Effect of Endosulfan on Male Reproductive Development

H N Saiyed, Aruna Dewan, V K Bhatnagar, U Shenoy, R Shenoy, H Rajmohan, Kumud Patel, Rekha Kashyap, P K Kulkarni, B Rajan and B C Lakkad

*Environmental Health Perspectives* 111 (16), 2003; 1958-1962
Commenting on the study, Dr. Jim Burkhart, science editor for EHP, says, "This is the first human study to ever measure the effects of endosulfan on the male reproductive system. Decades of spraying this pesticide, and only this pesticide, on the village provided a unique opportunity to analyze its impact. Although the sample size is somewhat limited, the results are quite compelling."