ESTIMATING THE IMPACT OF POISONING:
CHANGING PATTERNS OF MORTALITY IN CENTRAL LUZON, PHILIPPINES
IN RELATION TO PESTICIDE USE

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ABSTRACT

Misdiagnosis and under-reporting by the formal health care system may mask the extent of pesticide intoxication in developing countries. In a major rice growing area of the Philippines, widespread adoption of insecticides by small farmers was followed by a 27% increase in non-traumatic mortality among economically-active men (P < .001). Several factors suggest a causal link: highly toxic chemicals have been used under unsafe conditions, mortality has increased only in the age and sex class occupationally exposed, the death rate has declined among unexposed urban men, specific death rates have increased for those conditions likely to be confounded with insecticide poisoning and have declined for others, and both within and between years the pattern of mortality among men has reflected that of insecticide use. The results suggest strongly that the currently accepted figure of 10,000 deaths annually worldwide due to accidental intoxication is a substantial underestimate.

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INTRODUCTION

The spread of modern cereal varieties, and the adoption of modern farming practices and agrochemicals have made possible major increases in agricultural production in Southeast Asia. However, widespread use of synthetic pesticides by farmers and agricultural laborers, under inadequate safety conditions, has also exposed large numbers of people to occupational intoxication.

The hazard these workers face may be substantial. "Endrin", an organochlorine insecticide of high oral and dermal toxicity, has been widely marketed in the region. Based on results of a recent study (1), a person applying the insecticide with a backpack sprayer in good repair, using concentrations typical in the Philippines, and leaving unprotected, as is often the case, his hands, lower legs and feet would come into direct contact with 41 mg of active ingredient per hour. At that rate, a worker weighing 55 kg would be exposed to 33% of the mammalian dermal LD50 (the lethal dose for 50% of a population) in treating an average holding once with endrin*. This figure does not include exposure during handling of the concentrate and in mixing, which may be substantial though highly variable.

Efforts to estimate the actual impact of pesticide exposure on the health of field workers in developing countries encounter important methodological problems*. Clinical signs of intoxication, notably acetylcholinesterase depression, provide an objective measure; however, the uncertainty of the relationship between cholinesterase levels and morbidity (2) and difficulties in monitoring representative samples of small farmers or laborers over significant periods limit the conclusions that can be drawn by this method.

Retrospective studies based on reported cases have also been conducted. In Sri Lanka for example, 13,000 people are admitted to hospital each year for pesticide poisoning, of whom some 1,000 die (3). However, the accuracy of such estimates depends crucially on proper diagnosis and complete reporting. In developing countries, misdiagnosis of poisoning is made more likely by the absence of diagnostic tools, high patient-doctor ratios, unfamiliarity of health workers with the signs and symptoms of poisoning and lack of access by the poor to the formal health care system.

* Assuming 3 hours to treat a hectare; 2.5 ha/holding; a solution of 0.7 mg active ingredient/ml spray solution; 87% of the spray contacting the operator falling on the parts of the body left uncovered (4) and a dermal LD50 for endrin of 15 mg/kg (5).
A different form of retrospective analysis is employed in the present study. In an area of Central Luzon, Philippines where pesticide use has been relatively well studied and where the comparative ease of access to government services makes gross under-reporting of at least adult mortality unlikely, specific changes are predicted in death rates from what is known of the temporal and spatial patterns of use and the clinical toxicology of the compounds in question. A close fit between observation and expectation then allows one to estimate the excess mortality that has occurred. Specifically, it is hypothesized that: (1) increased mortality due to occupational intoxication will be concentrated among men, who are primarily involved in pesticide application; (2) no such effect will be apparent in unexposed urban groups; (3) the trend of death rate over the years will parallel that of pesticide use; (4) within the year, increased mortality will be concentrated in the months of greatest pesticide use and will closely reflect changes in the cropping pattern; (5) the specific death rates of the conditions most likely to be confused with pesticide poisoning will rise disproportionately and (6) these rates will be significantly correlated with that of diagnosed fatal poisoning.

Hypotheses regarding misdiagnosis are possible as well. In Central Luzon, two types of pesticide of marked acute toxicity have been widely used by small farmers: organophosphate (OP) and cyclodiene and hexachlorocyclohexane (CYC-HCH) organochlorine insecticides. Intoxication by each type can occur by the dermal, respiratory and oral routes. Symptoms of severe OP poisoning include generalised convulsions, psychic disturbances, intense cyanosis, bradycardia, pulmonary oedema and coma (6,7). Pneumonia, asthma and bronchospasm are frequently encountered sequelae (8-10). Unpublished observations by Dr. Nelia Maramba and her colleagues at the Philippines General Hospital indicate that when rural doctors were presented with the signs and symptoms of acute OP intoxication in mock examinations, they most frequently diagnosed a variety of cardio-vascular and respiratory conditions. I predict therefore that, as the use of OP insecticides rises, misdiagnosis of poisoning will inflate the combined death rates of cardio-vascular and respiratory diseases.

CYC-HCH intoxication presents very differently. The primary locus of action of these compounds is the CNS and severe poisoning is marked by convulsions, generally epileptiform in nature (11,12). Kubrich and Urban (13) describe a case of apparent dermal intoxication by endrin that under other circumstances would have been diagnosed as stroke. Thus, increasing use of and intoxication by CYC-HCH insecticides will, I predict, be followed by rising death rates attributed to epilepsy, brain tumor, stroke and related conditions (cerebral hemorrhage, embolism, aneurysm etc.) as a result of misdiagnosis.
METHODS

Pesticide use on the Central Luzon Plain, an area of intensive rice cultivation, rose markedly following the adoption of modern varieties in the late 1960's, and particularly as a result of the Masagana 99 credit scheme, introduced in 1972. A series of insect and virus disease outbreaks, beginning in 1971, served to increase insecticide use specifically. Between 1966 and 1979 insecticide applications on rice rose more than 500%. Compounds in widespread use during the 1970's included carbofuran, endrin, methyl parathion and monocrotophos (14,5). The liquid formulations sold in Central Luzon are classified as "extremely" or "highly hazardous" by WHO.

Aliaga, Jaen and Zaragoza are rural municipalities (combined 1980 population 96,000) in Nueva Ecija province. In typical villages, more than 80% of household heads are engaged in rice farming. Farmers typically applied insecticide 4-5 times per crop and treatments were concentrated in the vegetative stage, particularly during the month subsequent to transplanting. Men generally applied insecticides by backpack sprayer without protective clothing (locally unavailable). Since the late 1970's farmers' consumption of insecticides has remained constant or declined slightly.

Cabanatuan (population 138,000) is a nearby center within which there are both urban neighbourhoods where occupational exposure to insecticides is likely low and rural rice producing villages.

Population estimates were taken from the national censuses of 1960, 70, 75 and 80 (15) and by interpolation. Mortality statistics for 1961-84 were obtained from the civil registries, derived from death certificates. The causes ascribed were noted and entries assigned to one of 4 age classes: 1-5, 6-14 years and men and women 15-54 years. Deaths due to traumatic causes were excluded, save non-suicidal poisonings ascribed to pesticides or unspecified substances.

As consistent census breakdowns of the rural and urban populations of Cabanatuan were not available, indices of mortality by age class were calculated as the number of deaths in the urban or rural areas divided by the city's population in that year. This will be proportional to the death rate if the urban/rural mix remains constant. Cabanatuan has grown rapidly in recent years as a result of rural immigration and if, as appears likely, most immigrants settled in the urban neighbourhoods, a given proportionate change in the index of mortality would overestimate the true change in death rate in the urban areas and underestimate it in the rural areas.
For men and women, death rates in the rural municipalities and indices of mortality in Cabanatuan were adjusted to the city's age distribution in 1960 by the direct method.

Trends in mortality in the 1-5 and 6-14 years age classes were analysed by means of Armitage's test (16), and by least squares regression of arc sine-transformed rates for men and women (as these had been age-adjusted). However, as the use of insecticides has increased unevenly (rapidly in the years after 1972, slowly or not at all in the late 1970's), a more appropriate analysis of trend considers mortality in relation to two periods, one of low use (1961-71) and one of high (1972-84). I use the t-test to compare mean arc sine-transformed rates, except in the case of diagnosed poisoning, where a more conservative non-parametric method, the Mann-Whitney U-test is employed because of the few deaths in the early period. Changes in the proportions were analyzed by means of the appropriate Chi-square test.

RESULTS

Mortality by Age and Sex Classes
While non-traumatic mortality has increased significantly since 1961 among men, there has been a marked decline among women (fig. 1). The death rate has fallen as well among children 1-5 years ($\chi^2 = 58.5, P < .001$) and 6-14 years ($\chi^2 = 7.20, P < .01$). Note that for men there is no evidence of trend in the 11 years prior to 1972 ($r = -.05, ns$), the year low cost credit became widely available to farmers, nor in the years 1976-84, a period of rough constancy in insecticide use ($r = -.37, ns$). Comparing the periods before and after 1972, the mean non-traumatic death rate increased 27.4%, from 2.15 to 2.74 per 1000 ($t = 4.09, P < .001$).

Urban/Rural Comparisons
Significant and opposite changes in male mortality have occurred in the urban and rural sections of Cabanatuan (table 1): the index increased 29.3% in the villages ($t = 2.28, P < .05$) while declining 37.2% in the urban neighbourhoods ($t = -3.14, P < .05$). If, as suggested earlier, the city became more urban over the period, both trends would be accentuated. Among women in rural Cabanatuan, the index of mortality did not increase significantly ($t = 1.12, ns$), while as for men there was a marked decline in the urban areas, amounting to 52% ($t = -5.45, P < .001$).

Causes of Death
Mortality due to diagnosed poisoning increased 247% ($U = 29, P < .01$) and that due to potentially related conditions 41% ($t = 4.53, P < .001$) between the periods of low and high use of
insecticide (table 2). As predicted, there is a significant correlation between the two time series ($r = .47, .01 < P < .02$). The detailed pattern of increase in these cases has been similar to the trend of overall male mortality; death rates were low prior to 1972 (fatal diagnosed poisonings were recorded in only three of 11 years between 1961 and 1971), rising rapidly thereafter and remaining roughly constant after the late 1970's. In contrast, the death rate from all other causes, save cancer, has declined 33.7% ($t = -2.78, P < .02$) over the period.

Though this paper focuses on the impact of acute intoxication, chronic effects are also expected. Several insecticides in widespread use in Central Luzon are suspected carcinogens, including DDT and endrin (17,18). Though overall cancer rates (excluding brain tumor) have not increased significantly (table 2), marked changes have occurred in the death rates for specific cancers, notably leukemia. Growing evidence suggests a link between exposure to insecticides, both organochlorine and organophosphate, and subsequent development of this disease (19-21). In the three rural municipalities, mortality among men attributed to leukemia increased 580%, from 0.6 to $3.6 \times 10^{-5}$ between the 1961-71 and 1972-84 periods ($\chi^2 = 4.5, P < .05$). The rise has been most marked in recent years: 7 of the 11 cases recorded since 1961 occurred in the 6 years 1972-84.

The proportion of deaths attributed to acute pesticide poisoning and the conditions potentially confounded with it has increased significantly in both the rural municipalities ($\chi^2 = 20.7, P < .005$) and the rural sections of Cabanatuan ($\chi^2 = 15.7, P < .005$). No significant change is apparent in the urban neighbourhoods ($\chi^2 = 1.78, ns$).

Among the conditions that it was suggested were likely to be confounded with CYC-HCH intoxication, by far the most frequently recorded in the study area is stroke. While the specific death rate for all men rose significantly between the 1961-71 and 1972-81 periods ($\chi^2 = 49, P < .005$), the increase was greater among younger men normally at low risk of stroke (table 4A). Among those 15-24 years, no deaths attributed to stroke had been recorded before 1972, whereas 20 were noted from 1972 to 1982.

During the wet season of 1982, the Philippines Fertilizer and Pesticide Authority banned the use of endrin, previously the most widely used and acutely toxic CYC-HCH insecticide available to small farmers. In the two years prior and subsequent to the ban, the mortality attributed to stroke declined for all men ($\chi^2 = 4.8, P < .05$), but again to a significantly greater extent in the younger age class ($\chi^2 = 3.8, P < .05$; table 4B).

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**The Monthly Distribution of Mortality**

In the vicinity of Cabanatuan, the wet season crop is generally transplanted in late July and August and, since the completion of a large irrigation scheme in 1976, a dry season crop is planted in late January and February. As insecticide use is greatest immediately following transplanting, one would expect the increase in acute occupational poisoning to be concentrated in these months.

Figure 2 illustrates the monthly ratio of observed-to-expected mortality during two periods, where the expectation is taken from the monthly distribution of deaths from 1961 to 1971, when insecticide use was low. During the 1972-75 period (Fig. 2A), before irrigation made 2 crops a year possible, the ratio was greatest in August, the month of maximum insecticide use in the wet season. When double cropping became widespread (fig. 2B), the two largest peaks are observed in February, when insecticides are most intensively used during the dry season crop, and again in August. A straightforward method of testing the significance of this pattern is to calculate the prior probability of the two highest peaks coinciding with the months of greatest insecticide use in the wet and dry seasons: \( P = \frac{1}{12} \times \frac{1}{11} = .008 \).

Despite local differences in cropping schedules, August is a major period of transplanting and insecticide application during the wet season in the 3 entirely rural municipalities. Taking all rural areas together, the proportion of deaths among men occurring during August rose from 7.3% in 1961-71 to 10.1% in 1972-82 \( (\chi^2= 4.7, P < .05) \).

**DISCUSSION**

The data presented provide strong evidence linking a marked increase in mortality in Central Luzon and occupational exposure to insecticides: only men in rural areas have been affected, both within and between years male death rates have reflected the pattern of insecticide use, and increased mortality has been concentrated in those conditions potentially confounded with pesticide poisoning, a trend most strikingly seen in the close relation between endrin use and deaths attributed to stroke. The evidence is retrospective in nature; however, the close fit between observation and expectation lends credence to the postulated causal relation.

It is important however to consider other factors that may have contributed to the observed changes in mortality:

1) Impoverishment due to falling rural incomes in the region (14) might in part account for the changing monthly distribution of mortality, if its impact is greatest during periods of notable
stress. These may occur for men early in the agricultural season during land preparation. However, widespread reduction in the food supply of near-subsistence communities is generally thought to affect young children in greatest measure (22), whereas in the study area only death rates among men were found to have risen.

2) Increased tobacco consumption among men might contribute to some of the observed trends, notably an increase in respiratory and cardiovascular diseases. Conflicting results emerge from studies concerning the link between smoking and stroke (23-25), however none report a disproportionately increased risk for those under 35, or even 25 years, as found here. Moreover, though smoking appears to be at least as prevalent among urban as rural men, mortality has fallen markedly in the urban neighbourhoods.

3) Greater efficiency in the reporting of vital events would result in an apparent but spurious rise in death rates. However, specific biases in reporting are required to account for the selectiveness of the observed increases: death rates for men have risen faster than for women, those in August faster than in the rest of the year, etc.

The overall increase in non-traumatic mortality among rural men between the periods of low and high use of insecticides was estimated at 27%. The actual occurrence of fatal poisoning may well be greater than this figure suggests if one assumes that in the absence of exposure mortality would have declined, as it did among women and children in the rural areas and among men in urban Cabanatuan. Extrapolating, even on the basis of the 27% value, to other rice growing areas in the Philippines and elsewhere in Asia where pesticides have been widely adopted suggests an annual excess mortality of several tens of thousands. The figure of 10,000 deaths worldwide from accidental and occupational poisoning that is often cited (26-28) must on this evidence be considered a serious underestimate. That it is economically-active men, often the heads of households, who are most at risk of intoxication implies that the overall social impact is greater than such numbers alone indicate.

Further epidemiological research may be required to catalyse the political will to effectively confront the issue of poisoning in smallhold agriculture. Rigorous prospective or case-control studies may be impossible to carry out ethically and under rural conditions with the resources generally available to researchers. Similar techniques as here might be used in other areas where the registering of deaths has been reasonably complete and the pattern of pesticide use adequately documented. Participatory research techniques might also be considered as a means of awakening concern among a population at risk of intoxication.
A number of alternatives to exclusive reliance on synthetic insecticides in rice cultivation now exist, including varietal resistance, cultural and biological controls. These will require vigorous adaptive research to make them accessible to the majority of farmers. It is important that, as far as possible, medical and agronomic research and extension be integrated, that the diagnosis of the medical problem be followed by testing of pest control techniques that reduce exposure without sacrificing farm revenues.

ACKNOWLEDGEMENTS

I am indebted to E. Almayda for assistance in the mortality survey and to G.R. Conway, J.W. Frank, D.M. Gall, D. Gilbert, P.J. Lawther, P.E. Kenmore, J.A. Litsinger, G.A. Lloyd, B.P. Loevinsohn, and B.R. Trenbath for valuable comments. Financial support was provided by a fellowship from the Natural Sciences and Engineering Research Council of Canada.
REFERENCES


Table 1

Trends in indices of mortality among men 15 - 54 years in rural and urban areas of Cabanatuan, Philippines.

<table>
<thead>
<tr>
<th></th>
<th>1961-71</th>
<th>1972-81</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rural</td>
<td>1.84 ± 0.120 *</td>
<td>2.38 ± 0.138</td>
</tr>
<tr>
<td>Urban</td>
<td>1.64 ± 0.210</td>
<td>1.03 ± 0.058</td>
</tr>
</tbody>
</table>

* Mean index per thousand ± standard error.
Table 2

Trends in specific death rates among men 15-54 years in 3 rural municipalities in Nueva Ecija, Philippines.

<table>
<thead>
<tr>
<th></th>
<th>1961-71</th>
<th>1972-81</th>
</tr>
</thead>
<tbody>
<tr>
<td>diagnosed pesticide</td>
<td>2.39 ± 1.34</td>
<td>6.29 ± 2.30</td>
</tr>
<tr>
<td>poisoning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>all potentially con-</td>
<td>130 ± 9.20</td>
<td>183 ± 7.10</td>
</tr>
<tr>
<td>founded conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cancer (all sites except brain)</td>
<td>21.1 ± 3.49</td>
<td>25.9 ± 4.02</td>
</tr>
<tr>
<td>all other causes</td>
<td>62.0 ± 6.04</td>
<td>41.1 ± 4.62</td>
</tr>
</tbody>
</table>

* Mean rate per 100,000 ± standard error.
Table 3

Proportion of deaths attributed to diagnosed pesticide poisoning and the conditions potentially confounded with it among men 15-54 years in 3 rural municipalities and in rural and urban sections of Cabanatuan, Philippines.

<table>
<thead>
<tr>
<th>Location</th>
<th>1961-71</th>
<th>1972-84</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rural municipalities</td>
<td>46%</td>
<td>60%</td>
</tr>
<tr>
<td>(378)</td>
<td>(755)</td>
<td></td>
</tr>
<tr>
<td>Cabanatuan:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>rural</td>
<td>49%</td>
<td>51%</td>
</tr>
<tr>
<td>(412)</td>
<td>(908)</td>
<td></td>
</tr>
<tr>
<td>urban</td>
<td>53%</td>
<td>58%</td>
</tr>
<tr>
<td>(368)</td>
<td>(384)</td>
<td></td>
</tr>
</tbody>
</table>

* Values in parentheses are total deaths in the period.
Mortality attributed to stroke among men 15 - 54 years in Cabanatuan and three rural Philippine municipalities combined in: (A) periods of low and high endrin use; (B) the two years immediately prior and subsequent to the ban on endrin's use.

<table>
<thead>
<tr>
<th>Age class (years)</th>
<th>Death rate $\times 10^3$</th>
<th>Percent change</th>
<th>Death rate $\times 10^3$</th>
<th>Percent change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 - 34</td>
<td>4.39</td>
<td>18.0</td>
<td>+29%</td>
<td>26.0</td>
</tr>
<tr>
<td></td>
<td>(12) **</td>
<td>(70)</td>
<td></td>
<td>(27)</td>
</tr>
<tr>
<td>35 - 54</td>
<td>33.2</td>
<td>80.9</td>
<td>+144%</td>
<td>91.2</td>
</tr>
<tr>
<td></td>
<td>(41)</td>
<td>(135)</td>
<td></td>
<td>(38)</td>
</tr>
</tbody>
</table>

* Per 100,000. ** Values in parentheses are numbers of deaths.
FIGURE LEGENDS

Figure 1
Trends in non-traumatic mortality among men (A) and women (B) 15-54 years in three rural municipalities in Nueva Ecija, Philippines. The regression equations are: A) $Y = -41.8 + .0226X$ ($n=24, r=.61, P<.01$) and B) $Y = 46.9 - .0225X$ ($r=.58, P<.01$), where $Y$ is arc sin-transformed death rate.

Figure 2
Ratio of the observed to the expected number of deaths among men 15-54 years in the rural areas of Cabanatuan, Philippines.
A: a period of intensive insecticide use and predominantly single cropping. B: a period of intensive insecticide use and predominantly double cropping.
ANNUAL AGE-ADJUSTED DEATH RATE (10^3)
OBSERVED / EXPECTED MONTHLY MORTALITY

A 1972-75

B 1976-82

J F M A M J J A S O N D