

Influence of pesticide regulation on acute poisoning deaths in Sri Lanka

Darren M. Roberts,¹ Ayanthi Karunarathna,² Nick A. Buckley,³ Gamini Manuweera,⁴ M.H. Rezvi Sheriff,⁵ & Michael Eddleston⁶

Objectives To assess in a developing Asian country the impact of pesticide regulation on the number of deaths from poisoning. These regulations, which were implemented in Sri Lanka from the 1970s, aimed to reduce the number of deaths — the majority from self-poisoning — by limiting the availability and use of highly toxic pesticides.

Methods Information on legislative changes was obtained from the Ministry of Agriculture, national and district hospital admission data were obtained from the Sri Lanka Health Statistics Unit, and individual details of deaths by pesticide poisoning were obtained from a manual review of patients' notes and intensive care unit records in Anuradhapura.

Findings Between 1986 and 2000, the total national number of admissions due to poisoning doubled, and admissions due to pesticide poisoning increased by more than 50%. At the same time, the case fatality proportion (CFP) fell for total poisonings and for poisonings due to pesticides. In 1991–92, 72% of pesticide-induced deaths in Anuradhapura were caused by organophosphorus (OP) and carbamate pesticides — in particular, the WHO class I OPs monocrotophos and methamidophos. From 1991, the import of these pesticides was reduced gradually until they were banned for routine use in January 1995, with a corresponding fall in deaths. Unfortunately, their place in agricultural practice was taken by the WHO class II organochlorine endosulfan, which led to a rise in deaths from status epilepticus — from one in 1994 to 50 in 1998. Endosulfan was banned in 1998, and over the following three years the number of endosulfan deaths fell to three. However, at the end of the decade, the number of deaths from pesticides was at a similar level to that of 1991, with WHO class II OPs causing the most deaths. Although these drugs are less toxic than class I OPs, the management of class II OPs remains difficult because they are, nevertheless, still highly toxic, and their toxicity is exacerbated by the paucity of available facilities.

Conclusion The fall in CFP amidst a rising incidence of self-poisoning suggests that Sri Lanka's programmes of pesticide regulation were beneficial. However, a closer inspection of pesticide-induced deaths in one hospital revealed switching to other highly toxic pesticides, as one was banned and replaced in agricultural practice by another. Future regulation must predict this switching and bear in mind the ease of treatment of replacement pesticides. Furthermore, such regulations must be implemented alongside other strategies, such as integrated pest management, to reduce the overall pesticide availability for self-harm.

Keywords Insecticides, Carbamate/poisoning/supply and distribution; Insecticides, Organophosphate/poisoning/supply and distribution; Endosulfan/poisoning/supply and distribution; Poisoning/mortality; Legislation; Safety management; Agriculture; Sri Lanka (*source: MeSH, NLM*).

Mots clés Insecticides carbamate/intoxication/ressources et distribution; Insecticides organophosphorés/intoxication/ressources et distribution; Endosulfan/intoxication/ressources et distribution; Intoxication/mortalité; Législation; Gestion sécurité; Agriculture; Sri Lanka (*source: MeSH, INSERM*).

Palabras clave Insecticidas de carbamato/envenenamiento/provisión y distribución; Insecticidas organofosforados/envenenamiento/provisión y distribución; Endosulfano/envenenamiento/provisión y distribución; Envenenamiento/mortalidad; Legislación; Administración de la seguridad; Agricultura; Sri Lanka (*fuentes: DeCS, BIREME*).

Bulletin of the World Health Organization 2003;81:789-798

Voir page 796 le résumé en français. En la página 796 figura un resumen en español.

¹ Research Fellow, Ox-Col Collaboration, University of Colombo, Colombo, Sri Lanka; and Medical Officer, Division of Medicine, Royal Brisbane Hospital, Queensland, Australia.

² Pre-Intern, Ox-Col Collaboration, University of Colombo, Colombo, Sri Lanka.

³ Director and Associate Professor, Department of Clinical Pharmacology and Toxicology, Canberra Clinical School, ACT, Australia; and Ox-Col Collaboration, Department of Clinical Medicine, University of Colombo, Colombo, Sri Lanka.

⁴ Pesticide Registrar, Government Department of Agriculture, Peradeniya, Sri Lanka.

⁵ Professor and Head of Department, Ox-Col Collaboration, Department of Clinical Medicine, Faculty of Medicine, University of Colombo, Colombo, Sri Lanka.

⁶ Wellcome Trust Career Development Fellow, Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, England; and Ox-Col Collaboration, Department of Clinical Medicine, Faculty of Medicine, PO Box 271, 25 Kynsey Rd, Colombo-08, Sri Lanka (email: eddlestonm@eureka.lk). Correspondence should be sent to this author at the latter address.

Ref. No. 02-0319

Introduction

Deliberate self-poisoning is a major problem worldwide (1). However, there are marked differences in case fatality proportions (CFP) when comparing developed and developing countries (1–6). These differences have been attributed to the nature of the agents involved, given that self-harm is the primary intention and the choice of method is often secondary (7–9). Pesticides, such as organophosphorus compounds (OPs), are a common means of self-harm in the developing world (1), whereas pharmaceuticals feature widely in this respect in the developed world (10).

Pesticides have been used extensively in agriculture since the 1950s, promoted as a tool without which developing countries could not develop and become self-sufficient. However, intentional and occupational poisoning from pesticides is a major problem in these countries, with millions of cases and hundreds of thousands of deaths occurring each year (11–16). Management is difficult — there are few effective antidotes and many patients require intensive care, which is a rare resource in much of the developing world (1).

This situation has caused health authorities and legislators to consider regulating the use and availability of pesticides in an attempt to control their harmful effects. The main impetus to these activities was the publication in 1985 of a *Code of Conduct on the Distribution and Use of Pesticides* by the Food and Agriculture Organization (FAO) of the United Nations (17).

Several strategies have been implemented. The pesticide industry itself has established “safe-use” initiatives in which people are educated in the safer use of pesticides (18, 19). Governments and nongovernmental organizations (NGOs) have taken other approaches, such as introducing stricter regulations and encouraging the use of fewer pesticide applications within FAO’s integrated pest management (IPM) system (20). WHO and FAO have also encouraged countries to introduce legislation to restrict the availability of problem pesticides (17, 21, 22). Although this latter approach appears to have been successful in reducing pesticide-related death rates in some countries, such strategies have not always been found to reduce overall mortality (Table 1). Further studies are needed to assess the effectiveness of this approach.

Poisoning from pesticides is the most common cause of death in many rural districts of Sri Lanka (23), where almost all of the deaths are due to intentional self-poisoning (6). Following publication of FAO’s *Code of Conduct*, Sri Lanka has been actively assessing the role of pesticides and regulating their use (Box 1). This has taken place alongside efforts to implement IPM practice

Box 1. Pesticide harm reduction in Sri Lanka

Legislative restrictions and withdrawals on products for agricultural use

- Before 1980: chlordimeform, dichlorodiphenyltrichloroethane (DDT), dieldrin, endrin, methyl parathion, thallium sulfate
- 1980s: 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), aldrin, arsenic, captafol, ethyl parathion, hexachlorocyclohexane (HCH), leptophos, lindane, mercury compounds
- 1990s: dichloropropane, aldicarb, chlordane, methamidophos, monocrotophos, pentachlorophenol, quintozone (PCNB)
- 1998: endosulfan

Alternatives to pesticides

- Integrated pest management

Education

- Campaigns to train farmers, retailers, distributors, and the public (including schoolchildren) in the safe handling, use, and storage of pesticides

in paddy cultivation. As a result, WHO class I “extremely and highly hazardous” pesticides have been phased out, particular problem pesticides such as endosulfan (a WHO class II “moderately hazardous” pesticide) have been banned, and less pesticide has been used for paddy cultivation in some areas.

The purpose of this paper is to record the regulation of pesticides in Sri Lanka and to evaluate the impact of these regulations on the CFP from poisoning; and to record changes in the number of pesticide deaths in Anuradhapura General Hospital attributed to particular pesticides following this regulatory legislation.

Methods

Information on pesticide regulation was obtained from the records of the Pesticide Registrar, Ministry of Agriculture. The following information on poisoning was gathered retrospectively, as outlined below.

- National and district (Anuradhapura and Kurunegala) data on poisonings over a period of 15 years (1986–2000), provided by the Sri Lanka Health Statistics Unit (HSU) in Colombo, based on quarterly records from government hospitals in each district.
- Hospital data from the Statistics Office of Anuradhapura General Hospital over the previous five years (1997–2001). Anuradhapura hospital is a secondary referral centre for more

Table 1. Influence of availability of poisons and effects on mortality

Pesticide	Location	Action	Outcome	Reference
Endrin	Bengal, India	Restrictions on use	Decrease in the number of self-harm pesticide deaths but no change in the total number of self-harm deaths	9
Parathion	Jordan	Banned	Reduction in the number of self-harm deaths due to pesticides	44
Parathion	Rosario, Argentina	Banned	Reduction in all poisoning deaths	45, 46
Paraquat	Samoa	Reduced availability and raised awareness	Reduction in all poisoning deaths	47

than 750 000 people living in the North Central Province of Sri Lanka; most of this population are rural farmers (5, 24). Records were confirmed through a manual count of the number of patients discharged quarterly to detect any errors in transcription or calculation. These data included discharges (dead or alive) for all poisonings as classified under International Classification of Diseases (ICD) criteria.

- Intensive care unit (ICU) records from 1997 to 2001.
- Manual review of the notes of all patients referred to the hospital's Judicial Medical Officer (JMO), who routinely reviews all deaths caused by poisoning. All JMO records were available from 1991. The identity of the pesticide ingested was determined by the history provided on admission or signs recorded in the patients' notes. Blood samples were not available for confirmation of the pesticide involved. In most cases, however, the clinical syndrome clearly identified the class or type of pesticide responsible. The number of patient records found by manual review of the records was compared with the number of pesticide deaths recorded in the hospital record logs. Missing records were recorded as such.

To control for factors that may influence the decision to present to hospital (such as social unrest and war), data on spontaneous vaginal deliveries were also collected.

Results

Pesticide restrictions have been in force in Sri Lanka since the 1970s (Box 1). During the early 1990s the use of all WHO class I OP pesticides was gradually curbed by a restriction on import by 25% each year between 1991 and 1994, before being banned for routine use in January 1995. More recently, the import of endosulfan, an organochlorine locally associated with high rates of status epilepticus and deaths after self-poisoning, was banned. Nationwide stocks were predicted by the Ministry of Agriculture to last a maximum of two years.

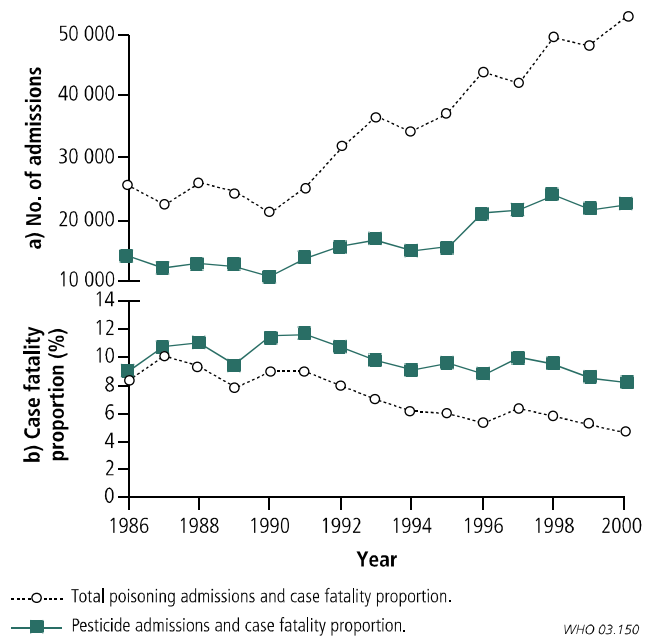
National and district level poisoning data

Our review of national and district data revealed that between 1986 and 2000 the number of "pesticide poisonings" and "total poisonings" increased both nationally (Fig. 1) and in the rural districts of Anuradhapura and Kurunegala (data not shown). In all cases the increase was greater for "total poisonings" (>100% increase) than for pesticide poisoning (~50% increase); most of the increase occurred between 1988 and 1998, but subsequently the incidence for pesticide poisoning stabilized. The increase in "total poisonings" coincided with an epidemic of yellow oleander (*Thevetia peruviana*) poisonings that occurred during this period in the North-Western and North-Central Provinces of Sri Lanka (24).

The CFP for "total poisonings" nationally fell from 9% to 5% during this same period — in particular, after 1991 (Fig. 1). The increase in the number of cases of poisoning by yellow oleander, which has a lower CFP than that of pesticides, may again explain this (24). The CFP for pesticide poisoning also increased nationally until 1991. Thereafter, there was a corresponding fall in CFP from 11% to 8% as WHO class I pesticides were gradually phased out.

The number of spontaneous vaginal deliveries was stable both nationally and in the districts throughout the period of investigation (data not shown), suggesting that the ongoing civil war did not affect the numbers of patients presenting to hospital.

Fig. 1. a) National number of admissions and b) case fatality proportion for total poisoning and pesticide poisoning, Sri Lanka, 1986–2000



Anuradhapura General Hospital

The number of admissions to Anuradhapura hospital for both total and pesticide poisonings increased from 1997 to 2001 (data not shown); the number of spontaneous vaginal deliveries was again stable. The increase in "total poisoning" admissions was the same as that of pesticides, indicating that the increase was almost totally due to an increase in pesticide admissions. In contrast to national and district data, the CFP for "pesticide poisoning" declined faster than the CFP for "total poisonings". Pesticide deaths as a percentage of total deaths by poisoning decreased from 83% in 1998 to 77% in 2001, which is consistent with the above decline in pesticide fatality rate.

Data for all patients who died from pesticide poisoning between 1991 and 2001 were retrieved by manual examination of patient records stored after the JMO review. A total of 1399 relevant patients' records were found (Fig. 2), ranging from 180 in 1998 to 80 in 1996. Comparison of the number of records found with the number of deaths recorded by the hospital Medical Statistics Office in their quarterly records indicated that 182 records were missing — 11.5% of all patient records. The number missing varied from 38 and 45 in 1996 and 1997, respectively, to none in 1991 and 1998.

At the beginning of the 1990s, OP and carbamate pesticides were the main cause of fatal pesticide poisonings, causing 72% of all such deaths during 1991 and 1992. The cases were fairly evenly distributed between patients ingesting class I OPs (methamidophos and monocrotophos), class II OPs (in particular dimethoate and fenthion), and unidentified pesticides that caused a cholinergic syndrome. Many of the latter patients were unconscious on admission and died without regaining consciousness. Their relatives did not know which pesticide had been ingested, but the poisons were probably the more toxic class I OPs.

The Pesticide Registrar made a decision in 1991 to restrict the import of class I OPs over four years and then severely restrict their use in routine agriculture, in an attempt to reduce the

number of deaths. During this period, the total annual number of pesticide deaths in Anuradhapura hospital fell from 150–170 in 1991–92 to 100–120 in 1995–96; in particular, the number of OP/carbamate deaths fell from 231 in 1991–92 to 88 in 1995–96. Notably, there was a fall in the number of deaths due to class II OP, as well as in those due to class I and unknown OPs.

As the availability of methamidophos and monocrotophos was restricted, the WHO class II organochlorine endosulfan (25) became the most popular insecticide in agricultural practice in Sri Lanka at that time. A combination of broad insecticidal activity, low cost, and trade incentives and promotion encouraged many farmers to switch to endosulfan (G. Manuweera, unpublished). This was reflected in the number of fatalities from endosulfan self-poisoning, from one to six deaths each year between 1991 and 1994 to 19 deaths in 1996 and 50 deaths in 1998.

Endosulfan was banned in 1998. The records from Anuradhapura hospital showed that the number of deaths due to endosulfan poisoning fell quickly from 50 in 1998, to 37, 5, and 3 in 1999, 2000, and 2001, respectively, as stocks ran out and farmers switched to other insecticides. This decrease was associated with a fall in the total number of deaths due to pesticides.

A review of ICU records for the years 1998–2001 showed a similar reduction in admissions and deaths from endosulfan. There were 10 admissions in 1998, 17 in 1999, two in 2000, and none in 2001. Although more patients were admitted to the ICU with OP poisoning (65, 72, 40, and 55 admissions, respectively, for the years 1998–2001) than endosulfan poisoning, the CFP for endosulfan patients who survived until being admitted to the unit was higher: 42% of endosulfan patients died in the ICU during 1998–99, in contrast to 29% of OP-poisoned patients during 1998–2001.

The true endosulfan mortality rate is likely to be higher than that in the ICU, given that 78% of endosulfan deaths occurred within 24 hours of presentation, with most of these occurring within six hours and before admission to the ICU. Most deaths were secondary to cardiorespiratory arrest amidst ongoing seizures; few deaths resulted from delayed complications such as pneumonia. Some patients were also discharged to the open ward for palliative care, and died there rather than in the ICU.

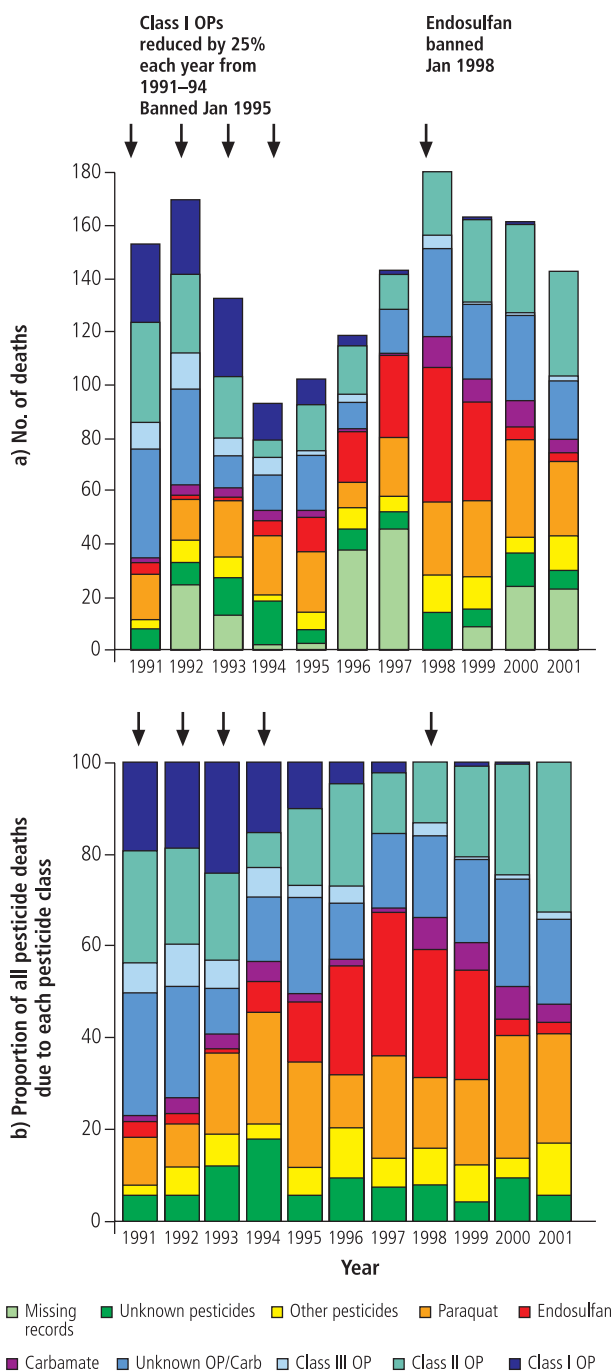
By 2001, WHO class II OP pesticides and paraquat were the most common substances used for fatal pesticide self-poisoning. The number of paraquat cases was fairly stable throughout the decade, averaging at least 24 deaths a year, with a peak of 37 in 2000, although there was a trend for paraquat to become a more important cause of death as the decade progressed, being responsible for 8.4% of deaths in 1991–92 and 20.8% of deaths in 2000–01.

There were 89 deaths due to poisoning from less-common pesticides: mostly the herbicides MCPA (4-chloro-2-methylphenoxyacetic acid) and propanil, and also some of the newer pesticides such as chlorflazuron and ethofenprox. The number of deaths due to propanil was exacerbated by the lack of availability of intravenous preparations of its antidote, methylene blue (26).

Discussion

The in-hospital mortality rate following poisoning is high in developing countries, approaching 15% in Sri Lanka compared with less than 1% in the United Kingdom (6, 8). Several factors affect the outcome of acute poisoning, including the nature of the poison, the dose consumed, the

Fig. 2. The number a) and proportion b) of deaths due to pesticide poisoning, for each type of pesticide in Anuradhapura General Hospital, 1991–2001^a



^aAs the class I organophosphorus pesticides (OPs) were phased out in the early 1990s, the number of deaths due to all OPs fell markedly. From 1994 until its ban in 1998, the number of deaths due to endosulfan increased steadily until a peak of 50 in 1998. The importance of endosulfan has been replaced by class II OPs (and to a lesser extent paraquat) after its ban. These changes are seen most clearly with the changes in the proportion of the number of deaths due to each class of pesticide: the fall in class I OPs, the rise and fall in endosulfan, the rising importance of class II OPs, and the steady importance of paraquat.

WHO 03.151

quality of medical facilities available, and the time between exposure and medical care (6, 27).

Most poisonings are acts of self-harm, but many of these patients are young and few wish to die (6–8, 28, 29). Many cases

of self-poisoning in Sri Lanka are without a history of previous attempts or extensive pre-meditation; rather, they represent an impulsive response to difficult, or even relatively trivial, situations (30, 31). Because a high proportion of the Sri Lankan population is involved in agriculture, there is ready access to highly toxic pesticides at these moments of stress (8). A very similar situation exists in China (32, 33).

During the past 20 years Sri Lanka has set up programmes to reduce the availability and use of pesticides in general, and some highly toxic pesticides in particular (Box 1). The purpose of our work was to assess the effect of these programmes on the number of total poisonings, and specifically pesticide poisonings, in Sri Lanka, and their respective CFP.

National and district epidemiology

Both national and rural district data show that while presentations for total poisonings increased from the late 1980s, survival actually improved. This is probably due, in part, to the increasing number of oleander poisonings and their lower CFP (24). There was also an increase in the number of presentations for pesticide poisoning and a decrease in CFP, although this decrease was less marked than for total poisonings.

It is clear that improvements have been made in reducing the number of deaths due to poisoning; however, there are problems with interpreting the data on national and district admissions and CFP, as discussed below.

- Double counting: national/district data are pooled from peripheral and secondary hospitals and are based on events rather than on individual patients. Most patients are referred for specialized care to a secondary hospital, producing a second registration; some are again transferred for tertiary care, which produces a third registration. Also, patients may be discharged alive but then readmitted with delayed but fatal complications, such as paraquat-induced pulmonary fibrosis. Overall, it is likely that each poisoning death is associated with at least one live discharge for the same event. This artificially raises the number of presentations and reduces the death rate, underestimating the true CFP from pesticides and minimizing the magnitude of change.
- Miscoding of medical records is an established problem when they are used for epidemiology studies (34). Problems with the coding of pesticide poisoning cases were observed for all years, suggesting that allocation of a death to either "OP/carbamate pesticides" or "other pesticides" is probably inaccurate (23).
- Changes in referral thresholds from smaller hospitals owing to changes in practice or experience of the referring doctor. Increased referral rates may reduce the CFP at referring and receiving hospitals, while increasing the number of admissions to the receiving hospital.
- Changes in resources, such as availability of ventilators or ambulances for transfers and adequate staffing levels, may influence rates of transfer and CFP.

With these caveats in mind, no reduction in the number of cases of pesticide poisoning has occurred during the implementation of the pesticide-limiting programmes. However, there has been a reduction in pesticide CFP nationally. The role of improved care is unclear — for example, no significant changes in medical management occurred during the past five years in Anuradhapura hospital to account for a 40% reduction in CFP. It seems more likely that programmes aimed at reducing the availability of toxic pesticides have had a significant effect.

Pesticides responsible for deaths in Anuradhapura General Hospital

During the 1990s, there were marked changes in the pesticides responsible for the majority of deaths in Anuradhapura hospital due to pesticide poisoning. At the beginning of the decade, OP insecticides predominated, with both the class I OPs methamidophos and monocrotophos and the class II OPs dimethoate and fenthion causing many deaths. Restrictions on the use of class I OPs during the first half of the decade coincided with a fall in deaths due to all pesticides and due to all OPs, including class II OPs.

This coincident fall in class II OP-induced deaths raises questions about the causal link between the legislative restriction and the reduction in the number of deaths. However, it is possible that people simply switched from OP insecticides en masse to the insecticide that then became popular, the WHO class II organochlorine endosulfan.

Deaths from endosulfan were rare during the early 1990s. Unfortunately, the switch from OPs to endosulfan was followed by a rapid increase in the number of deaths. Endosulfan causes status epilepticus that is very difficult to terminate with standard benzodiazepines and barbiturate-based therapy (25, 35). Many patients died from cardiorespiratory arrest within a few hours of arriving on the ward. Although the switch was from class I (and possibly class II) OPs to a class II organochlorine, management of the latter was much more difficult: a switch had been made from a very toxic but still treatable insecticide to a less toxic but untreatable pesticide.

As the scale of the problem of endosulfan poisoning became apparent, the pesticide was banned in 1998; this resulted, fortunately, in a rapid reduction in the number of endosulfan deaths. There was an apparently coincident fall in the total number of deaths from pesticides. A few confirmed endosulfan deaths still occurred in 2002 (M. Eddleston and D. Roberts, unpublished observations) but the majority of stocks seemed to have run out by the end of 1999, as predicted by the Ministry of Agriculture.

The rapid fall in the number of deaths from both class I OPs and endosulfan after their restriction suggests that, in Sri Lanka at least, regulation is able to prevent sale and agricultural use of particular pesticides.

Current situation

Currently the majority of deaths are due to class II OPs, in particular the dimethyl OPs fenthion and dimethoate, and paraquat. Management of the class II OP poisonings is still very difficult; there appears to be little response to oxime therapy (36, 37) and patients often require intubation and long-term ventilation, the provision of which is rare in the developing world.

There is currently no effective therapy for paraquat poisoning (38), and good supportive care probably makes no difference to the patient's outcome (unlike for OP poisoning). The quantity of paraquat ingested seems to be the sole determinant of outcome (38). The importance of paraquat in Anuradhapura has increased gradually over the past decade. With a CFP of around 50% (M. Eddleston, unpublished data) and no effective antidote, serious consideration must be given towards allowing use of only a less-concentrated preparation, which should increase the volume of pesticide that must be ingested to cause death.

Deaths from other pesticides were uncommon. Several deaths resulted from ingestion of newer and less toxic pesticides such as chlorfluazuron and ethofenprox. It is likely that some deaths were due to the complications of the aggressive gastric emptying techniques that are often employed following diagnosis of pesticide poisoning. In future, greater care must be taken when deciding whether to use such techniques. Some pesticides have such a low toxicity that conservative therapy with supportive care is probably the only justified approach.

Pesticide harm minimization through a hazard reduction approach

The results from our study of pesticide deaths in Anuradhapura suggest that regulatory approaches alone will not be completely effective in reducing the number of such deaths. It is likely that regulations will have to be implemented in partnership with other strategies.

A generic approach has been proposed for minimizing the hazards of working with pesticides, based on a hazard reduction model used in industrial sectors (19). This approach uses a combination of government and industry interventions in a hierarchy (Box 2) that is based on impact, practicalities, and time required for effective and lasting change. These interventions should be implemented at the same time, given that regulatory actions must be tied to programmes aimed at changing farmers' attitudes and cultural practices, while ensuring that recommended alternative products or practices are available, affordable, and practical at the local level (19, 20).

A similar approach could be taken to the problem of intentional self-poisoning with pesticides (Box 2). The first level would be regulatory and legislative actions to restrict the availability of the most toxic and/or untreatable pesticides, plus adoption of IPM in agriculture to reduce the use of pesticides in general. The second level would be to set up community systems to remove pesticides from households and hence keep them away from people at moments of stress. One option might be to install community pesticide stores with lockers for each individual. The third level is to improve the medical management

of pesticide self-poisoning to reduce the number of deaths — secondary prevention.

The most important elements will probably be regulatory and legislative actions and implementation of IPM to reduce the availability of highly toxic pesticides and all pesticides, respectively.

Regulation and legislation

Regulatory control aims to substitute “problem” pesticides with safer, less toxic pesticides. It may involve total bans or restrictions on the quantity of pesticides imported and/or distributed, based on agricultural need and availability of alternatives (17).

WHO's classification of pesticide toxicity (Table 2) has been used by regulators to help determine which pesticides should be restricted. This classification system is based on the LD₅₀, the dose of poison that kills 50% of the animal cohort studied. Pesticides are classified according to the species and route that has the lowest toxic dose. This is necessary given the wide variability in LD₅₀ between animals, and even within a species. It should be noted that this system was not designed to compare various pesticides in the context of self-poisoning, but instead for occupational exposures.

There are currently relatively few data on human pesticide poisoning. It is probable that extrapolating from LD₅₀ animal studies to self-poisoning in humans is complicated, particularly because most ill pesticide-poisoned humans receive antidotes not given to animals in the LD₅₀ studies. The examples of endosulfan and paraquat illustrate clearly that a WHO class II “moderately hazardous” pesticide could be more toxic than a WHO class I “extremely or highly hazardous” pesticide because of difficulties in treating patients with WHO class II pesticide poisoning.

It may be sensible, where evidence is available, to incorporate other factors into decisions about the regulation of pesticides including CFP, the availability and efficacy of antidotes/treatments, and the presence of treatable alternative pesticides. Local epidemiological research is required to supply this information to policy-makers.

Box 2. Hazard reduction model for harm minimization in occupational pesticide poisoning (19) and deliberate pesticide self-poisoning in three stages, based on hazard minimization strategies used in industry

Occupational pesticide poisoning

1. Engineering controls: elimination of hazards — that is, the most problematic pesticides in local use — using regulatory controls and legislation. Application of principles advocated within the Integrated Pest Management (IPM) paradigm, including the minimal use of pesticides, and use of non-chemical and biological control agents.

2. Implementation of administrative controls: maintenance of a trained core of people who can apply pesticides, provision of appropriate exposure monitoring and control measures for pesticide users, and restriction of home storage of pesticides.

3. Personal protective equipment: this has the lowest priority, given the concerns that it may give a false sense of protection, the anticipated poor compliance due to cost, and impracticalities in a hot climate.

Deliberate pesticide self-poisoning

Engineering controls: elimination of hazards — that is, the most problematic pesticides in local use — using regulatory controls and legislation. The medical consequences of any replacement pesticide must be considered. The application of principles advocated within the Integrated Pest Management (IPM) paradigm, including the minimal use of pesticides, and use of non-chemical and biological control agents.

Implementation of administrative controls: restriction of home storage of pesticides by, for example, supplying community stores with lockers for pesticide storage.

Improved medical management of pesticide poisoning: an important facet of control because better management will reduce the number of deaths. Requirements are the better availability of antidotes (both in central referral hospitals and ideally in peripheral health units) and ventilation facilities, better training, and better evidence for interventions.

Table 2. WHO classification of pesticide toxicity^a

Class	Property	Oral (LD ₅₀)		Dermal (LD ₅₀)	
		Solid	Liquid	Solid	Liquid
Ia	Extremely hazardous	≤5	<20	<10	<40
Ib	Highly hazardous	5–50	20–200	10–100	400–400
II	Moderately hazardous	50–500	200–2000	100–1000	400–4000
III	Slightly hazardous	>500	>2000	>1000	>4000
Active ingredients unlikely to present acute hazard					

^a Classified using animal LD₅₀s of the technical compound and formulations. The relative toxicity of compounds in human poisoning is complicated by the ease of treatment — for example, class I organophosphorus pesticides can be treated with atropine and oximes with some effect, whereas self-poisoning with class II organochlorines is practically untreatable in many locations (see ref. 48).

There are, however, several difficulties with regulatory controls. For example, (1) many of the older and acutely toxic pesticides result in a quick kill, have a broad spectrum of activity, are cheaper than their alternatives, if available, and have been in use for years. Difficulties result from immediate bans if issues of cost (including government subsidies) and farmer education are not considered. This can result in illegal importation and use, challenging effective implementation (20, 39). (2) Differences in legislation between countries may encourage illegal imports. This can be solved through a regional or international approach. For example, seven Central American countries are addressing this issue through a joint initiative to implement harmonized restrictions on the locally problematic pesticides (40). The effectiveness of the endosulfan ban in Sri Lanka may have been at least partly due to the relative ease in preventing illegal imports to an island. (3) To minimize trade of hazardous chemicals such as pesticides, the Rotterdam Convention was adopted in 1998 to legally enforce the UNEP and FAO Prior Informed Consent procedure that had been in operation since 1989. This procedure requires an importing country to formally consent to the importation of a chemical listed in the Convention. Where consent is not granted, exporting countries must ensure that exporters within its jurisdiction comply with this decision, sharing responsibility for illegal trade. The Convention provides for the distribution of information on these chemicals, including core information to be provided to an importing country, in addition to dissemination of decisions to refuse trade by such countries, with their justification (41).

In terms of overall public health, effective restrictions may be more appropriate than outright bans. Such an argument has been made for the organochlorine DDT (dichlorodiphenyltrichloroethane), which may be banned as part of the Persistent Organic Pollutants Convention (41). Some workers feel that it should not be banned, considering it to be one of the few affordable, effective tools for controlling malaria transmission in developing countries, while arguing that its effects on human health are still uncertain (42).

Integrated Pest Management

The promotion by industry and past short-term benefits of pesticides may induce farmers to use pesticides at frequent intervals without regard to the presence or absence of specific pests (11). It has been argued that such activities cause adverse effects on human health and on the environment (17, 20). IPM includes non-chemical and biological control agents, as well as

the use of pesticides on a needs basis, thereby aiming to foster the independence of the farmer as decision-maker.

Programmes to implement IPM and increase safety in the handling and use of pesticides are under way in Sri Lanka, but await full evaluation to determine their impact (43). However, preliminary studies have shown that farmers who graduate from the FAO programme and practice IPM use less pesticide and have an increased yield (43). A reduction in farmers' pesticide use and therefore stocks should reduce the availability of pesticides for self-harm.

IPM is dependent on the farmer's understanding and proactive role in the operation of the agricultural ecosystems of different crop types (17). It should not be confused with industry safe-use programmes, which differ from IPM because they focus on reducing pesticide hazards in the context of continued use. The benefits of safe use depend on uptake by users, the methods and types of pesticide use, and compliance with recommendations. It relies on appropriate labelling of containers and educating the user, and fails where there is illiteracy, multiple dialects or languages, and inadequate training, resources, and education (12, 13, 18). The pesticide industry has collaborated with the FAO on safe-use initiatives; however, there is still debate as to whether such initiatives have produced any sustainable benefits (19).

Conclusion

These data from Sri Lanka show a steady increase in the number of total and pesticide poisoning admissions coincident with a fall in CFP. During this time, regulatory activities have restricted the availability of pesticides perceived to be important causes of death from pesticide poisoning. Although these regulations may have led to a reduction in CFP, the evidence from close observation of trends in pesticide poisoning deaths from one hospital is more complicated. At the end of the decade, there was little difference in the total number of pesticide deaths, despite the marked reduction in deaths from the banned pesticides.

These results are significant for other countries of the Asia-Pacific region. Future work to reduce the number of pesticide deaths will need to blend regulatory activities into an integrated hazard minimization programme. This should consist of additional strategies such as IPM to reduce the use of pesticides generally, attempts to keep pesticides out of households where they can be used for self-harm, and improved medical management to reduce the death rate once pesticides have been

ingested. Programmes that address psychosocial factors leading to deliberate self-poisoning should also be a priority to complement these activities. Any proposed programme should be tested in a controlled study to check that the predicted beneficial outcomes actually occur. ■

Acknowledgements

We thank Sandya Basanayake, Udaye Rajakaruna, Ariyaworthi, Chandrika, and in particular Mahinda, of the Anuradhapura records office and staff at the Health Statistics Unit in Colombo for their

help in obtaining patient records, Dr Asoka Munasinghe, Medical Superintendent, Anuradhapura Hospital, for permission to review the hospital records, and Dr Henk van der Berg for his advice on IPM in Sri Lanka and review of the manuscript. ME is a Wellcome Trust Career Development Fellow in Tropical Clinical Pharmacology.

Funding: By grant GR063560MA from the Wellcome Trust's Tropical Interest Group to ME is acknowledged.

Conflicts of interest: none declared.

Résumé

Influence de la législation concernant les pesticides sur les décès par intoxication aiguë à Sri Lanka

Objectif Evaluer, dans un pays asiatique en développement, l'impact sur le nombre de décès par intoxication de la législation sur les pesticides. La réglementation, mise en application à Sri Lanka depuis les années 70, vise à réduire le nombre de décès par intoxication – la plupart volontaires – en limitant la disponibilité et l'utilisation des pesticides hautement toxiques.

Méthodes Les sources des données concernant l'évolution législative, les admissions dans les hôpitaux nationaux et de district et les données personnelles sur les décès par intoxication due aux pesticides sont respectivement le Ministère de l'Agriculture, l'unité des statistiques sanitaires de Sri Lanka et les dossiers individuels et l'enregistrement de l'unité de soins intensifs d'Anuradhapura.

Résultats Entre 1986 et 2000, le nombre total d'admissions dans le pays pour intoxication a doublé, et le nombre d'admissions pour intoxication par des pesticides a augmenté de plus de 50 %. En revanche, la létalité a chuté pour l'ensemble des intoxications et pour les intoxications par pesticide. En 1991-1992, 72 % des décès dus aux pesticides à Anuradhapura étaient dus aux organophosphorés et aux carbamates – en particulier au monocrotophos et au méthamidophos, organophosphorés de la classe I de l'OMS. A partir de 1991, l'importation de ces pesticides a diminué progressivement jusqu'à ce qu'ils soient interdits en pratique courante en janvier 1995, avec une chute correspondante des décès. Malheureusement, ils ont été remplacés dans l'agriculture par l'endosulfan, un organochloré de la classe II de

l'OMS, qui a conduit à une augmentation des décès par état de mal épileptique – de 1 en 1994 à 50 en 1998. L'endosulfan a été interdit en 1998 et, en trois ans, le nombre de décès imputables à ce pesticide est retombé à 3. Cependant, à la fin de la décennie, le nombre de décès dus aux pesticides était comparable à celui de 1991, les organophosphorés de classe II de l'OMS étant responsables de la plupart des cas. Si ces produits sont moins toxiques que les organophosphorés de classe I, la prise en charge des intoxications par les organophosphorés de classe II reste difficile, car ils sont encore très toxiques et leur toxicité est aggravée par la rareté des centres antipoisons.

Conclusion Malgré une augmentation de l'incidence des intoxications volontaires, la chute de la létalité laisse penser que les programmes sri lankais de réglementation concernant les pesticides ont été bénéfiques. Cependant, un examen plus attentif des décès dus aux pesticides dans un des hôpitaux a mis en évidence le passage à d'autres pesticides hautement toxiques, quand un pesticide est interdit et remplacé en agriculture par un autre. La réglementation ultérieure devra prévoir ce type de remplacement et ne pas négliger la facilité de traitement des intoxications par les nouveaux pesticides. Cette réglementation doit en outre être mise en œuvre parallèlement à d'autres stratégies, comme la lutte intégrée contre les ravageurs, de façon à diminuer globalement la disponibilité des pesticides dans un but d'auto-intoxication.

Resumen

Influencia de la regulación de los plaguicidas en las defunciones por intoxicación aguda en Sri Lanka

Objetivo Evaluar en un país asiático en desarrollo la repercusión de la regulación de los plaguicidas en el número de defunciones por intoxicación. Estas normas, que entraron en vigor en Sri Lanka a partir de los años setenta, tenían por objeto reducir el número de defunciones por intoxicación -autointoxicaciones deliberadas la mayoría de las veces- mediante la limitación de la disponibilidad y el uso de plaguicidas altamente tóxicos.

Métodos La información sobre los cambios legislativos procede del Ministerio de Agricultura, los datos de ingreso en hospitales nacionales y de distrito se obtuvieron de la Unidad de Estadísticas Sanitarias de Sri Lanka, y los datos particulares sobre las defunciones por intoxicación con plaguicidas son el resultado de un examen manual de las notas de los pacientes y de los registros de la unidad de cuidados intensivos de Anuradhapura.

Resultados Entre 1986 y 2000 se duplicó la cifra total de ingresos

por intoxicación a nivel nacional, y los ingresos por intoxicación con plaguicidas aumentaron en más de un 50%. Al mismo tiempo, la tasa de letalidad descendió para las intoxicaciones totales y para las intoxicaciones por plaguicidas. En 1991-1992, el 72% de las defunciones por plaguicidas registradas en Anuradhapura se debieron a plaguicidas organofosforados (OF) y de carbamato -en particular a los productos monocrotophos y metamidofos, clasificados por la OMS como OF de tipo I. A partir de 1991, la importación de estos plaguicidas se redujo gradualmente hasta que se prohibieron para uso corriente en enero de 1995, con la correspondiente caída de las defunciones. Lamentablemente, su desaparición en las tareas agrícolas dio paso al endosulfán organoclorado, un OF de tipo II que causó un aumento de las defunciones por status epilepticus, de una en 1994 a 50 en 1998. El endosulfán fue prohibido en 1998, y durante los tres

años siguientes el número de muertes por endosulfán se redujo a tres. Sin embargo, al final de la década el número de defunciones por plaguicidas había vuelto a ser similar al de 1991, atribuyéndose la mayoría de las defunciones a los OF de tipo II. Aunque estos productos son menos tóxicos que los OF de tipo I, su gestión sigue planteando problemas, pues son todavía muy tóxicos y su toxicidad se ve agravada por la escasez de servicios.

Conclusión La caída de la tasa de letalidad en el contexto de una incidencia creciente de casos de autointoxicación indica que los programas de regulación de los plaguicidas en Sri Lanka

fueron beneficiosos. Sin embargo, una inspección más atenta de la mortalidad por plaguicidas en un hospital reveló un desplazamiento hacia otros plaguicidas altamente tóxicos, pues al prohibirse el uso de uno de ellos en la agricultura no tardó en ser reemplazado por otro. En la futura reglamentación habría que prever tanto ese tipo de sustituciones como la posibilidad de tratar fácilmente las intoxicaciones por los plaguicidas de sustitución. Además, la regulación al efecto debe aplicarse al mismo tiempo que otras estrategias, como el manejo integrado de plagas, a fin de reducir la disponibilidad general de plaguicidas para autolesiones.

References

- Eddleston M. Patterns and problems of deliberate self-poisoning in the developing world. *Quarterly Journal of Medicine* 2000;93:715-31.
- Singh D, Tyagi S. Changing trends in acute poisoning in Chandrigah zone. A 25-year autopsy experience from a tertiary care hospital in northern India. *The American Journal of Forensic Medicine and Pathology* 1999;20:203-13.
- Singh S, Wig N, Chaudhary D, Sood NK, Sharma BK. Changing pattern of acute poisoning in adults: experience of a large north-west Indian hospital (1970-89). *The Journal of the Association of Physicians of India* 1997;45:194-7.
- Thomas M, Anandan S, Kuruvilla PJ, Singh PR, David S. Profile of hospital admissions following acute poisoning — experiences from a major teaching hospital in south India. *Adverse Drug Reactions and Toxicological Reviews* 2000;19:313-7.
- van der Hoek W, Konradsen F, Athukorala K, Wanigadewa T. Pesticide poisoning: a major health problem in Sri Lanka. *Social Science and Medicine* 1998;46:495-504.
- Eddleston M, Sheriff MHR, Hawton K. Deliberate self-harm in Sri Lanka: an overlooked tragedy in the developing world. *BMJ* 1998;317:133-5.
- Hettiarachchi J, Kodithuwakku GCS. Pattern of poisoning in rural Sri Lanka. *International Journal of Epidemiology* 1989;18:418-22.
- Hettiarachchi J, Kodithuwakku GCS. Self-poisoning in Sri Lanka: factors determining the choice of the poisoning agent. *Human Toxicology* 1989;8:507-10.
- Nandi DN, Mukherjee SP, Banerjee G, Ghosh A, Boral GC, Chowdhury A, et al. Is suicide preventable by restricting the availability of lethal agents? A rural survey of West Bengal. *Indian Journal of Psychiatry* 1979;21:251-5.
- Hawton K, Fagg J, Simkin S, Bale E, Bond A. Trends in deliberate self harm in Oxford, 1985-1995: implications for clinical services and the prevention of suicide. *British Journal of Psychiatry* 1997;171:556-60.
- Bull D. *A growing problem: pesticides and the third world poor*. Oxford: Oxfam; 1982.
- Dinham B. *The pesticide hazard. A global health and environmental audit*. London: Zed Books; 1993.
- Murray DL. *Cultivating crisis. The human cost of pesticides in Latin America*. Austin (TX): University of Texas Press; 1994.
- Karalliedde L, Eddleston M, Murray V. The global picture of organophosphate insecticide poisoning. In: Karalliedde L, Feldman F, Henry J, Marrs T, editors. *Organophosphates and health*. London: Imperial College Press; 2001. p. 431-71.
- Eddleston M, Karalliedde L, Buckley N, Fernando R, Hutchinson G, Isbister G, et al. Pesticide poisoning in the developing world — a minimum pesticides list. *Lancet* 2002;360:1163-7.
- Kishi M, Ladou J. International pesticide use. *International Journal of Occupational and Environmental Health* 2001;7:259-65.
- Food and Agriculture Organization of the United Nations. *International code of conduct on the distribution and use of pesticides (amended to include prior informed consent in Article 9 as adopted by the 25th session of the FAO conference in November 1989)*. Rome: Food and Agriculture Organization; 1990.
- Ellis WW. Private-public sector co-operation to improve pesticide safety standards in developing countries. *La Medicina del Lavoro* 1998;89 Suppl. 2:S112-S122.
- Murray DL, Taylor PL. Claim no easy victories: evaluating the pesticide industry's Global Safe Use campaign. *World Development* 2000;28:1735-49.
- Food and Agriculture Organization of the United Nations. *FAO pesticide management — FAO/OECD pesticide risk reduction survey, in analysis of government responses to the second questionnaire on the state of implementation of the international Code of Conduct on the Distribution and Use of Pesticides*. Rome, 1996.
- World Health Organization. *Primary prevention of mental, neurological and psychosocial disorders*. Geneva: World Health Organization; 1998. p. 75-90.
- World Health Organization. *World Health Report 2001. Mental health: new understanding, new hope*. Geneva: World Health Organization; 2001.
- Annual health bulletin, Sri Lanka, 2000*. Colombo, Sri Lanka: Ministry of Health; 2002.
- Eddleston M, Ariaratnam CA, Meyer PW, Perera G, Kularatne SAM, Attapatu M, et al. Epidemic of self-poisoning with seeds of the yellow oleander tree (*Thevetia peruviana*) in northern Sri Lanka. *Tropical Medicine and International Health* 1999;4:266-73.
- Environmental health criteria #40. Endosulfan*. Geneva: World Health Organization; 1984.
- Eddleston M, Rajapakse M, Roberts DM, Reginald K, Sheriff MHR, Dissanayake W, et al. Severe propanil (*N*-(3,4-dichlorophenyl) propanamide) pesticide self-poisoning. *Journal of Toxicology, Clinical Toxicology* 2002;40:847-54.
- Siwach SB, Gupta A. The profile of acute poisoning in Harayana-Rohtak Study. *The Journal of the Association of Physicians of India* 1995;43:756-9.
- Jeyaratnam J, Alwis J, Seneviratne RS, Copplestone JF. Survey of pesticide poisoning in Sri Lanka. *Bulletin of the World Health Organization* 1997;60:615-9.
- Senanayake N. Organophosphorus insecticide poisoning. *The Ceylon Medical Journal* 1998;43:22-9.
- Maracek J. Psychological approaches to understanding suicide. In: *Suicide in Sri Lanka*. Kandy: Institute of Fundamental Studies; 1989. p.16-24.
- Maracek J. Culture, gender, and suicidal behaviour in Sri Lanka. *Suicide and Life-Threatening Behavior* 1998;28:69-81.
- Phillips MR, Li X, Zhang Y. Suicide rates in China, 1995-99. *Lancet* 2002;359:835-40.
- Phillips MR, Yang G, Zhang Y, Wang L, Ji H, Zhou M. Risk factors for suicide in China: a national case-control psychological autopsy study. *Lancet* 2002;360:1728-36.
- Blanc PD. Surveillance of poisoning and drug overdose through hospital discharge coding, poison control center reporting, and the Drug Abuse Warning Network. *The American Journal of Emergency Medicine* 1993;11:14-9.

35. Singh N, Singh CP, Kumar H, Brar GK. Endosulfan poisoning: a study of 22 cases. *The Journal of the Association of Physicians of India* 1992;40:87-8.
36. Eddleston M, Szinicz L, Eyer P, Buckley N. Oximes in acute organophosphorus pesticide poisoning: a systematic review of clinical trials. *The Quarterly Journal of Medicine* 2002;95:275-83.
37. Eyer P, Kiderlen D, Meischner V, Szinicz L, Thiermann H, Worek F, et al. The current status of oximes in the treatment of OP poisoning — comparing two regimes. Rome: European Association of Poisons Centres and Clinical Toxicologists; May 2003. Abstract. *Journal of Toxicology, Clinical Toxicology* 2003;41:441-3.
38. Lock EA, Wilks MF. Paraquat. In: *Handbook of pesticide toxicology*, 2nd ed. San Diego (CA): Academic Press; 2001.
39. Karalliedde L, Feldman F, Henry J, Marrs T, editors. *Organophosphates and health*. London: Imperial College Press; 2001.
40. Wesseling C, Aragon A, Castillo L, Corriols M, Chaverri F, de la Cruz E, et al. Hazardous pesticides in Central America. *International Journal of Occupational and Environmental Health* 2001;7:287-94.
41. United Nations Environmental Program. Conference of plenipotentiaries on the Stockholm convention on persistent organic pollutants. UNEP/POPS/Conf/2. 2001. Available from: URL: <http://www.pops.int/>.
42. Attaran A, Roberts DR, Curtis CF, Kilama WL. Balancing risks on the backs of the poor. *Nature Medicine* 2000;6:729-31.
43. Perera B, Liyanage GW. National IPM Programme, Sri Lanka. *Programme Advisory Committee Meeting, FAO Inter-country Programme for Community IPM in Asia*. Yogyakarta, Indonesia: Food and Agriculture Organization; July 1999.
44. Abu Al-Ragheb S, Salhab AS. Pesticide mortality. A Jordanian experience. *The American Journal of Forensic Medicine and Pathology* 1989;10:221-5.
45. Piola JC, Prada DB. Influencia de medidas regulatorias en la morbilidad y mortalidad por talio y parathion en Rosario, Argentina [Influence of regulatory measures on morbidity and mortality due to thallium and parathion in Rosario, Argentina]. *Acta Toxicologica Argentina* 1999;7:41-3. In Spanish.
46. Piola JC, Prada DB, Evangelista M, Cagna B. Intoxicaciones con evolución letal atendidas en Rosario, entre 1990 y 1999 [Lethal poisoning cases seen in Rosario, Argentina, between 1990 and 1999]. *Revista Medica de Rosario* 2001;67:19-24. In Spanish.
47. Bowles JR. Suicide in Western Samoa. An example of a suicide prevention program in a developing country. In: *Preventative strategies on suicide*. Leiden: E. J.Brill; 1995. p. 173-206.
48. *WHO recommended classification of pesticides by hazard and guidelines to classification 2000–2001*. Geneva: World Health Organization; 2001. Available from: URL: http://www.who.int/pes/docs/Classif_Pestic_2000-02.pdf.