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* Agrichemical safety practices on farms in the Western Cape. London L. SA Med J 1994 ; 84 : 273-278.

* Notification of pesticide poisoning in the Western Cape 1987 - 1991. London L, Ehrlich R, Rafudien S, Krige F, Vurgarellis P. SA Med J 1994 ; 84 : 269-272.

* Critical Issues in agrichemical safety in South Africa. London L, Myers JE. Am J Ind Med 1995 ; 27(1) : 1-14.

* Repeatability and validity of a field kit for estimation of cholinesterase in whole blood. London L, Thomson ML, Sacks S, Fuller B, Bachmann OM, Myers JE. Occupational and Environmental Medicine 1995 ; 52 : 57-64.

* Biological Monitoring of workers exposed to organophosphate pesticides: Guidelines for field application. London L. Occupational Health Southern Africa July/August 1995 ; 1(4) : 13-17.

THE HEALTH HAZARDS OF CHEMICAL USE IN AGRICULTURE

INTRODUCTION

Despite playing an important role in crop protection and increasing food production, chemicals used in agriculture may have a range of unanticipated effects on human health. Such effects may range from overt and acute poisonings to gradual-onset chronic morbidity.

In South Africa, data on such morbidity are sparse, and subject to much underreporting as one of the included papers illustrates. The dearth of such data has much to do with the marginalised living and working conditions in agriculture and the lack of attention to occupational and environmental health on farms in the country. We have little sense of the extent of hazardous exposures in agriculture, nor of their health impacts on rural populations. Even less so, have methods for the control of poisoning by pesticides been investigated amongst farm workers in South Africa.

A public health response to this problem should aim at all levels of prevention (primary, secondary and tertiary), by characterising the extent and distribution of the problems caused by pesticides, identifying risk factors and groups at highest risk for poisoning, as well as testing intervention strategies and technologies.

The set of papers presented below attempts to do that by linking a series of investigations into different aspects of agrichemical hazards in South Africa, with a focus on the Western Cape.

The first paper examined various aspects of potential exposure to agrichemicals on farms in the Stellenbosch region, taking into account both environmental and occupational routes of exposure. The second paper describes the profile of agrichemical poisoning in the province from 1987 to 1991,

identifying high risk groups and characterising the completeness and nature of reported poisonings. The third paper developed from the author's growing realisation of the need to contextualise problems related to agrichemical exposures and effects within the overall legislative and public health framework in South Africa. This paper therefore identifies the key public health issues that need addressing with regard to pesticide safety. Finally, the last two papers address aspects related to workplace interventions for the prevention of agrichemical poisoning. One paper deals with the evaluation of a field kit (for validity and repeatability) for monitoring workers exposed to organophosphate and carbamate insecticides, while the last paper elaborates guidelines for the use of cholinesterase testing in the primary and secondary prevention of organophosphate and carbamate poisoning.

In this series, therefore, the papers attempt to address the problem of agrichemical hazards within a public health framework, tracing the problem from potential exposure to acute outcomes, through reviewing the legislative and occupational health environments, through to technologies and policy guidelines related to workplace intervention.

In doing so, the papers use the term "agrichemical" to refer to all chemicals used in agriculture for pest and weed control. This supersedes the term "pesticide" which has ambiguous meanings in the technical environment. Readers are therefore advised to understand the term "agrichemical" to include the generic aspects of chemical usage on crops in agriculture.

The research on which these papers was based was spawned by the involvement of the author in a larger research project investigating long-term neurobehavioural effects of organophosphate exposure on deciduous fruit farm workers over the period 1991 - 1994. This latter piece of research is not referred to here as it was the basis for another degree at the University of Cape Town [1]. However, because the research took place contemporaneously, it is still appropriate to acknowledge

the financial support of the International Development Research Centre and the Guy Elliot Fellowship in the Department of Medicine which contributed towards the papers presented here for fulfillment of the degree of Master of Medicine (Community Health).

Agrichemical safety practices on farms in the western Cape

L. LONDON

Abstract **In order to study agrichemical safety practices in a rural farming area in the western Cape, an audit of 45 randomly sampled farms was performed over 3 months in 1992. A response rate of 87% was achieved, and the survey results suggest that approximately 9% of permanent and 14% of seasonal farm workers are employed in jobs with potential exposure to agrichemicals. While protective equipment was widely available, gloves and masks were seldom used, with little enforcement or commercial support from the suppliers of the equipment. Farm workers receive little training on pesticide safety, but interest in the possibility of further training for workers was high. In the absence of a system of pesticide disposal, the presence of residual, unwanted and outdated stocks of pesticides in farmers' stores, and to a lesser extent the presence of empty containers, are identified as important problems. Current pesticide storage practices require improvement by simple industrial hygiene measures. Health facilities available to workers on most farms are extremely limited, particularly in the light of statutory requirements for occupational safety and health under the Machinery and Occupational Safety Act. It is argued that collective solutions to problems of pesticide safety are possible within the ambit of a public health response, particularly given the willingness of the farming community to identify and address potential health problems. As a result, initiatives to meet these needs are currently under way in the region.**

S Afr Med J 1994; 84: 273-278.

Despite their role in protecting crops and maintaining food production,[1,2] pesticides pose considerable health risks to people exposed through their work, the environment and intentional misuse.[1,3-5] Little information is available in South Africa on the extent of the problems related to pesticides and other agrichemicals[6] and on their usage and control on farms. Surveillance is imperfect[7] and considerable undernotification of incidents of pesticide poisoning in the country is evident.[8,9]

Control and safe handling of agrichemicals is a key aspect of the prevention of pesticide morbidity and mortality[10,11] and is the subject of substantial legislation with regard to the labelling, distribution and storage of pesticides.[6] However, among cases notified to the Department of National Health and Population Development, the most frequent source of the pesticide has been a farm pesticide store, and the majority of cases involve farmers, farm workers or their families.[12] This suggests that unauthorised access to pesticides is an important problem not addressed by existing legislation.

Safety training is a key aspect of prevention but appears to be poorly co-ordinated and unevenly distributed.[9,13] Two safety initiatives in the western Cape include the National Productivity Institute (NPI) Deciduous Fruit Division, who provide audiovisual self-help materials to fruit farmers for training on the safe application of agrichemicals, and the Rural Foundation (RF), whose field worker provides a basic industrial hygiene assessment to member farms of the RF on request. However, the extent to which these (and other) safety initiatives have been applied locally is unknown.

In order to identify some of the key needs for agrichemical safety in the farming community, an audit of pesticide safety and control conditions was conducted on a random sample of farms in a rural district of the western Cape over 3 months in 1992. The survey was aimed at providing information to the local authority health service on which to plan a public health response to the question of agrichemical safety.

The objectives of the study were to: (*i*) describe the size and workforce profile of farms in the region and identify the numbers and job types of farm workers potentially exposed to agrichemicals during the course of their work; (*ii*) describe the sources of agrichemical supplies, as well as attitudes towards their storage, control and disposal and practices in this regard; (*iii*) describe the prevalence of safety practices; (*iv*) describe the extent of health services available on farms and levels of safety training in relation to agrichemicals; and (*v*) assess the extent of record keeping for agrichemical use on farms and document any previous poisoning events on the farms surveyed in relation to notifications.

Methods

A random sample of 75 farms and smallholdings was drawn from a sampling frame of 884 rural holdings available from the health inspectorate at the local Regional Services Council Health Department. After non-agricultural holdings had been excluded, 45 farms and smallholdings were left in the sample. Measurement consisted of a semi-structured interview conducted with the farmer, farm manager or supervisor directly involved in production processes on the farms and an inspection of the farm's pesticide store. The questionnaire was piloted on a subsample of farms in the region early in 1992. All participants were assured of the anonymity of their individual responses.

Results

The response rate in the sample was 87%, with 6 farms declining to participate in the survey. No difference between participants and non-participants was noted regarding incidents of previous poisoning episodes recorded with the local authority.

Farm profile

The majority of farms surveyed were involved in production of grapes for wine (72%). Other common activities were fruit (46%) and vegetable farming (18%). Multiple crop production activities involving more than one product were common (56%). Eleven farms out of 35 who gave unequivocal answers (31%) reported being members of the RF. The distribution of farm size and workforce size is shown in Figs 1 and 2.

Department of Community Health, University of Cape Town
L. LONDON, M.B. CH.B., B.SC. HONS (EPIDEMIOL.), D.O.H.

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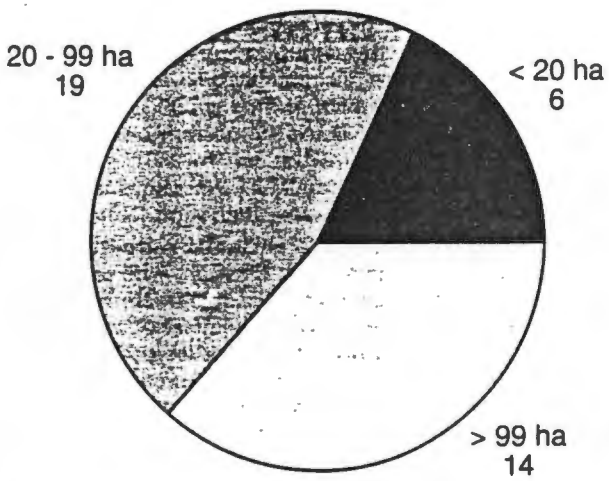

FIG. 1.
Distribution of farm size (in hectares) (39 farms).

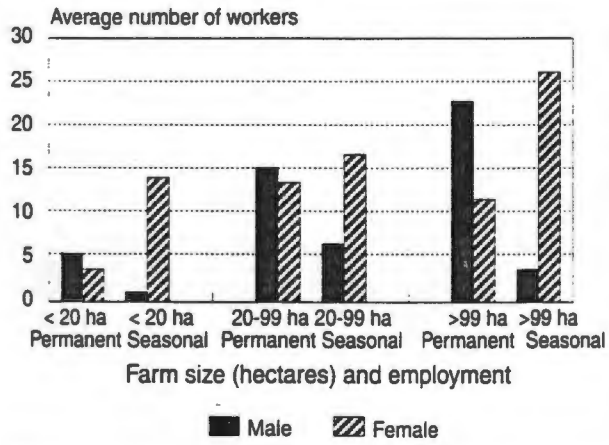

FIG. 2.
Average workforce by farm size, employment status and gender (39 farms).

Workforce size varied widely from 1 or 2 workers on smallholdings to over 100 on farms that were part of groups of holdings or agribusinesses. Seasonal labour was widely used, except for vegetable farming, and constituted roughly half of the total workforce (Fig. 2).

Contract migrant labour was used on only 3 farms. Continuity of re-employment of seasonal workers from one year to the next varied from 0% (i.e. total turnover from one season to next) to 100% (usually when the seasonal workforce consisted of the family of the same or a neighbouring farm's permanent workforce). Average return of seasonal labour over all farms using seasonal labour was 36%.

Agrichemical sources and storage, control and disposal attitudes and practices

The majority of farmers (72%) reported receiving the bulk of their agrichemicals directly from agrichemical companies rather than from a co-operative. Seventy-four per cent reported having a separate pesticide store that was usually locked, and Fig. 3 shows the numbers and type of personnel with access to the store.

The usual situation on most farms (82%) was that keys to the store were kept by the farmer, his manager or the foreman. On only 15 farms (38%) was it reported that more than one person had authorised access to the store.

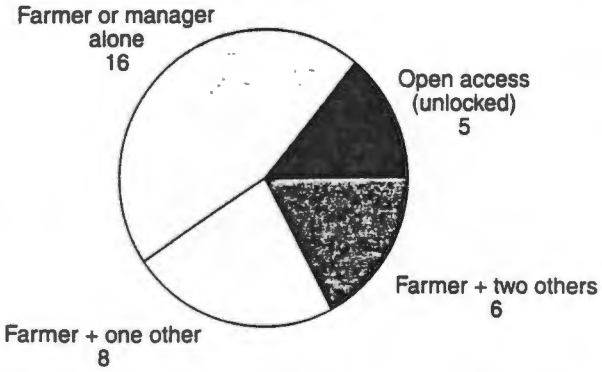

FIG. 3.
Access to pesticide stores (35 farms — 4 farms reported no formal store for pesticides).

Fig. 4 shows the results of a brief industrial hygiene inspection of the stores conducted at the time of interview. In most cases (56%) the store was found to be unlocked at the time of visiting. Another important finding was that a large number of farms (49%) kept material unrelated to pesticides (such as tools and diesel fuel) in the pesticide store. Empty containers outside the store (including containers for pesticides such as mancozeb, glyphosate, paraquat and diquat) and unlabelled containers in the store were also found, but less commonly.

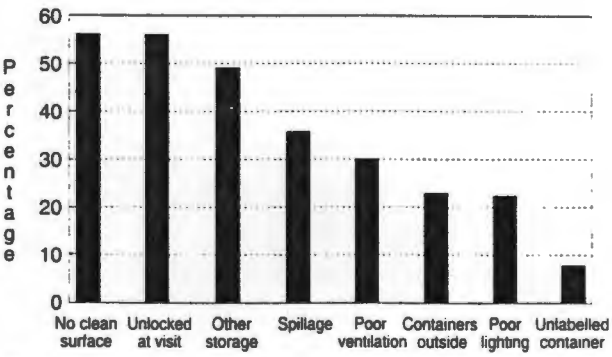

FIG. 4.
Industrial hygiene assessment based on inspection of stores.

Eleven farms reported having unwanted empty pesticide containers and 18 farms (46%) having residual pesticides in their stores of which they had not been able to dispose. The types of pesticide container and residual pesticide are listed in Table I.

Farmers most frequently reported disposing of empty pesticide containers by a combination of puncturing, burning and burying the containers in a specific site on their farms (89%). Thirty-one per cent of respondents experienced problems with getting rid of empty containers, and a similar proportion stated that they had to store up containers inside their store until there were enough to destroy. Two respondents reported disposing of empty containers at the municipal dump. None of the farms that washed out containers before destroying them had any plan to deal with the effluent water used to clean the containers. Only 1 farm was currently making use of a disposal service for empty containers, and 2 farmers expressed knowledge of a local container disposal service that had started recently.

While only 6 farmers reported re-using empty containers for purposes of storage of other chemicals, 19 out of 25 thought it possible to re-use containers of pesticides they thought were 'not dangerous'. Two-thirds

TABLE I.
Residual pesticides and containers (39 farms)

Empty pesticide containers	Residual pesticides
Azodrin	Azodrin
Bravo	Amitrole
Capsine	Bladex
Chlorpyrifos	Buctril
Dithane	Basaman
Dieldrin	Bayleton
Folimat	DDT
Folidol	Dieldrin
Glyphosate	Ethylene dibromide
Karathane	Eptam
Parathion	Folidol
Phosdrin	Folin
Sting	Gusathion
	Karathane
	Lead arsenate
	Maneb
	MCPA
	Planovin
	Shell-B-Amine
	Stomp
	Tedion
	Toxaphene
	Triadimenol
	Rogor
	Fruitop

expressed an interest in participating in a service that could recycle or dispose of empty pesticide containers.

Potentially exposed workforce

Thirty-two farms (82%) reported that the main route of pesticide application was by tractor spraying. Backpack spraying was the major method of application on 5 farms, including the nurseries and smallholdings, while a number of farms used backpack spraying as a supplementary form of pesticide application. The number of workers involved in spraying ranged from 1 to 12 per farm and was dependent on the size of the farm. The median number of tractor drivers involved in spraying was 2 per farm. In addition, 20% of the farms had supervisory staff who came into regular contact with pesticides by storing, mixing or handing pesticides to the sprayers. None of the farms had workers solely responsible for the maintenance of the pesticide store. Out of a total of 1 060 permanent workers in the sample, 8,5% were involved in work that brought them into direct contact with pesticides (mixing, packing, spraying or handling). In addition, a further group of workers (constituting about 14% of the seasonal workforce) were involved in other agricultural activities in the field, such as pruning or shaping vines, which brought them into indirect contact with pesticides that had been sprayed onto the vine, tree or crop.

Farmers or farm managers were involved in activities exposing them to pesticides on 28 farms (72%). In most cases (77%) farmers, managers or supervisory employees were responsible for packing and storage. In contrast, pesticides were frequently mixed by those workers involved in their application (71%), usually the tractor drivers. While there was some overlap in responsibilities for mixing, it appeared that application was usually the sole responsibility of drivers or labourers, while control of storage was usually the sole responsibility of the farmer or manager. The frequency with which different categories of personnel were involved in different aspects of pesticide handling is indicated in Fig. 5.

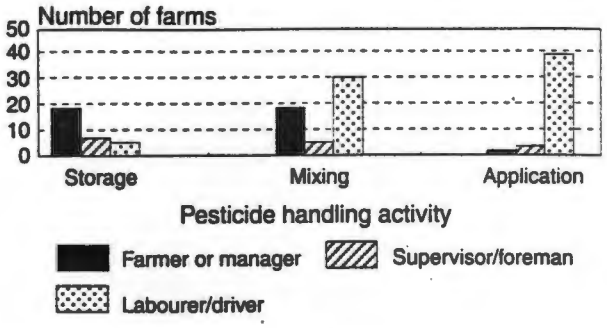

FIG. 5.
Responsibility for pesticides (39 farms) — category of personnel involved in storage, mixing and application. Responsibilities for different job activities may overlap (see text).

Farms on which workers were responsible for packing and mixing pesticides included 4 (13%) where the workers were reported to be illiterate.

Safety precautions in handling agrichemicals

Issuing of personal protective equipment (PPE) (including gloves, masks and overalls) for mixing and applying pesticides was widely reported. However, many farmers doubted that PPE was used regularly (Fig. 6). More than one farmer commented that it was difficult to get workers to wear protective equipment and only 2 claimed to enforce use of PPE by workers.

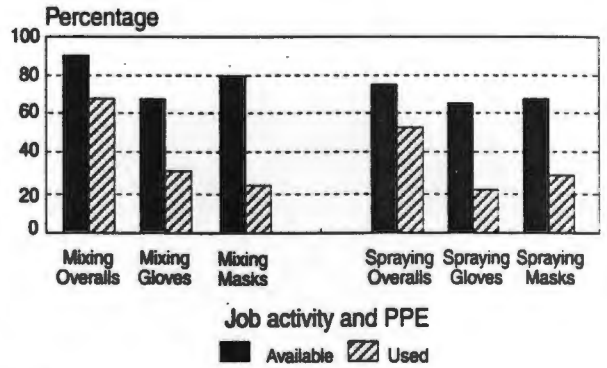

FIG. 6.
Personal protective equipment (39 farms) — availability and usage by type of PPE and by pesticide activity.

None of the farmers who provided masks reported receiving any follow-up from the co-operative from which the mask was purchased. Reporting of replacement of filters on the masks was very variable, ranging from once a week to once a month.

Health services

With the exception of 1 farm, the owner of which was a doctor, the only form of health service available on the farms was a first-aid box or boxes (62%). Twelve respondents (31%) reported that they had no form of first aid or health service on the farm. On farms that provided a first-aid box, the source of first aid was most commonly the wife (or mother) of the farmer or manager (36%), followed by the farmer or manager himself (31%) or other clerical staff on the farm (8%). On 2 farms workers had received specific first-aid training.

Sixteen out of 26 farmers indicated that they thought they would be able to recognise the signs and symptoms

if a worker were to be poisoned. Most said that in such a case they would take the worker to the nearest general practitioner or hospital, both of which were in all cases less than 20 km away.

Safety training

Training of the workforce on pesticide safety was low (Fig. 7). Most farms (60%) reported that they did not have any specific training other than that provided by the farmer or manager as part of the worker's general training. Only 4 farms (11%) had arranged for specific training on pesticide safety and handling for their workers and the remaining 29% reported no training of workers on pesticide safety at all.

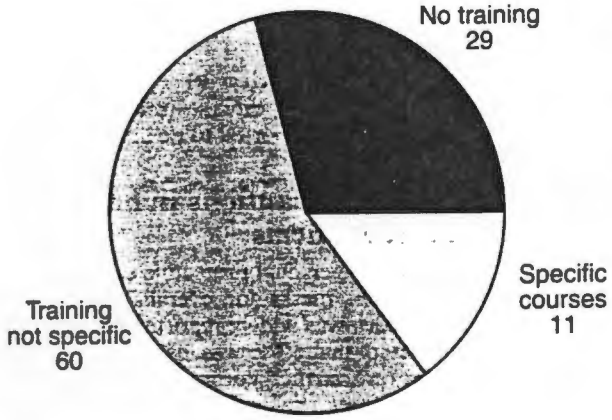

FIG. 7.
Training in pesticide safety (% of sample).

In terms of known educational initiatives in the region, only 3 of 35 farms (9%) had been exposed to the NPI video on pesticide application and 4 of the RF's 11 members in the survey had previously been audited as part of the RF's safety programme. Two farmers had been on special courses on pesticide handling and safety.

Concern about training on pesticide safety for the workforce was high, 31 out of 38 farmers (84%) indicating an interest in sending their workers on a training course on safe handling of pesticides.

Record keeping and previous morbidity

The extent of record keeping in relation to agrichemical application is set out in Table II.

TABLE II.
Record keeping of agrichemical applications (39 farms)

Records for	No. of farms	%
What was sprayed	33	85
When applied	31	80
Where applied	31	80
Quantity applied	26	67
Who applied*	15	58

*Data not available for 13 farms.

More than half of the farms only kept records for 2 years or less, the range for keeping of records being 1-13 years. Quality and duration of record keeping appeared to have no relationship to farm size or to whether there had ever previously been a case of poisoning on the farm. Frequently the records took the form of spray programmes, which usually (but not always) give information on the timing, nature, amount and site of application, but do not give data on which workers were exposed.

Seven farms (18%) reported that there had been incidents of poisoning in the past. The nature of these incidents was very diverse, and was not tightly defined. They included a parasuicide, an accident on duty (leading to a Workmen's Compensation claim) and 2 cases of symptoms which it was thought had been caused by pesticides but which were unconfirmed. For 3 cases notification could be traced at the local health authority. Three farmers or farm managers reported that they themselves had been poisoned by pesticides in the past.

Discussion

The random sample of farms included in this study appears to be a representative range of farm types in the area. In following up the 6 farms that failed to participate in the survey, little difference was found between their safety records or production activities and those of the rest of the sample. Moreover, with a response rate well in excess of 80%, the research should have good generalisability to the local region. Inasmuch as this area is regarded as a relatively 'enlightened' farming community, the survey results probably reflect one of the best-case scenarios in relation to farming practices in the western Cape more broadly and in South Africa as a whole.

In assessing occupational exposure to hazardous agrichemicals, it appears that most potentially exposed workers are tractor drivers and backpack sprayers primarily involved in pesticide application and, to a lesser extent, mixing activities. However, a significant number of supervisory staff or farmers themselves are exposed through their responsibility for the pesticide stores. These assessments of exposure require further qualitative elaboration in epidemiological studies.[14]

Farm-based records appear to be adequate for assessing short-term exposures on farms for the immediate past season, but are generally not available for assessing long-term exposure, especially where chronic health outcomes are under investigation. Exposure records are also not generally linked to individual workers, and further measures would need to be instituted to investigate health risks in individual subjects. Mixed production is a common feature of agriculture in the area and is probably likely to increase as farmers diversify their crop output,[15] which will add to the heterogeneity of chemical exposures among workers. Agrichemical exposures experienced by seasonal workers would be difficult to assess in the presence of high turnover from one season to another, so they would be a difficult population in which to perform any epidemiological study. Similarly, contract (migrant) labour is not substantially used in the area.

Availability of protective equipment in this study appears to be reasonably high, in contrast to actual use — less than a third of workers were reported to use gloves or masks in the course of performing hazardous activities. These are probably substantial overestimates of the true rates, given that the study chose to use data obtained from interviews with the farmers and managers, and was not designed to validate use in the field. These results are consistent with studies in underdeveloped countries around the world where use of protective equipment is low.[16,17]

Further investigation into the reasons for low use as well as training for appropriate use of PPE are indicated. A further deficit identified was the lack of follow-up provided by the retailers supplying masks for protective use, and there appears to be sound motivation for co-operatives to provide follow-up to individual farmers on how to use, maintain and replace their protective equipment.

Disposal, both of empty containers and of residual pesticides, is a significant problem.Current methods of disposal of empty containers on farms appear to meet minimum legal standards[18] but do not address the environmental problem of water effluent produced from rinsing containers. Moreover, re-use of containers does occur. Even though this re-use is reported as being specifically to transport other chemicals, there is a perception that containers of 'less hazardous' agrichemicals are safe to re-use. This might suggest that re-use of containers is more widespread than reported.

A more important hazard, from both an environmental and a personal health perspective, is the presence of substantial amounts of unwanted agrichemicals in pesticide stores on farms in the region (Table I). These include some extremely hazardous chemicals, of which a number are no longer registered for use. Many of these residual pesticides were inherited with the farms, and in 3 cases the containers were so rusted that removal was likely to result in breakage and spillage. On two other farms, containers present were so old that it was no longer possible to identify what was inside them because the labels were totally illegible.

Part of the explanation for this phenomenon may be the prohibitive costs and logistic difficulties of commercial waste disposal, as well as the reluctance of agrichemical companies to take responsibility for outdated chemicals. Only 1 farm reported that the agrichemical supplier had removed excess unwanted pesticide.

Given the considerable concern expressed by farmers, it is hardly surprising that the majority of the farms surveyed identified a need for a system for agrichemical disposal. These findings are remarkably similar to an unpublished study of pesticide hazards on farms in the Hex River region, where 51% of farmers reported having problems with unwanted containers or chemicals and identified a need for a disposal service (A. Reid — personal communication). These findings have formed the basis for a current pilot programme, located in the western Cape, to assess the viability of instituting a pesticide disposal service through the facilitation of the local Regional Services Council health authority.[19]

Storage and security of control of pesticides on farms need to be improved, particularly in light of the frequency of cases of notified poisonings in which unauthorised access to pesticides plays a role.[12] Simple measures such as keeping all non-chemical materials in a separate store would minimise the need to open the store and reduce the time during which access to dangerous chemicals is possible. Provision of clean working surfaces, adequate lighting and ventilation and the clearing of all spillage are simply applied measures that should be incorporated in training and support provided to farmers, managers and supervisors.

Health services on farms in the area appear to be limited, and the usual providers of first aid have little training, particularly in the recognition and treatment of pesticide poisoning. If poisoning occurs, it is the responsibility of the farmer alone to recognise the seriousness of the condition and get the worker to a doctor — this may be an impossible expectation if he has received no training. While the farms in the study area are relatively fortunate in being in close proximity to the local hospital or local general practitioners, there is definitely a need for an emergency service on farms. Moreover, this situation fails to meet the requirements of the Machinery and Occupational Safety Act, which governs workplace safety in South Africa at present.

Reported morbidity on the farms surveyed is difficult to assess given the lack of definition of a previous episode of poisoning. However, the fact that only 3 out of 7 cases could be traced in notifications appears to support findings in other studies that pesticide poisoning is substantially underreported.[6-10] Surveillance for disease caused by pesticides needs to be critically re-evaluated. Active surveillance, in the form of a regular monitoring programme for exposed workers, should be seriously considered as a public health intervention.

Levels of safety training are disturbingly low. Current safety initiatives investigated in this study (NPI video and safety audit by RF field worker) appear to have achieved very limited coverage. Few farmers had made use of any specific training courses for their workers (Fig. 7) or for their own education, in spite of frequently being exposed to pesticides in the course of their own work, and illiteracy of some of the workers involved in handling potentially hazardous chemicals (13% of farms) is a major obstacle to further training. However, there is strong interest in potential training on most farms, and local developments are likely to produce some response to this need.[19] Interestingly, during interviews farmers suggested that agrichemical companies could play an important role in this regard.

Conclusion

Deficiencies in a number of areas of pesticide safety have been identified. These include inadequate training and usage of protective equipment, shortcomings in storage practices, the absence of a disposal system for empty containers and residual pesticides, insufficient and inappropriate provisions for medical care on farms, undernotification and a lack of effective surveillance. However, many of these can be solved within the ambit of a public health approach, and three aspects (surveillance, training and disposal) are currently the subject of three major regional initiatives.

Moreover, many of the farmers in the study were willing to address the potential problems identified in the study. Given this attitude, and a growing concern for a healthy environment, there is ample reason to believe that a co-ordinated response to pesticide safety is possible. A strategy involving collaboration of all the parties concerned, including farmers, workers, agrichemical companies, development organisations, research institutions and health authorities, should bring about a considerable reduction in the acute and long-term risks arising from agrichemical usage in the farming community.

Part of this research was carried out while the author was the recipient of the Guy Elliot Fellowship at the University of Cape Town in 1991/92. The author wishes to thank Mr B. Slon and Mr T. Pollock for their assistance with data collection and the Western Cape Regional Services Council Health Department staff for their full co-operation. The co-operation, time and insights given to the author by the farmers, workers and managers who participated in the interviews, and the support of the International Development Research Centre in the development of this research, are also acknowledged.

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The effects of a single treatment of an acaricide, Acarosan, and a detergent, Metsan, on Der p 1 allergen levels in the carpets and mattresses of asthmatic children

A. MANJRA, D. BERMAN, A. TOERIEN, E. G. WEINBERG, P. C. POTTER

Abstract **Baseline levels of the house-dust mite allergen, Der p 1, were measured on the carpets and mattresses of 60 pure-mite-sensitive asthmatic children in the Cape Peninsula, by means of an enzyme-linked immunosorbent assay (ELISA). High levels of mite allergens were recorded (range 2 - 50 μg Der p 1/g dust). In order to investigate the efficacy of the application of acaricides to carpets and bedding, 3 groups of 20 children were studied. Carpets and mattresses in group A were treated with a detergent, Metsan (Snowchem), and in group B with Metsan combined with the acaricide, Acarosan (Noristan). Group C was a control group in which no treatment was applied. The level of airway hyperreactivity (PC20) to histamine was measured at the beginning of the study and again 3 months after acaricide treatment.**

Significant reductions in carpet Der p 1 levels were achieved in group A (22,83 v. 13,26 μg Der p 1/g dust; $P = 0,04$) and group B (21,76 v. 13,26 μg Der p 1/g dust; $P = 0,01$), but mite levels were not reduced in any of the mattresses treated. There was also no improvement in airway hyperreactivity in any of the groups.

This study clearly demonstrates that at present it is not possible to reduce Der p 1 antigen levels in mattresses in the Cape Peninsula with the available acaricides, even when one of these is combined with a detergent solution.

Until strategies are developed which will significantly reduce Der p 1 levels in the bedding of sensitive individuals, a reduction in ongoing airway inflammation and airway hyperreactivity cannot be expected.

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Allergy Clinic, Red Cross Children's Hospital, Cape Town
A. MANJRA, F.C.P. (S.A.), D.C.H. (S.A.)
D. BERMAN, B.A., DIP. MED. TECH.
A. TOERIEN, R.N., R.M.
E. G. WEINBERG, M.B. CH.B., F.C.P. (S.A.)
Allergology Unit, Department of Clinical Science and Immunology, University of Cape Town
P. C. POTTER, B.SC. HONS, M.D., F.C.P. (S.A.), D.C.H. (S.A.)

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Allergy to house-dust mites occurs in 67 - 80% of children with allergic disease in the Cape Peninsula.[1,2] Chronic exposure to perennial allergens, such as the house-dust mite, results in an inflammatory process in the airways[3,4] which in turn increases the airway nonspecific reactivity to cold air, exercise, tobacco smoke and specific allergen challenge. Mite-allergic asthmatic patients, when placed in a mite-free environment, experience a significant reduction in nonspecific bronchial hyperreactivity and in their symptoms.[5] Furthermore, their requirements for anti-inflammatory treatment with steroids or cromoglycate are reduced.

Although it has been known since 1955 that house-dust mites are found in the coastal regions of South Africa,[6] immunochemical determination of the allergen level of house-dust mite, *Dermatophagoides pteronyssinus* (Der p 1), has not previously been undertaken. The recent availability of such assays for Der p1 antigen[7] has made it possible to quantify and evaluate objectively the protocols currently recommended to reduce house-dust mite levels in patients' homes.

Several acaricides have been found to kill mites effectively under laboratory conditions.[8] Their acaricidal effects on mites in patients' homes are influenced by factors such as the age of the house, the level of mite infestation, the ambient humidity and temperature, the presence or absence of carpets and the nutrient supply for the mites.

We report the results of a prospective study which documents the levels of Der p 1 in the carpets and

Notification of pesticide poisoning in the western Cape, 1987 - 1991

L. LONDON, R. I. EHRLICH, S. RAFUDIEN, F. KRIGE, P. VURGARELLIS

Abstract **There is a paucity of data on pesticide-related morbidity and mortality in South Africa. A review of notifications to the western Cape office of the Department of National Health and Population Development from 1987 to 1991 was undertaken to describe the epidemiological profile of pesticide poisoning in the region. Two hundred and twenty-five cases of pesticide poisoning were identified, of which the majority were from rural areas. Farmers, farm workers and their families were most frequently involved in poisoning events, which included accidents arising outside of workplace production (44%), self-inflicted injury (35%) and direct occupational contamination (11%). Farm pesticide stores were the most frequent source of pesticide and a seasonal variation in the trend of poisoning events could be discerned; this corresponded to agricultural spraying practices in the region. The mortality rate was significantly higher among those with self-inflicted injury, particularly farm workers. A concurrent review of hospital admissions for 1991 found that 78% of cases had not been notified. In view of the key role of surveillance in reducing pesticide-related morbidity and mortality, a call is made to improve notification of pesticide poisoning so as to facilitate control of an important potential public health problem.**

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Despite their role in protecting crops and maintaining food production, pesticides pose considerable health risks to those exposed both occupationally and environmentally. The World Health Organisation estimates that 1 million unintentional acute poisonings occur worldwide every year, with between 5 000 and 20 000 fatalities.[1] In underdeveloped countries the major causes of pesticide-related morbidity and mortality are occupational exposure among rural workers[1-4] and suicide.[2,4-6] Accurate description of the extent of the problem is prevented by the absence of data on poisonings in many rural settings, and by the problem of underreporting.[1,2,4-6]

Research data available in South Africa on the extent of health problems related to pesticides and other agrichemicals, and on their usage and control, are scant. Poisoning caused by paraquat and organophosphate insecticides have been reported to be an important reason for admission to respiratory intensive care units of hospitals[7] while incidents of pesticide poisoning made up 9 - 13% of Poison Centre consultations at Red Cross Children's Hospital in Cape Town in 1987.[8] A similar study of childhood poisoning in the Orange Free State in 1988 found that 12% of poisonings involved pesticides.[9]

In terms of the Health Act, pesticide poisoning is a notifiable condition. Between 100 and 150 cases were notified in 1990 and 1991, with a case-fatality rate of about 7%.[10,11] However, incidence rates in South Africa based on notification are difficult to establish because of undernotification.[12,13] A study of registered deaths in 1977 found that fewer than 5% of deaths found to be due to pesticide poisoning at the Salt River police mortuary in Cape Town had been notified[14] while a review of records at a small rural western Cape hospital found that only 10% of the 90 cases of pesticide poisoning seen at the hospital in 1989 and 1990 had been notified.[15] Similarly, published reports of Poison Centre data from Bloemfontein,[9] Cape Town[8] and Johannesburg[15] include numbers of consultations for possible pesticide poisoning far in excess of national notifications.

In the absence of clear information on the extent and risk of acute poisoning, it is difficult to plan public health intervention aimed at controlling this important potential health hazard. To address this need for information, a review of all pesticide poisonings notified to the Western Cape Regional Office of the Department of National Health and Population Development (DNHPD) between 1987 and 1991 was undertaken. The study aimed (*i*) to describe the incidence and demographic profile of fatal and non-fatal pesticide poisonings in the western Cape; (*ii*) to identify any patterns in the circumstances surrounding pesticide poisoning, in particular, whether the incident was farm-related; and (*iii*) to identify any risk factors pertinent to primary and secondary prevention of poisonings.

In a separate exercise, a survey of all Cape Provincial Administration (CPA) and province-aided hospitals in the western Cape ($N = 55$) was undertaken to ascertain the number of hospital admissions for pesticide poisoning in 1991 and to gauge the extent of undernotification.

Methods

All cases of pesticide poisoning notified to the regional director of the DNHPD are referred to the local authority health inspectorate for investigation of the circumstances of the poisoning. Reports are then centralised at the regional office of the DNHPD. This study reviewed reports for the years 1987 to 1991. Data on the age, gender, educational level, residence and occupation of all subjects who suffered pesticide poisonings were collected, as well as information on the type and the source of pesticide involved, and whether the outcome was fatal. The immediate circumstances surrounding the event were recorded in terms of whether: (*i*) the poisoning was occupational, accidental or self-inflicted; and (*ii*) whether it occurred on a farm or at a site independent of a farm.

In order to assess patterns in the circumstances of poisonings, data on farm workers and non-farm workers were analysed separately. Included in the former category were farmers, those employed as farm workers and

Department of Community Health, University of Cape Town
L. LONDON, M.B. CH.B., B.SC. (EPIDEMIOL.), D.O.H.
R. I. EHRLICH, B.BUS.SCI., M.B. CH.B., D.O.H., F.F.C.H. (S.A.)
S. RAFUDIEN, B.SC.
Hospital and Health Services, Cape Provincial Administration
F. KRIGE, M.B. CH.B., M.PRAX.MED. (COMM. HEALTH), D.T.M. & H.
Department of National Health and Population Development, Cape Town
P. VURGARELLIS, M.B. CH.B., F.F.C.H. (S.A.)

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their families, while the category of non-farm worker included those subjects who were not connected with a farm in any way. Additional variables considered in the attempt to establish a pattern were the source of the poison, the immediate circumstances giving rise to the poisoning and seasonal variations in poisoning incidence.

The criterion for a child was an age of 16 years or younger. Where there was uncertainty about the chemical responsible for the poisoning, the local authority health inspector identified the most likely chemical implicated. Data were collected by a single trained reviewer (S.R.).

Superintendents of CPA- and province-aided hospitals in the western Cape region (Fig. 1) were surveyed by means of a postal questionnaire for details of patients admitted for pesticide poisoning in the period January to December 1991. A response rate of 91% was achieved. Teaching hospitals, particularly Tygerberg and Groote Schuur Hospitals, which do not form part of the administrative western Cape region of the CPA, were not included.

Differences in proportion of categorical data were compared by means of χ^2-tests, and odds ratios (ORs) were calculated as measures of association with 95% confidence intervals.[16] Exact limits were used where the cells in contingency tables were small.[16]

Results

Two hundred and twenty-five cases of pesticide poisoning were notified between 1987 and 1991. Table I lists the number of cases by year, and Fig. 1 shows the geographical distribution of notifications. Over 80% of cases notified were reported from rural areas of the western Cape.

TABLE I.
Pesticide poisonings in the western Cape — notifications to DNHPD, 1987 - 1991

Year	No. of poisonings
1987	58
1988	44
1989	36
1990	28
1991	50

Data on 9 subjects missing.

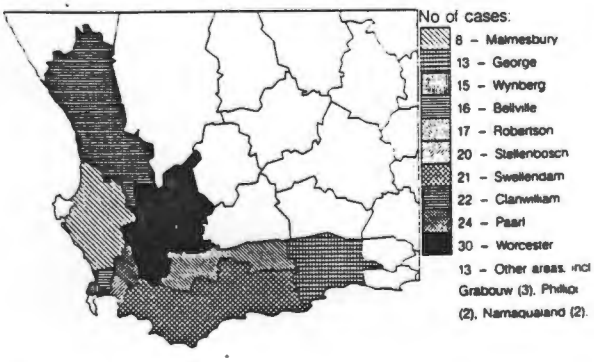


FIG. 1.
Geographical distribution of pesticide poisoning notifications, 1987 - 1991.

Age and gender distribution of cases are shown in Fig. 2. Thirty per cent of cases involved children 16 years old or younger, and 18% involved pre-school children. Males constituted 70% of all cases and 65% of children under 6 years of age. Only 12% of patients were white, the majority (78%) being coloured.

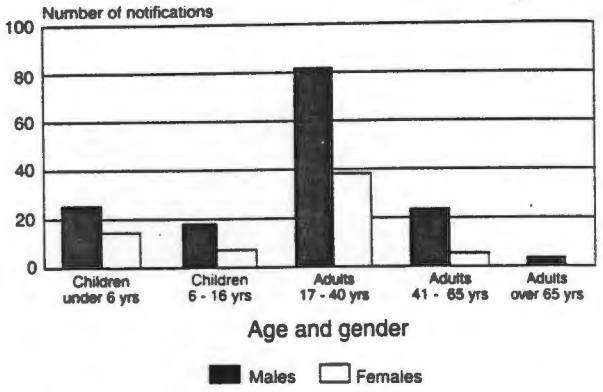
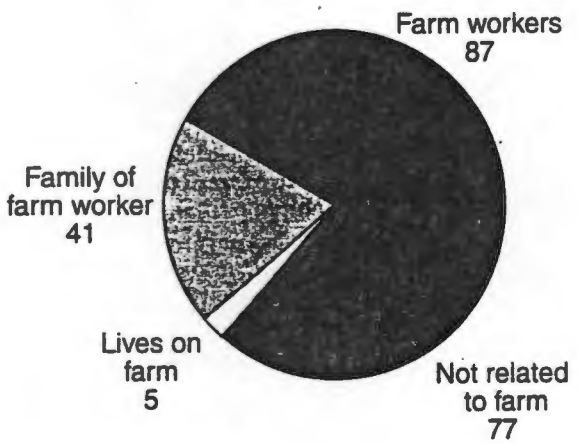


FIG. 2.
Demographic characteristics of pesticide notifications, 1987 - 1991.

The majority of cases (61%) of poisoning involved farm workers, farmers or their families (Fig. 3). This percentage was similar for children (66%) and included 7 who were reported to be farm workers. The commonest pesticide types implicated in poisoning events were organophosphates (68%), carbamates (9%) and organochlorines (5%). In only 6% of cases was the chemical responsible entirely unknown.



No data available on 8 subjects.

FIG. 3.
Characteristics of subjects.

The circumstances of poisonings are summarised in Fig. 4 and the seasonal variation in cases is shown in Fig. 5. Seventy-one per cent of childhood poisonings were accidents, but a small number were the result of occupational exposure (7%) and self-inflicted injury (5%). A seasonal variation was noted in the incidence of notified poisonings, with a rise from September to February, and a single peak in May. Analysis of this trend in respect of subgroups was not possible given the small numbers in the sample.

The commonest source of a poison was reported to be a farm pesticide store (40%), particularly where poisonings involved farm workers; the percentage was sometimes as high as 80%. For non-farm-related poisonings the commonest sources were household stock (49%) or over-the-counter purchases at a shop or co-operative (30%). Sources of poison in cases of childhood poisoning were evenly divided between farm stores (41%) and purchase in a shop (41%). However, among farm children who were poisoned, the most frequent source was the farm pesticide store (74%; $N = 23$). Only 10% of poisonings overall could be traced to an over-the-counter purchase.

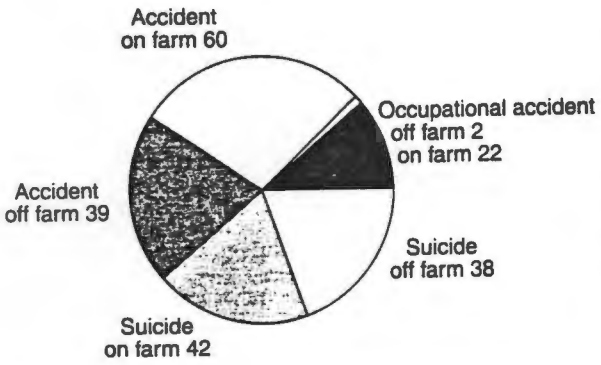


FIG. 4.
Circumstances of pesticide poisoning, 1987 - 1991.

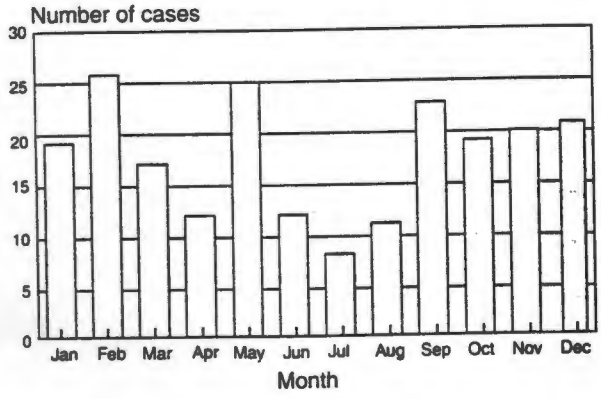


FIG. 5.
Seasonal variation in pesticide poisoning.

The overall case-fatality rate among notified poisonings was 12% and the rate among farm poisonings (14,6%) was not significantly different from that of non-farm poisonings. Among children, the case-fatality rate was 4% and was significantly lower than that of adults (OR = 0,26; 95% CI = 0,05 - 0,91). The risk of a fatal outcome was significantly higher in a suicide attempt (OR = 3,34; 95% CI 1,36 - 8,29) than in non-self-inflicted poisonings. Among those with a self-inflicted injury, the risk of a fatal outcome was higher among farm workers than others (OR = 4,13; 95% CI 1,06 - 19,36). The majority of patients (97%) received treatment within 48 hours of the event and there was no relationship between the duration until treatment and (*i*) likelihood of a fatal outcome; (*ii*) the age of the subject; and (*iii*) the type of subject.

Of the 17 cases in which the responsible pesticide could not be accurately identified, 11 were farm-related, a proportion not significantly different from that for the non-farm population. Fifty-nine per cent of adult farm workers who were involved in a poisoning had 5 years or less of schooling while the equivalent percentage for non-farm workers was 22%. This difference was statistically significant (OR = 5,55; 95% CI = 2,23 - 14,14).

Of the 135 cases of pesticide poisoning admitted to CPA hospitals in 1991, only 30 (22%) notifications could be traced at the DNHPD regional offices. A further 20 cases were reported by the hospitals as having been notified, but no notification could be traced.

Discussion

Surveillance has been identified by the WHO as a key element in control of the problem of acute pesticide poisoning.[1] Evidence in this study, consistent with experience elsewhere in South Africa[12,14,15] and overseas,[1,4,6,17] suggests that notification consistently underestimates the extent of acute poisoning events. This underreporting factor can be used to estimate the true incidence of pesticide poisoning, with population estimates for the region[18] as denominator and the number of yearly notifications as numerator. In this study, the population incidence rates for pesticide poisoning in the region for the years 1987 to 1991 would range from about 4/100 000 (1990) to 8,7/100 000 (1987) with the most recent rate being 7/100 000 in 1991. On the basis of census data for the denominator,[18] the incidence rate in 1991 for farm workers was approximately 25/100 000 and for the rural population of the region, 23/100 000.

However, hospital admissions for pesticide poisoning may represent a particular sub-population that are more likely to be notified than those patients who do not reach hospital.[4,17] For example, private practitioners may, for various reasons, be less likely to notify poisoning events.[19] Moreover, the survey was based on hospital self-reporting with the likely effect that hospitals may have tended to err on the side of overstatement of notification.

It is apparent that pesticide poisoning is a problem of the farming areas with over 80% of cases being reported from rural areas of the western Cape. While the western Cape contains only 11% of the total population and 17% of farm workers in the country,[18] 37% of all notified poisonings nationally in 1991[10] were reported from the region. There appear to be three patterns in the profile of pesticide poisoning: (*i*) accidental poisoning of adults and children, involving both a farm worker group and people unconnected with farms; (*ii*) self-inflicted injury among adults; and (*iii*) occupational poisoning involving adult farm workers.

Accidental poisoning constitutes 40% of reported notifications and 70% of childhood poisonings. Sources of poison were frequently farm stores, but, for non-rural subjects, purchase from a retailer was an important source. Self-inflicted injury remains an important concern in pesticide safety. Almost one-half of adult notifications involved suicide attempts, and there was a significantly higher risk of fatal outcome with self-inflicted injury compared with other causes, particularly in farm workers, who constituted more than one-half of the patients with self-inflicted injury. Unauthorised access to farm stores is clearly an important point of intervention to prevent pesticide mortality and morbidity. The higher risk of a fatal outcome among farm workers may be related to the larger quantities and higher concentrations kept in pesticide stores, and does not appear to be explained by possible delays in treatment.

Workplace poisoning in the course of occupational exposure forms a small but significant proportion of cases. It should be noted that many of the accidental events that occur on farms are indirectly linked to occupation, through access, location and familiarity. Such events should also be addressed in promoting workplace safety in the agricultural sector. There is a growing worldwide realisation of the diversity of work-related disease and of the many different ways in which work may impact on human health.[20]

Prevention of childhood poisoning should be an important target of pesticide safety programmes in public health. While poisoning accidents have been recognised as an important risk for children, there were also 4 cases of self-inflicted injury and 5 cases of work-related poisoning, reflecting the use of child labour in the agricultural setting. Studies overseas have identified children as particularly vulnerable to workplace pesticide poisoning.[3]

The above data locate the problem of notified pesticide poisoning primarily in the agricultural setting,

where farm workers as a group had much lower education levels than other patients with poisoning. Farm workers, farmers or their families were most frequently involved in accidents, both immediately in the course of their work and outside of formal work. They were also involved in 50% of the self-inflicted injury cases in which they experienced a poorer outcome. Farm stores were the most important source of the poison and seasonal variation in the patterns of poisoning suggest a trough in winter (Fig. 5). This trend appears to follow the seasonal pattern of use of pesticides on the grape and fruit farms that form the major component of the region's agricultural sector, and may reflect greater opportunity for access during the spraying season. The presence of a peak in May could be traced partly to the occurrence of two multi-case accidents in 1988 and 1991 involving accidental ingestion of pesticides. The data were too sparse to analyse sub-populations of subjects meaningfully.

Conclusion

Improved surveillance will enable public health authorities to assess more accurately the extent of the problem, identify important areas for preventive programmes and evaluate the impact of such interventions. Methods employed in other countries to achieve this objective have included the use of Poison Centre Surveillance Networks,[21,22] the use of hospital records,[23] review of statutory medical illness reports[24] and the introduction of active surveillance that relies on cholinesterase testing.[25]

Data in this study have identified patterns in poisoning events that require intervention, particularly with regard to access to chemicals. Given undernotification, it is unclear whether these patterns are generalisable to less severe cases that are less likely to be notified. In response to the results of this and other studies, a pilot surveillance project in a selected rural area of the western Cape is planned, which aims to develop a method to improve surveillance for pesticide poisoning.[26]

In addition, the health inspectors of the local authority remain the key health care promoters in the control and prevention of pesticide poisoning. Their vigilance and follow-up of notified cases, rapport with the farming community, and liaison with general practitioners can play an invaluable role in improving awareness and preventing future incidents. To optimise the running of a surveillance programme, documentation and reporting should be made as concise and useful as possible, and to some extent, improvements in these areas have been made with the introduction of a new form (Epidemiological Investigation: Toxicology, DNHPD, Pretoria, 1993).[26] Such changes will assist in meeting the WHO recommendations for establishing a standardised reporting system that will distinguish intentional from unintentional poisonings, and that will identify preventable factors.[1]

To implement any pesticide safety programme successfully, the public health authorities need to have the co-operation of all the parties involved in the agricultural setting. There are ample signs that such co-operation is possible,[26] and that improvement in surveillance as part of a programme to address pesticide safety is an attainable goal.

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Critical Issues for Agrichemical Safety in South Africa

L. London, MB ChB, DOH, BSc, and J.E. Myers, BSc, MB ChB, DTMH, MD

A review is made of the potential for environmental and occupational exposure to agrichemicals in South Africa. Data from the farming industry in the Western and Southern Cape regions of South Africa confirm substantial use of a range of insecticides, fungicides, and other agrichemicals. The potential for worker exposure to hazardous agrichemicals is also substantial but, to date, such exposures have been poorly characterized. Further data identify important deficiencies in industrial hygiene measures with regard to safekeeping of chemicals on farms, disposal of empty containers, use of protective equipment, and levels of safety training among farm workers. Evidence is presented for widespread underreporting of agrichemical morbidity and mortality. Surveys investigating acute health effects among farm workers with occupational exposure to agrichemicals in South Africa have produced conflicting results. The possibility of chronic health sequelae from low-dose long-term exposure is an underresearched area that is only now being investigated. A number of important obstacles to agrichemical safety are identified: the multiplicity of laws relating to pesticides administered by different departments resulting in poor coordination; the failure of existing occupational health legislation to address the agricultural workplace adequately; the unavailability and incoordination of safety training; the absence of adequate surveillance data; and inadequacies in statutory requirements with regard to waste disposal on farms. Drawing on experiences of local initiatives, possible solutions are identified that address the public health context of the problem.

Key words: pesticides, South Africa, occupational exposures, environmental contamination, industrial hygiene practices, safety training, legislation, farm workers

INTRODUCTION

Pesticides and related chemicals are widely used in farming and public health programs worldwide. Estimates of global expenditure on agrichemicals exceeded 13 billion US dollars in 1986 [Watterson, 1988] and usage of pesticides has increased markedly over the past decades [World Health Organization (WHO), 1990a; British Medical Association (BMA), 1992], particularly in the less developed countries [Forget, 1991; BMA, 1992]. Despite their role in improving food production [BMA, 1992], agrichemicals have considerable potential for adverse human and environ-

Occupational Health Research Unit, Department of Community Health, University of Cape Town, Rondebosch, South Africa.
Address reprint requests to J.E. Myers, Occupational Health Research Unit, Department of Community Health, University of Cape Town, Medical School, Observatory, 7925, South Africa.
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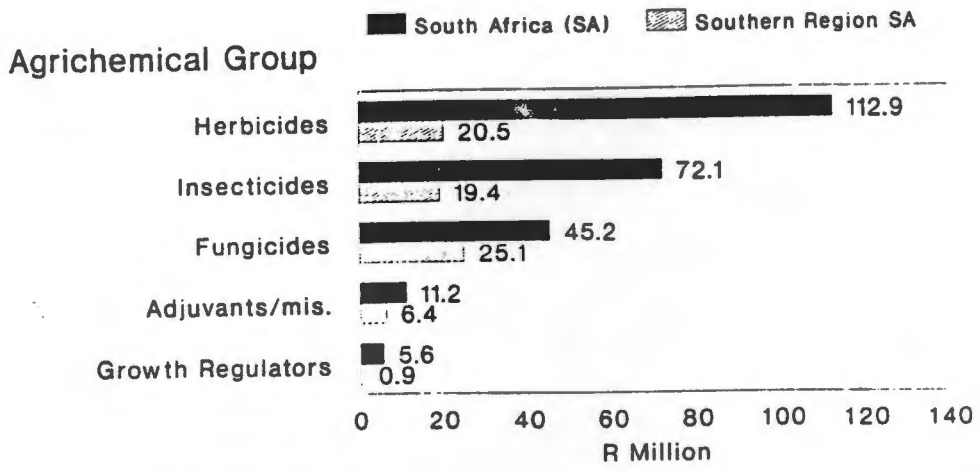

Source: London and Myers, 1993; Agricultural and Veterinary Chemicals Association (AVCASA), 1991.

Fig. 1. Agrichemical sales in 1990.

mental health effects [WHO, 1990a,b] and WHO estimates that one million cases of nonaccidental pesticide poisoning occur ever year [WHO, 1990b]. In the context of a global concern for human and environmental health [Davies, 1988; WHO, 1990b], there have been recent moves toward improving environmental health policy in South Africa [Department of Environmental Affairs, 1993]. This paper reviews the situation in South Africa with regard to agrichemical safety by examining the extent of possible hazardous exposures to agrichemicals and the implications for, and interrelationship between, occupational and environmental health. It reviews some of the existing data on agrichemical morbidity and mortality and the legislative framework in which agrichemical safety currently operates and goes on to identify key issues to be addressed in promoting agrichemical safety in South Africa.

HAZARDOUS EXPOSURES TO AGRICHEMICALS IN SOUTH AFRICA

The Agricultural and Veterinary Chemicals Association of South Africa (AVCASA) reports that $268 million was spent on agrichemicals in 1990 with the bulk of the market centered around crop protection in agriculture [London, 1992a]. Herbicides constitute the biggest proportion of the market (Fig. 1), particularly in the large scale maize farming regions.

However, assessment of human exposure is poorly served by figures on agrichemical expenditure. In South Africa, unlike the situation in other countries where there are statutory requirements for the reporting and monitoring of hazardous chemical exposures [Heikkila and Kauppinen, 1992], data on the quantities of different types of agrichemicals used in agriculture are not available. In 1978, the Department of Agriculture discontinued the collection of national reports from agrichemical companies on quantities of chemicals produced because of inaccuracies and unreliability of data [Barlin-Brinck, 1991; Emanuel, 1992]. As a result, no ongoing exposure surveillance data for agrichemicals are presently available in the country. The last

published figures for annual agrichemical use nationally are for 1978–1979 and amounted to 24,598 metric tons of active agrichemical, of which 39% was insecticides [Fourie, 1986].

OCCUPATIONAL EXPOSURE TO CHEMICALS IN AGRICULTURE

To address the paucity of quantitative information on chemical usage in agriculture, market research data from industry are utilized below to describe the usage patterns of agrichemicals in the southern region of South Africa. This region is dominated by fruit farming (pome, stone, vine, and citrus) and its pattern differs from the rest of the country (Fig. 1).

Data presented in Table I on patterns of agrichemical use in the region by main crop sector and by main chemical group are expressed as two measures of chemical quantity: 1) mass of active ingredient in Kg; and 2) mass of active ingredient standardized by LD50 (biological equivalents or BEs) [London and Myers, 1993]. The latter measure renders equivalent different chemicals based on their acute toxicity as represented by their LD50. From the data, it is clear that, for example, fungicides are most widely used in terms of quantity (4 million Kg), but that fumigants comprise the major biological hazard because of their high individual toxicity.

Using this approach, it is possible to analyze usage patterns in more detail. Table II presents data for insecticide use by insecticide category in the deciduous fruit industry, which forms the single largest agricultural activity in the region [Kassier, 1992]. Figure 2 lists the quantities (by Kg active ingredient and by BE) of the most commonly used individual agents in the same sector.

Among insecticides, organophosphates are the major component for deciduous fruit, and this is true of most other crop sectors in the region [London and Myers, 1993]. Moreover, of the six most commonly used individual chemicals in the sector by BE, four are organophosphates (Fig. 2). These data are potentially useful for generating exposure indices for workers in a particular agricultural sector to which an a priori exposure matrix may be applied [Nanni et al., 1993]. This method of estimating exposure is being implemented in a study investigating the potential long-term health effects of chronic exposure to agrichemicals utilized in the Western Cape region of South Africa.

Workers known to be at highest risk of exposure in agriculture include applicators and mixers [Moses, 1983; Coye and Fenske, 1988], particularly if working in confined spaces such as greenhouses or tunnels [London and Myers, 1993]. However, workers involved in routine farm work such as picking or thinning fruit may also be subject to indirect exposure from spray drift in the fields or by contact with chemical residues on crops and trees [Wicker and Guthrie, 1980; Davies et al., 1982; Griffith and Duncan, 1985]. In a random sample of 45 farms in a rural area of the Western Cape, approximately 9% of permanent workers and 14% of seasonal workers were employed in activities where such indirect exposures existed [London, 1992b].

In the same survey, usage of protective equipment (Fig. 3) and levels of training were low and industrial housekeeping extremely variable [London, 1992b]. These factors have been noted to influence actual exposures experienced by workers [Moses, 1983; Coye and Fenske, 1988; London and Myers, 1993]. Because of the multifactorial determinants of workplace exposure, further research is planned to

TABLE I. Agrichemical Usage Patterns in the Southern Region of South Africa by Main Crop Sector and Agrichemical Group, 1989*

	Deciduous	Vine	Citrus	Total
Insecticide				
Kg	231.569	54.790	112.370	567.122
BE	5.552	204	2.034	10.984
Fungicide				
Kg	724.470	2.149.780	25.780	4.067.396
BE	137	141	15	660
Herbicide				
Kg	139.240	211.190	35.030	714.552
BE	167	206	61	1.012
Fumigants				
Kg	—	14.760	4.710	130.713
BE	—	7.618	3.986	26.967
Growth reg				
Kg	3.020	3.480	1.300	14.796
BE	20	28	20	87
Acaricides				
Kg	39.460	5.000	1.150	48.502
BE	105	1	0.2	117
Seed treatment				
Kg	—	—	—	17.240
BE	—	—	—	18
Oil				
Kg	894.491	49.583	327.320	1.222.062
BE	—	—	—	—
Miscellaneous				
Kg	204.980	50	155.610	361.234
BE	4	0.1	0.1	5
Total				
Kg	2.237.230	2.488.633	663.270	7.143.618
BE	5.985	8.198.1	6.116.3	42.580

*Data from London and Myers [1993].

TABLE II. Insecticide Usage in Deciduous Fruit Farming, Southern Region of South Africa, 1989*

Insecticide group[a]	Kg active ingredient	Biological Equivalent
Organophosphates (17)	144.503	4.084
Carbamates (5)	11.840	20
Organochlorines (1)	32.728	449
Dinitrophenol (1)	32.711	991
Miscellaneous (12)	1.689	8
Total (36)	223.471	5.552

*Data from London and Myers [1993].
[a]Number of different agents is in parentheses.

validate job-exposure matrices for application to different agricultural sectors in South Africa.

Other than farming, occupations in which potential exposures to agrichemicals

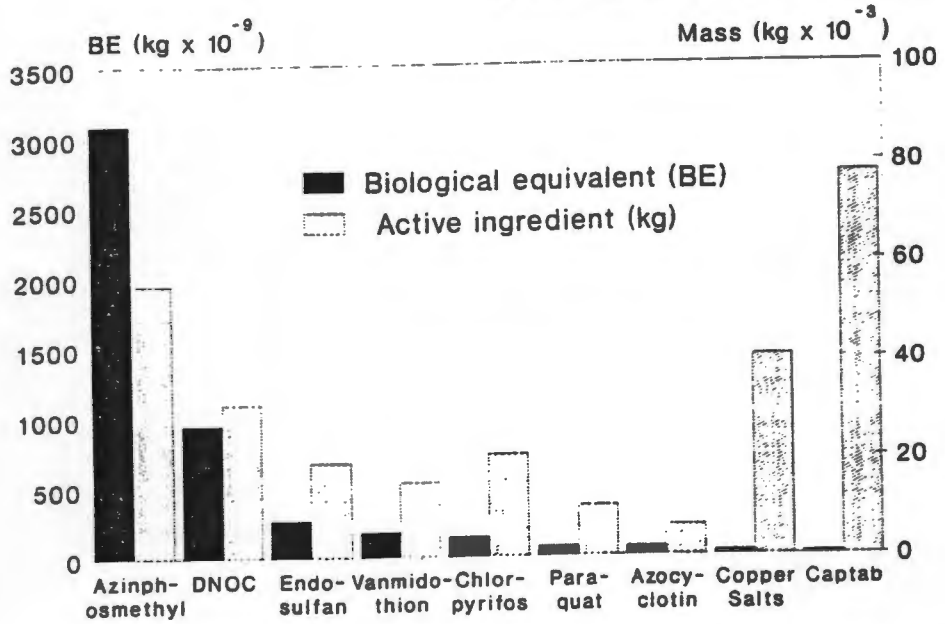

Fig. 2. Leading agrichemicals in 1989: deciduous fruit farming in Southern region of South Africa. Mineral oil (844.908 kg; 0 BEs), sulphur (321.152 kg; 0 BEs) not included. Source: London and Myers, 1993.

exist are listed in Table III [Moses, 1983; Coye and Fenske, 1988]. A study in 1989 of workers involved in a malaria control program in Natal found raised serum levels of DDT and its metabolites and evidence of impaired liver function [Bouwman et al., 1991] but the health implications for these workers remain unclear. While little production of pesticides occurs in South Africa, the occupational risks arising in the production process are demonstrated by the death of a worker due to organophosphate intoxication at a plant in the Transvaal in 1988 [Department of Justice, 1988]. However, the extent of many of these nonfarming exposures and their potential health effects have yet to be adequately quantified in South Africa.

IMPLICATIONS FOR ENVIRONMENTAL AND OCCUPATIONAL HEALTH

Evidence for the poor state of general occupational safety on farms in South Africa [Myers, 1990] is provided by annual reports of nonchemical occupational accidents in South Africa in which mortality in farming is twice that of nonagricultural industries [Workmen's Compensation Commissioner, 1988]. In addition, industrial hygiene practices for chemical safety in agriculture have been reported as inadequate [Emanuel, 1992]. In an audit of farm pesticide stores in the Western Cape, more than half were found to be unlocked at the time of inspection, and a number of farms had no secure locking facility. In addition, almost half of the farms had excess residual unwanted stocks of pesticides in their stores, including chemicals no longer registered for use; and about a third of farms were unable to dispose of empty containers because of prohibitive costs [London, 1992b]. These findings are replicated in research from other areas in the Cape [Reid, 1991, personal communication, Child Health Unit, Red Cross Children's Hospital, Cape Town; Emanuel, 1992].

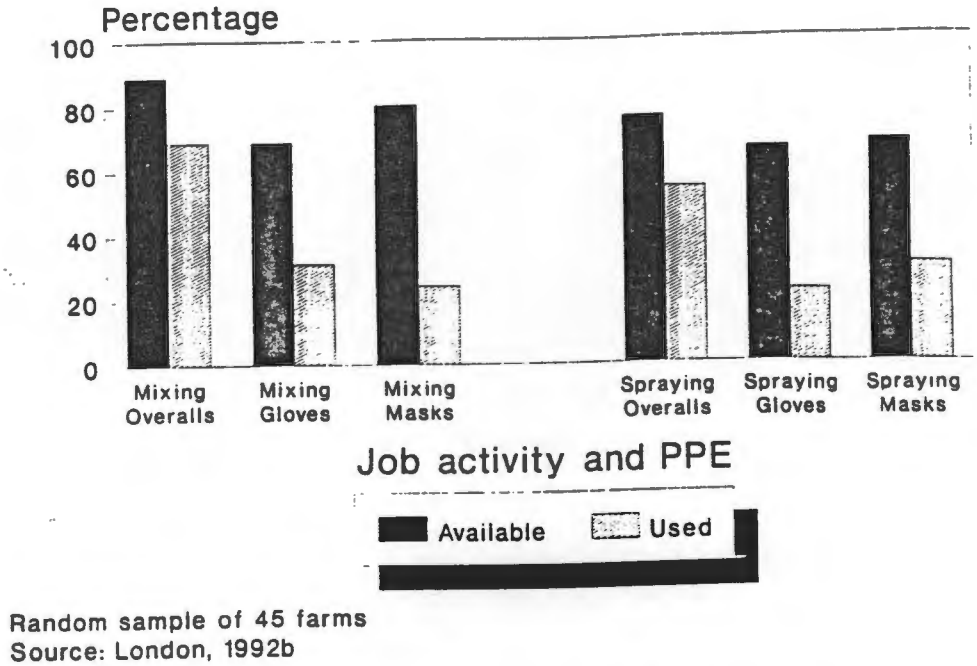

Fig. 3. Personal protective equipment availability/use on Western Cape farms.

TABLE III. Occupations With Potential Agrichemical Exposure*

- Agriculture
  - Direct: application, mixing, storage
  - Indirect: field work, spray drift
- Public health personnel: vector control
- Forestry workers
- Aerial spray pilots and maintenance staff
- Commercial pest control operators
- Malaria control workers
- Manufacture, formulation, and packaging workers
- Chemical transport
- Municipality/parks employees
- Railway workers applying wood preservatives
- Dock workers

*Data from Moses [1983] and Coye and Fenske [1988].

Given that many cases of notified pesticide poisoning are related to unauthorized access by rural residents to nearby pesticide stores on farms [London et al., 1993], such inadequacies in safety practices pose considerable public health risk. While this has been identified as an important problem by growers, the health authorities, and the agrichemical industry alike [Emanuel, 1992; Medical Association of South Africa (MASA), 1993], efforts to address this problem remain uncoordinated and underresourced.

While problems of poor industrial hygiene and inadequate safety practices are tragically ubiquitous in less developed countries [Pesticides Trust, 1987; Forget, 1991; BMA, 1992], this problem cannot be blamed on an inadequate technical in-

frastructure in South Africa, where extensive state support has been provided to white farm owners over past decades [Cooper, 1990]. Unlike most other less developed countries [Hoglund, 1990; Forget, 1991], the majority of South Africa's 1.19 million farm workers [Central Statistical Services, 1990] are not self-employed but employees on white-owned farms [Cooper, 1990]. Many different authors have identified the frequently harsh employment conditions existing for farm workers [Keenan and Sarakinsky 1987; Ball, 1990; Cooper, 1990; Bosch, 1991a] that have contributed to the lack of occupational and environmental health protection in the South African farming sector.

ENVIRONMENTAL CONTAMINATION

Few studies have investigated the extent of environmental contamination from agrichemical application in South Africa. Elevated levels of DDT and its metabolites have been found in breast milk of lactating mothers in a rural area of Natal where DDT is widely used for malaria vector control [Bouwman et al., 1990]. Another study among plantation workers in the Northern Transvaal exposed to organophosphates found that rural control subjects had lower cholinesterase levels than the occupationally exposed group and the authors' hypothesis was that widespread environmental contamination was responsible [Jaga et al., unpublished data].

While water table contamination by agrichemicals has been a major focus of public health research in the United States [Hogmire et al., 1990], little comparable data are available for South Africa. Two studies conducted in the Western and Northern Cape for the Department of Water Affairs found little evidence of ground water contamination by currently used pesticides [Weaver, 1993]. However, in the one study, surface water entering an irrigation scheme was found to have high levels of atrazine which was thought to have occurred as a result of run-off from surrounding maize growing areas [Weaver, 1993].

Because farm workers' residences in South Africa are frequently located within or adjacent to orchards, vineyards, or fields [London, 1992b], domestic contamination may arise from contamination of drinking or washing water, or by direct drift of spray into households. Reuse of contaminated containers for domestic purposes (drinking water, washing) has been shown to be responsible for a number of episodes of acute poisoning reported to the Department of National Health and Populations Development [London et al., 1993] and may be another significant source of environmental contamination [Emanuel, 1992]. These hypotheses concerning mechanisms of domestic exposure require further elaboration, since such routes may add considerably to the lifetime burden of chemical exposure of individuals in rural areas and may be important in the etiology of adverse health effects of chronic low-dose agrichemical exposures.

SAFETY TRAINING

Training facilities for pesticide safety appear to be poorly coordinated and not standardized. Less than 20% of farm workers in high exposure jobs receive safety training in handling pesticides [Emanuel, 1992; London, 1992b]. This is further aggravated by low levels of literacy among farm workers generally [De Graaf et al., 1990]. Levels of training of farmers have also been found to be low [London, 1992b].

Until recently, no legal obligation on employers existed to ensure training of

workers involved in handling pesticides. However, recent legislation now makes mandatory the training of safety representatives and workers who are in contact with potential occupational toxins [Department of Manpower, 1993]. Proposed changes to the Fertiliser, Farm Feed and Stock Remedies Act [Department of Agriculture, 1983] are said to require certification of all purchasers of pesticides [personal communication, Mr. P. Wessels, AVCASA, 1992]. While these changes would aim to encourage the extension of safety training, there are serious doubts as to the effectiveness in practice given the lack of clarity on the content and quality of training and doubts as to the enforceability of such regulations. Nonetheless, important interventions can be made by the Department of Manpower in setting statutory minimum standards for safety training.

Within the farming community, efforts to address the need for safety training have been sporadic. The Rural Foundation, a private sector initiative, runs a Farm Health Worker program focused on primary health care that covers approximately 660 farms and 80,000 rural farm residents in different areas around the country [Rural Foundation, 1993]. However, until recently, prevention of occupational and pesticide hazards has not been included in the program. Nonetheless, it is encouraging that the overwhelming majority of farmers (84%) referred to in the previous survey audit were supportive of the need for safety training of their workforces [London, 1992b] and that the deciduous fruit industry in particular is developing work groups to address preventive health needs in agriculture.

ADVERSE HEALTH EFFECTS OF PESTICIDES IN SOUTH AFRICA: WHAT DO WE KNOW?

As with many other health problems in South Africa, data on pesticide morbidity and mortality are scant. Current legislation requires the notification of all cases of pesticide poisoning to the Department of National Health and Population Development in terms of the Health Act [Department of National Health and Population Development, 1977]. Based on notifications, about 100–150 cases are notified nationally every year with a fatality rate of 5–10%.

Ample evidence of substantial undernotification of acute morbidity exists. Poison centers around the country consistently report consultations for possible pesticide poisoning far in excess of national notifications [London et al., 1993]. Incidents of pesticide poisoning accounted for between 9 and 13% of poison center consultations at the Red Cross Children's War Memorial Hospital in Cape Town in 1987 [Roberts et al., 1990], while a similar study of childhood poisoning in the Orange Free State in 1988 found that 12% of poisonings involved pesticides [Van der Werwe and Botha, 1991]. Data from poison center experience in one major teaching hospital in Cape Town found that agrichemicals were implicated in 38% of all consultations for poisoning queries involving nondrug chemicals, the majority of which came from nonagricultural settings [Muller et al., 1993].

Estimates of poisoning by pesticides based on more defined outcomes confirm the problem of underreporting. A study of fatalities seen at a Cape Town mortuary in 1979 suggested that only 5% of cases of fatal pesticide poisonings had been notified [Coetzee, 1981]. More recent surveys of hospital admissions suggested that approximately 20% of cases (fatal and nonfatal) were being notified [Emanuel, 1992; London et al., 1993]. Reasons for underreporting include the failure of health personnel

to notify, misdiagnosis of milder forms of poisoning, and difficulties of access to health care in rural areas.

While biological monitoring of workers in contact with pesticides, particularly cholinesterase monitoring in plasma and erythrocytes, has been used as the basis for active surveillance directed at worker safety in many countries [Coye et al., 1986; Ames et al., 1989], it has not been widely practiced in South Africa. One study of 47 spraymen on a fruit farm near Cape Town in 1989 found that 15% of workers involved in routine spraying had biochemical evidence of organophosphate exposure resulting in reduction of plasma cholinesterase activity [Innes et al., 1990]. Another cross-sectional study in the rural area of Venda in the Northern Transvaal found that coffee plantation workers had lower plasma cholinesterase levels than laboratory controls [Jaga et al., unpublished data].

However, results from a survey of 134 apple farm workers near Cape Town who applied agrichemicals found little change in serum and erythrocyte cholinesterase across spraying season when compared to packing store workers undergoing single measurements [Barnes et al., unpublished data]. These conflicting results may be attributed to poor study design and inadequate exposure assessment in these studies. Much work needs to be done to document the nature of the problem through simple but well-designed active surveillance programs.

The spectrum of chronic morbidity arising from pesticide exposure has been partly documented. This includes long-term neuropsychological sequelae following acute pesticide poisoning [Savage et al., 1988; Rosenstock et al., 1991] and peripheral neuropathy arising as a long-term consequence of acute pesticide intoxication with a number of organophosphate insecticides [WHO, 1986]. While measurement of neuropathy target esterase (NTE) has been advocated for predicting the onset of organophosphate-induced delayed peripheral neuropathy [Maroni et al., 1986; Lotti, 1986], markers for chronic exposure or of chronic biological effects are presently unavailable.

Increasing attention is being directed at the possibility of chronic neurotoxic morbidity arising from long-term low-dose exposures among farm workers who do not present with acute clinical pesticide-related disease [Ilani et al., 1988; Rosenstock et al., 1990; Daniell et al., 1992]. An investigation of the possible long-term psychological and neurological effects of chronic pesticide exposure is currently being undertaken in the fruit industry in the Western Cape.

LEGISLATIVE FRAMEWORK FOR AGRICHEMICAL SAFETY

Currently, pesticide safety legislation and administration in South Africa are characterized by extensive duplication, overlap, and poor coordination among a range of state departments. To a large extent, this reflects the situation with the regulation of nonagricultural hazardous chemicals in general, where the environmental, occupational, and scheduling responsibilities for health are divided across different state departments. Table IV summarizes the diverse pieces of legislation that pertain to agrichemical safety in South Africa at present, and the state departments to which they refer.

Because of multiple administrative bureaucracies, a potential for gaps exists in the legislative framework, and the respective inspectorates are largely understaffed and undertrained to enforce such legislative measures as do exist. While fairly rig-

TABLE IV. Legislative Framework for Agrichemical Safety in South Africa

State department	Legislation and scope
Agriculture	Fertiliser, Farm Feeds, and Stock Remedies Act (36/47) Registration, labeling, distribution classification toxicity
Health and Population Development	Health Act 63/77: notification Hazard Substance Act 15/73: class of toxicity, licensing Foodstuffs, Cosmetics Act (54/72): maximum permissible residues in food
Manpower	MOS Act: Occupational Safety Workmen's Compensation
Water Affairs	Environmental Conservation Act
Environmental Affairs	Environmental Conservation Act

orous legislative measures exist to control the importation, registration, distribution, retailing, and labeling of agrichemicals [Barlin-Brinck, 1991; London, 1992a], the prevention of hazards in the storage or application of pesticides in agriculture, safety training, and medical surveillance of potentially affected workers are not covered [Barlin-Brinck, 1991; Emanuel, 1992; London, 1992a]. This stands in sharp contrast to requirements in the United Kingdom [Ministry of Agriculture, Fisheries and Food, 1990] and the United States [Ames et al., 1989; Fillmore and Lessenger, 1993], where substantial statutory requirements exist to ensure agrichemical safety and health.

New legislation directed at general workplace safety in South Africa [Department of Manpower, 1993] covers agriculture, and medical monitoring of exposed farm workers will become mandatory. However, what these changes will mean in practice is unclear. The traditional exclusion of farm workers from protective labor legislation in the past, the isolation of rural farm workers, and the traditional authoritarian work environment and culture in agriculture [Keenan and Sarakinsky, 1987; Ball, 1990; Bosch, 1991a] have meant that farm workers as a group have developed little capacity to demand and obtain adequate health and safety measures in their workplaces. Despite the recent extension of collective bargaining rights to farm workers [Bosch, 1991b; Benjamin, 1993], unionization is marginal at present, and unlikely to address issues of health and safety as a priority. Therefore, the likelihood that preventive measures for health and safety in agriculture will be achieved through collective bargaining is slim for the near future at least.

Nonetheless, opportunity exists for the State to coordinate and streamline its administrative and regulatory functions in order to create a coherent framework for the promotion of chemical safety in agriculture. Evidence is emerging that environmental health policy is to be rationalized in the future [Department of Environmental Affairs, 1993]. Crucial inputs at the level of policy need to be made by all important role players, which should include the farming and the agrichemical industries, organized labor, nongovernmental organizations, environmental groups, and research institutions. Regulatory developments in South Africa are rapidly acquiring a tripartite character [Bosch, 1991a; Bilateralism Project, 1993], with equal participation from labor, capital, and the State. In addition, environmental groups represent another constituency with legitimate interests in the question of agrichemical safety. It remains to be seen if the environmental movement in South Africa, still in its relative infancy, can effectively influence environmental health policy.

INTEGRATED PEST MANAGEMENT

Agricultural practices globally have been significantly altered by the introduction of alternative nonchemical technologies such as the use of biopesticides or the use of natural insect predators to control pests [Watterson, 1988; BMA, 1992; Leslie and Cuperus, 1993]. In South Africa, the development of an integrated approach to pest control has been utilized in the deciduous fruit [Wooldridge and Botha, 1991] and citrus [Bedford et al., 1985] industries, but has yet to make a widespread impact on agricultural production as a whole. The development of local pest resistance and overseas market considerations are the main pressures driving the move towards nonchemical control of pests. The development of a mainstream approach to pest control that reduces reliance on chemical control merits greater attention.

CONCLUSIONS

Given the potential for conflicts of interests between differing parties, and the background of poor labor relations in the agricultural sector, chemical safety is a highly charged issue. Critical issues which need to be addressed are: 1) the implementation of appropriate and effective worker and employer education programs on agrichemical safety with standardization of content and quality of training; 2) improved workplace and environmental surveillance and monitoring; 3) the development of creative approaches to the question of toxic chemical waste in a setting traditionally unconcerned with industrial pollution; and 4) the promotion of ongoing research to address the extent of adverse health outcomes and the effectiveness of control measures, particularly with regard to possible environmental hazards and morbidity arising from chronic exposures.

Public health authorities have a key role in this regard, particularly in light of the need to address farm worker and rural community health in terms of a holistic developmental approach. A collaborative effort, involving all major players in the area, may be able to address many of these key issues. Recent experiences in the Western Cape fruit industry indicate that important initiatives with regard to research into chronic health effects of occupational exposures, surveillance for acute morbidity and mortality, models for agrichemical waste disposal, and health and safety training may be able to achieve important advances in the promotion of agrichemical safety.

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Repeatability and validity of a field kit for estimation of cholinesterase in whole blood

L London, M L Thompson, S Sacks, B Fuller, O M Bachmann, J E Myers

Abstract

***Objectives*—To evaluate a spectrophotometric field kit (Test-Mate-OP) for repeatability and validity in comparison with reference laboratory methods and to model its anticipated sensitivity and specificity based on these findings.**

***Methods*—76 farm workers between the age of 20 and 55, of whom 30 were pesticide applicators exposed to a range of organophosphates in the preceding 10 days, had blood taken for plasma cholinesterase (PCE) and erythrocyte cholinesterase (ECE) measurement by field kit or laboratory methods. Paired blinded duplicate samples were taken from subgroups in the sample to assess repeatability of laboratory and field kit methods. Field kits were also used to test venous blood in one subgroup. The variance obtained for the field kit tests was then applied to two hypothetical scenarios that used published action guidelines to model the kit's sensitivity and specificity.**

***Results*—Repeatability for PCE was much poorer and for ECE slightly poorer than that of laboratory measures. A substantial upward bias for field kit ECE relative to laboratory measurements was found. Sensitivity of the kit to a 40% drop in PCE was 67%, whereas that for ECE was 89%. Specificity of the kit with no change in mean of the population was 100% for ECE and 91% for PCE.**

***Conclusion*—Field kit ECE estimation seems to be sufficiently repeatable for surveillance activities, whereas PCE does not. Repeatability of both tests seems to be too low for use in epidemiological dose-response investigations. Further research is indicated to characterise the upward bias in ECE estimation on the kit.**

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Keywords: cholinesterase; field kit; repeatability

Occupational Health Research Unit, Department of Community Health, University of Cape Town, Anzio Road, Observatory
L London
O M Bachmann
J E Myers

Department of Statistical Sciences, University of Cape Town, Private Bag Rondebosch, 7700
M L Thompson

Department of Chemical Pathology, Groote Schuur Hospital, University of Cape Town, Anzio Road, Observatory, 7925
S Sacks
B Fuller

Correspondence to:
Dr L London, Occupational Health Research Unit, Department of Community Health, University of Cape Town, Anzio Road, Observatory 7925, South Africa.

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Agrichemicals are extensively used in farming and public health programmes worldwide and their potential for adverse health effects is considerable.[1 2] Biological monitoring of humans potentially exposed to agrichemicals has been widely recommended for the prevention of pesticide poisoning[3 4] and for purposes of epidemiological research.[5] Proposed changes to South African occupational health legislation[6] are likely to make medical monitoring of workers exposed to potentially hazardous chemicals mandatory and thus bring statutory requirements into line with international standards.[4 7] Given that farm workers will fall under the ambit of the new legislation,[6] attention is likely to be directed at identifying cheap and practical methods that are both reliable and valid for field monitoring of workers exposed to agrichemicals.

Organophosphates and carbamates constitute the most widely used insecticides in South Africa at present,[8 9] and measurement of serum and red blood cell cholinesterase is widely used to monitor exposed people.[1 3 6 10 11] Decreased plasma cholinesterase (PCE) activity is regarded as a marker of recent exposure, and in erythrocytes (ECE) of neuronal toxicity.[3] The magnitude of cholinesterase depression is also used as an action guide for removal of a worker from further exposure.[3 4]

Laboratory methods for estimating cholinesterase activity have been well described.[3 12] For public health purposes, however, methods of field cholinesterase estimation are advantageous. Field kits, with either tintometric or kinetic spectrophotometry, are available.[3 12] Studies have found that the kinetic spectrophotometry has better precision for estimation of erythrocyte cholinesterase than has the tintometer,[12] particularly when standardised for haemoglobin concentration in the blood.[13] This method is being used in developing countries as part of the East Africa pesticide network project[14] and has been reported as being sufficiently precise to obviate the need for laboratory specimens.[15] As a result of promising initial research results, the World Health Organisation is currently helping to develop the spectrophotometric method as a valid and reliable field device for estimation of cholinesterase.[16]

Published data on the precision and validity of such field methods are not available, and their usefulness in field studies on health effects of exposure to pesticides is still unclear. To fill some of these gaps, this study aimed to assess the repeatability and validity of the field kit for estimation of cholinesterase by the spectrophotometric method (Test-Mate OP kit)[12 13] in relation to standard laboratory methods based on the procedure of Ellman *et al.*[17] Farm workers in the Western Cape region of South Africa provided the specimens. These data were then used to model the sensitivity and specificity of the kit in

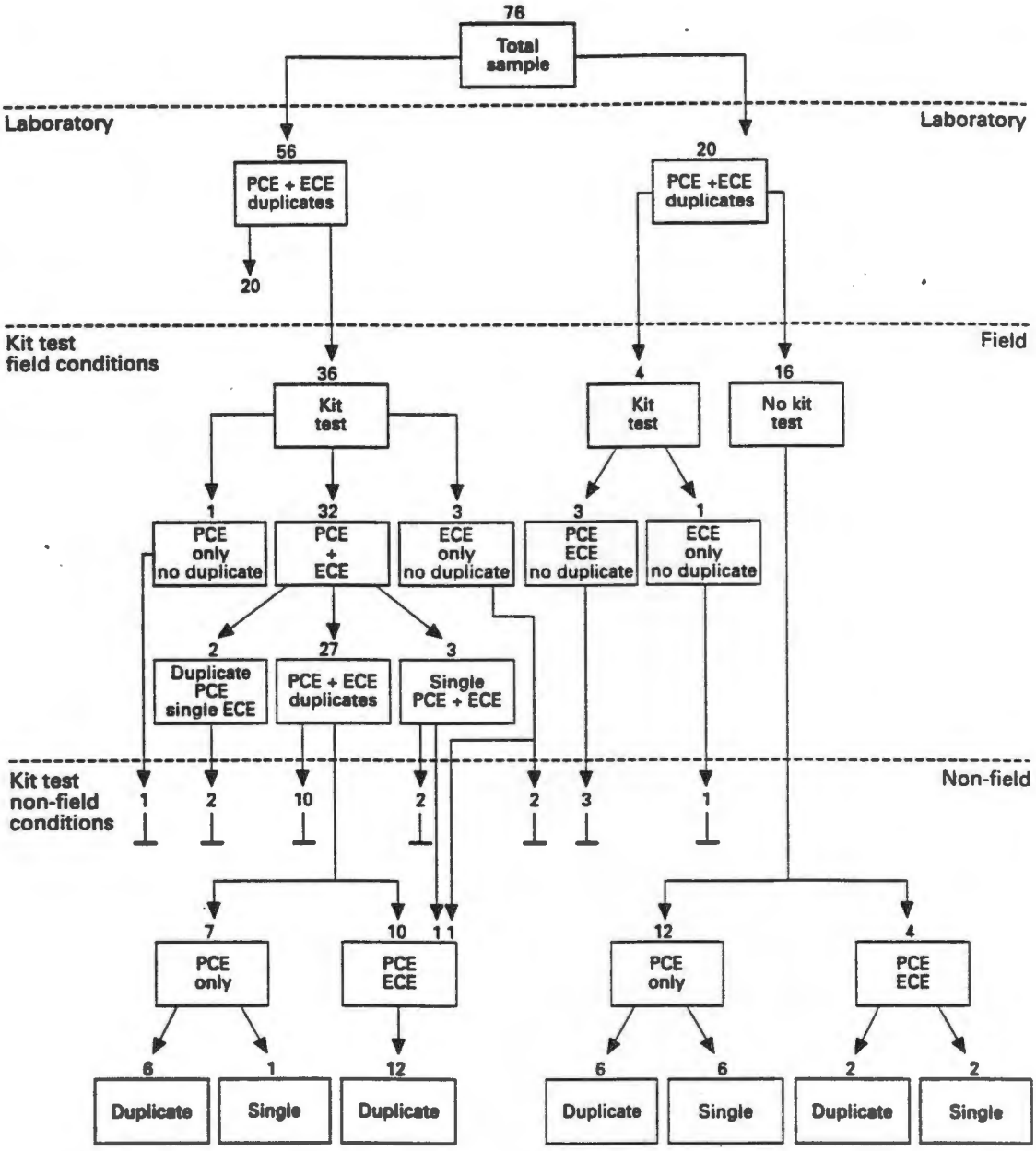


Figure 1 Cholinesterase testing in the study sample.

the detection of critical changes in cholinesterase activity. The study was performed as part of a larger investigation of potential long term adverse health effects arising from exposure to agrichemicals among fruit farm workers for whom laboratory estimations of PCE and ECE were being collected.

Methods

The total sample consisted of 76 subjects who received either field kit or laboratory estimations of PCE and ECE activity or both (fig 1). The sample was accumulated on three successive field trips during a period of three weeks in March 1993 and included 80% of the participants who attended for the larger neurotoxicity study already referred to. All subjects were male workers between the ages of 20 and 55, and included 30 workers involved in agrichemical application who had been exposed to a range of organophosphates within the past 10 days.

Field procedures for blood sampling were as follows: 10 ml of heparinised venous blood was taken from each subject for cholinesterase estimation. Fifty six subjects had a second sample taken with a false subject name for blinded laboratory repeat PCE and ECE estimations. Venous blood was kept on ice and reached the laboratory within eight hours of venepuncture. Field kit estimations were performed on 10 μl of blood derived from a finger prick according to methods described by the suppliers.[13 18] One examiner was responsible for all field kit estimations (MB). Attention was paid to avoid excessive thermal exposure or vibration damage to the device during transport, and temperature on the collection days ranged between 20 and 28° C.

Subgroups of subjects underwent repeat finger prick field tests (non-blinded) during the same sampling session for PCE and ECE. Also, parallel estimations of field kit PCE and ECE (duplicate and non-duplicate) were performed on heparinised venous blood from another subgroup of subjects on the same day under non-field conditions. Figure 1 shows the numbers in the groups. The differing numbers of subjects included in various tests and

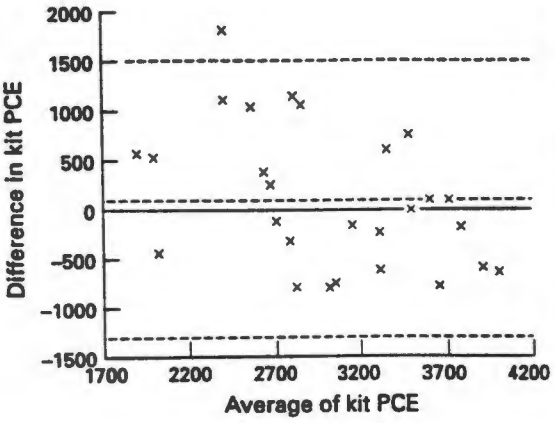


Figure 2 Repeatability: difference in field kit PCE v mean field kit PCE.

settings were the result of logistical constraints imposed by the field conditions under which data were collected as part of a larger study.

Laboratory estimation of cholinesterase was performed at the Chemical Pathology Laboratory at Groote Schuur Hospital, a large teaching hospital in Cape Town. The PCE was measured by the method of Knedel and Bottger with butyrylthiocholine as substrate[19] and ECE by the method of Ellman *et al*[17] with acetylthiocholine as substrate. Haemolysates for ECE were prepared as described previously.[20] Reagents were supplied as kits (Boehringer-Mannheim) and analyses were performed at 30°C with an automated analyser (Hitachi 704). Commercial quality control serum samples, two each for PCE and ECE (Precipath and Precinorm, Boehringer-Mannheim) were run within the batches of assays for PCE and ECE and good agreement was found with the stated mean values provided by the suppliers.

Field kit estimation for PCE uses butyrylthiocholine and ECE uses acetylthiocholine as a substrate and determines cholinesterase activity on whole blood by means of a battery powered computer driven colorimeter. The ECE field kit assay makes use of an inhibitor As1397 to prevent PCE interference in whole blood (R Magnotti, personal communication, 18 June 1992). Steps in the assay are guided by digital commands, key activated functions and computer generated timing to assist reproducibility. The kit has a photometric haemoglobinometer, and performs an automated adjustment for haemoglobin concentration as well as a correction for assay results to 25°C based on an inbuilt temperature sensor.[18]

For comparison between laboratory and kit methods, results obtained from the kit for PCE were corrected from 25° to 30°C by multiplying kit results by a temperature factor of 1·24 and by a factor of 1000 to adjust from U/ml to U/l, and multiplying laboratory results by (1-packed cell volume) to adjust to measurement on whole blood. For ECE, results were standardised by haemoglobin concentration,[13] and kit estimates were corrected to 30°C by multiplying by a factor of 1·28. Results for PCE (U/l) and ECE (U/g haemoglobin) are therefore given corrected to 30°C.

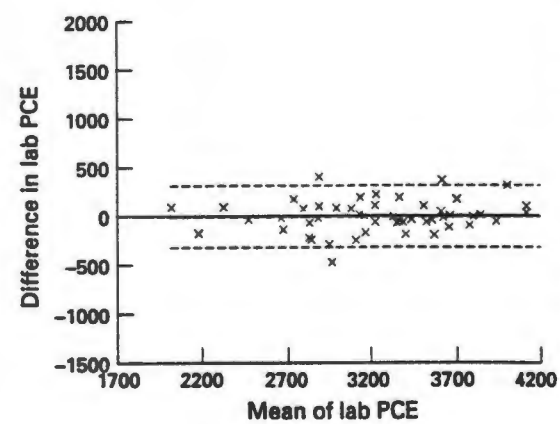


Figure 3 Repeatability: difference in laboratory PCE v mean laboratory PCE.

ANALYSIS

Three methods of determination of PCE and ECE are compared in this study: field application of the kit, non-field application of the kit, and laboratory. Repeatability of each method was assessed by comparing duplicate measurements taken with the same method (field kit, kit under non-field conditions, or laboratory) and kit (field or non-field) validity was assessed by comparing kit measures with those from the laboratory on the same subjects.

The statistical assessment of repeatability and validity has been discussed in some detail by Bland and Altman.[21] For each assessment, the Pearson's correlation coefficient was determined to establish the degree of linear agreement between the two measures under consideration (repeat measures under one method for reliability or comparison of one method with another for validity). The Pearson statistic was used after having first confirmed normality of the distributions. Plots were also constructed of the difference in the two measurements *v* their average.[21] Such plots enable one to graphically display the variability across repeat measurements and to identify any tendency for that variability to change with activity. For reasons of brevity, only the plots for repeatability and validity of PCE are presented.

The mean (SD)—that is, the bias—of the differences were also determined. The SD of the difference across duplicate measurements with the same method provides an estimate of the repeatability of that method. Two SDs is the definition of a repeatability coefficient adopted by the British Standards Institution,[22] and this was used to calculate a lower limit (mean difference − 2 SD) and an upper limit (mean difference + 2 SD) of agreement. The use of the SD as a measure of variability requires approximate normality of the differences, which was verified in each case. Analyses were carried out with the SAS and Statgraphics statistical packages.[23 24]

Comparison was then made to recognised activity standards for changes in cholinesterase activities[3 4] to assess how well the kit would perform as a monitoring tool. Based on the variability of kit results, and with the baselines obtained in the study for PCE and ECE, the probability was estimated of missing a

Table 1 Repeatability of cholinesterase measurements

Method* n	Mean	Correlation†	Mean difference (95% CI)‡	Limits of agreement (95% CI)§		
PCE:						
FK 29	3091·2	0·59	95·3 (−172·2 to 362·8)	Lower	−1311·6	(−1774·9 to −848·2)
				Upper	1502·2	(1038·8 to 1965·5)
NFK 26	3561·2	0·84	3·8 (−208·9 to 216·5)	Lower	−1049·2	(−1417·7 to −680·8)
				Upper	1056·8	(688·4 to 1425·3)
Lab 56	3374·9	0·97	−11·6 (−53·5 to 30·3)	Lower	−331·7	(−404·3 to −259·1)
				Upper	308·5	(235·9 to 381·1)
ECE:						
FK 27	45·1	0·85	1·3 (−0·10 to 2·70)	Lower	−5·76	(−8·18 to −3·34)
				Upper	8·36	(5·94 to 10·78)
NFK 14	45·7	0·32	1·3 (−1·64 to 4·24)	Lower	−8·90	(−14·00 to −3·80)
				Upper	11·50	(6·40 to 16·60)
Lab 56	36·0	0·96	−0·1 (−0·48 to 0·28)	Lower	−2·91	(−3·66 to −2·34)
				Upper	2·89	(2·14 to 3·46)

* FK = field kit; NFK = non-field kit; Lab = laboratory.
† Pearson's correlation between repeat measures.
‡ Average difference across repeat measures.
§ Lower limit = mean difference between repeat measures less 2 SDs of the difference between repeat measures.
Upper limit = mean difference between repeat measures plus 2 SDs of the difference between repeat measures.

30% drop in baseline cholinesterase in the presence of a true drop of 40% (false negatives), as well the probability of finding an apparent 30% drop in the presence of an unchanged "true" baseline (false positives) for both PCE and ECE.

Results

REPEATABILITY

PCE determinations

Figures 2 and 3 show plots of the difference in the duplicate PCE measurements *v* their average for the field kit and laboratory respectively, and indicate graphically the limits of agreement, and the mean difference based on repeat measures.[21] Table 1 shows these estimates with 95% confidence intervals (95% CIs), and the correlation coefficients based on repeat measures.

As is to be anticipated from duplicate measures, there is essentially no bias (the 95% CIs for all mean differences include 0), but the repeatability of the laboratory measurements of PCE is clearly far better than that of the field kit, with a much narrower 95% CI in the mean difference for laboratory measures. This is shown in the greater scatter of results of PCE estimations found for the kit (fig 2) than for the laboratory (fig 3). No trend in differences was found across a range of PCE measurements for either kit or laboratory measures.

The PCE repeatability coefficient (implicit in table 1 as the upper limit of agreement less the mean difference) for the field kit is 4·4 times greater than the repeatability coefficient for the laboratory and 1·3 times that of the kit under non-field conditions. This suggests worse agreement for repeat field kit PCE measurements relative to laboratory measurements, with some improvement when the kit is used under non-field rather than field conditions.

ECE determinations

Table 1 shows the estimates of the correlation between repeated measures of ECE on the field kit and in the laboratory, the mean differences, and the upper and lower limits of agreement.

Once again, the repeatability of the laboratory measurements is far better than that of both the field and non-field application of the kit. In this case, the repeatability of the non-field kit is worse than that of the field kit, but this is based on a small sample (n = 14). The repeatability coefficient of the field kit ECE, implicit in table 1 as the upper limit of agreement less the mean difference, is 2·4 times that of the laboratory. Although the field kit ECE still performed worse than the laboratory, this represents an improvement in quality when compared with the PCE repeatability.

VALIDITY

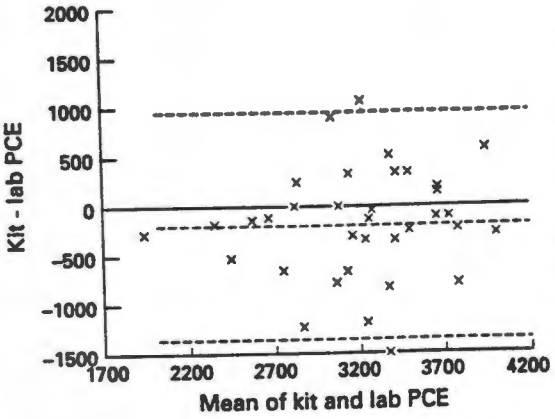
PCE determinations

Figure 4 shows a plot of the difference between kit (under field conditions) and laboratory PCE measurements *v* their average,

Table 2 Validity of cholinesterase measurements

Method n	Correlation	Mean difference (95% CI)	Limits of agreement (95% CI)		
PCE:					
FK 36	0·54	−217·4 (−405·7 to −29·1)	Lower	−1370·4	(−1696·6 to −1044·2)
			Upper	935·6	(609·4 to 1261·8)
NFK 35	0·82	−67·9 (−268·3 to 132·5)	Lower	−1277·4	(−1624·6 to −930·5)
			Upper	1141·7	(794·7 to 1488·8)
ECE:					
FK 39	0·68	8·2 (6·71 to 9·69)	Lower	−1·28	(−3·86 to 1·30)
			Upper	17·68	(15·10 to 20·26)
NFK 16	0·51	9·9 (7·40 to 12·40)	Lower	0·52	(−3·81 to 4·85)
			Upper	19·28	(14·95 to 23·61)

Footnotes as for table 1.



...e 4 Validity: ...ence between field kit ...laboratory PCE v ...age of field kit and ...atory PCE.

and graphically illustrates the mean difference and the limits of agreement. Again, a wide scatter is evident, with a slight downward bias of kit relative to laboratory. This is confirmed in table 2, which summarises data on the difference between laboratory, field, and non-field kit PCE measurements and provides estimates of correlation, bias, and upper and lower limits of agreement.

The downward bias of the kit measurements relative to the laboratory measurements is not substantial relative to the activity of PCE. For example, the mean difference between field kit and laboratory measures is of the order of 6% of mean laboratory PCE in table 1, and for non-field use of the kit the 95% CI of the differences includes 0. In absolute terms, field kit PCE may be from 1370·3 U/l below to 935·6 U/l above the laboratory readings for the same subject. The non-field kit application performs better than the field kit in terms of bias, but they are of comparable variability relative to the laboratory measurements.

ECE determinations

Table 2 shows analagous estimates of correlation, bias, and upper and lower limits of agreement for ECE measurements that compare laboratory methods with field and non-field kit determinations. The kit is biased upwards and, in contrast to PCE, the extent of the bias relative to the laboratory ECE activities is substantial. Field kit ECE may be 1·3 U/g haemoglobin below to 17·7 U/g haemoglobin above the laboratory readings and the mean difference between kit and laboratory measures is of the order of 23% of mean laboratory ECE. The variability of the field and non-field application of the kit relative to the laboratory is comparable.

Table 3 Probability of false negatives and false positives in detecting a decrease in cholinesterase activity

	*False negative**	*False positive†*
PCE	0·33	0·09
ECE	0·11	0·00

*False negative = a person's measurement after exposure is > 70% of his or her measurement before exposure when, in reality, the population mean concentrations are 40% lower.
†False positive = a person's measurement after exposure is < 70% of his or her measurement before exposure when, in reality, the population mean concentrations are unchanged.

Table 3 shows the estimates of probabilities of false positives and false negatives calculated from the variances estimated from repeat readings in our sample with an assumed 30% drop in baseline cholinesterase as a threshold for action. For PCE a 30% drop in activities from the observed field kit average of 3091·2 U/l would be 927·4 U/l and for ECE (average 45·1 U/g) would be 13·5 U/g. The kit would miss a true drop in PCE of 40% from baseline in 33% of cases, and a 40% drop in ECE in 11%. A full exposition of the method of calculation is contained in the appendix.

Discussion

Data from this study suggest limitations to the validity and repeatability of the field kit relative to laboratory measurements. The repeatability of PCE and ECE of the kit seems much poorer than that of the laboratory (table 1) and for PCE, this is probably a conservative assessment. The adjustment of laboratory results for PCE described earlier involved a second measured variable (packed cell volume) that is subject to its own variability. The combination of two measured variables, each with its own spread, will increase the variability of the adjusted laboratory measures and overestimate the laboratory repeatability coefficient, with the result that the true picture may be worse than that reflected in this study for PCE.

Poor kit repeatability for PCE and ECE seems to be partly a feature of the kit itself. We would attribute this to a number of possible factors—for example, the field kit is operated by non-laboratory personnel and is subject to changes in ambient temperature, vibration and movement, and other environmental variables, as well as being subject to internal instrument error. In contrast, the separation and washing steps required for laboratory ECE measurement are done by trained technicians and the laboratory analyser operates in a controlled environment, has strict temperature and voltage control, and uses fully automated pipetting and mixing steps.

Even when venous blood was used as the source for kit estimations (non-field conditions), which may be expected to obviate many of the field obstacles to optimal test performance, (including haemoconcentration in successive drops of finger prick blood), the repeatability of the kit PCE determinations improved somewhat, but remained substantially worse than that of the laboratory. It must also be borne in mind that the kit is intended for use in field conditions and that this is where its usefulness most needs to be evaluated.

The validity assessment in this study suggested that relative to the laboratory, the field kit readings of PCE were systematically low, and that there was also a more substantial upward bias relative to the laboratory in the kit ECE readings. In the examination of plots of difference against the mean[21] no evidence was present that the

extent of the bias varied across the range of cholinesterase readings.

Clearly, the kit and laboratory results for ECE were not comparable. One explanation for the results may lie in the different manner in which interference by PCE in the measurement of ECE is prevented. In the laboratory, this is accomplished by physical separation of plasma and erythrocytes, whereas the kit relies on As1397 to inhibit PCE in whole blood. Incomplete inhibition of the PCE in the field kit may be responsible for the overestimation of ECE. Another explanation may be the presence of residual acetylcholinesterase activity in serum,[25] reported to be of the order of 10%.[26] If either of these factors are constant across a range of ECE activities, as suggested by our data, it may be possible to adjust for this overestimation by applying a conversion factor, and further research is needed to clarify this possibility.

A different approach to validity is to establish normal ranges for the field kit based on appropriate reference populations. However, data on this has yet to be reported in the scientific literature, and the difficulties of locating an appropriate control group, particularly in South Africa, are considerable. High levels of alcohol consumption, chronic liver disease, malnutrition, and anaemia are known determinants of PCE and ECE activities[3] and are factors that are prevalent among both farm workers and non-farm worker populations in South Africa. Also, the possibility of environmental contamination due to agrichemicals in rural areas would further complicate the use of rural control subjects to establish normal ranges.

A preferred method of estimation of cholinesterase to identify affected workers is to use subjects as their own controls in prospective measurements over a season, and this is recommended in the field kit manual.[18] The comparison of a cholinesterase result with a subject's baseline value before exposure is the object of biological monitoring in the workplace to enable prompt preventive action to be taken. California regulations rely on a decrease from baseline activities of 30% of either PCE or ECE to warrant further action (repeat test) and of 40% in ECE and 50% in PCE to spur removal from exposure.[3]

Based on the repeatability found in this study, and with the observed baselines (table 3), the kit seems to miss a true drop in PCE of 40% from baseline in 33% of cases. The equivalent probability for a 40% drop in ECE is 11%, which is more satisfactory. The poor performance of the kit PCE may be partly due to exposed study subjects who have PCE activities already lower than normal. From the same calculations as in the appendix, but with higher baselines for PCE—that is, 4000 and 6000—the frequency of false negatives drops to 29% and 20% respectively, but still remains unacceptably high.

Moreover, these results reflect an optimistic assessment as they are based on measurements taken at a single point in time. Greater variability would be introduced with additional measurements at different points in time, which would therefore decrease the likelihood of detecting real changes in cholinesterase activities. Follow up data are presently being analysed to illucidate the effects of this added variability on the ability of the kit to detect changes in PCE and ECE over time.

High levels of instrument variability also compromise the usefulness of the kit in epidemiological studies to investigate dose response relations. This is exacerbated where within and between individual variation in the measured variable may be high, as has been reported for cholinesterase activity.[3] Estimates of maximum variation in PCE activity of healthy subjects are of the order of 9%[3] to 14%,[27] whereas that for between person variability may be substantially higher.[3 28] If a measurement device itself has poor repeatability, the chances of non-differential misclassification are greatly enhanced, and the value of the field kit with a repeatability coefficient as high as shown by our data, may render the kit of limited value for detecting exposure-outcome effects. This served as an important motivation for a decision to rely on laboratory measures of cholinesterase in our larger study of chronic neurotoxic effects.

An issue not assessed in this study is the effect of different readers on kit repeatability and validity as all kit measurements were performed by a single observer (MB). Given that one researcher performed all the kit tests in a standardised manner, we think that non-instrument human error was kept to a minimum in this study. This is consistent with our experience in piloting the device in 1992 where a different reader (LL) found a similar upward bias in kit ECE and poorer repeatability for both kit ECE and PCE relative to the laboratory, although the levels of variability of the methods differed from those of the current study.

An additional reason for the use of field monitoring devices may be economic. In our experience, however, in a developing country, the costs of the field kit tests are not insubstantial when compared with those of laboratory tests. For example, laboratory costs for PCE and ECE assays are about $4 and $5–20 respectively, whereas the costs of purchasing the kit and reagents for the first 200 PCE and ECE assays were of a similar order ($5). With increasing numbers of tests, the average costs for the field kit decrease because of economy of scale. Unless the kit is to be used for a large number of tests, this cost saving will not be substantial.

Conclusion

Despite the undoubted value of a field instrument, to be used on farms to obtain immediate cholinesterase results with minimal reader training, limitations are apparent in the performance of the field kit for cholinesterase measurement relative to laboratory measurements. These include the presence of an upward bias of ECE as measured on the kit

relative to the laboratory, and more importantly, poor kit repeatability relative to laboratory measurements, particularly for PCE.

These shortcomings seriously detract from the potential usefulness of the kit for epidemiological studies to investigate dose response relations, and for surveillance purposes. Because the ECE repeatability of the field kit is somewhat better than PCE, the estimation of ECE by the field kit may be sufficient for purposes of biological monitoring with the use of a model based on California regulations. The ease and simplicity of use of the kit needs to be balanced against its lack of repeatability in the field.

Several issues for future research into the kit have been raised in this study. These include the characterisation of the constancy of the upward bias in ECE estimation and the reasons for this bias, the elaboration of the sources of variation that contributed to poor repeatability of the kit results, and field research into the impact of less than ideal field conditions on kit performance, which is especially important for its use in developing countries where field methods are most needed.[29] In particular, the effect of multiple observers and instruments remains unexplored, and the use of slightly different observer technique in giving the test may play an important part in adding to the variability inherent in the instrument. It would be particularly useful if studies sought to evaluate and validate techniques for assay performance, particularly given that the prime objective of the kit is for field use where robustness of the methods is essential.

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Appendix: Estimation of false positives and false negatives in cholinesterase tests with the field kit

Let the baseline measurement (of PCE or ECE) for a person in a particular population be X_1 and the subsequent measurement for that person be X_2, and assume that $X_i \sim N(\mu_i, \sigma_i^2)$, $i = 1,2$. Assume further that $X_1 - X_2 \sim N(\mu_{diff}, \sigma_{diff}^2)$.

The threshold for action with regard to a person is a drop in cholinesterase to below 70% of the baseline measure. Thus if $X_2 < 0{\cdot}7\ X_1$ then further action is indicated.

False positives occur if:
$X_2 < 0{\cdot}7\ X_1$ but, in fact, $\mu_{diff} = 0$.

False negatives occur if:
$X_2 \geq 0{\cdot}7\ X_1$ but, in fact, $\mu_{diff} = c$, where $c \geq 0{\cdot}3\ \mu_1$.

To be able to estimate the sensitivity and specificity of this action threshold, we use the sample values of the various model parameters. Specifically, we assume for PCE that:

$\mu_1 = 3140{\cdot}0$
$\sigma_1 = 589{\cdot}7$
$\sigma_2 = 863{\cdot}4$
$\sigma_{diff} = 703{\cdot}4$
$\text{cov}(X_1, X_2) = 300396{\cdot}7$

It must be kept in mind, however, that σ_{diff}^2 and $\text{cov}(X_1, X_2)$ are not based on repeat measurements separated by a period of time—for example: before and after the season, and so we are almost certainly underestimating the variability and hence giving too optimistic an assessment of the usefulness of the field kit in this context.

The probability of action being signalled is then given by:
$P(X_2 < 0{\cdot}7X_1)$ or $P(0{\cdot}7X_1 - X_2 > 0)$.
Now $0{\cdot}7X_1 - X_2 \sim N(\mu_{diff} - 0{\cdot}3\mu_1, \quad \sigma_{diff}^2 - 0{\cdot}51\ \sigma_1^2 + 0{\cdot}6\ \text{cov}(X_1, X_2))$.
Under the null hypothesis that $\mu_{diff} = 0$, we have that:
$P(X_2 < 0{\cdot}7X_1) = 1 - P(Z_{N(0,1)} < 1{\cdot}34) = 0{\cdot}09$.
Thus we estimate that if there is no change in mean PCE activity, 9% of workers will be falsely diagnosed as having PCE activities that have fallen below the threshold. This means that the specificity of this PCE action procedure, when applied through the field kit, is 91%. It must be kept in mind that this may be an optimistic assessment.

We consider further the proportion of subjects who would not be detected by this action procedure in the situation where the true mean PCE activities have dropped by 40%. Under the alternative hypothesis that $\mu_{diff} = 0{\cdot}4\ \mu_1$, we have:
$P(X_2 \geq 0{\cdot}7X_1) = P(Z_{N(0,1)} \leq -0{\cdot}45) = 0{\cdot}33$.
Thus if the true mean PCE activity of the subjects has, in fact, dropped by 40%, 33% of such subjects will not be detected by this action threshold. This means that the sensitivity of the PCE action procedure (in the presence of a 40% drop in PCE activity) is 67%.

The calculations for the field kit ECE follow similarly, where we assume (again with sample values) that:

$\mu_1 = 45{\cdot}5$
$\sigma_1 = 6{\cdot}42$
$\sigma_2 = 6{\cdot}68$
$\sigma_{diff} = 3{\cdot}53$
$\text{cov}(X_1, X_2) = 36{\cdot}624$.

Table 3 shows these results.

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Biological Monitoring of workers exposed to Organophosphate pesticides: Guidelines for field application

L London

Cholinesterase-inhibiting pesticides are a major source of morbidity and mortality in a wide range of working populations. Guidelines are presented for the use of cholinesterase testing to monitor the health of workers exposed to organophosphates and carbamates so as to prevent pesticide-related disease. Occupational health practitioners are urged to plan, implement and evaluate programmes for biological monitoring of exposed workers using the guidelines set out in this paper.

Organophosphates (OPs) and other cholinesterase-inhibiting pesticides are widely used in South Africa for pest control in agriculture[1] with over R60 million spent on OPs in South Africa in 1990[2]. The acute toxic effects of OP exposure have been well described (see Table 1) and poisoning due to OPs and carbamates remain an important cause of admission to respiratory intensive care units at hospitals around the country.[5,6] There is evidence that morbidity due to pesticides is substantially under-reported, particularly in the agricultural setting. [1,2]

Table 1. Organophosphate and carbamate poisoning: Acute toxicity[1]

- Mild poisoning:[2]
  - dizziness, headache, tiredness
  - moderate bronchial spasm
  - increased sweating, salivation and lacrimation
  - nausea
  - pinpoint pupils
- Moderate : Above symptoms, plus
  - abrupt weakness
  - blurred vision
  - profuse salivation, sweating
  - significant bronchospasm, bronchial hypersecretion
  - muscle fasciculation, hypertonia, hand tremor
  - gait disturbance
  - urination, diarrhoea and vomiting
  - chest pain
- Severe : Above plus
  - abrupt tremor
  - convulsions
  - acute psychiatric disturbance
  - loss of consciousness
  - cyanosis and respiratory failure
  - coma[3]

Source: 14

Footnotes:

1. Chronic exposure to organophosphates may lead to tolerance of lower levels of cholinesterase activity. This may result in further small acute exposures producing disproportionate toxicity with possible fatalities.
2. Mild symptoms may resemble flu-like illness without fever.
3. Death may arise due to cardiac or respiratory failure.

L London, Department of Community Health, University of Cape Town

Biological monitoring has been widely recommended as a key method for the prevention of adverse health effect amongst workers exposed to pesticides.[7,8] The role of biological monitoring is to detect early biochemical or physiological changes before these lead to reversible or irreversible disease and illness. This paper summarises existent knowledge with regard to monitoring practices for OP pesticides worldwide and offers guidelines for local occupational health practitioners seeking to implement suitable biological monitoring programmes for workers exposed to cholinesterase inhibiting pesticides. This is of particular relevance in South Africa today, given the imminence of the Hazardous Chemical Substances regulations under the Occupational Health and Safety Act which includes cholinesterase-inhibiting chemicals amongst its list.[9]

Targets for biological monitoring programmes

1. Which workers should be monitored?

A wide range of workers, not only those in agricultural production, may be exposed to OPs (Table 2).[1] Workers involved in the manufacture, formulation, preparation, packaging, transport, storage, mixing and application of pesticides will have the highest exposures to pesticides, and therefore have the highest health risks.

Table 2. Occupations with potential agrichemical exposure

- Agriculture:
  - Direct: Application, mixing, storage
  - Indirect: Field work, spray drift, contact with foliar residues
- Public Health personnel: vector control
- Forestry workers
- Aerial spray and maintenance staff
- Commercial pest control operators
- Manufacture, formulation and packaging agrichemicals
- Transport of chemicals
- Municipality or parks employees
- Railway workers applying wood preservatives
- Dock workers

Source:1

2. What type of monitoring is available?

There are two main methods of monitoring exposures to potentially hazardous chemicals:[10]

a. Environmental monitoring of the chemical or its residue in the environment (air, foliage, soil) or in contact with humans (overalls, skin contact)

b. Monitoring of the intact chemical or its metabolite in the tissue or fluids of the body (Biological Monitoring), or the effect of the chemical on enzyme systems within the human body (Biological Effect monitoring).

Many variables determine the actual extent of chemical absorption through dermal or respiratory routes such as the use of protective equipment, safety practices, climatic conditions, individual susceptibility, contaminant disease,

properties of the formulation and the chemical, etc. Because it integrates all these factors, biological monitoring is regarded as a more accurate assessment of human exposure.[7,10]

3. What chemicals may be monitored?

For most organophosphate and carbamate pesticides, a fairly simple measure of biological effect is available. The enzyme cholinesterase, which is inhibited by the carbamate and organophosphate pesticides may be measured in the peripheral blood.[3,4] The toxicity of OPs and carbamates is mediated by the binding of these pesticides to the enzyme cholinesterase in the human nervous system, causing an accumulation of chemical neurotransmitters. Measurement of the effect of these pesticides on similar enzymes in the blood, enables one to detect a decrease in enzyme activity before symptoms develop and can therefore be used to prevent poisoning. Lowered levels of cholinesterase activity in the blood therefore indicate exposure to these chemicals.[11-14]

Two forms of cholinesterase are present in the peripheral blood, one in the red blood cells, and the other in the plasma. Of the two, plasma cholinesterase is regarded as most sensitive to recent absorption of OPs and carbamates, while the red blood cell cholinesterase reflects more closely the concurrent effect in the nervous system.[3,11] In a monitoring programme it is preferable that both enzymes are monitored[14]. Where financial resources are limited, the red cell cholinesterase is preferred as the best assay because it reflects more closely the physiological effect of the chemicals on the worker's nervous system.

For most other pesticides, such simple methods of biological effect monitoring are generally not available. Tests to monitor workers for exposure to pesticides other than organophosphates and carbamates are generally technically complex, time-consuming and costly since they involve measurement of the intact pesticide or its metabolite in the blood or urine of the exposed worker, or the intact pesticide in the environment.[7,8] Accordingly, these tests are generally not recommended for routine monitoring unless the chemical to which workers are exposed is known to be highly toxic or carcinogenic (eg: pentachlorophenol).[15]

Management of a cholinesterase monitoring programme

Certain questions need to be addressed by those responsible for the management of biological monitoring programmes for OPs and carbamate exposure prior to implementation. These are summarised below.

A checklist before implementing a monitoring programme

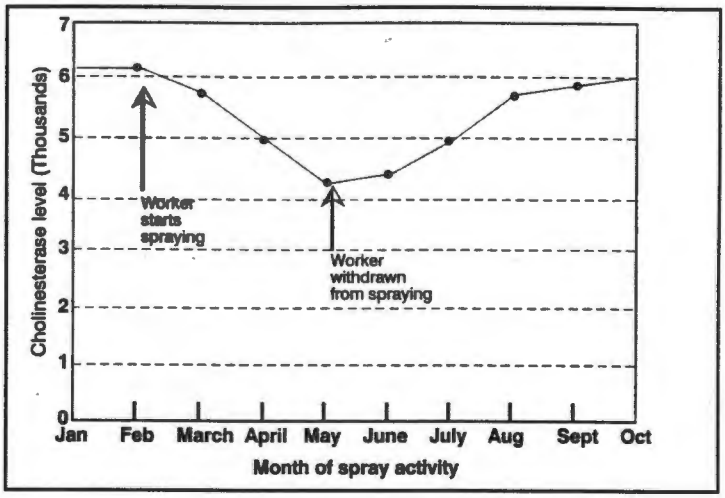
It is helpful to use a checklist of questions before implementing a monitoring programme:

- What are the objectives of the programme? Are they clear?
- If prevention is to be the objective of the programme, what protocols will be followed to ensure that the objective can be met? Are these protocols clear to all personnel involved?
- Will the information recorded enable you to audit the programme?
- Is the programme linked to an education package?
- Is the programme going to be sustainable?

1. How can one determine whether a cholinesterase level is low, or has dropped?

Because cholinesterase levels are known to differ widely between individuals,[11,16] irrespective of their exposure to chemicals, the optimal method of determining what is normal for an individual is to establish his or her baseline level. This can be compared to enzyme levels after exposure to determine whether a significant drop has occurred. Figure 1 illustrates a hypothetical scenario where serial testing for cholinesterase level is performed before, during and after exposure. By withdrawing the worker from exposure timeously, he or she may be prevented from becoming symptomatic, and may safely be returned to work once their cholinesterase has returned to normal.

Figure 1. Serial Cholinesterase Testing Utility for preventive actions



In the absence of a baseline for an individual worker, it is often extremely difficult to determine whether a worker's cholinesterase has decreased. Laboratories may quote normal ranges for cholinesterase levels, but because the variation between individuals is so high, these "normal" ranges are not helpful for biological monitoring. For example, a worker with no significant exposures to organophosphates or carbamates may have cholinesterase levels well below the "normal" ranges simply because of genetic variability. The normal ranges developed for laboratory use are generally based on statistical distributions, and bear little relevance to the practical applications of biological monitoring. For this reason, it is advisable to develop individual baselines for each worker in the monitoring programme, rather than to rely on normal ranges to identify exposed workers.

2. How does one establish a baseline cholinesterase level?

Baseline cholinesterase levels are best determined before a subject begins work, or has experienced any exposure to OPs or carbamates. Such tests should form a routine part of pre-placement medical examinations.[14] Alternatively, if a potentially-exposed worker is already in employ, he or she could be tested for a baseline level in the course of the year as long as they have no exposures to organophosphates or carbamates within the previous two to three months. This is sufficient time for the red blood cell cholinesterase to recover after significant exposure.[11] It is critically important to ensure that when testing to establish a baseline, the worker has been free of any exposure and that they are not in any way still below their "true" normal.

In addition to inter-individual variation, there is also substantial day-to-day biological fluctuation within individuals.[11] While these differences may be small (CIs of the order of 4 to 10%), it may still affect the level at which

an individual's baseline is established, especially if the precision of the method used to measure cholinesterase is low. For this reason, a preferable method uses the mean of two measurements to establish a baseline level of cholinesterase for subsequent comparisons. When a worker's baseline cholinesterase is based on two readings, precision of the baseline estimate is increased and smaller decrements in cholinesterase may be used to identify significant declines.

3. How much of a decrease in cholinesterase is significant?

There is evidence for a correlation between the level of decline in cholinesterase and the development of poisoning symptoms.[3,11,14] A decline of 40% or more in plasma cholinesterase (ie down to 60% of baseline levels or lower) is generally thought to be associated with symptoms, while for red blood cell cholinesterase the decline required to produce symptoms is 30% or more (ie down to 70% of baseline levels or lower). Evidence also suggests that the rapidity of a decline in cholinesterase may be as important in causing symptoms.[11]

In order to prevent the onset of symptomatic disease, declines of magnitude less than those required to produce symptoms should warrant preventive actions. At the same time, it is important to distinguish benign daily fluctuation from a significant decline warranting further action. Given that daily biological fluctuation in cholinesterase within a single individual should not exceed 10 to 15%,[11] declines of between 10 and 30% (red cell cholinesterase) and between 10 and 50% (plasma cholinesterase) represent significant declines that could be used to prompt preventive action.[11,12]

4. What type of preventive action should be prompted by a drop in cholinesterase?

Preventive actions may include the investigation of the work environment, re-testing the worker or removing the worker from any further exposure. Table 3 is based on regulations of the California Health Department and lists the preventive actions that should be taken at different levels of cholinesterase decline from baseline.[11,12]

Table 3. Action thresholds for cholinesterase depression

Level of decline from baseline	Appropriate action
1. Plasma Cholinesterase	
By 15 - 25%	Re-test worker
By 25 - 40%	Re-test worker
	Investigate safety conditions
By 40% or more	Remove worker from exposure
	Investigate safety conditions
11. Red Cell Cholinesterase	
By 15 - 25%	Re-test worker
By 25 - 30%	Re-test worker
	Investigate safety conditions
By 30% or more	Remove worker from exposure
	Investigate safety conditions

Sources: 11,12

Worker removed from exposure as a result of a decline in cholinesterase, should not return to work until the red blood cell cholinesterase has risen to at least 90% of the baseline value (ie within "normal" variability). Alternative work allocations must be available for these workers while their cholinesterase levels remain depressed.

5. How frequently should testing be done?

Regularity of monitoring is critical for the success of a biological monitoring programme. Testing should happen at least once (and preferably more regularly than this) during the spraying season, particularly around peak spraying time. For example, California regulations prescribe that workers having more than 6 full days exposure to organophosphates or carbamates within a 30 day cycle and that workers with more than 40 hours contact with pesticides in a weeks' schedule should be tested for evidence of cholinesterase depression.[12] Other factors particular to the work setting may also be used to prompt testing, such as continuous work with pesticides in a closed environment, or known accidental exposures. Workers found to have depressed cholinesterase levels should be followed up until their cholinesterases have returned to normal (within 90% of their baseline level).

Record Keeping

Record keeping is an essential component of good industrial hygiene practice as well as comprising an important requirement of the imminent Hazardous Chemical Substance Regulations under the Occupational Health and Safety Act. In terms of these regulations, all workplaces where organophosphate chemicals are used will be required to perform appropriate medical monitoring of exposed workers, and to be able to demonstrate evidence of such monitoring to the Department of Labour inspectorate.[9]

Additional reasons for maintaining adequate records are the need for proper documentation for potential compensation requirements, and the potential for many of the cholinesterase compounds to cause long-term chronic health effects.[17] Good monitoring data during the course of employment will be essential in interpreting chronic neurological and other disorders arising in workers, as well as in assisting future research into many of the long-term hazards of ongoing chemical exposures.

Technical Resources

Cholinesterase testing is generally available from commercial and University laboratories at competitive rates. Testing therefore requires the presence of professional staff available to draw blood from the workers, transporting the blood under ice to the relevant laboratory, and awaiting the laboratory result. One drawback is the potential delay between the taking of the blood and receipt of the result, or worse still, loss of the sample, or the result, in transit.

An additional consideration is the need to ensure adequate laboratory quality control of cholinesterase estimation.[14,18] This is particularly the case for the red cell cholinesterase assay, for which the methodology is fairly complex and susceptible to many sources of error. Laboratories contracted to provide cholinesterase analyses should provide reasonable account of their efforts to ensure quality control, or preferably, demonstrate that they are part of a laboratory quality control programme for the tests in question. Such a programme is in place for lead monitoring in the workplace (National Centre for Occupational Health in Johannesburg) and should be extended to cholinesterase monitoring.

An alternative technology for cholinesterase estimation involves the use of field kits based on finger prick devices. A number of such devices are available, although their reliability and validity are not widely described. One such field kit (the TestMate OP) has been tested under field and non-field conditions in the Western Cape and shown to have sufficient reliability as to be able to apply the

California regulations with reasonable robustness.[19] Such technology may be easily applied by field staff (not necessarily health professionals) with sufficient training, and the benefits of immediate results in the field may outweigh the slight loss of precision involved.

Preventive actions linked to biological monitoring

Biological monitoring will provide a useful means of preventing disease due to exposure to organophosphates and carbamates. However, it cannot serve as a substitute for other methods of pesticide safety, such as engineering controls, correct use of personal protective equipment, administrative controls and worker education and training, all of which should be integrated in a comprehensive health and safety programme at the workplace, and which are feasible in the agricultural setting.

Where biological monitoring is implemented, it can be used to spur a wide range of preventive actions. Investigation of the workplace must be done to identify behavioural, structural and organisational sources of exposure amenable to intervention. Appropriate training and hygiene measures should then follow.

Because a biological monitoring programme involves invasive procedures (the taking of blood), workers should only participate after giving full informed consent. This consideration is a further argument for having monitoring programmes supplemented by education and training as part of a comprehensive health and safety programme.

Evaluation of a biological monitoring programme

Once a monitoring system is in place, it should be regularly evaluated to ensure that it is effective and efficient.[12] Too often, programmes run routinely to meet statutory requirements without attention to effectiveness. For example, quality control is often neglected in many monitoring programmes, particularly with regard to laboratory results. An efficient programme can be a waste of time and resources if data from the laboratories is invalid.

Depending on the scope of the programme, its objectives and the amount of resources available, evaluation of a monitoring programme could examine a wide range of benefits.

Firstly, the programme needs to establish that it is achieving the prevention of disease due to organophosphates and carbamate pesticides. Surveillance for cases of poisonings reported at work and outside the workplace involving exposed workers can provide information on outcome effectiveness. Collaboration between farm health personnel and local health authority staff in sharing information around notified pesticide poisonings can improve two-way information flow in order to achieve this objective.

Secondly, assessment should be done of the process outputs of the programme such as the number of workers monitored, tests performed, and preventive actions (retesting, workplace investigations, withdrawal from exposure, etc.) triggered by the programme. This is an indication of the number of workers protected from potential disease by the application of the programme.

Thirdly, programme efficiency should be assessed. This would include an examination of whether tests were performed in the correct manner, and at the appropriate times, whether the appropriate workers were monitored or whether there were any important omissions from the programme. Costs, both direct and indirect should be measured and compared to a similar assessment of benefits in financial terms. Lastly, monitoring programmes may have benefits that are more difficult to quantify such as improved workplace morale and productivity, as well as increased job satisfaction amongst occupational health service staff.

Cholinesterase testing in occupational medicine practice

There are occasions when cholinesterase testing will be used to detect the presence of mild illness in workers exposed to organophosphates and carbamate pesticides who present with non-specific symptoms such as headache, nausea or dizziness. These workers may be suffering from early or mild organophosphate poisoning. Under such circumstances, comparison of the result to a baseline will enable the clinician to reach a simple diagnosis.

However, clinicians are often faced with a situation where no baseline is available, and where the single cholinesterase result is within, or only slightly below "normal" laboratory range. Under these circumstances, serial testing of cholinesterase after withdrawing the worker from exposure may be useful to confirm mild cases of poisoning. If the cholinesterase level gradually increases by more than 10 to 15% over time, and then plateaus out with continuing abstinence from exposure, this is compatible with a retrospective confirmation of cholinesterase inhibition as the cause of the worker's illness.[20] The use of cholinesterase testing here is for secondary prevention (early diagnosis) rather than for primary prevention, the usual intention of biological monitoring.

Conclusion

Biological monitoring can play a crucial role in preventing morbidity and mortality due to pesticides. Its implementation may also contribute considerably to raising the awareness of workers, management and health professionals at the workplace regarding the hazardous nature of the chemicals used. Occupational health practitioners are urged to use these guidelines to develop monitoring programmes to reduce the adverse impact of agrichemicals on the health of exposed workers.

Summary Protocol for a biological monitoring programme for workers exposed to organophosphate carbamate pesticides

1. Planning Monitoring Programme
   Decision with regard to:
   - Objectives
   - Who participates
   - Frequency of testing
   - Alternative job sites
   - Responsibilities for investigation
   - Training
   - How to evaluate
   - What technologies to use
2. Baseline Cholinesterase Testing:
   - Pre-employment or at least 2 months without exposure.
3. Interval testing:
   - At least once a season
   - Every month if more than 6 days exposure per month
   - Other indications may be appropriate
4. Depending on level of Cholinesterase: (see Table 3)
   - Re-test
   - Investigate
   - Withdraw from exposure
   - Wait till Cholinesterase back to normal

The Department of Community Health, has produced the material contained in this article in the form of a stand-alone monograph called "Biological monitoring of workers exposed to pesticides: Guidelines for field application. Occupational Health Research Unit Monograph". This may be obtained by writing to the Occupational Health Research Unit, Department of Community Health, University of Cape Town Medical School, Anzio Road, Observatory, 7925, or faxing (021) 4066163. OH

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CONCLUSION

The data in these papers confirm the extensive potential for exposure to agrichemicals through occupational and environmental routes in a fairly typical rural farming locality in the Western Cape. When read in conjunction with the review of notified poisonings in the region, which identified farm workers and their families as being at high risk, and farm sources of agrichemicals as the major source of chemicals involved in notified poisonings, the need for intervention is clear. Furthermore, the evidence of under-reporting in existing surveillance systems points to the need for a critical assessment of current surveillance practices, and to explore novel ways of improving surveillance methods. Such initiatives are currently underway in collaboration with the Health Departments of the Cape Metropolitan Council (Stellenbosch) and the Bree Rivier Regional Services Council.

What kinds of interventions are needed to improve agrichemical safety? At the workplace, the recent Hazardous Chemical Regulations [2] in terms of the Occupational Health and Safety Act [3], will demand rigorous measures from agricultural employers embracing the full range of training, risk assessment, environmental measurements and biological monitoring. Research to support the application of these measures in the most effective and efficient manner is urgently needed. In addition, assessment of the extent of real exposures arising from environmental routes is needed, as are improvements in the surveillance systems in place for the prevention and control of agrichemical-related morbidity and mortality.

The papers presented here are the first attempt to begin systematically to characterise the full public health impact of agrichemicals in South Africa. To my knowledge, only one previous paper has been published in the peer-reviewed literature to address the health effects of agrichemicals on the health of farm workers [4]. It is hoped that this work will

contribute to encouraging other researchers and public health practitioners to focus more attention on the health problems arising from the unsafe storage, use and disposal of agrichemicals in rural farming areas, and thereby to contribute to improving the working and living conditions of farm workers in South Africa.

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